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*HMAA
13th
Balatonfüred
Meeting*



Greetings

Dear Colleagues, Future Colleagues, and Guests,

It is my pleasure to welcome you to the Hungarian Medical Association of America (HMAA) Summer Conference in Balatonfüred!

The HMAA was founded 51 years ago by a handful of Hungarian physicians living in the United States. They wanted to build a bridge to the motherland and improve healthcare both in the United States and Hungary. They established a fellowship program to benefit Hungarian medical students who wanted to do clinical rotations in the United States. They also started a scientific meeting in Sarasota to learn, exchange ideas, and enjoy each other's friendship.

In 2008, a new tradition was born: the Hungarian Chapter of the HMAA organized a Summer Conference in Balatonfüred. This conference has also become a lasting success. Highlights include presentations by medical students, lectures by professors, wine tasting at night and, of course, a water polo game.

Welcome again! Enjoy the meeting!



A handwritten signature in blue ink, appearing to read 'Andras Khor'.

Andras Khor, MD, PhD
President HMAA

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B. Multidisciplinary session I.: CARDIOVASCULAR DISEASES

B/1 COMPREHENSIVE ASSESSMENT OF INTRACRANIAL ANEURYSM RUPTURE IN THE POPULATION OF VOJVODINA

Emőke Anna Csernus

University of Novi Sad

Keywords: intracranial aneurysm, neurosurgical clipping, endovascular coil

Aims: Management of intracranial aneurysm (IA) rupture still carries high rates of mortality and long-term morbidity. This study aims to assess management, outcome, and aneurysmal morphology in individuals treated with the diagnosis of ruptured or nonruptured aneurysms in our patient population.

Methods: A retrospective analytical study was conducted reviewing records of 240 patients admitted to the Clinical Center of Vojvodina with IA between 2014 and 2016. 142 subjects underwent a more extended analysis, divided into ruptured (123) and nonruptured (19) groups. Finally, relative risk assessment of neurosurgical clipping, endovascular coiling, and conservative treatment modalities was performed across several patient subgroups.

Results: The sample's mean age was 58 years and was 70% female. Aneurysms were located most frequently on the Acom/ACA. In the ruptured group, 85% of aneurysms presented in the anterior circulation with 56,1% of them being 5-10 mm in diameter. Mean aspect ratios were 2.4 [ruptured] and 2.6 [nonruptured]. 41% of patients received clipping, 29.2% coiling, and 29.2% conservative treatment. Overall mortality was 33%. Complication incidence was 67.4% across all groups with 10% of rebleed. The relative risk assessment indicated endovascular coiling was both the preferred interventional modality overall, as well as in the majority of subgroups of age, Fisher and WFNS grades, lumen size, and aneurysm location.

Conclusions: The results are in agreement with recent randomized trials and follow-up studies in that less invasive approaches, like endovascular coiling, are favored for most subgroups of patients with respect to outcome. Close surveillance and education of patients with risk factors is highly recommended.

B/2 ZERO-FLUOROSCOPY STRATEGY FOR CATHETERABLATION OF PAROXYSMAL SUPRAVENTRICULAR ARRHYTHMIAS: SINGLE-CENTER STUDY

Dorottya Debreceňi, Dr. Péter Kupó, Dr. Eszter Fődi, Prof. Dr. Tamás Simor
PTE KK Szívgyógyászati Klinika

Keywords: ablation, zero-fluoroscopy, learning curve, PSVT

Aims: Data regarding the comparison of the minimal/zero fluoroscopy and the conventional fluoroscopy-assisted approach in the treatment of paroxysmal supraventricular tachycardias (PSVTs) are limited, furthermore data regarding the impact of electroanatomic mapping systems (EAMSs) on the procedural time are controversial. We aimed to compare the conventionally fluoroscopy-assisted with the minimal/zero fluoroscopy approach guided by electroanatomic mapping systems in the treatment of PSVTs.

Methods: Between September 2017 and September 2018, 98 patients undergoing electrophysiologic study with or without ablation due to PSVT, performed by a single operator with no previous experience with the use of EAMS were included in our retrospective single-center study. 36 patients underwent an EAMS-guided procedure (Group

1), while in the cases of 62 patients the procedure was performed conventionally (Group 2).
Results: In Group 1, 91.7% of the procedures were performed without the use of radiation. The success rate was 100% in both groups without any complication. The use of EAMS reduced radiation time (0 vs 2.2 min, $p<0.0001$), with longer procedure time (70.0 vs 52.5 min, $p=0.035$). There was no difference either in the number of RF applications (7.5 vs. 7.5, or in the ablation time 218.0 vs 224.5 s, $p=0.80$ each). The analysis of the procedural time of cases with the EnSite NavX system assisted AVNRT ablations showed a non-significant trend of decreasing duration ($r=0.048$, $p=0.32$).
Conclusions: The EAMS-guided approach for the treatment of PSVTs is a feasible and safe method that reduces fluoroscopy time and does not influence the number of applications, ablation time, success or complication rates.
Support:-

B/3 COMPARISON OF THE EFFICIENCY OF X-RAY GUIDED AND INTRACARDIAL ECHOCARDIOGRAPHY GUIDED CAVOTRICUSPIDAL ISTHMUS ABLATION

Jakab Veronika Anna, Prof. Dr. Tamás Simor, Dr. Péter Kupó
Heart Institute, University of Pécs

Keywords: atrial flutter, ICE, catheter ablation, CTI ablation, cardiology

Aims: Cavotricuspidal isthmus ablation, which is therapy to atrial flutter, is usually an X-ray guided procedure. The Department of Cardiology started to use intracardial echocardiography (ICE) as a new visualization tool in the past year for CTI ablations. Our aim was to compare the two different techniques in this procedure.
Methods: We enrolled 56 patients to our study (ICE guided: 22 patients, mean age: 61.5 ± 13.9 years; X-ray guided: 34 patients, mean age: 61.9 ± 9 years). They had cavotricuspidal isthmus ablation between January 1st, 2016 and December 31st, 2017. We analysed the procedural data and the rate of recidivism observed during follow-up retrospectively.

Results: Comparing the two groups acute success rate and radiation time we discovered significant difference (ICE=100%, X-ray=82,3%, $p=0,07$; ICE= 4.6 ± 3.0 minutes; X-ray= 15.4 ± 5.3 minutes, $p<0.0001$). There was no significant difference between procedural time and rate of recidivism observed during follow-up in the two groups (ICE= 79.6 ± 23.9 , X-ray= 87.6 ± 35.8 ; ICE=0%, X-ray=5,9%).

Conclusions: The use of ICE catheter during CTI ablations significantly lowers radiation time furthermore higher acute success rate can be achieved.

B/4 THE CLINICAL RELEVANCE OF HYPO-ATTENUATED LEAFLET THICKENING AFTER transcatheter AORTIC VALVE IMPLANTATION

Jávorszky Natasa, Karády Júlia, Astrid Apor, Kolossváry Márton, Nagy Anikó Ilona, Szilveszter Bálint, Bartykowszki Andrea, Papp Roland, Molnár Levente, Jermendy Ádám Levente, Panajotu Alexis, Suhai Ferenc Imre, Varga Andrea, Maurovich-Horvat Pál, Béla Merkely

Semmelweis University Heart and Vascular Center

Keywords: HALT, TAVI, Quantitative, Cardiac Computed Tomography (CT)

Aims: There is no consensus over the standardized definition of hypo-attenuated leaflet thickening (HALT) and its clinical relevance is poorly understood. We sought to establish a standard quantitative measurement of HALT and aimed to determine the predictors and clinical significance of HALT after transcatheter aortic valve implantation (TAVI).

Methods: In this single-center observational study we prospectively enrolled patients who previously underwent TAVI. At inclusion cardiac computed tomography angiography (CTA), transthoracic echocardiography and brain magnetic resonance imaging (MRI) was performed. Volumetric quantification of HALT was performed on cardiac CTA images by segmenting the inner volume of the TAVI frame at the level of the leaflets and applying a threshold of -200 to 200 Hounsfield units. Clinical predictors of HALT volume, and its association with ischemic brain MRI lesions and all-cause mortality was evaluated.

Results: In total, we analyzed 111 patients (56.7% female, 80.3 +/- 7.4 years). The mean HALT volume was 111.0 +/- 163.4 mm³. After multivariate adjustment, aortic peak gradient remained a significant predictor of HALT volume (beta-coefficient: 23.3; 95%CI:6.3-40.2; p= 0.008). HALT volume was not associated with ischemic brain MRI lesions (all p>0.05) and did not predict all-cause death (median follow-up: 20 months [IQR:18-23]; HR:1.0; 95%CI:1.0-1.0; p=0.15).

Conclusions: Aortic peak gradient was the only independent predictor of HALT volume. Our results suggest that HALT negatively affects TAVI valve function, but we found no association of HALT volume with cerebrovascular ischemic lesions or increased risk for all-cause mortality. Support:-

B/5 PULMONARY VEIN RECONNECTION OBSERVED WITH MULTIELECTRODE MAPPING LATE AFTER SECOND-GENERATION CRYOBALLOON OR CONTACT FORCE SENSING RADIOFREQUENCY CATHETER ABLATION FOR ATRIAL FIBRILLATION

Krisztián István Kássa¹, Zsófia Nagy², Zsuzsanna Kis², Zoltán Som², Levente Csákány², Tamás Major², Csaba Földesi², Attila Kardos²

1 Semmelweis University Budapest, 2 Gottsegen György Hungarian Institute of Cardiology Budapest Department of Electrophysiology

Keywords: atrial fibrillation, ablation, reconnection, mapping, cryoballoon

Aims: Late pulmonary vein reconnection (PVR) determines recurrence of atrial fibrillation (AF) after pulmonary vein isolation (PVI) procedures. The PVR rate was reported to be lower following the second-generation cryoballoon (CB) compared to contact-force sensing radiofrequency (CF-RF) ablation using circular mapping catheters.

Methods: A total of 66 [31 (47%) women, mean age=63±11.6 years] patients underwent redo ablation due to AF recurrence after index PVI accomplished with CB (n=37 pts) or CF-RF (n=29 pts). All repeated procedures were achieved in sinus rhythm using bipolar voltage map with multielectrode mapping catheter and CARTO 3 Confidence Module (mean number of points=1012±602). We examined the reconnection pattern of the antral lesion sets.

Results: Among 109 PVs in the CF-RF group, 82 (75.2%) showed conduction gaps (2.9 per patient). Whereas among

143 PVs in the CB group, 107 (74.8%) showed PVR (2.9 per patient) ($p=0.81$). After CF-RF ablation, the inferior and the posterior part of the right inferior PV and the right carina showed conduction gaps more likely. In the CB group, the left atrial appendage-left superior PV ridge and the superior segment of the left superior PV were most frequently reconnected. In the CB group late PVR was associated with higher nadir temperature ($-52.8 \pm 5.3^\circ\text{C}$ vs $-42.2 \pm 8.6^\circ\text{C}$, $p=0.031$), while in the CF-RF group the mean CF was lower in the reconnected PVs as compared to those PVs which remained isolated (10 ± 3.2 g vs 18.8 ± 4.9 g, $p<0.05$).

Conclusions: In our single-center analysis no difference was observed in the PVR incidence and the antral lesion sets after CB or CF-RF ablation.

Support: Nothing to declare

B/6 PREDICTIVE VALUE OF RIGHT VENTRICULAR MECHANICS ON POSTOPERATIVE RIGHT VENTRICULAR FUNCTION IN PATIENTS UNDERGOING MITRAL VALVE SURGERY

Erika Kisapál 1, Márton Tokodi 1, Bálint K Lakatos 1, Zoltán Tóssér 2, Kristóf Rác 3, Ádám Soltész 3, István Hartyánszky 1, Endre Németh 3, Attila Kovács 1, Béla Merkely 1

1 Heart and Vascular Center, Semmelweis University; 2 Argus Cognitive, Inc.; 3 Department of Anesthesiology and Intensive Therapy

Keywords: right ventricle, echocardiography, mitral regurgitation

Aims: Severe mitral regurgitation induces significant changes not only in the left, but also in the right ventricular (RV) morphology and function. The PREPARE-MVR study (Prediction of Early Postoperative Right ventricular failure in Mitral Valve Replacement/Repair patients) aims to identify preoperative parameters which may predict perioperative RV failure in patients undergoing MVR.

Methods: We prospectively enrolled 38 patients (63 ± 11 years, 74% males) undergoing MVR. Transthoracic 3D echocardiography was performed preoperatively and at intensive care unit discharge. 3D model of the RV was reconstructed and RV end-diastolic volume (EDV) along with RV ejection fraction (RVEF) were calculated. For in-depth analysis of RV mechanics, we decomposed the motion of the RV to compute longitudinal (LEF) and radial ejection fraction (REF). Right heart catheterization was performed to monitor RV stroke work index (RVSWi). Results: RV morphology as assessed by EDV was unaffected by surgery (preoperative vs postoperative; 142 ± 42 vs 143 ± 46 mL, $p=NS$). RVEF was slightly decreased after MVR (50 ± 6 vs 48 ± 7 %, $p<0.01$), whereas RV contraction pattern has changed notably. Before the surgery, the longitudinal shortening was the major contributor to RVEF (LEF/RVEF vs REF/RVEF; 0.48 ± 0.09 vs 0.43 ± 0.13 , $p<0.05$), while after MVR the radial motion became the dominant component (0.31 ± 0.13 vs 0.56 ± 0.12 , $p<0.001$). Preoperative LEF was an independent predictor of postoperative RV failure defined as impaired RVSWi (OR=1.27 [1.05 – 1.63], $p<0.05$).

Conclusions: MVR induces a shift in RV mechanical pattern. Advanced measures of RV mechanics are related to invasively measured parameters of RV contractility and may predict postoperative RV failure.

B/7 THE CLINICAL RELEVANCE OF CYTOMEGALOVIRUS IN THE MANAGEMENT OF HEART TRANSPLANT RECIPIENTS

Orsolya Szalai¹, Nóra Parázs¹, Alexandra Assabiny¹, Zsófia Szakál-Tóth¹, Ákos Király¹, Zoltán Tarjányi¹, Tímea Teszák¹, Marina Varga², Dávid Becker¹, Balázs Sax¹, Béla Merkely¹

1. Semmelweis University, Heart and Vascular Center, 2. Semmelweis University, Department of Transplantation and Surgery

Keywords: HTX, cytomegalovirus, CMV, cardiac allograft vasculopathy, CAV

Aims: Cytomegalovirus (CMV) infection can appear as asymptomatic viraemia, viral syndrome or tissue-invasive disease after any solid organ transplantation. CMV increases the risk of cardiac allograft vasculopathy (CAV), the specific coronary artery disease of heart transplant recipients and acute cardiac rejection as well. In our retrospective study, we examined the clinical relevance of CMV-infections among heart transplant recipients in the Heart and Vascular Center of Semmelweis University.

Methods: We gathered data from 116 patients transplanted between 2014-2017. Patients were classified according to the donor (D) and recipient (R) CMV immunoglobulin-G serological status: low-to-medium (D-/R- or D-/R+ or D+/R+) and high-risk (D+/R-) groups. We performed regular CMV-PCR measurements and at least annual coronary artery imaging to screen for vasculopathy.

Results: 15% of our patients were in the high-risk group for CMV-disease. CMV-viraemia (CMV-PCR > 150 copies/ml) occurred in significantly higher ratio of high risk patients (67% vs. 35% p=0.017).

Altogether 23 patients developed CAV. The incidence of vasculopathy was significantly higher in the high-risk group (44% vs. 15% p=0.0087), albeit we could not prove significant correlation between CMV-viraemia and the development of CAV.

Conclusions: CMV-viraemia occurred in a high percent of heart transplant recipients, however CMV-disease and CAV were presented more frequently in the high-risk group. Despite viraemia being common, merely 6% of patients developed CMV-disease. This outcome confirms the effectivity of the strict CMV-surveillance and immediate therapeutic response. We consider this strategy particularly beneficial for high-risk patients.

B/8 Correlation between the amplitude of the ST segment elevation and the extent of the myocardial scar tissue determined by LGE-MRI in patients with STEMI

Supervisor: dr. prof. Benedek Imre, Főorvos, Marosvásárhelyi Kardiológia klinika

Author: Katona Orsolya-Brigitta

University of Marosvásárhely

No English abstract available

C. Multidisciplinary session II.: ANATOMY-PATHOLOGY

C/1 EXAMINATION OF THE HEARING SYSTEM IN PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP)-DEFICIENT AND VAD- MICE

Authors: Gyurok Gergő Péter¹, Fülöp Balázs Dániel¹, Humli Viktória^{2, 3}, Zelles Tibor^{3, 2}, Szepes Judit³, Ott Virág¹, Reglődi Dóra¹, Gaszner Balázs¹, Németh Adrienn⁴, Tamás Andrea¹

¹Anatómiai Intézet, MTA-PTE PACAP Kutatócsoport, Idegtudományi Centrum, Pécsi Tudományegyetem, Általános Orvostudományi Kar, Pécs ²Gyógyszerkutató kutatócsoport, MTA KOKI, Budapest ³Farmakológiai és Farmakoterápiás Intézet, Általános Orvostudományi Kar, Semmelweis Egyetem, Budapest ⁴Fül-Orr-Gégészeti és Fej-Nyaksebészeti Klinika, Klinikai Központ, Általános Orvostudományi Kar, Pécsi Tudományegyetem, Pécs

No English abstract available

C/2 ION CHANNEL EXPRESSION AND FUNCTION ON PROGENITOR CELLS ISOLATED FROM OSTEOARTHRITIC ARTICULAR CARTILAGE

Kothalawala William Jayasekara 1, dr. Matta Csaba 2

1, 2: University of Debrecen, Department of Anatomy, Histology and Embriology

Keywords: osteoarthritis, ion channel, cartilage, BK-channel, chondrocyte

Aims: Osteoarthritis (OA) is a degenerative disorder affecting all components of joints. The disease is not yet curable. According to our hypothesis, the expression and function of the membrane proteins of chondrocytes and chondroprogenitor cells are altered in the inflammatory micro-environment characteristic to OA. The role of these proteins in the pathogenesis of OA is currently unclear. In our work, we tried to understand the function of these ion channels in OA progenitor cells. Our preliminary results showed different expression of genes encoding multiple ion channels which we wanted to confirm.

Methods: Following RNA isolation from in vitro cultured chondrogenic progenitor cells derived from human OA articular cartilage, the expression of selected ion channel genes was analysed by RT-qPCR. The mRNA levels were normalized to the reference gene RPS18. We also cultured the cells in the presence of inhibitors or activators of ion channels and investigated their effects on cell proliferation, viability and electrophysiological properties.

Results: The expression pattern of alpha and beta subunits of the high-conductance Ca²⁺-activated K⁺-channel (BKCa) showed a difference compared to the mesenchymal stem cells (MSC) used as the reference cell population. Using the activators and inhibitors the cells showed no difference in viability, yet there was a decrease in the proliferation pattern of cells cultured in the presence of paxillin.

Conclusions: As many drugs act by modulating the function of ion channels, understanding the ion channel composition and function of this chondrogenic progenitor cell population may contribute to the development of new target drugs.

Support: Supported by the New National Excellence Program of the Ministry of Human Resources.

C/3 FROM SKIN TO PRIMARY CELL CULTURES: HUMAN CUTANEOUS MELANOCYTES IN VITRO

Emese Zsigrai, Patrik Kovács, Róza Zákány, Tibor Hajdú

University of Debrecen, Faculty of Medicine, Department of Anatomy, Histology and Embryology

Keywords: in vitro, primary cell culture, human, cutaneous, melanocytes

Aims: Melanocytes of the skin are pigment producing cells located in hair follicles and in the basal layer of the epidermis. Primary melanocyte cultures can serve as a useful in vitro model for the better understanding of pigment cell disease pathogenesis and behavior. For this purpose, we aimed to isolate melanocytes from human skin and to establish primary cell cultures.

Methods: To this end, we used human juvenile prepuce samples for our experiments (obtained from the Department of Pediatrics, University of Debrecen, under the license of the appropriate authorities). After several steps of sterilization and overnight incubation in dispase II the epidermis can be removed from the tissue. Followed by trypsinization and centrifugation, the resuspended pellet can be plated in a desired density. The addition of special mitogens and factors to the culture medium enhances melanocyte selection and proliferation from the initial cell population.

Results: Morphological analysis of hematoxylin-eosin stained cultures showed bi-, tri- and multipolar, gracile, pigment containing cells. Light microscopy using full bright field optics also proved the presence of dendritic, pigmented cells in the culture. Fluorescent microscopic evaluation of melanocyte specific protein expression (MITF, TYRP1) proved positive immune signals in every cell in each examined visual field. Presence of contaminating cells (keratinocytes, fibroblasts) was not detected.

Conclusions: Based on the thorough verification processes we can state that the isolation of our primary melanocyte cultures is successful (n=6). The cost-efficient method, the flexible protocol and the sustainable source of samples provides an ideal approach for isolation and culturing of cutaneous melanocytes.

C/4 THE ROLE OF QUANTITATIVE COMPUTED TOMOGRAPHY (CT) BASED TEXTURE ANALYSIS (QTA) IN THE HISTOPATHOLOGICAL DIAGNOSIS OF LUNG ADENOCARCINOMA

Andrea Fülöp^{1, 2}, Dr. Zsolt Megyesfalvi^{2, 3}, Dr. Zoltán Lohinai Ph.D.^{2, 3}, Szabolcs Gergely^{1, 2}, Csilla Kugler^{2, 3}, Botond Megyesfalvi²

1. University of Medicine, Pharmacy, Science and Technology of Marosvásárhely, Marosvásárhely, 2. Department of Thoracic Surgery, Semmelweis University, Budapest, 3. National Koranyi Institute of Pulmonology, Budapest

Keywords: NSCLC, adenocarcinoma, QTA, machine learning, COPD

Aims: Quantitative computed tomography (CT) based texture analysis (QTA) represents a non-invasive diagnostic method in different cancer types by converting digital images into high-dimensional mineable data. Our aim was to evaluate the accuracy of machine learning based QTA in the diagnosis of histopathological type and associated comorbidities in non-small cell lung cancer (NSCLC) patients.

Methods: QTA was applied separately on 50 contrast-enhanced CT images of 32 adenocarcinoma, 12 squamous cell carcinoma and 6 other NSCLC type patients, including 38% of patients with chronic obstructive pulmonary disease (COPD). Three-dimensional tumor segmentation was performed using 3D Slicer, thus obtaining 104 CT parameters. The parameters were further reduced by principal component analysis (PCA) to eight principal

components. Histopathological subtypes were differentiated based on machine learning algorithms using Naïve Bayes and K-means clustering.

Results: Machine learning algorithms clearly differentiated lung adenocarcinoma from other histopathological types with an accuracy of 68%. Moreover, we found a significant difference in three CT parameters according to histopathological types including Skewness ($p=0.018$), 10-Percentile ($p=0.041$) and Gray-Level Non-Uniformity ($p=0.040$). We identified a principal component that is characteristic ($p=0.002$) to the presence of COPD. Furthermore, based on cluster analysis, advanced-stage NSCLC patients can be classified into two major subgroups according to their principal components.

Conclusions: Our findings suggest that QTA might represent a unique diagnostic method for lung adenocarcinoma and associated COPD. Accordingly, QTA based characterization of a tumor's histopathological features could help guide clinicians in order to enhance early treatment management especially when invasive tumor sampling is not possible.

Support: The authors have no financial support to report.

C/5 PROGNOSTIC SIGNIFICANCE OF IMMUNOHISTOCHEMICAL CLASSIFICATION OF ADENOCARCINOMAS OF AMPULLA OF VATER

Alexander Schlegel, Ildiko Illyés, Katalin Borka

2nd. Department of Pathology, Semmelweis University Budapest, Hungary

Keywords: ampulla of Vater, cancer, immunohistochemistry, mucin, prognosis

Aims: Tumors of the ampulla of Vater present their-self in a heterogenous way, due to anatomical complexity. Our aim was to analyze different immunohistochemical (IHC) markers alone and in combination to classify these tumors and characterize prognosis.

Methods: 51 pancreatoduodenectomy specimens of ampullary adenocarcinoma were reviewed between 2013-2018. Tissue microarray (TMA) was used for immunohistochemical staining of CK7, CK20, CDX2, MUC1, MUC2, MUC5AC, MUC6 and CLDN-3,-4. Allred scoring system was used by two different investigators and results were harmonized. IHC subtypes were categorized according to international classification (Ang et al.). Correlation between IHC profiles, histological data (T-stage, N-stage) and overall survival data were analyzed (Kaplan-Meier curves, chi square, Fischer's exact test).

Results: Single IHC markers do not predict a poor survival except of CLDN-3. Intestinal IHC subtype had a better prognostic tendency (survival $p=0,07$, T-stage, N-stage) compared to pancreatobiliary subtype. Although it was analyzed elsewhere, MUC5AC does not give a poor survival. CLDN-3 positivity showed a significantly better survival ($p=0,0023$), a lower T-stage ($p=0,0274$) and a better tendency in N-stage ($p=0,15$). CLDN-4 showed a continuous positivity in all cases.

Conclusions: The IHC evaluation of the ampullary adenocarcinomas has an impact on the prognosis: especially CLDN-3 or the combination with other IHC markers. Immunohistochemical evaluation should be routine procedure in every case of ampullary adenocarcinomas in order to choose the adequate therapy (radiochemotherapy).

Support: 14383/2017/EKU

C/6 SOLID-PSEUDOPAPILLARY NEOPLASMS OF THE PANCREAS – CLINICOPATHOLOGICAL INVESTIGATION OF AN ENIGMATIC TUMOR

Viktória Kis-Orha, Attila Zalatnai

First Department of Pathology and Experimental Cancer Research, Semmelweis University

Keywords: Solid-pseudopapillary neoplasm, pancreas, review, immunohistochemistry

Aims: Solid-pseudopapillary neoplasm (SPN) is a rare, enigmatic entity of the pancreas, which was first described by V. Frantz in 1959. Since then its terminology has continuously changed, but the name has remained descriptive, indicating that the histogenesis is still obscure. The neoplasm -generally occurring in young women- has a unique behavior. Although the survival after surgical excision is excellent, the expected prognosis is not exactly predictable.

Methods: Between 2007 and 2018 12 SPN cases have been diagnosed at our Institute. We have analyzed their tissue samples microscopically by using different histological and immunohistochemical techniques. In addition, we have performed deep literature search to make a summary of this entity.

Results: We have found a lot of contradictions in the literature, that proves the vague behavior of the neoplasm. According to the literature and our experience we have summarized the clinicopathological features, the expected behavior, the molecular alterations, the immune phenotype and the putative histogenesis of SPN.

Conclusions: The histological characteristic findings would help to differentiate SPN from other, look-alike tumors, moreover we make suggestions about the desirable content of the histological report.

C/7 INDUCED PLURIPOTENT STEM CELL BASED IN VITRO MODELLING OF THE CARDIOVASCULAR MANIFESTATIONS OF DiGEORGE SYNDROME

Brigitta Rita Szabó^{1, 2}, Tünde Berecz^{1, 2}, Andrea Molnár², Ágota Apáti¹

1. Institute of Enzymology, Research Centre for Natural Sciences, Budapest, Hungary, 2. Heart and Vascular Center, Semmelweis University, Budapest, Hungary

Keywords: DiGeorge, cardiovascular, iPSC, cardiomyocytes, frequency

Aims: DiGeorge syndrome caused by the hemizygous microdeletion of the 22q11.2 chromosome region can affect multiple organ systems. However, the size of this deletion does not correlate with the severity of the clinical manifestation. Our aim was to create such an in vitro disease-specific model that enables us to examine the mechanisms resulting in these different clinical phenotypes.

Methods: Human induced pluripotent stem cells (iPSC) and their differentiated derivatives are new, promising models for studying disease related phenotypes. Therefore, we generated iPSCs from peripheral blood of members of a family where the disease is present in three generations. We compared the iPSC derived cardiomyocytes (iPSC-CM) of the affected progeny and mother to the healthy grandmother and a commercially available control cell line. To functionally characterize the iPSC-CMs we used High Content microscopy to obtain real time videos of the beating clusters on which we performed frequency analysis. In addition, we investigated the expression of certain mRNAs.

Results: During the cardiac differentiation an increase in frequency was present in case of all the cell lines. The frequency analysis of the iPSC-CMs revealed that the progeny had a significantly higher beating frequency than the mother and the control lines.

Conclusions: We were able to differentiate iPSC-CMs from both the DiGeorge affected and the healthy iPSCs. We

found that the affected iPSC-CMs showed an altered beating pattern compared to the healthy ones. The mRNA expression levels suggest changes in the Ca²⁺ homeostasis and the sarcomere structure but these findings need further investigation.

Support: Supported by the National Brain Research Program of Hungary (NAP 2017-1.2.1-NKP-2017-00002 and KTIA_NAP_13-2014-0011), and by the National Research, Development and Innovation Office (NVKP_16-1-2016-0017 and OTKA- K128369).

D. Multidisciplinary session III.: NEUROSCIENCE

D/1 PRECOGNIZE PILOT STUDY: A NOVEL DIAGNOSTIC APPROACH FOR ALZHEIMER'S DISEASE?

Dalida Borbála Berente^{1*}, Zsolt Bálint¹, Sára Lality¹, Viktória Rosenfeld¹, Viktória Kis-Orha¹, Anna Király¹, András Attila Horváth²

¹Faculty of Medicine Semmelweis University Budapest Hungary, ²National Institute of Clinical Neurosciences Budapest Hungary

Keywords: Alzheimer's disease, visuomotor, neuropsychology, imaging

Aims: Dementia affects 50 million people worldwide, two-thirds of whom have Alzheimer's disease. Thus, making extensive research is important. Visuospatial impairment appears in the early stages of cognitive decline. Our aim is to develop a complex diagnostic approach for Alzheimer's disease based on testing visuospatial abilities.

Methods: Two groups of participants were selected. The Control group consists of individuals without neurological disorders. The Affected group comprises subjects with memory complaints or Alzheimer's disease. The study took place at the National Institute of Clinical Neurosciences. It included a self-developed diagnostic algorithm testing visuomotor abilities using eye-hand coordination paradigms, neuropsychological testing using Addenbrooke's Cognitive Examination (ACE) and structural and functional MRI scans.

Results: Eighteen individuals were included. Fifteen in the Control group and three in the Affected group. The averages of counts were higher in the Affected group compared to the first group in every task. Mouse-move average: 578 and 1080; respectively. There is a significant negative correlation between visuospatial ACE scores and Precognize counts both in the Control and Affected group. Control: mouse-move right hand Precognize-ACE visuospatial $r=-0,12$. Affected: mouse move right hand Precognize ACE visuospatial $r=-0,99$.

Conclusions: This is a pilot study with low number of patients in the Affected group. However, even with this low number of participants a significant correlation is present between the patients' ACE visuospatial scores and Precognize counts. ACE is a widely accepted sensitive diagnostic tool in Alzheimer's disease. Our results are promising in providing an easier and widely available diagnostic tool for dementia.

D/2 MACROSTRUCTURAL SLEEP CHANGES IN ALZHEIMER'S DISEASE: CANDIDATES FOR EARLY DIAGNOSIS?

Anna Csilla Kegyes-Brassai, András Horváth

National Institute of Clinical Neurosciences

Keywords: Alzheimer, sleep changes, neuropsychology, cognitive decline

Aims: Sleep-wake abnormalities are very common in Alzheimer's disease (AD) affecting 30-50% of the patients. Previous studies showed, that sleep, amyloid- β peptide (A β) accumulation and the pathologic process of AD have

strong connections. Evidence has shown that sleep–wake cycle directly influences the levels of A β in the brain, while accumulation of the A β results in impaired sleep pattern. Sleep disorders and AD may influence each other. Thus, to consider sleep changes is important in the treatment and the diagnosis of AD. **Methods:** The aim of the study was to analyze the sleep pattern in AD, comparing 30 AD patients to 30 healthy controls with similar sex and age ratio. Detailed neuropsychologic examination was executed including Addenbrooke's Cognitive Examination (ACE). Patients were involved in a 2-year long prospective follow-up. Sleep structure was analyzed with polysomnography for 1 night. For statistical analyses two-tailed, independent samples T-test and Pearson-correlation was applied. **Results:** There was a significant decrease in sleep duration, efficiency and sleep onset latency in AD group ($p<0.05$). Relative S1, S2 and S3 duration decrease also have found by AD patients. There was a strong positive correlation between the ACE score and relative S3 and REM duration. Patients with initially lower ACE scores declined faster.

Conclusions: Our findings support the hypothesis that sleep disturbances reflect the clinical stages of AD. Analysis of slow-wave and REM sleep might support the differential diagnosis of neurocognitive disorders and could be involved in the proper diagnosis of AD in the earliest stage opening new perspectives for more effective treatment.

Support: the 5th keyword: polysomnography

D/3 EFFECT OF EPILEPTIFORM DISCHARGES ON THE PROGRESSION OF ALZHEIMER'S- DISEASE

Viktória Kis-Orha, András Horváth, Anita Kamondi
National Institute of Clinical Neurosciences, Semmelweis University

Keywords: Epilepsy, Alzheimer, EEG, Neuropsychology, Cognitive decline

Aims: Evidence suggests that patients with Alzheimer's disease (AD) have a higher chance to have epileptic seizures. However, only a few studies observed the potential harm of epileptiform discharges on the progression of cognitive decline. Animal studies suggest that these might be important contributors of Alzheimer pathology through the increased transcellular amyloid transport. The aim of our study was to examine AD patients using long-term EEG recording with a prospective longitudinal follow-up to estimate the effect of epileptic discharges.

Methods: We selected 40 patients (20 with epileptiform discharges and 20 without epileptic activity) meeting the criteria for probable AD and followed them during 3 years. Patients with epileptic seizures were excluded. The patients underwent rigorous clinical investigation including long-term (24hours) EEG monitoring and repeated detailed neuropsychology. Repeated measure general linear model was applied for statistical analysis. Point-serial correlation was applied to measure the connection between spiking rate and progression.

Results: Patients with epileptiform discharges showed more prominent decline in the neuropsychological results during the 2-year follow-up even with an age, gender and severity

weighted statistical model ($p < 0.001$). Correlation analysis revealed significant positive correlation between the progression of cognitive decline and the amount of spikes ($r = +0.42$; $p < 0.05$).

Conclusions: Epilepsy is a common comorbidity of AD. Epileptiform potentials represent an underrecognized phenomenon in Alzheimer patients, however, epileptiform discharges could accelerate the progression of AD, so accurate assessment of AD-related epilepsy is essential because antiepileptic drugs might represent a new therapeutic strategy in AD.

D/4 EPILEPTIFORM DISCHARGES AND DEGENERATION OF PAPEZ-CIRCLE IN ALZHEIMER'S DISEASE

Sára Lality, András Horváth, Anita Kamondi
National Institute of Clinical Neurosciences

Keywords: epilepsy, Alzheimer's, Papez-circle, dementia, neurodegeneration

Aims: Alzheimer's disease (AD) is the leading cause of cognitive decline in the elderly. Recent studies reported that AD patients frequently present epileptic seizures. Since we are not able to treat AD, we are searching for potentially modifiable comorbid contributors. There is a heated debate on the importance of epileptiform spikes without epileptic seizures in AD. The aim of our study was to analyze the connection between epileptic activity and the atrophy of brain structures in AD.

Methods: We selected 20 patients (10 with epileptiform discharges and 10 without epileptic activity including epileptiform discharges or seizures). Detailed neuropsychology was performed together with structural brain MRI analysis. Freesurfer software was applied for estimating the volume and thickness of brain structures. ANOVA analysis was performed to demonstrate intergroup differences. Severity was added as a covariate to the model. Point-serial correlation was applied to measure the connection between epileptic activity and atrophy. Results: Patients with epileptiform discharges showed significantly smaller hippocampal volumes, and entorhinal, anterior cingulate, prefrontal and precuneal thickness with a severity weighted statistical model ($p = 0.032$). Correlation analysis revealed significant positive correlation between atrophy scores and epileptic spiking ($r = +0.31$; $p < 0.05$).

Conclusions: Epilepsy is a common comorbidity of AD. Our results reveal a new insight for the importance of epileptiform potentials in dementia and proving that epilepsy is an important contributor of neurodegeneration. The pattern of accelerated atrophy follows the stations of Papez-circle reinforcing the theory that neurodegeneration process corresponds to the functional brain networks.

D/5 INTRACRANIAL HEMORRHAGIC COMPLICATIONS OF ENDOVASCULAR TREATMENT OF ACUTE ISCHEMIC STROKE IN THE NATIONAL INSTITUTE OF CLINICAL NEUROSCIENCES

Emma Orosz, Balázs Kis, István Szikora
Department of Neurointerventions, National Institute of Clinical Neurosciences, Semmelweis University, Budapest

Keywords: ischemic stroke, intracranial hemorrhage, mechanical thrombectomy

Aims: As a result of the expanding indication zone of endovascular treatment of acute ischemic stroke it is important to examine the complications which can affect clinical outcome. Analysis of hemorrhagic complications after endovascular treatment of acute ischemic stroke in 2017 and 2018 regarding clinical factors, treatment features and clinical outcome.

Methods: We made a retrospective analysis from the prospectively collected data of the treated cases. We recorded hemorrhagic complications in 122 patients out of the 459 treated cases. We created two subgroups for the hemorrhage, we put all kind of hemorrhagic complications in one group and made another group for the subarachnoid hemorrhage. We made a statistical analysis based on epidemiology, ischemic condition, localization of large vessel occlusion and periprocedural antithrombotic therapy.

Results: Significantly higher hemorrhage rate in males (Fisher's probe $p=0.044$). There is an association between the emerge of hemorrhage and the anterior Willis location. The association is significant with the lower ASPECT numbers (Mood test $p<0.001$) and with the increasing onset to recanalization time (t-probe $p=0.0476$). Combined therapy didn't augment the number of all hemorrhagic complications, but it can affect the appearance of parenchymal hematoma. Hemorrhagic complications have a bad effect on the clinical outcome.

Conclusions: Intracranial hemorrhagic complications in the endovascularly treated patient group can be related with patient features and therapeutic methods. Significant modifying factors are the gender, the localization and the onset to recanalization time.

D/6 EXAMINATION OF "DARK CELL PHENOMENON" IN A RODENT MRI MODEL

Dorottya Kata Szabó

Department of Radiology UP MS

Keywords: dark cell, rat, ADC, MRT, brain trauma, electric shock

Aims: INTRODUCTION: „Dark cell phenomenon” is the compaction of neurons caused by different noxae. Its main feature is reversibility, our aim was to examine this reversibility by advanced rodent MRI techniques. **METHODS:** 10 Wistar Hun rats in general anesthesia underwent cranial electroshock performed by a condensator capable of delivering 250V DC. The process of the MRI examinations was the following: T1, T2 maps, ADC (apparent diffusion coefficient) and MRT (magnetization transfer ratio) images were acquired first as a “baseline” before the electric trauma, right after it (in 20 minutes), 6 h in 9 cases, and 20 hours later in 3 cases. Regions of interests (ROIs) in the hippocampus and the cortex were observed with FSL FMRIB. Average intensities were measured in every animal's every timepoints and were compared to predicted values calculated from a control region in the brainstem. We used Man Whitney and Kruskal Wallis ANOVA after Shapiro-Wilk normality test.

RESULTS: After evaluating the ADC and MTR images, our results were the following: we experienced a tendency of decrease in MTR ROIs. Measured values compared to predicted values showed a relative increasement ($p=0.06-0.14$). On ADC images we found intensity increasement on the immediate images followed by a decrease on the 6h images ($p>0.0011$ in every case). Compared to predicted values our results showed a steeper intensity decrease ($p=0.08-0.32$).

CONCLUSION: According to our results we assume movement of water molecules opposite to the edema in regions underwent electric noxa, which can be caused by neuronal compaction and regeneration.

D/7 PROSTAGLANDIN E2: CONSTRICTS OR DILATES HUMAN CEREBRAL ARTERIOLES?

Andras Czigler M.D.1, 2, Luca Toth M.D.1, 2, Nikolett Szarka M.D.1, 2, András Büki MD, Ph.D.1, Peter Toth M.D., Ph.D.1, 2, 3, 4

1) Cerebrovascular Laboratory, Department of Neurosurgery and Szentagothai Research Center, University of Pecs Medical School, Pecs, Hungary 2) Department of Translational Medicine, University of Pecs Medical School, Pecs, Hungary 3) Reynolds Oklahoma Center on Aging, Donald W. Reynolds Department of Geriatric Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK USA 4) MTA-PTE Clinical Neuroscience MR Research Group, Pecs, Hungary

Keywords: PGE2, Vasospasm, Vasodilation, Neurovascular coupling,

Aims: Prostaglandin E2 (PGE2) has been suggested to contribute to both vasodilation and vasoconstriction in the human brain in physiological and pathological conditions. For example, it is involved in subarachnoid hemorrhage-induced vasospasm and in neurovascular coupling-related dilation of cerebral vessels. Despite these controversies, responses of human cerebral arterioles to PGE2 have not been extensively studied yet.

Methods: Following written informed consent, we isolated arterioles from cortical samples from patients undergoing neurosurgical removal of cerebral tumors (n=25, age= 53.7 ± 2.9). To determine the vasomotor effect of PGE2 we assessed the evoked isotonic force of the arterioles in response to different concentrations of PGE2 (10⁻⁹ to 3x10⁻⁵ mol/l). In a different set of experiments, in order to identify the role of PGE2 receptors, EP4 receptor antagonist BGC 20-1531 and EP1 receptor inhibitor SC-51322 was added with PGE2 to the organ bath.

Results: In functionally intact parenchymal arterioles, low concentrations (10⁻⁸ mol/l and 10⁻⁶ mol/l) of PGE2 caused a significant dose-dependent dilation, but vasoconstriction at higher concentration (>10⁻⁶ mol/l). The dose-dependent dilation was inhibited by the EP4 receptor blocker BGC201531. In the presence of EP1 inhibitor SC-51322, higher concentrations of PGE2 did not induce vasoconstriction. Vascular mRNA and protein expression of vasodilator EP4 receptors was significantly higher than that of vasoconstrictor EP1 receptors in human cerebral arterioles

Conclusions: Our results support the role of PGE2 in neurovascular coupling and could provide an explanation of the involvement of PGE2 in vasospasm after subarachnoid hemorrhage.

E. Multidisciplinary session IV.: HEALTH SCIENCES

E/1 DANCE-MEDICINE IN HUNGARY AS A PREVENTIVE AND REHABILITATIVE CARE FOR PROFESSIONAL DANCERS

Kristof Kerekes

United for Artist Foundation, KK Moves Health Center

Keywords: Dancemedicine, Rehabilitation, Prevention, Injuries, Health-care

Aims: In Hungary dance medicine is a quite hidden branch of sport-medicine. Only a few expert specialized for professional dancers' injuries even though currently in this small country more than 2000 professional dancers work day by day. From 2015, Kristof Kerekes, dance-medicine specialist represents this field, whose aim is to create full-support for Hungarian artists so as highly supported system around world does. During the presentation, Hungarian dancers' health status will be shown and the already achieved goals by United for Artists Foundation and KK Moves Health Center.

Methods: In our survey, we have collected data by physical examinations and questionnaires with active professional dancers in Hungary working for main theaters. We worked with nutrition experts, physiotherapists and mental hygiene specialists.

Results: Our results show the excessive amount of physical injuries achieved by wrong technical support or everyday overload. In our survey we could collect data about body image disturbance and the nutrition based relations which ended up physical injuries.

Conclusions: With the support of the medical team we have already achieved results in dancers prevention and rehabilitation procedures while we are working on the upcoming and accelerating steps of covering and supporting all artists in this country.

E/2 RESEARCH OF ANTIOXIDANT CAPACITY AND ANTIMICROBIAL EFFECTS OF LAVENDER VARIETIES

Tímea Biczók, Dr. Benedek Csilla, Burgettiné Dr. Böszörményi Erzsébet

Semmelweis University, Faculty of Health Sciences, Institute of Applied Health Sciences, Department of Dietetics and Nutrition Sciences, Semmelweis University, Faculty of Health Sciences, Institute for Health Promotion and Clinical Methodology, Department for Epidemiology

Keywords: lavender, aqueous extract, colorimetry, antioxidant capacity

Aims: Next to growing popularity, lavender was chosen as the herb of the year in 2018 by the Hungarian Society for Pharmaceutical Society. The composition, microbiological and physiological effects of its essential oil have been analyzed in numerous studies, but the characteristics of its aqueous extracts, decoctions and infusions are not well-known.

Methods: During this research, over 10 varieties of lavender species (*Lavandula angustifolia*; *Lavandula intermedia*) were studied. Samples were collected in different regions of Hungary, using two drying methods from which decoctions were made. The colors of lavender decoctions were analyzed by a colorimeter. Antioxidant capacity, total polyphenol, flavonoid and anthocyanin contents of samples were measured by a spectrophotometer. In order to study the antimicrobial activity of lavender, four pathogens were selected from strain collections: *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pyogenes* and *Candida albicans*. Samples were tested on ELISA 96-well plates in liquid environment based on absorbance by a new measurement technique.

Results: Results show significant differences among lavender varieties, even for same species. While antioxidant characteristics are mainly related to assumed nutrient content of the soil, anthocyanin content correlates with the

color of lavender decoctions. The method of drying has an effect on the flavonoid content. There were also significant differences among different lavender varieties in terms of antimicrobial activity.

Conclusions: Results can be considered as niche for domestic species and terroirs, completing the information available in literature and confirming curative characteristics explored before. Although it is preferred for soothing and stress-relieving effects, our research shows that consumption of lavender tea can be recommended for other beneficial effects.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

E/3 RISK-BASED SCREENING OF PREDIABETES AND DIABETES MELLITUS IN AN UNDERPRIVILEGED VILLAGE - THE ROLE OF THE GENERAL PRACTITIONER AND THE ADVANCED PRACTICE NURSE WITH COMMUNITY SPECIFICATION IN THE RECOGNITION AND SECONDARY PREVENTION

Henrietta Galvács, János Szabó MD, Zoltán Balogh PhD

Károly Rácz School of PhD Studies, Semmelweis University, Budapest, "JVZSE" Health Service and Nonprofit Ltd., Heves, Heves county, Department of Nursing, Institute of Applied Health Sciences, Faculty of Health Sciences, Semmelweis University, Budapest

Keywords: prediabetes, screening test, HbA1c, glucose tolerance test

Aims: Diabetes mellitus (DM) is one of the most serious worldwide endemics today. Thus, we aimed to reveal the prevalence of pre-DM and DM in the population (18-75 years of age) of Átány, Heves county (an underprivileged village) with help of the registered GP. In addition, we aimed to elucidate the difference between laboratory diagnostics screening methods (glucose tolerance test vs. HbA1c) and the definition of the strongest predictor in the disease onset.

Methods: The FINDRISC questionnaire was used to determinate the risk of DM. In the case of patients with increased or high risk, we used glucose tolerance test and glycated hemoglobin test to determine the condition of their carbohydrate metabolism.

Results: Data of 406 persons were collected with the FINDRISC questionnaire. We have found with Kruskal-Wallis test a significant correlation between the rising of diabetes risk and age and body mass index. The glucose tolerance test revealed prediabetes in 26,31%, and not previously diagnosed DM in 9,43% of the patients. The level of HbA1c revealed 50,94% prevalence of prediabetes and 11,32% prevalence of DM. The strongest predictors of prediabetes and DM was age, positive family anamnesis and hypertension. Chi-Square Test showed weak correlations with smoking and physical activity.

Conclusions: The present study revealed high incidence of prediabetes and diabetes mellitus in the population of this underprivileged village, pointing to the importance of risk recognition, early detection, prevention with changes in lifestyle and appropriate therapeutic interventions, all of which can be assigned to AP Nurse with community specialization and general practitioners, which can reduce the morbidity and mortality.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

E/4 THE RELATIONSHIP BETWEEN PERINATAL DEPRESSION AND SOCIAL SUPPORT

Júlia Hegedűsné Talabér, Eszter Lefkovics, Zsolt Somogyvári, László Szabó, János Rigó, Ildikó Baji

Semmelweis University Faculty of Health Sciences Department of Family Care Methodology, Semmelweis University Faculty of Health Sciences Department of Applied Psychology, Department of Clinical Studies in Obstetrics and Gynecology, 1st Department of Obstetrics and Gynecology, Semmelweis University

Keywords: perinatal depression, social support, pregnancy, postpartum

Aims: Perinatal period, optimally, is a joyful phase in the life of families. The incidence of mental illness, especially depression, is high in this vulnerable period. Incidence of prenatal depression in women is approx. 7-17%. This is a high risk of postpartum depression, which is approx. 22% among women. Social support is an important protective factor for perinatal depression. One of the most important aims of our research is to investigate the symptoms of depression and perceived social support in the perinatal period.

Methods: In our follow-up research, the women were involved at the 1st Department of Obstetrics and Gynecology, Semmelweis University in Budapest with a questionnaire method in three phases: the 3rd trimester of pregnancy, 3-5 days postpartum and 6-8 months after birth. 2238 respondents completed questionnaires. We examined the depressive symptoms by the EPDS questionnaire and the received social support by the MSPSS questionnaire on 3 sub-scales: friends, family and others.

Results: Clinical depression occurs in 11.56% of pregnant women and 8.47% in 6-8 months after delivery. Pregnant women with prenatal depressive symptoms consider their social support to be significantly lower than mentally healthy women. The same is true for perceived support from other people. Conclusions: Social support is an important protective factor for perinatal depression, which can be provided by not only direct relatives, but also professionals in care.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

E/5 NUTRITIONAL INTAKE AND BODY COMPOSITION OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Hajnalka Krisztina Oláh, Dr. Erzsébet Pálfi, Dr. Gábor Veres

Semmelweis University, Faculty of Health Sciences, Department of Dietetics and Nutrition Sciences, Director of the Pediatric Institute-Clinic of the University of Debrecen,

Keywords: inflammatory bowel disease, IBD, nutritional intake, body composition

Aims: Pediatric inflammatory bowel diseases have a huge impact on nutrition and body composition. The aim of this paper is to assess nutritional intake and body composition in a longitudinal follow-up study. Methods: 38 patients from the Department of Pediatrics I, Semmelweis University were involved. Nutritional intake was assessed by using 3-day food record, body composition was examined with InBody 720 body composition analyzer. The results were analyzed with NutriComp DietCAD, Microsoft Excel 2013 and IBM SPSS Statistics 22 software.

Results: Patients treated with biological and conventional therapy had a higher intake of vegetable protein and carbohydrate from starch than those treated with exclusive enteral nutrition (EEN) in the remission phase. The EEN group had a higher intake of iron compared to the conventional therapy group. Protein intake and fat-free mass had a significant positive correlation, while added sugar correlated with body fat mass in the same way.

Energy intakes were mostly adequate to that of the healthy recommendation, but protein intakes were higher than that. Consumption of added sugar was higher during the active phases. Body fat mass in patients in the biological therapy group overstepped the healthy median during their first 3 measures significantly, and the fat-free mass in the EEN group stayed under it at their first measurement.

Conclusions: Our results confirm that it is essential to measure body composition and not only monitor body weight. The patients should be advised based on their body composition, therapy and phase of the disease.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

E/6 POSTPARTUM FEMALE SEXUAL DYSFUNCTIONS IN HUNGARY: A CROSS-SECTIONAL STUDY

Katalin Szöllősi, László Szabó,

Department of Family Care and Methodology, Faculty of Health Sciences, Semmelweis University, Budapest
Károly Rácz School of PhD Studies, Semmelweis University, Budapest Heim Pál Children's Hospital, Budapest

Keywords: body image, postpartum, sexual dysfunction, sexual life, urinary

Aims: Although female sexual dysfunctions are common among women in the postpartum period, the profile of these disturbances has not yet been well investigated in Hungary.

Methods: This was a cross-sectional study including patients from two maternity clinics in Budapest. 113 women were recruited into our study 3 months after their childbirth. Data was collected from medical reports and by using self-developed questions and validated questionnaires in order to assess potential predictors, such as the mode of delivery, parity, urinary incontinence and body image. Sexual functions were evaluated by the Hungarian version of Female Sexual Function Index (FSFI). The Hungarian version of Body Image Questionnaire-Short Form14 (BSQ-SF14) was applied for assessing body image.

Results: 82,3% of the participants began to have sexual intercourse within three months postpartum, 53,98% of them reported sexual dysfunctions. Modes of delivery, parity, hemorrhoids, time of intercourse resumption were not associated with female sexual dysfunctions. We found correlation at a tendential level between urinary incontinence and sexual dysfunctions ($p=0,003$, $R=0,26$). We found negative correlation at a tendential level between the total score of BSQ-SF14 and FSFI ($p=0,03$, $R=-0,269$). Only 32,74% of women reported discussing sexual life with health care professionals, however 67,25% of them would have had the need to be asked.

Conclusions: The prevalence of female sexual dysfunctions was relatively high after childbirth. We found that incontinence and body image were associated with sexual dysfunctions, other risk factors remained unknown. Despite regular contact with health care professionals, women rarely get any information about postpartum sexual health issues.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

E/7 FACTORS ASSOCIATED WITH POSTURAL CONTROL IN NURSING HOME RESIDENTS

Réka Laura Erdős, dr. Éva Kovács, Izabella Jónásné Sztruhár

Semmelweis University, Faculty of Health Sciences, Institute of Basic Health Sciences, Department of Morphology and Physiology, Old Age Home of the Municipality of Budapest,

Keywords: postural control, elderly, Berg Balance Scale, fall prevention

Aims: Decline of the sensory and motor systems in older people negatively affects postural control. This increases the risk of falls, which is especially dangerous for older people in long-term care. Being aware of the quality of postural control and the factors affecting it among elderly people is crucial in implementing an effective fall prevention program. This cross-sectional study aimed to measure postural control and the demographic, health-related, and functional factors presumed to be correlated with it among nursing home residents. Another aim was to find valid screening tools based on these factors.

Methods: 71 residents of a nursing home in Hungary were included. Postural control was measured using Berg Balance Scale. Grip strength, 30 second chair stand test, and Timed Up and Go test were used to measure global strength of the upper and lower extremities, and functional mobility, respectively. The results of the three functional tests were dichotomized using age-specific reference values published in literature. Cohen's d was calculated to examine strength of relationship between the variables.

Results: Postural control was significantly worse in those who did not reach the age-specific reference values in any of the three functional tests. Effect sizes were large for functional mobility and medium for strength of upper extremities and lower extremities. Multi-morbidity and sex had no effect on postural control in our sample.

Conclusions: Among nursing home residents postural control is related to functional mobility and strength. Thus, routine testing of these skills among elderly people is an important task of the physiotherapist.

Support: Higher Education Institutional Excellence Program, Semmelweis University / Semmelweis Egyetem, Felsőoktatási Intézményi Kiválósági Program.

F. Multidisciplinary poster session I. – BIOCHEMISTRY/MOLECULAR BIOLOGY

F/1 CHARACTERIZATION OF ERA-DOMINATED SUPER-ENHANCERS IN BREAST CANCER CELLS

Noura Faraj, Dóra Bojcsuk, Edina Erdős, Balint L. Balint
University of Debrecen

Keywords: Super-enhancers, Breast cancer, E2, Transcription regulation, eRNA

Aims: Approximately, 75% of breast cancer women express estrogen receptor alpha (ER α - positive). ER α - driven super-enhancer (SEs) are clusters of long regulatory regions which are marked with high H3K27ac and production of enhancer RNA (eRNA). SEs are crucial players in cancer development and progression. However, SE's role in cancer is still under investigation. Here, we present the genomic characterization of the ER α -driven SEs in the breast cancer-driven MCF-7 cell line.

Methods: For this, MCF-7 cells were cultured and treated with estradiol (E2). Then we evaluated ER α and H3K27ac enrichment of four selected SE constituents located at the CUEDC1 gene region over control, by implementing chromatin immunoprecipitation followed by quantitative PCR (ChIP-qPCR). For investigating eRNA production, total RNA was isolated by TRIzol/chloroform, then RT-QPCR was performed and GRO-Seq data was also analyzed.

Results: Our study demonstrates that within a SE region, one enhancer, called mother enhancer, had stronger

activity than the others, known as daughter enhancers. Upon estradiol treatment, ER α and H3K27ac are enriched dramatically at the mother enhancer region compared to those at daughter enhancer regions. This is due to that ER α -driven super-enhancer region becomes more open and more transcriptional regulators are recruited. Moreover, our results indicate that expression levels of eRNA at mother enhancer are significantly higher than those at daughter enhancer regions in E2-treated cells.

Conclusions: Our practical results validate the former findings which were obtained by in-silico analysis. Hence, this study might give a better understanding for the ER α driven molecular mechanisms that are associated with breast cancer.

Support: This work was supported by NKFIH K-129166 grant entitled "Chromatin level determinants of cellular identity", MOLMEDEX FUN-OMICS (GINOP-2.3.3-15-2016-00007) grant and Debrecen Venture Catapult Program (EFOP-3.6.1-16-2016-00022) grant implemented through the New Hungary Development Plan co-financed by the European Social Fund and the European Regional Development Fund.

F/2 PERINATAL STRESS INDUCED SHORT- AND LONG-TERM MEMORY TRACES IN C. ELEGANS MODEL

Márton Csaba, Eszter Gecse, Dr. Csaba Sőti

Semmelweis University, Department of Medical Chemistry, Molecular Biology and Pathobiochemistry

Keywords: C. elegans, Learning, Memory, Stress, Imprinting

Aims: A peculiar way of associative learning is called imprinting, which forms after birth. The long-term effects of the perinatal memory traces are poorly described, and it is a challenging task to investigate it in humans. In order to find a solution for studying the early and harmful impressions I used an unusual model: Ceanorhabditis elegans. With my experiments I tried to give an answer for the question: Are the perinatal toxic stresses capable of disturbing short-term the behavioral patterns of the individual and leaving a long-lasting mark?

Methods: As a negative effect I used toxins with different points of action in the first 24 hours. This could be associated with the E. coli bacterial lawn's (food) sensorial inputs (smell, taste). Out of toxic stimuluses I chose the optimal stressor agent. I tracked the mitochondrial stress responses with a hsp-6::gfp strain and I investigated its relations with the aversive behavioral changes. These worm's food choice preferences were observed on the 1st and the 4th day.

Results: My results show that antimycin (AM) and paraquat exposure induce aversive reactions. AM exposure inducing developmental effects and hsp6::gfp expression. The toxic stress causes the different level of hsp-6 based on the worm's behavior: If the worms showed aversion, the hsp-6 levels were lower compared to the staying group. My results do not show significant food aversion in adults.

Conclusions: To sum up, I invented a model for investigate the early stress exposures effects on the behavior, and I found correlations between this and the tissue stress responses.

Support: MOL:MT18K-004

ÚNKP: ÚNKP-18-2-I-SE-7

F/3 THE EFFECT OF EXPRESSION LEVEL ON THE SIGNALING EFFICIENCY OF TYPE-1 CANNABINOID RECEPTOR (CB1R) IN HETEROLOGOUS EXPRESSION SYSTEMS

Viktória Bea Horváth /presenter/, Gergő Szanda /tutor/
Department of Physiology, Semmelweis University

Keywords: Cannabinoid Receptor CB1, Protein Biosynthesis, Plasmid, Leptin

Aims: Endocannabinoids (ECs) enhance food intake via pleiotropic actions of the CB1Rs, whereas leptin, on the other hand, decreases EC levels in the hypothalamus and this effect contributes to leptin's anorexigenic actions. We hypothesized that leptin not only reduces EC levels but also interferes with CB1R signaling. Therefore, we aimed to study leptin's effect on CB1R signaling in cells expressing recombinant receptors.

Methods: Human embryonic kidney cells (HEK293T) were used. Expression of CB1R and leptin receptor (LepR) along with ERK phosphorylation was measured by western blot.

Results: Transfecting HEK293T cells simultaneously with LepR and CB1R construct resulted in drastically reduced LepR expression as compared to LepR transfection alone. We presumed that this reduction of LepR expression was due to the overload of the cell's protein synthesis system by large amounts of recombinant CB1R. In order to overcome this hindrance, we replaced the cytomegalovirus (CMV) promoter with the human herpes virus thymidine kinase promoter (TK) within our CB1R construct. The expression of the TK-CB1R was reduced approximately by two orders of magnitude when using the same amount of plasmid DNA. However, reduced receptor expression did not interfere with signaling efficiency as CB1R agonist – ERK phosphorylation dose response curves were virtually identical with both CMV-CB1R and TK-CB1R constructs. (Nonetheless, TK-CB1Rs attenuated LepR expression to the same extent as CMV-CB1Rs.)

Conclusions: Our results indicate that reduced CB1R expression driven by weak promoters may be sufficient to saturate the cell's endogenous signal transduction machinery and such may be beneficial when examining receptor function.

Support: NKFI-6/FK-124038

F/4 INVESTIGATION OF THE ANTI-TUMOR EFFECTS OF 19 NOVEL TAMOXIFEN DERIVATIVES ON VARIOUS NEOPLASTIC CELL LINES

Márton Kalabay[1], Zsófia Szász[1], Orsolya Láng[1], László Kőhidai[1]

1: Institute of Genetics, Cell- and Immunobiology, Semmelweis University

Keywords: tamoxifen, cytotoxicity, impedimetry, cell cycle, apoptosis

Aims: The selective estrogen receptor modulator tamoxifen is a well-known anti-tumor compound, which can modulate multiple cellular physiological pathways. Previous investigations of the drug documented, that structural modifications of the parent molecule may result significantly increased activity in different models.

Methods: Tamoxifen and 19 analogues were investigated in 5 tumor cell lines (PANC-1, COLO205, A2048, EBC-1, MCF7). The antiproliferative effects (IC50) were evaluated by impedimetry (xCELLigence SP) and colorimetric alamarBlue assay. Effects on the cell cycle elicited by the analogues were observed with flow cytometry after propidium iodide staining.

Results: Tamoxifen performed antitumor effects in each cell line (IC50: PANC-1 – 33.7 uM, Colo205 – 12.0 uM, A2058 – 13.5 uM, EBC-1 – 8.2 uM). Incorporation of ferrocene as well as halogenation resulted significantly increased anti-tumor effect in PANC-1 (IC50: T15 – 15.0 uM, T6 – 29.6 uM) and in COLO205 (IC50: T15 – 2.5 uM, T6 – 9.9 uM) cells. Halogenation could increase the anti-tumor effects even in the MCF-7 cells. Cell cycle analysis confirmed that presence of ferrocene residue (subG1: 40.7%) can enhance the basic apoptotic character of

tamoxifen (subG1: 7.9%), while the halogenated derivate resulted G2/M phase arrest in PANC-1 cells.
Conclusions: Modification of the tamoxifen parent molecule with ferrocene or halogene residue results potentially increased anti-tumor character. The observed effect could be the result of the induction of apoptosis or a cell cycle arrest.

F/5 INVESTIGATING THE ROLE OF PHOSPHOLIPASE C γ 2 IN AUTOANTIBODY-INDUCED DERMATITIS

Kata Szilveszter, Attila Mócsai

Department of Physiology, Semmelweis University School of Medicine, Budapest, Hungary

Keywords: autoimmune, antibodies, inflammation, skin, phospholipase

Aims: Epidermolysis bullosa acquisita (EBA) is an autoimmune blistering skin disease characterized by autoantibody formation against collagen type VII (C7). Phospholipase C γ 2 (PLC γ 2) is an important member of the immune receptor signaling pathway. We aimed to find and optimize a proper method for the isolation of anti-C7 antibodies, then study the role of PLC γ 2 in the pathogenesis of EBA-like dermatitis model. Methods: Rabbits were immunized with GST-C7 fusion protein. We tried two methods to isolate anti-C7 antibodies from its blood-serum, Melon Gel and Protein G based affinity chromatography. The efficiency of these methods was controlled by gel electrophoresis. Next we injected the antibodies into wild type and PLC γ 2 deficient (PLC γ 2 $^{-/-}$) bone marrow chimeras. We observed the size of affected skin area and the severity of the symptoms every second day until 14 days. We made ear histological sections.
Results: We could isolate nearly equal amount of protein with the two methods, but we found more contamination in the samples, when we used Melon Gel. In the dermatitis model, wild type mice developed skin lesions, upon anti-C7 antibody treatment. Inflammatory infiltration was observed in histological samples. On the other hand PLC γ 2 $^{-/-}$ animals remained protected from the disease, we couldn't find any differences between this and the control group.

Conclusions: Protein G based antibody purification method appeared to be more capable of the isolation of anti-C7 antibody than the Melon Gel in respect of efficiency and purity. We found that the PLC γ 2 has a crucial role in the development of autoimmune dermatitis model.

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F/6 GENETIC BACKGROUND INFLUENCE THE PROGRESSION OF RENAL FIBROSIS IN TGF-BETA TRANSGENIC MICE

Omolegho Momoh, Dr. Gábor Kökény, Dr. Miklos Mozes
Semmelweis Institute of Pathophysiology

Keywords: Nephrology, Transgenic mice, TGF-beta, Genetics, Renal fibrosis,

Aims: It has been shown that genetic background determines the progression of experimental glomerulosclerosis in mice. We have previously described renal fibrosis with mild or severe phenotype in Alb/TGF- β 1 (TGF- β) transgenic mice on inhomogenous (CBAXB6) genetic background. Our aim was to examine the influence of genetic background on TGF- β induced renal fibrosis in transgenic mice, and to elucidate the molecular details of strain dependent progression of fibrosis.

Methods: We used previously generated congenic B6-TGF- β (23 generations) transgenic mice and CBAXB6-TGF- β transgenic hybrid mice. Wild type B6 and CBAXB6 hybrids were used as controls. Survival, plasma TGF- β level, proteinuria, renal histology, immunohistochemistry and mRNA expression were analyzed.

Results: Both B6-TGF- β and CBAXB6-TGF- β hybrid mice had the same elevated plasma TGF- β levels. CBAXB6-TGF- β hybrids had dramatically shorter survival than B6-TGF- β mice. B6-TGF- β mice had significantly less proteinuria and only mild glomerulosclerosis as compared to CBAXB6-TGF- β hybrid mice. Expression levels of renal TGF- β , collagen I and collagen III mRNA were ~2 fold higher, and TIMP-1 expression was 100 fold higher in CBAXB6-TGF- β hybrids as compared to B6-TGF- β mice. No significant difference was found in mRNA expression of other TGF- β target genes, including MMPs, Smad molecules, biglycan and decorin. **Conclusions:** Our data demonstrate a direct relationship between genetic background and the progression of TGF- β induced renal fibrosis in TGF- β transgenic mice, with shorter renal survival associated with increased renal TIMP-1 mRNA expression.

Support: Semmelweis Institute of Pathophysiology

F/7 DETECTION OF OSTEOCLAST DEVELOPMENT BY A NOVEL FLUORESCENT MICROSCOPIC METHOD

Nagy Simon Péter¹, Dr. Győri Dávid, Dr. Mócsai Attila
Semmelweis University, Physiology Department

Keywords: osteoclast, Syk, rheumatoid arthritis, inflammation, osteoporosis

Aims: Osteoclasts are multinucleated giant cells which are essentials for bone resorption. Myeloid precursors differentiate into preosteoclasts in the presence of RANKL (biochemical maturation) and then fuse together to form mature osteoclasts. The expression of osteoclast-specific genes (e.g. cathepsin K) are highly upregulated during osteoclast development. Our aim was to set up a reporter system which is capable of following the gene expression changes during osteoclast development and to study the role of Syk tyrosine kinase in this process.

Methods: A new mouse strain was generated by crossing mTmG mice (capable of red to green fluorescence switch upon Cre-mediated excision) with Ctsk gene promoter driven Cre expressing CtskCre mice (mTmG CtskCre). Bone marrow cells from mTmG CtskCre mice and mTmG controls were isolated and differentiated into osteoclasts or macrophages. The fluorescent proteins were detected by fluorescent microscopy and Western blot techniques. R406 molecule was used to inhibit Syk kinase.

Results: The mTmG osteoclast and mTmG CtskCre macrophage cultures showed only red fluorescence. However, when mTmG CtskCre cells were differentiated into osteoclasts we were able to detect green fluorescence within the cultures, corresponding to multinuclear cellular structures. The presence of green fluorescent protein (eGFP) in the mTmG CtskCre osteoclast cultures was confirmed by Western blot. We could not detect any eGFP in control cultures. R406 dose-dependently inhibited the appearance of green fluorescence.

Conclusions: Taken together, we set up a novel reporter system capable of following the process of osteoclast

biochemical maturation and confirmed the role of Syk kinase in this process

F/8 CHANGES IN THE COLOCALIZATION BETWEEN Kv1.3 AND LIPID RAFTS IN RESPONSE TO ALTERATIONS IN STEROL CONTENT OF THE CELL MEMBRANE

Bence Cs. Szabó, Máté Szabó, Florina Zákány MD, Péter Nagy MD PhD DSc, Tamás Kovács MD PhD
Department of Biophysics and Cell Biology, University of Debrecen

Keywords: membrane sterols, Kv1.3, lipid rafts, quantitative image analysis

Aims: The preferential lipid raft localization has been demonstrated in Kv1.3 voltage-gated potassium channels, which may modify its structural and functional properties. Our previous studies demonstrated that treatment with the major lipid raft constituent cholesterol exerts remarkable effects on electrophysiological parameters of Kv1.3. However, the exact molecular mechanisms of these alterations are unknown.

Methods: In our experiments, we analyzed the effects of cholesterol and 7-dehydrocholesterol (7DHC) on the lipid raft localization of Kv1.3. For microscopic analysis of the colocalization of the channels and lipid rafts, HEK-293 cells were transiently transfected with plasmids encoding Kv1.3. After loading of the cells with cholesterol or 7DHC, channels and rafts were visualized by confocal or stimulated emission depletion (STED) microscopy. During image analysis, the Pearson correlation coefficients between channel and raft marker signals were determined.

Results: First, we tested our method by analyzing the colocalization between two known raft markers, cholera toxin-B subunit and GFP-GPI. As expected, highly positive values of the correlation coefficient were found. Coefficients of similar magnitudes were determined between intensities of the raft marker and the antibodies against ion channels, demonstrating the preferential raft localization of Kv1.3. Furthermore, the extent of colocalization significantly increased in response to treatments with cholesterol and 7DHC. Our results were confirmed with STED microscopy providing much better (46-60 nm) resolution.

Conclusions: In conclusion, changes in the distribution of Kv1.3 between different membrane microdomains might at least partially mediate the effects of sterols on these channels.

Support:

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DETEP

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F/9 VASOREGULATORY EFFECTS OF THE 18:2 LYSOPHOSPHATIDIC ACID (LPA) DEPENDS ON AGE

Krisztina Vén, Noémi Karsai, Margit Kerék, Anna Monori-Kiss, Zoltán Benyó and Éva Ruisanchez
Institute of Clinical Experimental Research

Keywords: vasoconstriction, vasorelaxation, LPA, age, wire myography

Aims: Our research group has recently reported that LPA1 receptor activation in the endothelium induces vasorelaxation, while in the vascular smooth muscle (VSM) it evokes cyclooxygenase1 (COX1) activation with consequential thromboxane A2 (TXA2) release, which elicits vasoconstriction. During platelet-activation mainly

18:2 LPA is liberated. Since vascular diseases are more common in the elderly, in this study we aimed to observe the age-related changes of the 18:2 LPA induced vasoconstriction and -relaxation and to determine other influential predictors.

Methods: Wild-type and LPA1 receptor knock-out (KO), 8-80 weeks old, male and female murine aorta segments were isolated, vasoregulatory effects of the 18:2 LPA were tested with wire myography. To measure the TXA2 released by 18:2 LPA, we used TXB2 ELISA assay.

Results: The highest vasoconstrictor effect of the 18:2 LPA was seen in the middle of the age range, in the 32-weeks old population. The constriction was significantly influenced by body weight and gender over 32 weeks, while these predictive factors had no significant effect under 32 weeks. The LPA released TXA2 was significantly higher in the 32-weeks population compared to the 8-weeks group. LPA mediated vasorelaxation decreased in the 80-week group. The vasoregulation was induced by LPA1 receptor activation apart from age and gender.

Conclusions: In conclusion 18:2 LPA appears to have the strongest vasoconstrictor activity at the age of 32 weeks, which can be due to the higher TXA2 release. This is particularly interesting in the case of endothelial injury and platelet activation where LPA can contribute to the progression of vasospasm.

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F/10 Adaptations and late effects of high-performance sport on the cardiometabolic system

Topic: Sport Sciences

Authors: Mark Kantor^{1,2}, Akos Koller^{1,3,4}, Adam Lelbach^{1,2,3,4,5}

Semmelweis University, Faculty of Health Sciences

Keywords: high-performance sports, regular exercise, hypertension

Aims: Competitive sports exert great demands -among others- on the cardiometabolic system. In different sport types the exercise intensity and nutritional loads are different, as well as the prevalence of cardiometabolic diseases. Non-competitive, regular, dynamic physical activities are the most important factors preventing hypertension (Pedersen, 2015). However, Berge et al. (2015) measured significantly higher systolic and diastolic blood pressures in athletes doing strength-sport compared to that of endurance-trained athletes. Interestingly, the post-career effects of competitive sport are less investigated and known. We propose that elevated blood pressure and metabolic syndrome progressively develop post-career in strength athletes.

Methods: We have reviewed and critically analyzed the available literature (PubMed) regarding the post-career cardiometabolic effects of competitive sports.

Results: Overweight American football players suffered from dyslipidemia and related cardiometabolic diseases (Tucker, 2009). Guo et al. (2013) found significantly increased cardiometabolic risk in heaviest-weight-class strength sportsmen, compared to all other weight categories. Also, in strength sportsmen after finishing competitive sport career, the prevalence of diabetes and metabolic syndrome were found to be significantly higher, than in any other sport types (Buell, 2008; Kujala, 1994; Miller, 2008). Strength sports can increase arterial stiffness (Gojanovic, 2010), as well. In contrast, moderate aerobic exercise effectively improves the cardiometabolic risk factors in overweight sportsmen with metabolic syndrome (Guo, 2015).

Conclusions: Although regular exercise is essential in delaying, the post-career effects of high-performance sports -especially strength sports- likely have negative impact on cardiometabolic aging.

G. Multidisciplinary poster session II. – CARDIOVASCULAR

G/1 COMPARING CRYOBALLOON ABLATION WITH RADIOFREQUENCY ABLATION FOR PAROXYSMAL ATRIAL FIBRILLATION

Dorottya Debreceni, Dr. Péter Kupó, Dr. Eszter Földi, Prof. Dr. Tamás Simor
PTE KK Szívgyógyászati Klinika

Keywords: ablation, atrial fibrillation, cryoballoon, blanking period

Aims: The atrial fibrillation is the most common sustained arrhythmia. According to the current guidelines, catheter ablation of drug refractory paroxysmal atrial fibrillation is a class I level A indication. We have two methods for pulmonary-vein isolation: radiofrequency ablation (RF) is the most common technique and the cryoballoon ablation (CB) which is available in Pécs from September 2017. Our aim was to compare the procedural and 12-months outcome of patients after radiofrequency and cryoballoon ablation.

Methods: 45 patients with paroxysmal atrial fibrillation (RF= 30 patients, aged 58.3 ± 11.3 years; CB= 15 patients, aged 56 ± 14.4 years) were enrolled. We constructed the procedural data and the check examination results (1-3-6-12 months) retrospectively.

Results: Procedure and fluoroscopy time were: RF= 150.8 ± 44.4 min and 22.6 ± 7.26 min; CB= 101.2 ± 31.9 min ($p < 0.001$) and 25.2 ± 16.1 min ($p = 0.56$). The acute success rate was 100% in both groups. We registered the number of the complications after the ablations: RF= 3 (10%); CB= 2 (13%). 12-months later freedom from atrial fibrillation was achieved in 73% of patients who underwent radiofrequency ablation and in 80% of patients treated with cryoballoon.

Conclusions: In this single center study there was no significant difference between the two methods with regard to the freedom from paroxysmal atrial fibrillation. The benefit of cryoballoon method is the significant shorter procedure time.

Support:-

G/2 HYPOXIA-REOXIGENIZATION INDUCES RELEASE OF EXTRACELLULAR VESICULAR HRCR AND miR-223 IN CARDIOMYOCYTES

Balazs Hornyak, Szabina Mecsei, Árpád Kovács, Hargita Hegyesi, Edit Buzas
Semmelweis University Department of Genetics, Cell- and Immunobiology

Keywords: HRCR, MI, miR-223, extracellular vesicles, ncRNA

Aims: Ischemic heart conditions including myocardial infarction (MI) lead to potentially permanent heart damage. Crosstalk between different non-codingRNAs (ncRNAs) -including microRNAs (miRs) and circularRNAs (circRNAs)- have been discovered to play important regulatory roles in pathophysiological processes. Extracellular vesicles (EVs) have the ability to carry ncRNAs and have been shown to play an important communicatory role in MI. Here we assessed cardiac EVs enclosing ncRNAs HRCR, miR-223, linc-p21, and MHRT in hypoxia as potential biomarkers for early heart damage detection.

Methods: Primary neonatal cardiomyocytes (CMC) culture from one-day-old neonatal C57BL/6 mice were established and 5-day-old cells underwent hypoxia (4h) / reoxygenization (16h) experiments. Cell viability was assessed using Annexin-V FITC/PI staining by flow cytometry. Fractions of extracellular vesicles (EVs) were isolated with filtration and differential centrifugation methods. The presence of medium size (mEVs) and small size EVs (sEVs) were confirmed by flow cytometry. RNAs were isolated from CMCs, sEVs, mEVs. Differences in expression levels were determined using qPCR. The uptake of EVs by cardiomyocytes were confirmed by fluorescent labelling with PKH-26 dye.

Results: EVs exhibited the expected size, and expressed marker proteins CD63, CD81, CD9 on sEVs, and AnnexinV on mEVs. We report a significant increase in expression levels of miR-223 and circHRCR in CMCs after hypoxia. Expression levels of linc-p21 and MHRT did not change after hypoxic injury. Both miR-223 and circHRCR are present in EVs, however only the abundance of circHRCR changed after hypoxia.

Conclusions: Here we are first to show that both circHRCR and miR-223 are present in CMC-derived EVs.

G/3 ANALYSIS OF PREDICTIVE FACTORS FOR PROPAFENONE PROARRHYTHMIA. DOES EXERCISE ECG PLAY A ROLE DURING LONG TERM PROPAFENONE TREATMENT?

Edina Nagy-Baló MD, Krisztina Medvés-Vácz MD

University of Debrecen, Department of Cardiology and Cardiovascular Surgery, Debrecen, Hungary

Keywords: propafenone, proarrhythmia, ECG, tachycardiomyopathy, predictors

Aims: Propafenone proarrhythmia (PPA) is a potentially life-threatening complication of propafenone therapy (PT). PPA is defined as significant QRS widening on resting ECG during PT or wide QRS tachycardia during follow up. Limited data exist assessing the potential predictors for PPA in structurally normal heart patients and the benefit of exercise ECG (EECG). We aimed to investigate the predictors for PPA and to study the role of EECG.

Methods: 142 patients with structurally normal heart treated with propafenone between 01.2010 and 09.2017 were enrolled if they were on ongoing PT or PT was stopped because of PPA. Patients on ongoing PT (n=114) underwent an EECG and we considered it to be positive if an increase of baseline QRS duration was ≥ 40 msec (n=10).

Results: Comparing patients with positive and negative EECG the duration of PT (97.1 vs 40.2 months; $p=0.001$) were significantly different. During a mean follow-up of 46 ± 50 months 1 PPA (10%) occurred in patients with positive EECG. Age, sex, comorbidities, history of recovered tachycardiomyopathy (TCMP), duration of PT, dose of propafenone, dose of beta blocker, ejection fraction, left atrial diameter were analyzed as potential predictive

factors. On a multivariate analysis only history of TCMP was predictive for PPA (HR:7.995 CI:2.456-26.028; p=0.001). Besides, longer duration of PT was predictive for a positive EECG (HR:1.016 CI:1.006-1.028; p=0.002). **Conclusions:** Recovered TCMP is an independent predictor of PPA in patients with apparently normal heart. EECG's impact in prediction of PPA is controversial as the result of EECG may be changed during treatment and positive EECG occurred rarely.

G/4 INCOMPLETE STRUCTURAL REVERSE REMODELING FROM LATE-STAGE LEFT VENTRICULAR HYPERTROPHY IMPEDES THE RECOVERY OF DIASTOLIC FUNCTION IN RATS

Christian Karime, Bálint András Barta, Mihály Ruppert, Tamás Radovits
Heart and Vascular Center, Semmelweis University

Keywords: Pressure-overload, Reverse remodeling, Cardiac function

Aims: Pressure overload-induced left ventricular hypertrophy (LVH) regresses after pressure unloading. However, distinct structural alterations become less reversible during the progression of LVH, influencing the restoration of cardiac function. Here, we investigated how a reverse remodeling process from early- versus late-stage LVH affects different aspects of left ventricular function.

Methods: Pressure overload was induced in rats for 6, 12 or 18 weeks. Sham-operated animals served as controls. Pressure unloading was evoked by removing the aortic constriction at week 6 (early-debanded) or week 12 (late-debanded). The following alterations were then assessed: structural (by echocardiography and histology), molecular (by western blot and qRT-PCR), and functional (pressure-volume analysis).

Results: Myocardial hypertrophy regressed to a similar extent in both early and late-debanded groups, with no differences detected on the macroscopic (left ventricular mass, heart weight-to-tibial length ratio), microscopic (cardiomyocyte diameter) and gene expression (beta-to-alpha myosin heavy chain mRNA ratio) level. In contrast, resorption of interstitial and perivascular fibrosis was only detected in the early-debanded group, persisting in the late-debanded group. The incomplete structural reverse remodeling in the late-debanded group resulted in the normalization of ventriculo-arterial coupling, and thus the restoration of systolic function. However, residual diastolic dysfunction in active relaxation and passive stiffness was noted to be more severe in the late-debanded group.

Conclusions: Early debanding led to complete structural reverse remodeling (reduced hypertrophy and fibrosis) and full restoration of left ventricular function. In contrast, myocardial fibrosis persisted after late debanding, impeding the normalization of diastolic but not systolic function.

G/5 DIFFERENCES OF RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY BY GENDER

Flóra Zsófia Kulcsár, Walter Schwertner
Semmelweis Heart and Cardiovascular Center

Keywords: pacemaker, gender, heart failure, machine learning

Aims: Our aims were to assess the long-term clinical response to CRT by gender.

Methods: We evaluated the long-term outcome of patients implanted CRT device in our high-volume single center clinic. Primary endpoint was all-cause mortality. Kaplan-Meier and multivariate Cox regression analyses were used to evaluate mortality from any cause stratified by gender. Moreover, independent mortality predictors were also assessed by short-, mid- and long-term outcomes respectively by gender using machine learning technics such as Kullback-Leibler divergency score.

Results: In our clinic 2403 CRT implanted patients were registered from 2000 to 2017, 606 female and 1797 male patients were implanted. During the median follow-up of 4.0 years, 1218 patients died and reached the primary endpoint in the total patient cohort, 239 female and 979 male patients. There was a significant mortality benefit in female patients compared to male patients (HR=0.61, 95%CI: 0.54-0.69, $p<0.001$), which was also remained after adjusting for relevant clinical covariates. When 1-, 3- and 5-years mortality predictors were assessed by machine learning technics, between the early mortality predictors age, creatinine and urea were the most relevant parameters in the total patient cohort, while age is even more important over time and instead of renal parameters. By gender, in female patients weight and uric acid might be more relevant compared to male patients.

Conclusions: Female gender is an independent mortality predictor in CRT implanted patients. When clinical parameters were assessed between male and female patients, age, renal parameters, uric acid and weight might be relevant and changing predictors over time.

Support: Annamária Kosztin MD Béla Merkely MD, PhD, DSc

G/6 COMPARISON OF DSE, INVASIVE FFR AND CT-FFR IN PATIENTS WHO HAD PREVIOUS MYOCARDIAL INFARCTION

Judit Simon, Bálint Szilveszter, Ahres Abdelkrim, Balázs Jablonkai, Márton Kolossváry, Béla Merkely, Pál Maurovich-Horvat, Péter Andrásy

Heart and Vascular Center of Semmelweis University, Bajcsy-Zsilinszky Hospital

Keywords: Dobutamine stress echocardiography, CT, fractional flow reserve

Aims: Management of moderate non-culprit coronary lesions is controversial compared to significant NCL where revascularization improves the clinical outcome. Dobutamine stress echocardiography (DSE) and invasive fractional flow reserve (FFR) are accepted methods for detecting myocardial ischemia. Our aim was to determine the diagnostic performance of CT-FFR compared to DSE and invasive FFR.

Methods: In this prospective trial, DSE, FFR and CT-FFR were performed in every patient with MI and at least one moderate NCL (30-70% diameter stenosis). Wall motion abnormality in at least two contiguous myocardial segments on DSE, and FFR value 0.8 in invasive FFR and CT-FFR as well were determined as abnormal.

Results: Between March 2017 and December 2018, 51 patients (age 58.2 ± 10.4 , 74.5% male) were enrolled and 71 NCLs (40 LAD, 13 LCx, 18 RCA) were investigated. DSE, FFR and CT-FFR were positive in 32.3%, 32.9% and 22.5% of all lesions, respectively. FFR values were higher with CT-FFR compared to invasive FFR (0.85 ± 0.11 vs. $0.83\pm0.08, 0.05$). Compared to DSE, sensitivity, specificity, positive and negative predictive (PPV) (NPV) and diagnostic accuracy of CT-FFR were 40.9%, 85.7%, 56.2%, 76.3% and 71.8%. Same values were 39.1%, 85.4%, 56.2%, 74.5% and 70.4% compared to invasive FFR, respectively. Correspondence of CT-FFR with DSE ($k=0.29$) and with FFR ($k=0.27$) was weak.

Conclusions: Our results demonstrated excellent specificity, poor sensitivity and PPV and acceptable NPV of CT-FFR compared to DSE and FFR.

G/7 EFFECT OF SINGLE VENTRICULAR PREMATURE CONTRACTIONS ON LONG-TERM CLINICAL OUTCOME IN PATIENTS AFTER CARDIAC RESYNCHRONIZATION THERAPY IMPLANTATION

Richard Bence Masszi, Water Schwertner, Dr. Annamaria Kosztin
Városmajor Heart and Vascular Center, Semmelweis University

Keywords: heart failure, CRT, pacemaker, VES, ablation

Aims: Data on the effect of single premature ventricular contractions (PVCs) on clinical and echocardiographic response after cardiac resynchronization therapy (CRT) implantation is scarce. Methods: In our prospective study, 125 symptomatic heart failure (HF) patients (NYHA II-IVa) with reduced left ventricular ejection fraction ($EF \leq 35\%$) and wide QRS ($\geq 130\text{ms}$) underwent CRT implantation and were followed for 4 years. The primary endpoint was all-cause mortality at 2 and 4 years, the secondary endpoint was echocardiographic reverse remodeling assessed by $\geq 15\%$ improvement in EF, left ventricular end-systolic volume (ESV) or left atrial volume (LAV) after 6 months. The number of PVCs were assessed by device interrogation at 1 month after CRT implantation.

Results: During the 4 years of follow-up time 22 (33%) patients died and reached the primary endpoint from those 67 patients who attended 1 month follow up, and number of PVCs could be assessed, which median value was 11401. Patients with higher number of PVCs showed a higher risk of early all-cause mortality (HR 0.44, 95%CI 0.17-1.00; $p=0.04$), however when long term mortality was investigated, only a trend was found (HR 0.55; 95%CI 0.24-1.30; $p=0.11$). When secondary endpoints were investigated, patients with less PVCs than the median had a 4.8 times higher odds for LAV reverse remodeling 6 months after CRT implantation.

Conclusions: In patients underwent CRT implantation, greater amount of PVCs are associated with higher early but not long-term all-cause mortality and predicts atrial remodeling. Our results are pointing at the importance of PVCs as a response marker and warrant further investigations.

Support: Annamaria Kosztin

G/8 PSYCHOLOGICAL FACTORS AFFECTING MARFAN SYNDROME PATIENTS WITH OR WITHOUT CARDIAC SURGERY

Roland Stengl^{1, 2}, Bernadett Ruskó^{1, 2}, Miklós Pólos^{1, 2}, Kálmán Benke^{1, 2}, Bence Ágg^{1, 2, 3}, Andrea Székely⁴, András Szabó⁴, Elektra Bartha^{1, 2}, Zoltán Szabolcs^{1, 2}

¹Heart and Vascular Center, Semmelweis University, Budapest, Hungary, ²Hungarian Marfan Foundation, Budapest, Hungary, ³Department of Pharmacology and Pharmacotherapy, Semmelweis University, Budapest, Hungary, ⁴Department of Anesthesiology and Intensive Therapy, Budapest, Hungary

Keywords: Marfan syndrome, pain, psychology, anxiety, multidisciplinary

Aims: Marfan syndrome (MFS) is a rare systemic connective tissue disorder. Studies have been focusing mostly on the physical aspects, therefore literature on psychological and psychosocial burdens of the disease is sparse and

even the existing studies have small sample sizes. Therefore the aim of the present study was to assess the psychological and psychosocial aspects of the disease to improve the management of MFS patients. **Methods:** 66 adult patients with MFS were enrolled prospectively between 04.2016 - 11.2018 in this questionnaire-based study. Demographical and surgical data were collected and compared to the HUNGAROSTUDY (HS) population by using propensity matched method. Data management and analysis were performed using statistical software, reliability was calculated by using Cronbach's alpha. **Results:** Marfan patients had a moderate pain-related disability and sleep disturbances, however they were more satisfied with their lives and considered themselves happier than the average Hungarian population (HS group). Their score on the MMSE, BECK, STAI and STAI-T tests showed no significant difference. The HS group had a higher percentage of current smokers and higher pack-year unit. MFS patients were divided into operated (OP) and non-operated (NOP) groups. The OP group rated their subjective health condition lower and alcohol consumption was higher among them. Sleep disturbances were more common among NOP patients. **Conclusions:** Marfan patients' psychosocial life differs from the average Hungarian population and differences also exist between operated and non-operated MFS patients. These should be evaluated and taken into consideration to provide an optimal, multidisciplinary management for patients with MFS. **Support:** This study was supported by the National Research, Development and Innovation Office of Hungary (NKFIH; NVKP-16-1-2016-0017, „National Heart Program”), by the Higher Education Institutional Excellence Program of the Ministry of Human Capacities in Hungary, within the framework of the Therapeutic Development thematic program of the Semmelweis University.

G/9 DETERMINATION OF OPTIMAL CALCIUM SCORE THRESHOLD FOR 256-SLICE CORONARY CT ANGIOGRAPHY

Lili Száraz, Judit Simon, Márton Kolossváry, Bálint Szilveszter, Zsófia Drobni, Béla Merkely, Pál Maurovich-Horvat
Cardiovascular Imaging Research Group, Heart and Vascular Center, Semmelweis University, Budapest, Hungary

Keywords: Coronary CT Angiography, Coronary Calcium Score, Threshold

Aims: The diagnostic performance of coronary CT angiography (CCTA) is limited in patients with high coronary calcium score (CAC Score). In these cases coronary calcium results in an increased number of false positive scans. Therefore, our aim was to establish the optimal threshold of CAC Score for state-of-the-art scanner to perform or defer coronary CTA.

Methods: Consecutive patients with suspected coronary artery disease (CAD) who were referred to CCTA were included into our retrospective study. The patients were divided onto two groups based on the presence or absence of severe coronary artery stenosis on CCTA. Total and vessel-based CAC Score values were compared between the two groups. 95% specificity were considered clinically acceptable threshold.

Results: In total, we have studied 4865 patients. A CAC Score threshold of 700 had a specificity of 95.3% to identify patients with severe stenosis or non-diagnostic CCTA. The vessel-based CAC Score threshold in case of the left anterior descending (LAD) coronary artery was 320, in the left circumflex (LCx) coronary artery it was 100 and in the right coronary artery (RCA) it was 200.

Conclusions: Our results suggest that above a total CAC Score of 700, LAD score of 320, LCx score of 100, and RCA score of 200 due to heavy calcification CCTA should be deferred.

G/10 Skin microcirculation responses to ischemia and heat in trained and untrained individuals

Topic: Health-Sciences

Authors: Anna Pato, Zoltan Nemeth, Csaba Nyakas, Akos Koller
Semmelweis University, Faculty of Health Sciences

Keywords: occlusion, thermoregulation, microcirculation, exercise, heart r

Aims: The skin microcirculation has to supply the skin with sufficient oxygen and nutrients and contribute to the thermoregulation of the body. Thus, adaptation of skin microcirculation is important to achieve high levels of physical (sport) performance. We hypothesized that increases in perfusion of microcirculation is greater in response to local heat stimulus, than to local ischemic/ hypoxic challenge. Also, that heat-induced perfusion changes are greater in trained than non-trained individuals.

Methods: We have used Perimed5000 Laser Doppler flowmetry (LDF) to continuously measure perfusion (perfusion unit, PU, an arbitrary number), temperature (T) and pO₂ of the skin in various conditions. To achieve ischemia, the upper arm was occluded for 2 min, then released (followed by reactive hyperemia), whereas the temperature of skin was increased locally from control (~32.0 to 44°C) by a special LDF probe. The resting blood pressure and heart rate were also measured.

Results: In response to occlusion and release perfusion (PU) increased (from 10.4±1.2 to 48.8±25.5, 469.23±30.1% increase), T did not change, whereas pO₂ decreased to low levels. Increasing local T (from 32±1.02 to 44°C) elicited great increases in PU (from 10.4±1.2 to 237±73, a 2278.9±143.8% increase). Changes in skin perfusion in response to heat were correlated with the resting heart rate of individuals, whereas the magnitude of reactive hyperemia did not.

Conclusions: Thus, we propose that thermoregulation physiologically is more important than maintenance of skin blood flow and heat-induced regulation of skin blood flow is better developed in trained than in untrained individuals.

G/11 Relationship between different cardiovascular radiological phenotypes

Authors: Pirooska Márton, Zöldi Luca, Janositz Gréta, Gyulay Kata, Jokkel Zsófia, Debreczeni Rebeka, Persely Alíz, Szabó Gergely, Szabó Helga, Hernyes Anita, Tárnoki Dávid László, Tárnoki Ádám Domonkos
Department of Radiology, Semmelweis University, Budapest, Hungary

Introduction: Nowadays the role of arterial stiffness as a cardiovascular risk factor is unquestionable. However, its exact role in cardiovascular pathologies and its relationship with other cardiovascular phenotypes are not yet fully understood. Our aim was to study the relationship between different cardiovascular radiological phenotypes, including intima-media thickness (IMT), plaque formation and hemodynamic parameters, focusing on arterial stiffness. We also attempted to investigate the inheritance of these parameters.

Methods: We examined 46 Hungarian twin pairs (age: 54.8 ± 13.9 , 27 monozygotic (MZ), 19 dizygotic (DZ) pairs). We measured their peripheral blood pressure and hemodynamic values related to arterial stiffness (Arteriograph, TensioMed). We also measured the IMT, plaque burden, and local elastic properties of the carotid and femoral arteries (Samsung Prestige). We correlated these parameters, and did several t-test to compare these radiologic phenotypes and hemodynamic parameters, then we also carried out a twin study to estimate the inheritance of the examined phenotypes.

Results: Arterial stiffness is closely related to plaque burden ($r: 0.292$, $p < 0.05$ between aortic pulse wave velocity (PWVao) and total plaque volume, PWVao was significantly greater in the group with plaque burden, than in the group without $p < 0.05$), but has no significant correlation with IMT values. Both arterial stiffness and IMT showed correlation with blood pressure values. In the group with high arterial stiffness (PWVao > 12 m/s), aortic pulse pressure (PPao) and central blood pressure (SBPao) were significantly greater, than in the group with low arterial stiffness ($p < 0.01$). The IMT of the femoral arteries correlated with SBP (left: $r = 0.233$, right: $r = 0.291$, $p < 0.05$). Local elastic parameters did not show significant correlation with regional stiffness. The conducted twin study showed medium heritability of arterial stiffness ($A = 0.5$).

Conclusion: The results confirm that the process of arterial stiffness and atherosclerosis are closely related, but since PWVao has been correlated primarily with plaque parameters and not with IMT, this relationship occurs at a later stage of atherosclerosis. IMT values and arterial stiffness, although not significantly correlated with each other, both showed a strong correlation with blood pressure values. The twin study has shown, that there are probably significant genetic effects behind the development of arterial stiffness.

H: EMERGENCY- ANAESTHESIOLOGY – INTENSIVE CARE- PULMONOLOGY-RHEUMATOLOGY

H/1 THE CORRELATION BETWEEN CARDIOPULMONARY PARAMETERS AND ARTERIAL STIFFNESS IN CROSS-SECTION STUDY IN SYSTEMIC SCLEROSIS

Marianna Kalászi, Prof. Dr. Gabriella Szűcs, Dr. Edit Végh

Department of Rheumatology, University of Debrecen, Department of Rheumatology, University of Debrecen,
Department of Rheumatology, University of Debrecen

Keywords: systemic sclerosis, arterial stiffness, cardiopulmonary parameter

Aims: The systemic sclerosis (SSc) is a chronic heterogeneous autoimmune disease characterized by dysfunction of the immune system, generalized fibrosis and microvascular abnormalities. In SSc the cardiovascular and pulmonary involvements play the main role in the disease-related morbidity and mortality. In a previous retrospective study in 2017, we found significant positive correlation between the general pulmonary outcome and arterial stiffness values measured. Based on our previous results, we started a cross-section study to find correlation between the recent arterial stiffness parameters (flow-mediated vasodilatation (FMD), intima-media thickness (IMT, pulse wave velocity (PWV)) and definitive functional pulmonary parameters (FVC%, FEV1). We seeked for further correlations with other parameters including ejection fraction(EF), diastolic dysfunction and right ventricle pressure.

Methods: This study recruited 18 SSc patients (13 lcSs and 5 dcSsc subtype) followed by the Rheumatology Department of University of Debrecen. The examinations were performed in the last one year.

Results: We found positive correlation between the EF and age ($p=0.015$) and FVC% ($p=0.016$). The PWV was increased in patients with lcSSc compared to patients with dcSsc (PWV= 8.847m/s vs. 6.486m/s, $p=0.006$). The arterial stiffness did not show significant correlation with the definitive pulmonary parameters. In our study, we did not find correlation between the recent arterial stiffness values and the EF, pJK and diastolic dysfunction.

Conclusions: We could not find significant correlation between the arterial stiffness parameters and the functional pulmonary values. We presume that the lack of the correlation could be due to the low number of patients or the low number of abnormal pulmonary findings.

Support: Új Nemzeti Kiválósági Program

H/2 KRAS MUTATIONS PREDICT RESPONSE AND OUTCOME IN ADVANCED LUNG ADENOCARCINOMA PATIENTS RECEIVING FIRST-LINE BEVACIZUMAB AND PLATINUM-BASED CHEMOTHERAPY

Aron Kristof Ghimesy, Aron Bertram Gellert, Erzsebet Schlegl, Balazs Hegedus, Erzsebet Raso, Tamas Barbai, Jozsef Timar, Gyula Ostoros, Judit Moldvay, Ferenc Renyi- Vamos, Zoltan Lohinai, Mir Alireza Hoda, Thomas Klikovits, Walter Klepetko, Viktoria Laszlo, Balazs Dome

Department of Thoracic Surgery, National Institute of Oncology-Semmelweis University, Department of Tumor Biology, National Koranyi Institute of Pulmonology, Department of Thoracic Surgery, Ruhrlandklinik, University Duisburg-Essen, 2nd Department of Pathology, Semmelweis University, Tumor Progression Research Group, Hungarian Academy of Sciences-Semmelweis University, 8th Department of Pulmonology, National Koranyi Institute of Pulmonology, Division of Thoracic Surgery, Department of Surgery, Comprehensive Cancer Centre Vienna, Medical University Vienna, Austria.

Keywords: KRAS mutations, advanced lung adenocarcinoma, bevacizumab,

Aims: Bevacizumab, combined with platinum-based chemotherapy, has been widely used in the treatment of in advanced-stage lung adenocarcinoma (LADC). Although KRAS mutation is the most common genetic, its prognostic and predictive role remains unclear.

Methods: The correlations of KRAS mutational status with clinicopathological variables including progression-free and overall survival (PFS and OS, respectively) were retrospectively analyzed in 501 Caucasian stage III-IV LADC patients receiving first-line platinum-based chemotherapy(CT) with or without bevacizumab(BEV).

Results: Of 247 BEV/CT and 254 CT patients, 95 (38.5%) and 75 (29.5%) had mutations in KRAS, respectively. KRAS mutation correlated with smoking ($P=0.009$) and female gender ($P=0.003$) in the BEV/CT group. We found no difference in OS between patients with KRAS mutant versus KRAS wild-type tumors in the CT alone group ($P=0.6771$). Notably, patients with KRAS-mutant tumors demonstrated significantly shorter PFS ($P=0.0255$) and OS ($P=0.0186$) in response to BEV/CT compared to KRAS wild-type patients. KRAS mutation was an independent predictor of shorter PFS (hazard ratio, 0.597; $P=0.011$) and OS (hazard ratio, 0.645; $P=0.012$) in the BEV/CT group.

Conclusions: KRAS mutant LADC patients receiving BEV/CT treatment exhibited inferior PFS and OS compared to those with KRAS wild-type advanced LADC. KRAS mutations may define a subset of LADC patients unsuitable for antiangiogenic therapy with BEV.

H/3 ARTIFICIAL INTELLIGENCE-BASED ALGORITHM MIGHT IDENTIFY RESPONDERS TO IMMUNOTHERAPY IN NON-SMALL CELL LUNG CANCER (NSCLC)

Szabolcs Gergely^{1, 2}, Dr. Zoltán Lohinai Ph.D.^{2, 3}, Dr. Zsolt Megyesfalvi^{2, 3}, Andrea Fülöp^{1, 2}, Botond Megyesfalvi², Csilla Kugler^{2, 3}

1. University of Medicine, Pharmacy, Science and Technology of Marosvásárhely, 2. Department of Thoracic Surgery, Semmelweis University, 3. National Koranyi Institute of Pulmonology, Budapest

Keywords: QTA, artificial intelligence, NSCLC, PD-L1, Immunotherapy

Aims: Response rate to immunotherapy in high tumor programmed death-ligand 1 (PD-L1) population in non-small cell lung cancer (NSCLC) is only about 20-30%. Quantitative computed tomography (CT) based texture analysis (QTA), a non-invasive approach might complement conventional imaging and histopathological tumor assessment in NSCLC. We aimed to investigate the predictive and prognostic role of machine learning associated QTA in NSCLC patients in terms of response to immunotherapy and PD-L1 expression.

Methods: We analyzed pretreatment contrast-enhanced CT scans of 50 advanced-stage NSCLC patients treated with anti-PD immunotherapy. QTA was applied to primary tumors using the 4.8.1 version of 3D Slicer software obtaining 104 CT continuous CT parameters that describe tumor pixel distribution. Principal component analysis (PCA) was performed on the derived parameters and eight principal components were identified. Data were analyzed with artificial intelligence (AI) approaches based on Naïve Bayes algorithm and K-means clustering. Mann-Whitney U test was performed to compare the 104 continuous CT parameters alone.

Results: I identified patients with favorable response to immunotherapy and high PD-L1 expression ($\geq 50\%$) with an accuracy of 66% and 57%, respectively. There were significant differences in 23 CT parameters in the PD-L1 $\geq 50\%$ vs $< 50\%$ subgroups. We found one out of eight primary components that significantly differed in patients with high PD-L1 expression $\geq 50\%$ (vs. patients with low PD-L1 $< 50\%$; $p=0.007$).

Conclusions: Our results highlight the potential predictive value of AI-based QTA in the prediction of response to immunotherapy and tumor PD-L1 expression that might help clinicians to select patients for immunotherapy administration.

Support: The authors have no financial support to report.

H/4 COMPARATIVE TARGETED RNA SEQUENCING IN SMALL CELL LUNG CARCINOMA REVEALS CHANGE IN NEUROENDOCRINE PATTERN IN PRIMARY TUMOR VERSUS LYMPH NODE METASTASES

Zsolt Megyesfalvi M.D., Zoltan Lohinai M.D.

Thoracic Surgery Department, Semmelweis University and National Institute of Oncology; Tumor Biology Department, National Koranyi Institute of Pulmonology

Keywords: SCLC, neuroendocrine tumor, gene expression

Aims: Recent preclinical cell line data presented at World Conference on Lung Cancer 2018 suggest that neuroendocrine (NE) pattern of small cell lung cancer (SCLC) has strong therapeutic relevance. NE high tumors are associated with immune desert and NE low tumors are considered immune oasis phenotype.

Methods: Targeted RNA-sequencing of 2560 genes was performed on 32 matched surgically resected SCLC patients primary tumors and lymph node (LN) metastases. We performed a cluster analysis and heat map to divide patients into NE high and NE low subtypes by using the top NE associated genes.

Results: Cluster analysis clearly identified SCLC NE subtypes according to primary tumor (NE high vs. low, 20 vs. 12, respectively) and LNs (NE high vs. low, 23 vs. 9, respectively). In case of five patients, a change in NE pattern was observed, suggesting a possible inter-tumor heterogeneity regarding NE differentiation. Moreover, a significant downregulation of NE associated genes CAV1, CAV2 and ANXA3 was found in LN metastases compared to primary tumor. A lower expression of NE associated key RNA genes REST and Myc, and the higher expression of DLL3 in NE high subtype are in accordance with the preclinical findings and confirms the accuracy of the cluster analysis performed.

Conclusions: Our data confirm the results of preclinical studies and show NE low and high differentiation clusters in SCLC. NE pattern of the LN metastatic lesions might not reflect the NE phenotype of the primary tumor, consequently, treatment decisions including immunotherapy administration needs to be further investigated.

Support: The authors have no financial support to report.

H/5 FIRST PERIOD OF VATS LOBECTOMY IN OUR WARD BETWEEN 2011 AND 2017

Daniel Urban¹, Otto Kovacs¹, Choroumzadeh Dashti Parham², Zoltan Szanto¹

1 Ward of General and Thoracic surgery, Hetényi Géza County Hospital Szolnok; 2 Ward of Anesthesiology and Intensive Care, Hetényi Géza County Hospital Szolnok

Keywords: VATS lobectomy, lung cancer, adenocarcinoma, routine procedure

Aims: The mortality of the malignant lung cancer is still growing especially in Hungary. There is no efficient method for prevention and usually the recognition is in the progressive stage. Objectives was to analyse the data of 6,5 years periods and oncological follow-up. Our results were compared to the international literature.

Methods: 173 VATS lobectomies were proceeded on our ward. There were 105 men and 68 women patients. The mean age was 64,1 years. The mean time of operations was about 120 minutes. The mean follow-up was 19,5 months.

Results: From 173 VATS lobectomies there were 8 benign cases. The most frequent primer malignant pattern was the adenocarcinoma with 111 cases after these 32 cases planocellular carcinomas, 6 small-cell lung cancers, 4 carcinoids and 4 other primary lung tumors. Four patients had pulmonary metastases. In 118 cases neoadjuvant therapy was given. The distribution of tumor stage: IA 40, IB 53, IIA 30, IIB 17, IIIA 21. There were 9 local recurrences, 27 metastases. In case of 8 patients conversion was necessary. In postoperative period 20 recurrent airleak were observed. Because of this there was 10 reoperation from which 7 were VATS and 3 were thoracotomy. During the postoperative period the authors did not lose patient.

Conclusions: To sum up our data follows the international trends. The VATS lobectomy becomes a routine procedure in our Hospital. The oncological treatment and the recurrence of tumors are correlate with the results of international literatures.

H/6 CT QUANTITATIVE TEXTURE ANALYSIS (QTA) MIGHT PREDICT LYMPH NODE AND DISTANT ORGAN METASTASES IN NON-SMALL CELL LUNG CANCER (NSCLC)

Csilla Kugler, Andrea Fülöp, Szabolcs Gergely, Botond Megyesfalvi

National Koranyi Institute of Pulmonology, Budapest; Department of Thoracic Surgery, Semmelweis University, Budapest; University of Medicine, Pharmacy, Science and Technology of Marosvásárhely

Keywords: machine learning, NSCLC, lymph node, metastases, CT-QTA

Aims: Machine learning based quantitative CT texture analysis (QTA) might be a potential tool in the early prediction of metastases by extracting a large number of quantitative features from CT images which reflect the distribution of pixels, thus detecting subtle changes beyond simple visual assessment on the primary tumors. The aim of our study was to investigate the role of QTA in non-small cell lung cancer (NSCLC) patients according to lymph node (LN) and distant organ metastases.

Methods: Pretreatment contrast-enhanced CT images of 50 advanced-stage NSCLC patients were analyzed with 3D Slicer version 4.8.1. After tumor segmentation, image processing identified 104 CT parameters. Next, primary component analysis (PCA) reduced the parameters to eight independent principal components. These eight principal components were analyzed using machine learning approaches based on Naïve Bayes algorithm and K-means clustering. Statistical analyses were performed with Mann-Whitney U test.

Results: QTA identified patients with LN and distant organ metastases with an accuracy of 66% and 68%, respectively. We found a significant difference using all 104 primary tumor CT parameters in four parameters according to LN metastases and seven parameters according to distant organ metastases. Furthermore, we identified two primary components with one displaying significant differences according to the presence of LN metastases ($p=0.049$) and distant organ metastases ($p=0.011$).

Conclusions: QTA of CT images might serve as a promising non-invasive diagnostic tool to predict the presence of LN and distant organ metastases in NSCLC, however, further studies on “Big Data” are needed to define the exact prognostic value.

Support: Dr. Zsolt Megyesfalvi, Dr. Zoltán Lohinai Ph.D.

H/7 RIGID BRONCHOSCOPY UTILIZING TRANSLARYNGEAL HUMIDIFIED RAPID-INSUFFLATION VENTILATORY EXCHANGE

Anna Kornafeld¹, MD; Ryan Chadha², MD; Sebastian Fernandez-Bussy¹, MD

¹ Department of Pulmonary and Critical Care, Mayo Clinic, Jacksonville, FL, USA, ² Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Jacksonville, FL, USA

Keywords: rigid bronchoscopy, stent placement, THRIVE, ventilation, oxygen

Aims: To date, oxygenating and ventilating via rigid bronchoscopy required standard hand or jet ventilation. Recently, Humidified Rapid-Insufflation Ventilatory Exchange, traditionally via the transnasal approach has been utilized effectively for oxygenation in the anesthesia and ICU settings. However, there are no studies looking at the usage of Translaryngeal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE) during rigid bronchoscopy.

Methods: Patient was a 60-year-old male with tracheobronchomalacia presented for stent placement via rigid bronchoscopy. The patient was induced under general anesthesia and had an arterial line placed. Laryngeal mask was placed for airway exam, then rigid bronchoscope attached to the THRIVE was placed with subsequent uneventful stenting. He was subsequently emerged from anesthesia and taken to our recovery room with no complications noted.

To see the efficacy of oxygenation and ventilation, data points were collected at the beginning, every 10 minutes, and at the end of the procedure including oxygen saturation (SpO₂), partial pressure of oxygen, partial pressure of carbon dioxide (PaCO₂), pH, heart rate, blood pressure, pre- and post-procedure end tidal carbon dioxide (ETCO₂).

Results: There were no hemodynamic changes and patient maintained his SpO₂ throughout the procedure (94% to 99%). His PaCO₂ rose from 41 to 115mmHg, and his pre-ETCO₂ was 48 mmHg; post-ETCO₂ was 84 mmHg.

Conclusions: In our case, THRIVE utilization via the rigid bronchoscope allowed for adequate oxygenation with some ventilation, but resulted in significant hypercarbia. This case shows THRIVE may be useful in certain patient populations as long as clinicians are aware of the potential complications.

I. SPECIAL TEACHING SESSION: MTT session

I/1 Expression of IDO1-2, iNOS and interferon-inducible GTPases in Chlamydia-infected murine lung

Dóra Paróczai^{1,2}, Tímea Raffai², Dávid Kókai², Anita Bogdanov², Gábor Veres³, László Vécsei⁴, Szilárd Poliska⁵, László Tiszlavicz⁶, Ferenc Somogyvári², Valéria Endrész², Katalin Burián²

1Department of Pulmonology, Faculty of Medicine, University of Szeged - Deszk (Hungary), 2Department of Medical Microbiology and Immunobiology, University of Szeged - Szeged (Hungary), 3MTA-SZTE Neuroscience Research Group, Szeged - Szeged (Hungary), 4Department of Neurology, Faculty of Medicine, Albert Szent-Györgyi Clinical Center, University of Szeged - Szeged (Hungary), 5Genomic Medicine and Bioinformatics Core Facility, Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Debrecen - Debrecen (Hungary), 6Department of Pathology, Faculty of Medicine, Albert Szent-Györgyi Clinical Center, University of Szeged - Szeged (Hungary)

Introduction: Chlamydiae can infect a wide variety of cells, including human inflammatory and epithelial cells. *Chlamydia pneumoniae* (*C. pneumoniae*) and *Chlamydia muridarum* (*C. muridarum*) are involved in modelling human infections in murine lung tissues and investigating immune responses, gene expressions and histopathology.

Aims: As the functions of several genes, including indolamine-2,3-dioxygenase 1,2 (*IDO 1,2*) in chlamydia infection *in vivo* have not been well described, we designed a study to examine host gene expressions, implicated in the elimination of the murine and human *Chlamydia* strains.

Methods: BALB/c mice were infected with *C. muridarum* or *C. pneumoniae* and sacrificed on day 7 post-infection to gain lung tissues for RNA extraction and immunohistochemistry. We performed RNA sequencing and qPCR to analyse interferon-inducible (IFN-inducible) GTPases, IDO1,2 and even chemokine expressions. By using the high-performance liquid chromatography (HPLC), the tryptophan and kynurenine concentrations in lung tissues were determined.

Results: The transcriptome analysis of *C. muridarum* infected lung tissues revealed the significant upregulation of IFN-inducible GTPases, iNOS and CXCL chemokines. IDO genes were highly induced: we detected in *C. muridarum* infection a 20.4 ± 11.3 fold of *IDO1* and 38.2 ± 25.2 fold of *IDO2*, in case of *C. pneumoniae* 15.5 ± 14.1 fold of *IDO1* and 88.9 ± 73.9 fold of *IDO2* upregulation. The kynurenine/ tryptophan ratios ranged between 0.12-0.22 in the *C. muridarum* infected samples, 0.13-0.20 in the *C. pneumoniae* infected samples, indicating that IDO 1,2 were functionally active.

Conclusions: Our study emphasizes the similarities of *Chlamydia* elimination between humans and mice, regarding novel antichlamydial gene expressions in *Chlamydia*-induced lung infections.

I/2 VASCULAR ADHESION MOLECULES IN OSA AND ITS COMORBIDITIES

PÉTER HORVÁTH, MD (BUDAPEST, HU)

No abstract available.

I/3 EXPLORING THE GUT MICROBIOME TO FIGHT LUNG CANCER / MICROBIOM ÉS COPD/TÜDŐRÁK

Zoltan Lohinai, MD, PhD

National Koranyi Institute of Pulmonology, Budapest

The etiology of COPD and lung cancer has been linked to numerous factors including the gut microflora. The microbiome is the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space. By definition, the human metagenome/microbiome is the collective genome of all bacteria, archaea, fungi, protists, and viruses in the human body. Overall, around 100 trillion bacteria live in our human body. Ninety five percent of our microbiota located in the gastrointestinal tract. Recently, airway dysbiosis have been associated with lung diseases. Changes in the lung and gut microbiome diversity might provide new insights into carcinogenesis and disease screening. Recent study revealed that the gut microbiome diversity showed correlations in clinical responses from diverse cancer patients to immune checkpoint inhibitor therapy. Furthermore, fecal microbiota transplantation from patients with epithelial tumors who responded to immune checkpoint inhibitor into germ-free mice decreased the antitumor effects of Programmed death receptor-1 (PD-1) blockade. However, the presence and potential biomarker role of gastrointestinal (GI) microbiome in lung cancer has not been fully explored. There is an ongoing study in our Institution, that aim to investigate the biomarker role of microbiome in lung cancer patients. We performed shotgun metagenomic sequencing to identify more than 20.000 different bacteria at the same time. In our study, we aim to evaluate the associations of diversity in GI bacteria and response to oncotherapy in non-small cell lung cancer. Ultimately, microbiome associations should be translated into practical applications in order to accelerate the diagnosis of cancer or precancer, to increase the efficacy of oncotherapy.

I/4 IMMUNOTHERAPY IN SMALL CELL LUNG CANCER: WHY IMMUNE CELLS ARE WAITING OUTSIDE IN THE WORLD'S MOST AGGRESSIVE CANCER?

David Dora¹, Zoltan Lohinai²

¹Semmelweis University, Department of Anatomy, Histology and Developmental Biology, Budapest

²National Koranyi Institute of Pulmonology, Budapest

The way we evaluate small cell lung cancer (SCLC) has significantly changed recently, however today the diagnosis of SCLC is mainly determined based on simple morphological pattern with no major therapeutic advancements in this recalcitrant cancer. Lack of our understanding of key immunological mechanisms including immune checkpoints, immune cell infiltration and their inter-tumor and intra-tumor heterogeneity might be a key to the long term failure of significant efficacy of immunotherapies. Latest preclinical data show that SCLC is not a single disease entity, rather a continuous spectrum of cells that express different neuroendocrine (NE) patterns. SCLC might be classified into NE high and NE low subtypes that have major differences in morphology, growth properties, genetic alterations, and immunogenicity. NE high is immune desert and NE low is associated with immune oasis phenotype based on *in vitro* data. In this translational retrospective study we aim to characterize the immune microenvironment in human SCLC samples to identify new targets for therapy.

We provide a thorough immunohistochemical (IHC) analysis on primary tumor and matched lymph node samples of 32 resected early-stage histologically confirmed SCLC patients. Formalin fixed paraffin embedded (FFPE) tissue microarrays (TMAs) were prepared for IHC. Patients were clustered in NE low and NE high groups based on RNAseq data using NE associated key genes as previously described. Immunohistochemistry was performed to reveal the dispersion of leukocyte and T-lymphocyte infiltration between the stroma and tumor nests.

Our preliminary results show that the stroma is significantly more infiltrated by immune cells both in primary tumors and LN metastases compared to tumor nests with remarkably higher immune cell density in NE low tumors. Increased expression of emerging immune checkpoints were associated with NE subtypes. Furthermore, immune checkpoints were positively correlated with higher immune cell density both in primary and lymph node metastases. To our knowledge this is the first human study that demonstrates the proper histological localization and distribution pattern of immune cell types in NE low and NE high tumors in SCLC, providing insight for further translational and clinical studies on immunotherapies.

J. Multidisciplinary session VI.: ORTOPEDICS-OTORHINOLARYNGOLOGY

J/1 A PATIENT-SPECIFIC FINITE ELEMENT STUDY OF PERCUTANEOUS CEMENT DISCOPLASTY INDUCED STABILITY IN LUMBAL MOTION SEGMENTS

Ferenc Bereczki, László Kiss, Péter Endre Éltés, Áron Lazáry

In Silico Biomechanics Laboratory, National Center for Spinal Disorders, H-1126 Budapest, Királyhágó u. 1-3.

Keywords: Finite Element, Discoplasty, Aging Spine, 3D geometry, Stenosis

Aims: In case of elderly patients for symptomatic degenerative disc disease of the lumbar spine, standard surgical procedures are often limited due to severe comorbidities. During the minimally invasive percutaneous cement discoplasty (PCD) introduced by our Institution, bone cement (polymethylmethacrylate, PMMA) is injected into the degenerated disc spaces showing vacuum phenomena, via a postero-laterally positioned Jamshidi needle. The aim of this pilot study is to investigate the stabilizing effect of PCD with the use of patient-specific finite element models.

Methods: We used postoperative thin-slice computed tomography (CT) images of patients (n=3, age: 59, 83, 66 years) who underwent PCD. In silico segmentation process was used for creating the 3D geometries of the treated motion segments, and the injected bone cement. From these geometries, finite element models were created with the use of uniform 1 mm edge length linear tetrahedrons. The upper endplate, of the cranial vertebrae model was loaded to simulate the physiological forces present in prone position, and during extension of the motion segment.

Results: After post-processing the simulations, we visualized the pedicles of the cranial vertebrae in a horizontal plane. We predicted less pedicle displacement in motion segments with greater PMMA-endplate contact surfaces. This phenomenon will be statistically investigated later a larger cohort.

Conclusions: Patient-specific finite element simulations can be used to obtain important data, and to detect technical flaws regarding an operation procedure. The workflow developed by our research team allows the patient-specific investigation of larger patient groups treated with PCD in the future.

Support: OTKA FK123884

J/2 PRECLINICAL AND CLINICAL STUDY OF COST-EFFECTIVE, FUNCTIONAL UPPER LIMB PROSTHESIS AND THEIR DEVELOPMENT PROCESS BY EEG ANALYSIS AND 3D TECHNOLOGIES

Dávid Berki

Department of Biophysics, University of Pécs, Faculty of Medicine

Keywords: prosthesis, 3D printing, cost-effective, myoelectric, EEG

Aims: The aim of the study is to investigate proprietary, cost-effective, personalized functional prosthetic upper limbs for children and adults with transradial amputation. We have developed a myoelectrically controlled prosthesis using 3D technologies. Our objective is to develop a BCI system controlled by EEG signal processing. This could provide opportunity for a wider application of this method. Long term objective is to develop a 3D printed upper limb prosthesis that is capable for separate movements of fingers.

Methods: We have created our current prototype based on a ready to use product. The palmar component has been made of flexible PLA composite by FFF AM technology. Dorsal component and forearm have been created using hard PLA plastics. Braided plastic cords running in tunnels along the fingers provide connection with Micro Linear Actuator 7N in the palm. The frame of forearm contains a 5000 mAh battery, a processor, and some wires that connect one of the myoelectric sensors to our system. The other sensor does the same using Bluetooth connection; thereby it is not necessary to connect the device to a computer during use.

Results: We have developed a program code allowing complex sequences of motion to be executed sequentially. The completed myoelectrically controlled upper limb prosthesis is capable of real-time motion, based on 3D printing and the components used and the prototype is affordable. Using 3D printing is fully customizable to meet the needs of individuals.

Conclusions: Further studies of myoelectric and EEG control will be designed based on preliminary results.

Support: Prof. Miklós Nyitrai M.D., Péter Maróti M.D., Csaba Csóka, PTE 3D Projekt, Attila Péntek, Dániel Puskás, Lília Anik, Mátyás Bene, Ákos Árvai, István Hernádi M.D., Balázs Knakker

J/3 MONITORING THE LOCAL AND SYSTEMIC ACUTE CHANGES CAUSED BY ISCHEMIA-REPERFUSION OF THE HIND LIMB IN RATS

Dominik Gyenes¹, Csaba Körei², Katalin Pető³

1 Faculty of Medicine, University of Debrecen, 2 Kenézy Gyula Hospital, Department of Traumatology, hand and wrist surgery, 3 Department of Operative Techniques and Surgical Research, University of Debrecen

Keywords: surgery, prevention, ischemia, reperfusion, inflammation

Aims: In the case of traumatic injuries and during orthopedic surgery, we often encounter the blood disorder of the limbs. Monitoring the damage caused by ischemia-reperfusion can provide useful information to the clinic.

Methods: Fifteen anesthetized Wistar rats were cannulated in the common carotid artery to measure the blood pressure invasively. There was no other intervention in the control group. In the I/R groups, the lower right limb was strangulated for 120 minutes using tourniquet. Blood samples were taken to measure hematological, micro-rheological and blood gas parameters before and during the reperfusion. The microcirculation was examined with a Laser-Doppler tissue flow meter. We also measured the temperature of the soles and the blood pressure.

Results: White blood cell count significantly increased in the I/R group ($p < 0.001$). Red blood cell count and hemoglobin compared to the baseline ($p < 0.001$; $p < 0.05$) and to the control ($p < 0.01$; $p < 0.001$) decreased. The red blood cell deformability parameter was lower than in the control group ($p < 0.05$), while red blood cell aggregation was significantly impaired in both control ($p < 0.01$) and pre-operative ($p < 0.05$) groups. In the I/R group, the arterial mean pressure, hematocrit ($p < 0.01$), blood pH ($p < 0.05$), pO_2 decreased, pCO_2 , K^+ ($p < 0.0001$), glucose ($p < 0.05$) and creatinine ($p < 0.01$) increased relatively. There was no significant difference in tissue microcirculation, sole temperature.

Conclusions: The 120-minute limb ischemia caused significant acute changes in several hematological parameters. Metabolic changes due to ischemia led to acidosis, deterioration of micro-rheological parameters, different ionic concentration deviations. The model may later be useful for further investigation of pre-, post-conditioning methods recommended to prevent damage.

Support: Talent Management Program (DETEP), Students' Scientific Association (TDT)

J/4 FINITE ELEMENT ANALYSIS BASED LUMBOSACRAL REVISION SURGERY USING AN INDIVIDUAL NAVIGATION TEMPLATE

Benjamin Hajnal, Péter Endre Éltés
National Center for Spinal Disorders

Keywords: patient-specific, FEA, 3D printing, revision surgery, lumbar

Aims: Revision surgery in case of a lumbosacral non-union can be challenging, especially if an implant-related failure is present. In the S1 segment, the proper insertion of new screws during revision surgery can be extremely difficult without surgical navigation. We present a navigational template, using 3D modelling methods combined

with finite element analysis (FEA) and computer assisted design (CAD).

Methods: A step-by-step approach was developed to manage the clinical problem. (1) Quantitative CT based patient-specific FE model of the sacrum was created. (2) CAD model of the pedicle screw was inserted in the sacrum model in a bicortical convergent and a monocortical divergent position. (3) Static FEAs were performed. (4) A template with the two screw-guiding structures was designed and created for the sacrum using 3D design and 3D printing technologies. (5) Critical steps of the surgery were performed on the patient's 3D printed sacrum to evaluate the accuracy of the template.

Results: Based on the FEA results, the modified bicortical convergent screw position was more stable than the divergent position. The template fitted the 3D printed sacrum's surface and screw insertion was completed successfully. We could confirm that the achieved screw position was sufficiently accurate.

Conclusions: The patient-specific navigational template allows the surgeon to insert the screw into its optimal position considering the local bone material properties and the challenging geometrical situation. Its advantages compared to conventional surgical navigation techniques are the relatively low cost and minimized intraoperative X-ray exposure.

Support: -

J/5 SELECTIVE EPITYMPANIC DYSENTILATION SYNDROME

Barbara T. Bölcsföldi 1, István Szanyi, M.D. 2

1. Faculty of Medicine, University of Pecs, 2. Department of Otorhinolaryngology, University of Pecs

Keywords: middle ear, isthmus, dysventilation, cholesteatoma, endoscopy

Aims: There are three factors which effect the ventilation of the middle ear: the eustachian tube function, the buffer function and the transmucosal gas exchange of the middle ear. The eustachian tube plays a role in the middle ear's ventilation and keeps up the atmospheric pressure. The disorder of the eustachian tube function causes negative middle ear pressure leading to chronic diseases. The anatomic knowledge through endoscopic ear surgery could help to find a new factor, namely the blockage of the ventilation pathways causing a selective epitympanic dysventilation syndrome.

Methods: Cadaver dissections were carried out with endoscopic technique. During the dissections new anatomic structures were identified - epitympanic diaphragm, the tensor fold and the isthmus- which play a role in the ventilation of the middle ear.

Results: A photo documentation was prepared about each step of the dissections. The anatomic structures involved in the dysventilation syndrome were identified. Graphic pictures were drawn of the middle ear endoscopic anatomy.

Conclusions: Selective epitympanic dysventilation syndrome may evolve even if the eustachian tube functions are well, but the ventilation pathways are blocked. The syndrome can be diagnosed when 4 symptoms persist parallelly: 1) attic retraction pocket or cholesteatoma, 2) type "A" tympanogram or a normal eustachian tube function test 3) total epitympanic diaphragm 4) isthmus blockage. Discovering the syndrome and recovering ventilation in the middle ear could prevent the development of pathological diseases.

Support: -

J/6 THE ROLE OF IL-1A AND IL-1B SINGLE-NUCLEOTIDE POLYMORPHISMS IN THE DEVELOPMENT AND PROGRESSION OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW

Anita Györffi 1, Szófia Szentpéteri, MD, DMD 2, Mihály Vaszilkó, MD, DMD, PhD 2

1. Faculty of Medicine, Semmelweis University, 2. Department of Oro-Maxillofacial Surgery and Stomatology, Semmelweis University

Keywords: MRONJ, Interleukin-1alpha, Interleukin-1beta, SNP, Genetics

Aims: Many researches prove the role of interleukin-1 (IL-1) family of cytokines and receptors in chronic inflammatory process. The aim of our study is to investigate the role of defined interleukin-1 gene cluster polymorphisms in the progression of medication-related osteonecrosis of the jaw (MRONJ).

Methods: Since 2017 we have been doing the genetic testing of patients suffering from MRONJ. DNA samples were collected from buccal epithelial cells. The genetic examination was made by DentiGen test. DentiGen test is suitable for the detection of the IL-1A-889 and IL-1B+3953 polymorphism. The genetic tests were made by Istenhegyi GeneDiagnostic Center. We followed - up our patient and registered the stage reduction, the healing and the recidivation.

Results: We have collected the samples of 90 MRONJ patients. The samples of the MRONJ patients have been processed and evaluated. From the group 51 patients (56.6%) carry unfavorable allelic variants. We haven't found any significant connection between the stage reduction ($p=0.081$), or between the healing ($p=0.139$) and the examined polymorphisms. Significant association ($p=0.012$) was found between the recidivation of the disease and the unfavorable polymorphisms.

Conclusions: In our investigation we found significant association between the recidivation and the carrying of unfavorable polymorphism. Further, we plan to set up a control group to clarify the role of polymorphisms in the development of MRONJ.

K. MORNING HIGHLIGHTED LECTURE

K/1 ONE HUNDRED YEARS OF SURGICAL RESEARCH: INNOVATION, ERROR, FRAUD, POLICY

Prof. Dr. József Sándor (SE, Budapest)

No abstract available

L. Multidisciplinary session VII.: OBSTETRICS AND GYNECOLOGY – PEDIATRICS

L/1. PHAGOCYTIC FUNCTION OF MONOCYTES AND NEUTROPHIL GRANULOCYTES BEFORE AND AFTER SURGERY IN ENDOMETRIOSIS

Luca Lukács, Anna Rebeka Kovács MD, László Pál Phd., Rudolf Lampé MD

Department of Obstetrics and Gynecology, University of Debrecen, Department of Preventive Medicine, University of Debrecen

Keywords: endometriosis, phagocytosis, monocyte, granulocyte, immunology

Aims: Endometriosis is estimated to affect 10-15% of reproductive-aged women and causes infertility worldwide. The symptoms are significantly worsening the quality of life in patients. Pathophysiology of endometriosis is still unclear but immunological disorders became conspicuous recently. Our aim was to investigate whether the phagocytic activity of monocytes and neutrophil granulocytes are affected by the presence/removal of the endometrial lesions.

Methods: We examined peripheral blood samples from patients with endometriosis before surgery (n=26) and on the 7th postoperative day (n=13). We also investigated pre- and postoperative samples (n=14-14) from surgical control group (SCG) and healthy women (n=23). After separation of monocytes and granulocytes, the cells were incubated with opsonized fluorescein isothio-cyanate-labeled zymosan A particles as a target of phagocytosis. We calculated the phagocytic index (PI) by using fluorescence microscope.

Results: Preoperative PIs of both monocytes and granulocytes derived from patients with endometriosis were significantly lower than PIs of these cells from healthy women. Phagocytic function of leukocytes from postoperative patients' samples increased significantly compared to preoperative values and did not differ from the PIs of cells from healthy women. In the SCG significant difference between pre-and postoperative values was not detected.

Conclusions: Based on our results we assume that endometrial lesions and/or their microenvironment may produce factors, which depress the phagocytic function of monocytes and granulocytes. Since postoperative PIs of patients with endometriosis increased significantly, we assume that these factors were reduced or eliminated after removal of the lesions. Considering the results of the SCG, the surgical intervention has no influence on phagocytic function.

Support: EFOP-3.6.3-VEKOP-16-2017-00009, own resources of the Department of Obstetrics and Gynecology, University of Debrecen

L/2 THE USE OF CHOLINE PET/CT FOR RESTAGING OF PROSTATE CANCER PATIENTS

Diána Nikolett Szabó¹, Ildikó Garai², Péter Ágoston^{1, 3}, Csaba Polgár^{1, 3}

1: Semmelweis University, Budapest, Hungary, 2: ScanoMed, Debrecen, Hungary, 3: National Institute of Oncology, Centre of Radiotherapy

Keywords: choline PET/CT, prostate cancer, PSA, restaging, altered therapy

Aims: Prostate cancer is the third most common cancer of men in Hungary, mainly affecting the elderly population. After primary treatment in localised cases, regular check-up is important to detect possible

recurrence with measurement of PSA levels. In case of biochemical relapse, the results of traditional restaging imaging techniques determine further therapy. In Debrecen it is possible to have whole body choline PET/CT restaging. The National Health Insurance Fund of Hungary may reimburse the cost of the test with appropriate indication on a fairly reasonable basis. The aim of the present study was to compare the traditional restaging methods with choline PET/CT, to determine the ratio of positive choline PET/CT depending on pre-PET/CT PSA levels and to assess the effect of choline PET/CT on post-scan therapy.

Methods: Data of 51 prostate cancer patients treated at the National Institute of Oncology and their 59 restaging choline PET/CT were analyzed.

Results: Traditional restaging methods included bone scintigraphy, pelvic MR, abdominal CT, chest and spine MR. Of the 59 cases 25 were positive (19,8%). 35 of the 59 restaging choline PET/CT were positive (60,3%). Choline PET/CT changed the therapy of 29 patients (49.1%). Ratio of positive choline PET/CT depending on pre-PET/CT PSA values: 0-2 ng/ml: 43.2% (17); 2-10 ng/ml: 70.8% (24); > 10 ng/ml: 92.3% (13).

Conclusions: Choline PET/CT is more sensitive than conventional methods in the detection of recurrence and its results altered the therapy in half of the patients. Its sensitivity is highly improved over PSA value of 2 ng/ml.

L/3 MUCOSECTOMY DISRUPTING ENTERIC NERVOUS SYSTEM CONTRIBUTES TO FLAP CONTRACTION IN AUGMENTATION ILEOCYSTOPLASTY WITH SERO-MUSCULAR ILEAL FLAP

Daniel Urban, Daniel Hajnal, Raimondo Cervellione, Gabriella Varga, Tamas Cserni
Institute of Surgical Research, University of Szeged

Keywords: Bladder augmentation, ileal flap, contraction, mucosectomy, pig

Aims: Bladder augmentation with demucosalized ileal flap is a promising alternative approach for mucus free bladder augmentation, however the contraction of the flaps is still a major concern. Intact enteric nervous system (ENS) is essential to maintain intestinal integrity. Abnormal myenteric plexus with missing ganglia or nitrergic inhibitory neurons are thought to be responsible for conditions like Hirschsprung disease, Intestinal Neuronal Dysplasia or Hypoganglionosis where failure of the relaxation of the intestinal muscle results in motility disorder i.e. bowel obstruction. In mammals submucosal plexus contains NOS + inhibitory motoneurons responsible for muscle relaxation. We hypothesised mucosectomy disrupting (ENS) may be contributing to flap contraction.

Methods: Ileal mucosectomy was performed in 5 anesthetised pigs. In group I. only the mucosa was scraped off with forceps (sero-musculo-submucosal flap) while in Group II. the mucosa and submucosa was peeled off in one layer (sero-muscular flap). The width of the flaps was measured before and after mucosectomy. The ENS was assessed by Neurofilament and Nitric-oxid-synthetase immunohistochemistry.

Results: The flaps contracted from the original 100% width to 81,68 +/- 4,25 % in Group I. and to 72,675 +/- 5,36 in Group II. ($p = 0,002$). Equal Variance Test showed significant difference between Group I. and II. ($p=0.009$). The Neurofilament and Nitric-oxid-synthetase immunohistochemistry revealed the submucosus nervous plexus containing Nitric-oxid-synthetase+ neurons was separated from the myenteric plexus in Group II.

Conclusions: Mucosectomy results in significant flap contraction. The contraction is more severe when submucosa removed, this may be explained with disrupted ENS.

L/4 LAPAROSCOPY IN HEIM PÁL'S NATIONAL INSTITUTE OF PEDIATRICS: RESULTS OF THE PAST 10 YEARS FOCUSED ON COMPLICATIONS

Eszter Gradwohl, Balázs Fadgyas dr., Zoltán Ringwald dr., Gábor Garai dr.,
Heim Pál's National Institute of Pediatrics

Keywords: laparoscopy, pediatrics, complications, MIS, preoperative

Aims: Minimally Invasive Surgery (MIS) was started in adult practice in the last decades and developed rapidly, therefore MIS can be managed in younger and younger children.

Methods: A retrospective study was accomplished. Patients were studied between January 2009. and December 2018. Type of surgery, epidemiological data, type of penetration (Hassan technique or Veress-needle), intraabdominal pressure, complications were examined.

Results: In the study period 738 laparoscopic surgery were performed (appendectomy: 349, cholecystectomy: 132, inguinal hernia: 49, varicocele:63, ovarian surgery: 60, pyloromyotomy: 14, others:71). The youngest patient was 1 month old, the oldest 18 years old. The chosen insufflation method was Hassan technique 398 times, Veress-needle 324 times, (no data in 16 cases). Intraoperative complications were found in 25 cases. Intraoperative hemorrhage was detected 3 times (1 PIRS, 2 appendectomy). Gall bladder injuries due to intraoperative manipulation was detected 12 times, umbilical wound contamination 3 times, 6 times the appendix perforated during the laparoscopic manipulation, serosal injury occurred once. Postoperative complication was detected 41 times. Complication of the wounding occurred 9 times, postoperative hydrocele 12 times (PIRS 1, varicocele 11), passage disorder 6 times after appendectomy, intraabdominal abscesses were found in 5 patients.

During the ten-year period reoperation was necessary 9 times.

Conclusions: In the past 10 years the frequency of laparoscopic surgery increased significantly. Due to the low number of complications we believe the preoperative examinations could be more permissive.

L/5 HOW DOES EARLY HYPERGLYCAEMIA AFFECT THE CARDIOVASCULAR SYSTEM?

Márton Ferenc Schandl
Department of Neonatology

No English abstract available

L/6 EFFECTS OF HOLDER PASTEURIZATION ON LEVELS OF METABOLIC HORMONES IN HUMAN MILK

Réka A. Vass^{1, 2}; Edward F. Bell³; Tarah T. Colaizy³; Mendi L. Schmelzel³; Karen J. Johnson³; Jacky R. Walker³; Tibor Ertl^{1, 2*}; Robert D. Roghair^{3*}

1 Departments of Neonatology and Obstetrics & Gynecology, University of Pécs Medical School, Pécs, Hungary **2** MTA-PTE Human Reproduction Scientific Research Group, University of Pécs, Pécs, Hungary **3** Department of Pediatrics, University of Iowa, Iowa City, Iowa, USA

Keywords: HoP, breast milk, FSH, LH, TSH, insulin, cortisol

Aims: During human development, environmental conditions can be communicated by signaling molecules delivered across the placenta or within breast milk. Preterm infants are deprived of the transplacental hormone transfer that occurs during pregnancy, but they have two potential sources, their own mothers and milk bank donors. When donor milk replaces maternal milk, Holder pasteurization (HoP) is required, but that process may further impact the concentration of metabolic hormones.

Methods: Breastmilk samples by 26 mothers who gave birth to preterm infants hospitalized in the University of Iowa Children's Hospital. At the Mother's Milk Bank of Iowa, 31 donor mothers breastfeeding their term infants were recruited. Leptin, cortisol, insulin, luteinizing hormone, thyroid-stimulating hormone, and follicle-stimulating hormone were measured in the preterm milk and donor milk samples by custom magnetic bead array before and after HoP.

Results: Leptin concentration was significantly decreased by HoP in both cohorts. Cortisol concentration was not affected by HoP, but HoP donor milk contained significantly higher cortisol level compared to the preterm milk samples. Insulin concentration was not influenced by cohort or HoP. Pituitary glycoprotein hormones were present in similar amounts in human milk produced for preterm infants and term infants, but HoP increased the concentration of TSH, decreased the LH level, and did not influence FSH concentration.

Conclusions: In a hormone-specific fashion, the content of breast milk is impacted by maternal factors and HoP. Further research is necessary to define the breast milk feeding practices that best mirror intrauterine hormone exposure and optimize the development of highly vulnerable preterm infants.

Support: This project was supported by the Iowa-Pécs Neonatology Collaborative Research Fund, Department of Pediatrics, University of Iowa, and GINOP-2.3.2-15-2016-00021 „The use of chip-technology in increasing the effectiveness of human in vitro fertilization”.

L/7 NONINVASIVE CARDIOVASCULAR RISK ESTIMATION METHOD IN PREPUBERTY CHILDREN

Júlia Varga¹, Prof. Dr. Dénes Molnár², Dr. Sarolta Stomfai³
University of Pécs, Department of Pediatrics

Keywords: cardiovascular risk, prepuberty, IDEFICS, noninvasive, prevention

Aims: The development of cardiovascular diseases begins in childhood, though we lack consensus criteria concerning early risk status which could be the premise of targeted intervention. The aim of the present investigation is to introduce a new, noninvasive risk estimation method for prepuberty children in the frame of IDEFICS study (Identification and prevention of Dietary- and lifestyle-induced health Effects in Children and infants).

Methods: 4858 children (boys: 2513, age range: 2,1-9,9 years, bodyweight [mean±SD] 24.41±7.04 kg; BMI: 16.69±2.34) of the total IDEFICS population having all parameters of the applied risk estimation method were selected. The data consists of two types of input parameters: individual (BMI, waist-to-height ratio, blood pressure, weight small /large for gestational age, breastfeeding) and family history (early cardiovascular disease,

diabetes type 2, hypertension and dyslipidemia). These parameters were analyzed together and the global score was validated by the presence of pathological cardiometabolic laboratory parameters (fasting blood glucose, total cholesterol, HDL-cholesterol, triglyceride, HOMA-index, HbA1c, CRP). The laboratory parameters were categorized by the IDEFICS population's 90 percentiles (in case of HDL 10 percentiles) limit value, according to age and sex.

Results: Children having 3 or more abnormal input variables have a significant higher (OR>1.7 [CI:1.4-2.0]) chance to provide abnormal laboratory values. We can also find out, that each individual and family parameters have differing effects for the laboratory parameters.

Conclusions: Our results indicate that it is possible to develop a simple, noninvasive tool detecting children bearing cardiovascular risk and may be useful for prevention.

L/8 PEDIATRIC ACUTE PANCREATITIS FOLLOW-UP – INTERNATIONAL, MULTICENTRIC RETROSPECTIVE COMPARATIVE STUDY

Váncsa Szilárd, dr Török Imola, dr Mosztbacher Dóra, prof dr Hegyi Péter – Marosvásárhely
University of Marosvásárhely

No English abstract available

LS1. Highlighted topic:

LS2. Highlighted session: Update in neuroimaging 2019

LS2/1 MICROSTRUCTURAL DAMAGE TO THE FRONTO-STRIATAL CIRCUITRY MAY PLAY A ROLE IN THE DEVELOPMENT OF RESISTANCE TO FATIGUE-LOWERING MEDICATIONS IN PATIENTS WITH MULTIPLE SCLEROSIS

Miklos Palotai¹, Michele Cavallari¹, Ismail Koubiyr^{1,2}, Alfredo Morales Pinzon¹, Brian C. Healy^{3,4}, Bonnie Glanz³, Howard L. Weiner³, Tanuja Chitnis³, Charles R.G. Guttmann¹

¹ Center for Neurological Imaging, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

² INSERM U1215, Neurocentre Magendie, Bordeaux, France

³ Partners Multiple Sclerosis Center, Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

⁴ Biostatistics Center, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

Background

Recent comparative drug studies contradict previous findings regarding fatigue treatment in patients with multiple sclerosis (MS). We investigated the association of fatigue-lowering treatment with brain diffusion abnormalities.

Methods

Patient stratification: 1. Treatment Resistant Sustained Fatigue (TRSF): were on anti-fatigue and/or anti-depressant and/or anxiolytic medication and the latest two Modified Fatigue Impact Scale (MFIS) score ≥ 38 ; 2. Treatment-Controlled Low Fatigue (TCLF): were on anti-fatigue and/or anti-depressant and/or anxiolytic medication and the latest MFIS < 38 , and have at least one previous MFIS ≥ 38 ; 3. Treatment-Naïve Never Fatigued (TNNF): received none of the above-mentioned medications and MFIS was always < 38 (5 assessments minimum). Accordingly, we selected from the CLIMB Study cohort 65 patients with relapsing-remitting or secondary-progressive MS (23TRSF/16TCLF/26TNNF). 3T brain MRI was used to perform voxel-wise comparison of fractional anisotropy (FA) between the groups.

Results

We found reduced FA in multiple frontal, parietal, temporal, occipital, deep grey matter (DGM) and infratentorial areas in TRSF versus TCLF or TNNF patients, controlling for age+sex+disease duration+physical disability. When controlling also for T2LV, FA remained significantly lower in several frontal, parietal, temporal, occipital, DGM and infratentorial areas in TRSF versus TNNF patients, but TRSF versus TCLF patients showed lower FA only in fronto-striatal areas. When controlling also for depression, the signal (ie, lower FA) showed similar distribution in TRSF versus TNNF patients, but no significant difference remained between TRSF and TCLF patients. No difference was observed between TCLF and TNNF.

Conclusion

Fronto-striatal FA may serve as a biomarker for differentiating responders and non-responders to fatigue lowering medications.

Disclosures

Dr. Palotai reports no disclosures.

Dr. Cavallari reports no disclosures. Grant support: Neurogenic Determinants of Fatigue in Multiple Sclerosis (National Multiple Sclerosis Society, RG-1501-03141); Delirium, Dementia, and the Vulnerable Brain: An Integrative Approach (National Institutes of Health, 2P01AG031720-06A1).

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Dr. Morales Pinzon reports no disclosures.

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Dr. Weiner reports grants from National Institutes of Health, National Multiple Sclerosis Society, Verily Life Sciences, Genentech, Inc., Google Life Sciences, EMD Serono, Inc., Biogen, Teva Pharmaceuticals, and Novartis; grants and consulting from Sanofi US Services, Inc.; consulting and advising from Tilos Therapeutics; consulting and advising from Tiziana Life Sciences; consulting and advising from IM Therapeutics; personal fees, consulting and advising from vTv Therapeutics; personal fees, consulting and advising from MedDay Pharmaceuticals.

Dr. Chitnis has served on advisory boards for Biogen, Novartis, and Sanofi-Genzyme; received research support from Biogen, Novartis, Octave, Serono and Verily; has participated in clinical trials sponsored by Sanofi-Genzyme and Novartis.

Dr. Guttmann has nothing to disclose that could constitute a conflict of interest for this work. Dr. Guttmann has received research funding from Sanofi, the National Multiple Sclerosis Society, and the International Progressive Multiple Sclerosis Alliance as well as travel support from Roche Pharmaceuticals.

LS2/2 THE EFFECTS OF BINGE DRINKING ON ANXIETY-LIKE, DEPRESSION-LIKE AND SOCIAL BEHAVIORS

Balázs Simon^{1,2}, Miklós Palotai^{1,3}, Zsolt Bagosi¹

¹Department of Pathophysiology, Faculty of Medicine, University of Szeged, Hungary

²Department of Surgery, St Johns Hospital, Budapest, Hungary

³Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Introduction

Binge drinking is an increasing public health issue that is defined as consuming a large amount of alcohol in a short period of time. The aim of the present study was to determine the effects of binge drinking on anxiety, depression, sociability and preference for social novelty.

Methods

For this purpose, male C57BL/6 mice were exposed to drinking in the dark, a classical method used to investigate binge drinking in animals. In accordance with this method, the circadian rhythm of the mice was inverted for 14 days, and then their bottles of water were replaced with bottles of alcohol of 20% for 4 days. The mice had access to alcohol for 2 hours per day on the first 3 days and for 4 hours on the 4th day during the dark period of their circadian cycle. On the 4th day and the 5th day the mice were investigated in an elevated plus-maze test and a forced swim test for anxiety and depression-like behavior, respectively. In addition, on the 4th day the mice were evaluated in a three-chamber social interaction test for social behavior.

Results

On the 4th day binge drinking produced anxiolytic and antidepressant effects in mice. In contrast, on the 5th day binge drinking induced anxiety and depression. On the 4th day the mice exposed to binge drinking exhibited increased sociability, but decreased preference for social novelty.

Conclusion

The present study suggests that binge drinking exerts contrasting effects on anxiety-like, depression-like and social behaviors in mice.

Keywords: binge drinking, anxiety, depression, sociability, preference for social novelty

Acknowledgement: This study was supported by EFOP-3.6.2-16-2017-00006.

LS3. Burning topic: ONCORHEUMATOLOGY

LS3/1 ONCORHEUMATOLOGY AND ONCOIMMUNOLOGY: ASSOCIATIONS OF RHEUMATIC, MALIGNANT DISEASES AND THEIR THERAPIES

Zoltán Szekanecz¹, Éva Szekanecz²

University of Debrecen, Faculty of Medicine, ¹Division of Rheumatology and ²Department of Oncology, Debrecen, Hungary

Sustained systemic inflammation may lead to increased risk of malignancies. Chronic B-cell stimulation may lead to the development of lymphomas in SLE, rheumatoid arthritis (RA) or systemic sclerosis (SSc). Solid tumors may occur in tissues mostly affected by the underlying disease. For example, lung cancer is more common in SSc or RA, partly due to smoking. We have been conducting numerous studies on patients with autoimmune rheumatic conditions. We assessed the prevalence of secondary malignancies, the production of soluble tumor antigens. We also reviewed current knowledge about the possible carcinogenicity of antirheumatic therapies.

We found significantly higher prevalence of malignancies among patients with RA, SSc and SLE. We will discuss the possible oncogenic effects of antirheumatic drugs. We detected increased levels of soluble tumor antigens in RA, SSc and SLE.

To date, thousands of cancer patients have been treated by checkpoint inhibitors. Along with the growing number of treated patients, numerous cases developed autoimmune phenomena or even full-blown autoimmune disease. Mucositis, arthralgia, sicca syndrome or myalgia/myositis are among the most common manifestations. Here we will summarize the current understanding of checkpoint inhibition-triggered autoimmunity and present a recent case of Raynaud's phenomenon after nivolumab therapy.

There are numerous relationships between rheumatic and malignant diseases. Our studies may draw attention to the importance of collaboration between medical specialties including rheumatology, immunology and oncology.

LS4. BURNING TOPIC: LANGUAGE SKILLS AND DEMENTIA

LS4/1 Challenges of teaching LSP for beginners

Éva Édes (SE Nyelvi Intézet)

keywords: FOS (French for Specific Purposes), TV5MONDE, communication skills, audio-visual documents, teaching aids

With the curriculum reform, LSP teaching is reformed at Semmelweis University. The new courses „Introduction to language for medical/dental/pharmaceutical purposes” have been improved so that students can acquire authentic language turns and panels used in professional situations from an elementary level. In addition to literacy and communication practices, we also develop documentation skills.

The interest in these courses is growing because of dental tourism. This lecture introduces the main aspects of practice-centered training in professional communication through the methodology of French language courses. In many cases, students would also like to improve their general language skills, so they will also receive guidance on using a general language resource in the 90-minute weekly courses.

The “Apprendre” page of TV5MONDE offers an excellent opportunity for autodidact learning.

LS4/2 Network abnormalities in Alzheimer’s disease: understanding the disease mechanism of dementia

^{1,2}András Horváth MD, PhD

¹National Institute of Clinical Neurosciences

²Semmelweis University, Department of Anatomy, Histology and Embryology

Introduction: Alzheimer’s Disease (AD) is considered as an oscillopathy with impaired functional connectivity among the crucial brain areas. Recent studies highlighted many clinical features of altered neural networks in AD including higher risk for epileptic seizures, epileptiform discharges, macro-and microstructural sleep changes, impaired visuo-motor and spatial navigation skills. The aim of our work is to understand the role of clinically evident network changes in the progression of cognitive deterioration.

Methods: In the framework of National Brain Research Program, we examined >150 patients with various neurodegenerative diseases and age matched healthy individuals. We executed structural, functional magnetic resonance imaging and 24-hour ambulatory electroencephalography to measure network properties. We also followed these patients for 3 years with detailed neuropsychology. We described the prevalence of epileptic seizures, epileptic discharges, the semiology of epileptic activity and its effect on the cognitive performance of AD patients. We measured the sleep macrostructure and its prognostic value.

Results: We identified epileptic seizures in 28% and EDs in 57% of our patients. Epileptic seizures were mostly temporal focal seizures with impaired awareness. Patients with earlier onset of dementia and in a more advanced disease stage had a higher risk for epilepsy. Epileptic seizures were associated to higher level of atrophy of limbic structures being in line with the spiking rate and spiking pattern. Epileptic discharges changed significantly the cortical networks and accelerated the progression of cognitive decline. AD patients showed prominent reduction of slow-wave sleep and REM sleep. Slow-wave sleep decrease was associated to higher level of atrophy while REM sleep decrease indicated faster level of cognitive impairment.

Conclusions: Network alterations namely epileptic activity and sleep changes are common findings in AD even in the initial phases. They might serve as diagnostic markers for the precise identification of dementia and might play a prominent role in the pathogenesis of AD. Accurate diagnostic methods are essential since they could serve as a basis for novel screening methods and represent potential therapeutic targets.

M. Multidisciplinary session VIII.: BIOCHEMISTRY/MOLECULAR BIOLOGY – GENETICS- PHARMACOLOGY - MICROBIOLOGY

M/1 THE CONNECTION BETWEEN THE CAROTID, FEMORAL ARTERY ATHEROSCLEROSIS MARKERS AND TELOMERE LENGTH, MTDNA COPY NUMBER

Janositz Gréta¹, Melicher Dóra^{2, 3}, Illés Anett⁴, Gyulay Kata¹, Jokkel Zsófia¹, Zsupos Rebeka, Bérczi Viktor¹, Szabó Helga¹, Hernyes Anita¹, Tárnoki Dávid L.¹, Tárnoki Ádám D.¹

1 Department of Radiology, Semmelweis University, Budapest, Hungary 2 Department of Genetics, Cell- and Immunobiology, Semmelweis University, Budapest, Hungary 3 MTA-SE Immunoproteogenomics Extracellular Vesicle Research Group, Budapest, Hungary 4 Institute of Genomic Medicine and Rare Disorders, Semmelweis University, Budapest, Hungary

Keywords: oxidative stress, twin studies, epigenetics, ultrasound, plaque

Aims: The development of atherosclerosis is a response to injury, associated with local and particularly systematic inflammation. This could be marked by increased cell turnover and mitochondrial dysfunction. These phenomena are accompanied by shortened telomere length (TL) and decreased mitochondrial DNA copy number (mtDNAcn). Ultrasound methods allow comprehensive analysis of the carotid and femoral artery, enabling the early detection of subclinical atherosclerosis. The aim of this study was to examine the connection between atherosclerosis markers and mtDNAcn, TL.

Methods: 102 Hungarian twins (62 monozygotic, 40 dizygotic; 63% female, mean age 54±15 years) were enrolled in the study. Participants underwent carotid and femoral 3D ultrasound examination (Samsung RS85, arterial analysis, 15MHz transducer) and blood samples were collected. The DNA was first extracted from the previously isolated peripheral blood mononuclear cells (PBMC) and then with qPCR standard curve method the TL and mtDNAcn were analyzed.

Results: TL was significantly correlated with left common carotid artery (CCA) Young's elastic modulus ($r=0.233$) and pulse wave velocity (PWV) ($r=0.236$) (all $p<0.05$). No further significant association was found for the correlation of TL, mtDNAcn with IMT, local arterial stiffness and plaque data on carotid or femoral arteries. MtDNAcn and TL was not significantly associated with the presence of carotid or femoral plaques. Borderline significance was shown by the presence of femoral plaques for decreased mtDNAcn ($p=0.008$).

Conclusions: The majority of the examined atherosclerosis markers on the carotid and femoral artery are not connected with the studied biomarkers, in turn the increased carotid stiffness is associated with shortened TL.

M/2 LONGITUDINAL STUDY OF RELATIONSHIPS BETWEEN MITOCHONDRIAL DNA COPY NUMBER, TELOMERE LENGTH AND CAROTID IMT IN TWINS

Jokkel Zsófia¹, Melicher Dóra^{2, 3}, Illés Anett⁴, Bikov András⁵, Szabó Helga¹, Hernyes Anita¹, Molnár Andrea Ágnes¹, Molnár Mária Judit⁴, Buzás Edit^{1, 2, 3}, Falus András², Tárnoki Ádám Domonkos¹, Tárnoki Dávid László¹

1 Department of Radiology, Semmelweis University, Budapest, Hungary. 2 Department of Genetics, Cell- and Immunobiology, Semmelweis University, Budapest, Hungary. 3 MTA-SE Immunoproteogenomics Extracellular

Vesicle Research Group, Budapest, Hungary. 4 Institute of Genomic Medicine and Rare Disorders, Semmelweis University, Budapest, Hungary. 5 Department of Pulmonology, Semmelweis University, Budapest, Hungary.

Keywords: Genetics, Vascular disease, Cellular aging, Ultrasound, Twins

Aims: Mitochondrial DNA (mtDNA) copy number and telomere length (TL) has already been associated with numerous diseases and different manifestations of aging. Our aim was to compare the changes in mtDNA copy number, TL, carotid intima media thickness (IMT) and arterial stiffness over time.

Methods: 4 monozygotic (MZ) and 1 dizygotic (DZ) twin pairs (6 female, 4 male; mean age 43 ± 17 years) underwent a phlebotomy, oscillometric arterial stiffness (aortic pulse wave velocity, PWV) assessment and carotid ultrasound in 2009-10 and 2017. IMT of the common and internal carotid artery (CCA, ICA) was calculated bilaterally. MtDNA copy number (mtDNAcn) and TL changes have been analyzed between the two study waves.

Results: We found negative correlation between the right Δ ICA IMT and the Δ mtDNAcn ($r = -0.682$; $p = 0.06$) and positive correlation between the right Δ ICA IMT and the Δ TL ($r = 0.773$, $p = 0.02$), however, no significant correlation was found with the left Δ ICA, bilateral Δ CCA IMT and aortic PWV with the investigated biomarkers.

Conclusions: Our pilot study confirmed on limited sample size, that the change of right ICA IMT is associated with the change of the investigated biomarkers over 8 years. Further studies are needed to understand the exact pathomechanism.

M/3 THE ROLE OF MICRORNA IN THE REGULATION OF PROGRAMMED LIVER REGENERATION

Petra Rozman, Dr. Attila Szijártó, Dr. Dóra Krisztina Tihanyi

Semmelweis University; Semmelweis University, 1st Department of Surgery; Semmelweis University, 1st Department of Surgery

Keywords: MiRNA, liver regeneration, PVL, ALPPS, liver surgery

Aims: ALPPS (Associating Liver Partition and Portal Vein Ligation for Staged Hepatectomy) led the growth of residual parenchyma in a shorter time than conventional PVL (vena porta ligation) techniques. Recent studies have shown that micro-RNAs (miRNAs) play an important role in liver regeneration. The aim of our study was to investigate the role of miRNAs involved in PVL- and ALPPS induced liver regeneration.

Methods: Male Wistar rats ($n = 90$, 220-250g) were divided into three groups: PVL ($n=36$), ALPPS ($n=36$) and sham ($n=36$) operation. Rats were sacrificed after 0-4-12-24-48-72-168hours. Liver microcirculation was measured with an "O2C" (oxygen to see) system. The regeneration rate of the liver lobes and the serum AST (aspartate aminotransferase) were determined. Microarray analysis was performed on samples taken from regenerating lobes in the 4-hour group to analyze miRNA expression pattern. MiRNAs with a significance level of at least $p < 0.05$ were subjected to further target analysis using the DAVID 6.8 (<https://david.ncifcrf.gov/>) target prediction database.

Results: The liver regeneration rate was significantly higher at 48 and 72 hours in the ALPPS group compared to the PVL group ($p < 0.01$). Following ALPPS, microcirculation and serum AST concentrations of liver lobes did not show a significant difference compared to the PVL group. In the microarray analysis, 83 significant miRNAs were identified (ALPPS vs. PVL). Using target prediction database 7 miRNAs relevant for liver regeneration were identified: miR-21-5p, miR-155-5p, miR-200b-3p, miR-350, miR-455-5p, miR-1848-5p.

Conclusions: In the background of ALPPS-induced faster and higher regeneration, miRNA-mediated regulation can play an important role.

M/4 THE MOLECULAR BASIS OF THE INTERACTION BETWEEN COAGULATION FACTOR XIII AND FIBRINOGEN

Eniko Sebestyen, Krisztina Péntes-Daku

Division of Clinical Laboratory Science, University of Debrecen, Faculty of Medicine

Keywords: FXIII, fibrinogen, coagulation, thrombosis, interaction

Aims: Coagulation factor XIII (FXIII) consists of two A and two B subunits, its active form stabilizes the clot by crosslinking fibrin chains. Fibrinogen is made of three pairs of chains ($A\alpha$, $B\beta$, γ). Plasma fibrinogen can be separated by ion exchange chromatography into 3 fractions: Peak1 containing $\gamma A/\gamma A$ chains (85%), Peak2 with $\gamma A/\gamma'$ (15%) chains and γ'/γ' (0.5%) fraction. The plasma FXIII circulates in the blood bound to fibrinogen. By characterizing this interaction, we may be able to synthesize a peptide that binds to FXIII and decreases its activity and consequently thrombus formation.

Methods: Our aim was to characterize the binding of FXIII to the different fibrinogen isoforms by surface plasmon resonance technique (SPR) and isothermal titration calorimetry (ITC). We used Biacore systems for the SPR measurements and we immobilized FXIII-B and Peak1 fibrinogen as the ligand. As analyte, we used FXIII-B, Peak1, Peak2, and a 9-amino-acid long γA ($\gamma A9$) peptide, which we made by peptide synthesis. We studied the interaction between FXIII and $\gamma A9$ on a microcalorimeter (Microcal ITC 200).

Results: Peak1 and Peak2 fibrinogen bind to FXIII-B with almost the same affinity (K_d in the range of 10^{-6}) and the $\gamma A9$ binds to FXIII-B with a two magnitudes higher affinity (K_d in the range of 10^{-8}).

Conclusions: In conclusion, we can confirm that the FXIII-B subunit is associated with fibrinogen. The binding is a complex mechanism involving both γA and γ' chains.

M/5 THE MEASUREMENT OF THE DIPOLE POTENTIAL WITH A NOVEL HIGH-THROUGHPUT FLOW CYTOMETRIC METHOD

Máté Szabó, Florina Zákány MD, Bence Cs. Szabó, Zoltán Varga PhD DSc, Péter Nagy MD PhD DSc, Tamás Kovács MD PhD

Department of Biophysics and Cell Biology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

Keywords: dipole potential, hypercholesterolemia, polyunsaturated fatty ac

Aims: The least-known component of membrane potentials, the dipole potential (DP) originates from the preferential alignment of molecular dipoles at the membrane-water interface, generating a large positive (~300mV) potential creating an immensely strong intramembrane electric field. Consistently, DP influences a multitude of membrane-coupled events, including ion channel gating, ErbB activation, etc. The magnitude of DP is mainly determined by the lipid composition of cell membrane. Since it is entirely located within the membrane, it is difficult to measure in living cells, however, we developed a flow cytometric technique to determine DP. Our aim was to examine effects of changes in the composition of cell membrane in disease models and human samples.

Methods: As models of hypercholesterolemia and Smith-Lemli-Opitz-syndrome, we treated THP1, JY cells or human PBMC with cholesterol or 7-dehydrocholesterol (7DHC), respectively. To test the beneficial effects of Mediterranean diet, we treated cells with polyunsaturated fatty acids. Then we measured the magnitude of DP with our novel emission ratiometric approach using flow cytometry.

Results: Loading of cells with cholesterol or 7DHC resulted in dose-dependent increases in DP. As demonstrating the importance of diet, ω -3 fatty acid decreased, while ω -6 or saturated fatty acid increased the magnitude of DP. In our ongoing studies, we are determining alterations in the DP in samples from hypercholesterolemic and hypertriglyceridemic patients compared to control individuals.

Conclusions: In conclusion, we determined the effects of changes in membrane composition on DP in in vitro disease models with our novel technique.

M/6 DRUG CANDIDATE BGP-15 IMPROVES CARDIAC FUNCTION BY ACTIVATING THE PROTEIN KINASE G PATHWAY

Ticián Wilisicz 1, Zoltán Szilvássy 2, Béla Juhász 2, Mariann Bombicz 2, Dániel Priksz 2, Balázs Varga 2

1 Faculty of Medicine, University of Debrecen, 2 Department of Pharmacology and Pharmacotherapy, University of Debrecen

Keywords: Heart failure, Dyslipidemia, BGP-15, Echocardiography, cGMP-PKG

Aims: Pharmacological treatment of heart failure represents a major unmet need. Recent evidence suggests that hidroximic-acid derivative small molecule BGP-15 improves muscle function and strength, restores cardiac function, and reduces arrhythmic episodes in animal models of muscular dystrophy, heart failure or diabetic cardiomyopathy. Our aim in this present study was to evaluate the effects of BGP-15 in a rabbit model of atherosclerotic cardiovascular disease.

Methods: New-Zealand male rabbits were divided into 3 groups: (I) healthy control (normal chow); (II) dyslipidemic (DD) group (atherogenic chow); (III) atherogenic chow+BGP-15-treatment (DD+BGP-15 group, 10 mg/kg, p.o.), for 16 weeks. Serum parameters were determined at the endpoint of the study, and echocardiography was carried out to estimate cardiac function. Western Blot and ELISA assays were carried out to determine myocardial cGMP levels and VASP protein phosphorylation to determine the activity of the cGMP-PKG signaling pathway.

Results: Serum parameters were unaffected by BGP-15-treatment. The drug candidate restored diastolic function (E and A wave, DecT, e'/a', E/e', IVRT) and improved Tei-index compared to untreated DD rabbits. Myocardial cGMP levels, along with the phosphorylation of VASP protein was significantly elevated in the left ventricle samples of BGP-15-treated rabbits in comparison to the DD animals.

Conclusions: Even though BGP-15 treatment did not affect serum parameters, it considerably enhanced diastolic function, partly by modulating the cGMP-PKG pathway. As BGP-15 has excellent safety profile, it may offer a new therapeutic approach in atherosclerotic cardiovascular disease.

Support: Talent Management Program (DETEP), Students' Scientific Association (TDT)

M/7 IMPACT OF PER OS ANTIBIOTIC TREATMENTS ON THE GASTROINTESTINAL COLONIZATION WITH A MULTIRESTANT KLEBSIELLA PNEUMONIAE STRAIN

Ferenc Balázs Farkas, Judit Domokos, Béla Kocsis, Eszter Ostorházi, Dóra Szabó

Medical Microbiology Institute of Semmelweis University

Keywords: AMR, microbiota, gene transfer, colonization, in vivo

Aims: Colonization resistance refers to the ability of microbiota to prevent expansion and persistence of exogenously acquired bacterial species. Antibiotic therapy can damage this ability. Our goal was to determine the effect of different per os antibiotic treatments on colonization rate and resistance gene copy numbers in intestinally carried *K. pneumoniae* (KP5825) in mice. This strain expressed a PMQR gene, an ESBL gene (CTX-M-15) as well as a carbapenemase enzyme.

Methods: C57BL/6 mice were colonized with 5×10^6 CFU of KP5825 orally after 2 weeks of ampicillin pretreatment. Then mice were divided into 6 groups receiving antibiotic treatments for 15 days: 0.5g/L and 0.1g/L of ampicillin (AMP), ceftazidime (CAZ), ciprofloxacin (CIP) was administered in the drinking water (6th group: control). Every three days fresh fecal pellets were collected. In the second phase of our experiments the V3-V4 region of the 16S rRNA gene was sequenced to determine the microbiota composition in the animals. We used qPCR technique to determine the KP5825 DNA quantities and assess the resistance gene copy numbers.

Results: Our results show a significant perturbation in the microbiota. We could also observe that after 15 days KP5825 decreased significantly ($p < 0.004$) in the control group and in the CIP treatment groups ($p < 0.0001$, $p < 0.002$). Furthermore, qPCR results show that higher dose CAZ treatment lead to 4-fold increase in CTX-M plasmid quantities.

Conclusions: Thus, the CAZ had higher power on the dissemination of resistance genes than CIP. This raises the possibility of in vivo plasmid transfer, which we intend to investigate in our future experiments.

N. Multidisciplinary poster session III. –ANATOMY -PATHOLOGY - RADIOLOGY - PHARMACOLOGY

N/1 CHANGES IN NOTCH SIGNALING IN THE TEETH OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP)-DEFICIENT MICE

Balazs Daniel Fulop¹, Balazs Sandor^{1, 2}, Eszter Szentleleky³, Edina Karanyicz³, Dora Reglodi¹, Roza Zakany³, Tamas Juhasz^{3*}, Andrea Tamas^{1*}

*These authors contributed equally to this work.

¹Department of Anatomy, MTA-PTE PACAP Research Team, Centre for Neuroscience, University of Pecs, Hungary

²Department of Dentistry, Oral and Maxillofacial Surgery, University of Pecs, Hungary; ³Department of Anatomy, Histology and Embryology, Faculty of Medicine, University of Debrecen, Hungary.

Keywords: PACAP, teeth development, signaling, Notch

Aims: PACAP is a regulatory neuropeptide of the glucagon/secretin/VIP peptide family affecting tooth development partly via Shh (Sonic hedgehog) signaling cascade. The role of Notch signaling in tooth development is well described. We wanted to elucidate the possible connection between PACAP and Notch signaling pathway during tooth development.

Methods: We applied immunohistochemistry of Notch receptors (Notch1, 2, 3, 4), their ligands (DLL1, 3, 4,

Jagged1, 2) and intracellular target molecules (CSL, TACE, Numb) in the molar teeth of 5-day-old wild type, homozygous and heterozygous PACAP-deficient mice. We have measured the immunopositivity of the enamel producing ameloblast cells and dentin producing odontoblast cells in the case of all Notch signaling pathway molecules.

Results: We found elevated Notch2 receptor and DLL1 expression in the ameloblast cells of PACAP-deficient mice compared to the wild-type ones. The expression of CSL yielded similar results both in the ameloblast and odontoblast cells. Jagged1 ligand showed higher expression in the odontoblast cells of homozygous PACAP-deficient mice than in the wild-type mice. The other elements of Notch signaling have not shown significant differences between the genotype groups.

Conclusions: The lack of PACAP leads to upregulation of several elements of the Notch signaling pathway in the odontoblast and ameloblast cells. We presume Shh dependent and independent processes. Notch signaling, similarly to PACAP, is responsible for affecting cell proliferation and apoptosis. We hypothesize that Notch could serve as a salvage pathway in the case of the lack of PACAP.

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N/2 INTERLEUKIN-1 MEDIATES CHRONIC RESTRAINT STRESS-INDUCED PAIN IN A MOUSE MODEL

Barbara Fulop¹, Agnes Hunyady¹, Eva Borbely¹, Nikolett Szentes¹, Ádám Dénes², Nikolett Lénárt², Zsuzsanna Helyes¹

1Department of Pharmacology and Pharmacotherapy, Medical School and János Szentágothai Research Centre, University of Pécs, Hungary 2Momentum Laboratory of Neuroimmunology, Institute of Experimental Medicine, Budapest, Hungary

Keywords: fibromyalgia, stress-induced pain, restraining stress, IL-1

Aims: Fibromyalgia is a musculoskeletal pain syndrome of unknown mechanism, but chronic distress is a well-established ethiological factor. Since its treatment is unsolved, it is important to reveal the pathomechanisms and identify new therapeutic target(s). Interleukin-1 (IL-1) mediates neuroinflammation related to both stress and pain, but the relationship between these pathways is unclear. Therefore, we studied the role of IL-1 in a mouse model of chronic restraint stress-induced pain.

Methods: Female IL-1 $\alpha\beta$ deficient (knockout: KO) and C57Bl/6J wildtype (WT) mice were restrained for 6 hours daily for 4 weeks. The thermo- and mechanonociceptive thresholds were determined weekly by increasing temperature hot plate and dynamic plantar aesthesiometry, cold tolerance by withdrawal latency from icy water. Light-dark box, tail suspension and forced swim tests were performed to evaluate behavioral changes, thymus/adrenal-gland weights were at the end of the experiment.

Results: In WT mice restraint induced significant, approximately 25% decrease of the mechanonociceptive threshold (mechanical hyperalgesia) after 2 weeks and 70% decrease of the cold tolerance after one week, but the thermonociceptive threshold did not change. In IL-1 KO mice mechanical hyperalgesia was significantly smaller during the experiment, but cold hyperalgesia only at one week. There was no stress induced difference between the groups in behavioral tests, or in the weight of thymus/adrenal-gland.

Conclusions: We provide evidence that IL-1 mediates chronic stress-induced mechanical hyperalgesia in which neuroinflammation and central sensitization are involved, and plays a triggering role in cold hyperalgesia related to mainly peripheral mechanisms. This suggests potential therapeutic benefit of using IL-1 blocking drugs.

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N/3 EZH2 MUTATION SCREENING IN HUNGARIAN FOLLICULAR LYMPHOMA PATIENTS: PAVING THE WAY TO EPIGENETIC THERAPY

Bence Bártai¹, Noémi Nagy¹, Ambrus Gángó¹, Csaba Bödör¹

1. Hungarian Academy of Sciences-Semmelweis University Momentum Molecular Oncohematology Research Group, 1st Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest, Hungary

Keywords: EZH2, epigenetics, follicular lymphoma, diagnostics, therapy

Aims: Mutations emerging in epigenetic regulators play a major role in the pathogenesis of follicular lymphoma. The EZH2 histone methyltransferase harboring gain-of-function mutations in 25% of the patients emerged as a promising therapeutic target. The EZH2 inhibitor tazemetostat proved to be effective in a phase II clinical trial for the treatment of follicular lymphoma, demonstrating increased efficacy in patients harboring EZH2 mutations. To identify the patients most likely benefiting from an EZH2 inhibitor therapy, we aimed to perform EZH2 mutation analysis in a cohort of Hungarian follicular lymphoma patients.

Methods: We evaluated the EZH2 mutation status of 321 patients with follicular lymphoma, by performing a digital droplet PCR (ddPCR) mutation analysis of the Y646, A682, and A692 hotspots in DNA samples from bone marrow or lymph node biopsy specimens. We also analyzed the association of EZH2 mutation status and clinical data.

Results: Gain-of-function EZH2 mutations were identified in 24.3% (78/321) of the patients. In most cases the mutation resulted in Y646N (35%, 28/81), Y646F (20%, 16/81), or Y646S (16%, 13/81) amino acid change. In contrast with previous studies suggesting a superior progression-free survival in EZH2 mutant patients, we found no significant correlation between EZH2 mutation status and survival data.

Conclusions: In this study, 24.3% of follicular lymphoma patients harbored EZH2 mutations providing rationale for their recruitment into an EZH2 inhibitor clinical trial in the future. We also optimized EZH2 mutation testing using a highly sensitive ddPCR assay and included this test in the routine molecular diagnostic algorithm of follicular lymphoma.

Support: The study was supported by the KH17-126718 grant of the Hungarian National Research, Development and Innovation Office (NKFIH) and the Momentum grant (LP-95021) of the Hungarian Academy of Sciences.

N/4 RADIOMIC ANALYSIS IN SOLID TUMORS OF THE PANCREAS

Frank V, Shariati S, Budai B, Pencz B, Borka K, Kaposi PN

Department of Radiology, Semmelweis University, Budapest, Hungary, 2nd Department of Pathology, Semmelweis University, Budapest, Hungary

Keywords: pancreatic adenocarcinoma, radiomic analysis, machine learning

Aims: Assessing tissue heterogeneity in malignant lesions using CT Texture analysis can be used to differentiate pancreatic adenocarcinoma from disease-free parenchyma.

Methods: Thirty-nine pre-operative CT scans with resectable pancreatic adenocarcinoma were retrospectively collected. One case was excluded due to chemotherapy. CT series slice thickness were reconstructed in the arterial phase to 3mm. The whole pancreases and the tumors were manually segmented and underweight texture analysis using the 3D Slicer program. First, second and higher-order radiomic parameters (RP) were calculated on images transformed by using wavelet and Laplacian of Gaussian filters. The RPs were used in principal component analysis (PCA) and in a machine learning based prediction model.

Results: At first 1209 RPs of the 29 lesions and of the lesion-free pancreases from 26 patients with adenocarcinoma were used for PCA which revealed a dominant pattern and divided the data points into two groups. The best two RPs were selected with recursive feature elimination. A support vector machine based prediction model was constructed where the dataset was split into training and a test set, and it was able to separate the adenocarcinoma from the lesion-free pancreases with 96.55% accuracy. The receiver operating characteristics curve was also created where the area under curve was 95.26%.

Conclusions: Cross-validated prediction models based on radiomic analysis may be used successfully in the detection of pancreatic adenocarcinoma.

N/5 EARLY- AND LONG-TERM PATENCY AFTER ENDOVASCULAR TREATMENT OF PATIENTS WITH INFRARENAL AORTIC STENOSIS

Ákos Bérczi, Edit Dósa

The Heart and Vascular Center, Semmelweis University

Keywords: Interventional radiology, stent, aorta, endovascular, stenosis

Aims: For patients with infrarenal aortic stenosis (IAS) the following endosurgical treatment options exist: 1. percutaneous transluminal angioplasty (PTA), 2. aortic stenting, and 3. aortobiliac stenting. The aim of this study was to determine the success of IAS interventions.

Methods: Fifty-two symptomatic patients (33 females; median age: 60 [56-67] years) with IAS who underwent endovascular treatment between 2001 and 2017 were retrospectively analyzed. Patient, vessel, lesion, and balloon/stent characteristics were examined. Follow-up included peripheral pulse palpation, ankle-brachial index measurement, and ultrasound examination. Kaplan-Meier analysis was used as statistical method.

Results: The cause of IAS was vasculitis in two patients (4%) and atherosclerosis in 50 (96%). Thirteen percent of the patients were ≤ 50 years, 73% were smokers, 88% had hypertension, 21% were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$), and 8% had chronic kidney disease. The median length of IAS was 17.6 (10.8-27.2) mm, while the grade of IAS was 70 (70-80)%. Severe calcification was present in 19% of the patients. In four cases (8%) PTA, in 34 (65%) aortic stenting, and in 14 (27%) kissing stenting was performed. The median follow-up time was 63 (18-96) months. The primary patency rate was 100% at 6 months, 96% at 12 and 24 months, and 83% at 60 and 120 months. Restenosis developed in six patients (12%); reintervention was carried out in four cases (8%).

Conclusions: Interventions in patients with IAS can be performed with excellent patency rates.

N/6 MICRORNA-MRNA NETWORK ALTERATIONS UNDER HYPERCHOLESTEROLEMIA IN RAT MYOCARDIUM

Bence Ágg, András Makkos, Tamás Baranyai, Borbála Vető, Nóra Faragó, Ágnes Zvara, Zoltán Giricz, Dániel V. Veres, Péter Csermely, Tamás Arányi László G. Puskás, Zoltán V. Varga, Péter Ferdinandy

Department of Pharmacology and Pharmacotherapy Semmelweis University Budapest Hungary

Keywords: hypercholesterolemia, miRNA, network, bioinformatics, myocardial d

Aims: Hypercholesterolemia as a risk factor leads to coronary heart disease and impairs systolic and diastolic cardiac function as an independent factor. We aimed to explore novel hypercholesterolemia-induced microRNA mediated pathway alterations in the heart with an unbiased microRNA-mRNA interaction analysis.

Methods: Male Wistar rats were fed either with or without cholesterol supplemented chow (2% cholesterol and 0.25% cholate, ad libitum) for 12 weeks. Hearts were perfused in a Langendorff system and microRNA was extracted from the myocardium and microRNA microarray analysis was performed. Using microRNA-mRNA interaction database, mRNAs with at least 4 interacting upregulated microRNAs were identified by a network theoretical approach. Selected mRNA targets were validated by qRT-PCR and Western blot analysis. Selected microRNA-mRNA interactions were further validated by luciferase-assay.

Results: 47 microRNAs were up- and 10 microRNAs were downregulated in the hypercholesterolemic rat hearts as compared to the normocholesterolemic control hearts. To find mRNA hubs, a classical microRNA-target network was constructed, in which 11 mRNA target hubs were identified. Adrenoceptor beta 2 (Adrb2) and calcineurin B type 1 (CNB1) showed downregulation at protein level due to hypercholesterolemia. Interaction between two selected targeting microRNAs and the 3' untranslated region of Adrb2 mRNA was proven by luciferase reporter assay.

Conclusions: According to our results we assume that the downregulation of Adrb2 and the decreased production of the CNB1 protein as product of Ppp3r1 gene, is involved in the mechanism of hypercholesterolemia-induced cardiac dysfunction.

N/7 GLYCINE TRANSPORTER TYPE-1: A NOVEL TARGET IN THE MANAGEMENT OF NEUROPATHIC PAIN

Róbert Stollmayer, Amir Mohammadzadeh, Mihály Balogh, Kornél Király, Szilvia Barsi, Laszlo Köles, Zoltan S. Zadori, Laszlo G. Harsing, Jr., Mahmoud Al-Khrasani

Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, Semmelweis University, Nagyvárad tér 4, P.O. Box 370, H-1445 Budapest, Hungary

Keywords: GlyT-1; sarcosine; neuropathic pain; analgesia; in vivo model

Aims: Glycine transporters are an exciting target in pain research. So far there is no consensus on their antinociception, however many promising results had been born.

Aims: Assessment of the analgetic effect of the GlyT-1 inhibitor, sarcosine after acute and chronic administration

in thermal (tail-flick), inflammatory (formalin) and mononeuropathic pain models.

Methods: Male Wistar rats were used. Reactions to thermal stimuli were measured after acute and chronic sc. sarcosine treatment. In formalin test, prior to intraplantar injection of formalin rats were acutely or chronically treated with sarcosine, then nociceptive reactions were counted for 60 min, which was further subdivided into phase I (0-10min) and phase II (10-60min). Neuropathic pain model: pain was evoked by partial sciatic nerve ligation. The developed allodynia was measured by dynamic plantar aesthesiometer (DPA). Sham operated rats were used as a control. The antiallodynic effect of sarcosine was measured after acute and chronic treatment.

Results: Sarcosine proved to have analgesic effect in thermal pain model following chronic treatment. In inflammatory pain model sarcosine failed to produced analgesia in either phases. Interestingly, in neuropathic pain sarcosine does produce analgesia following both acute and chronic treatments.

Conclusions: Acute inhibition of GlyT-1 failed to affect thermal or inflammatory nociception under the presence conditions. After chronic treatment thermal nociception was alleviated. Both acute and chronic GlyT-1 inhibition produced antiallodynic effect. Inhibition of GlyT-1 could provide a new opportunity for the management of neuropathic pain, which is a huge challenge in clinical practice.

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O. Multidisciplinary poster session IV. – NEUROSCIENCE -

OBSTETRICS AND GYNECOLOGY - PEDIATRICS-OPHTHALMOLOGY

O/1 THE ROLE OF P2X7 RECEPTOR IN THE MATERNAL IMMUNE ACTIVATION MODEL OF AUTISM SPECTRUM DISORDER

Pablo Antonio Fritz-Ruenes, Beáta Sperlágh, Lilla Otrókcsi

Institute of Experimental Medicine, Hungarian Academy of Sciences

Keywords: Behavior Test, Inflammation, NLRP3 Inflammasome, Poly(I:C), ATP

Aims: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder that is defined by core abnormalities in communication, social and repetitive behaviors. Meta-analyses indicated the role of maternal immune activation (MIA) caused by infection during pregnancy as a risk factor strongly associated with the emergence of ASD in offspring. The P2X7 receptor could play a key role in this mechanism as its activation through the NLRP3 inflammasome serves as a maturation signal for processing of proinflammatory cytokines and leads to inflammation.

Methods: We administered poly(I:C) which causes MIA or ATP to mice on given days of pregnancy. Then we carried out behavior tests on offspring at 8 weeks of age. We performed social preference test, self-grooming, marble burying and rotarod test. After behavior tests mice were sacrificed to collect samples and measure Purkinje cell count.

Results: In the offspring of ATP treated wild type mice similarly to the maternal poly (I:C) treatment autistic phenotype was observed meaning social deficit, increased repetitive behavior, motor coordination deficit and Purkinje cell loss. These ATP induced alterations were not observed in P2X7 receptor deficient mice. The maternal

NLRP3 inflammasome antagonist pretreatment prevented social deficit, increased marble burying, motor coordination impairment and Purkinje cell loss whereas increased self-grooming was not affected by the treatment.

Conclusions: We showed that poly(I:C) and ATP treatment induces autism-like behavior and Purkinje cell loss in the offspring with the activation of P2X7 receptor and the participation of NLRP3 inflammasome signaling pathway.

Support: Hungarian Research and Development Fund (Grant K116654 to B.S), Hungarian Brain Research Program [2017-1.2.1-NKP-2017-00002 to B.S.] and Gedeon Richter plc. (RG-IPI-2016-TP10-0012) and the European Union's Horizon 2020 Research and Innovation Program under the Marie Skłodowska-Curie grant agreement No. 766124.

O/2 MICROBLEEDS BECOME INVISIBLE ON ACUTE-SUBACUTE HUMAN SUSCEPTIBILITY WEIGHTED MRI?

Bálint Soma Környei, Luca Tóth MD

Department of Radiology, Department of Neurosurgery UP MS

Keywords: TBI, microbleed, lesion number, SWI, MRI

Aims: Diffuse axonal injury (DAI) is a common and severe pathological component of traumatic brain injury (TBI), „microbleeds” developing alongside with DAI are reliable marker of this pathology. Susceptibility weighted (SWI) MRI is a sensitive method for microbleed visualization however recent studies revealed that lesions can become invisible in the acute-subacute period.

Methods: We performed a retrospective study on 195 patients who suffered TBI: criteria of exclusion were comorbidities causing microbleeds, anticoagulant therapy, deficient documentation or MRI images of poor quality, thus 85 patients could be involved in the study. For the lesions' precise definition, we performed SWI images' co-registration to high resolution T1 weighted images (FSL FMRIB). We defined TBI severity according to Mayo classification, recorded age, lesion number and elapsed time between the trauma and MRI imaging and examined the temporal changes of average lesion numbers. With a multilinear regression we also revealed which clinical parameters influence the lesion number.

Results: According to the multilinear regression, in the examined population neither the TBI severity ($p=0,5165$) nor age ($p=0,0685$) influenced lesion number. However, we registered a significant decrease and re-increase of average lesion number in the acute-subacute interval (24h=5,9; 24-48h=1,8; 48-72h=6,6; KW: $p=0,00175$; Conoven post hoc: $p<0.05$) while chi square test did not show significant results for TBI severity in the specified time intervals.

Conclusions: According to our findings we can assume that microbleeds can become “invisible” on human SWI MRI likewise in rodent studies. Human SWI MRI can be recommended to be performed within the first 24h after trauma or after 48h.

Support: Supported BY the ÚNKP-18-2-I-PTE-201 New National Excellence Program of the Ministry of Human Capacities”

O/3 THE ROLE OF GUT MICROBIOTA IN NICOTINE ADDICTION-RELATED PROCESSES

Alina Lakosa, Morgane Besson

Integrative Neurobiology of Cholinergic Systems, Institute Pasteur, Paris

Keywords: addiction, microbiota, anxiety, withdrawal, nicotine

Aims: A growing body of evidence suggests important role for the microbiota-gut-brain axis in neuropsychiatric disorders. Although smoking is a major public health issue, few studies examined its role in nicotine addiction. Previous experiments in our laboratory showed a potentiation in the acute action of nicotine on the reward system when gut microbiota was depleted. My task was to investigate the effect of microbiota in withdrawal syndrome after chronic exposure to nicotine and the effect on the level of anxiety, as there is a strong comorbidity in anxiety and tobacco consumption.

Methods: 4 groups of mice (n=12-15) were set up: subcutaneous minipumps delivered nicotine or saline for 28 day and antibiotic-cocktail was used to break down intestinal flora. Behavioral experiments included Open Field (OF), Elevated Plus Maze(EPM), Dark-Light Box(DLB), Novel Place Recognition(NPR). On the 28th day nicotine-withdrawal was precipitated with mecamlamine injection. Severity of the withdrawal was measured with DLB and with the quantification of somatic signs (shaking, chewing, tremor, etc.). Statistical analysis included two-way ANOVA, post-hoc and student t-tests.

Results: Mice treated with antibiotics showed elevated level of anxiety: impaired short-term memory, decreased locomotion in OF and EPM and decreased %time spent on the open arms in EPM. Depletion of gut microbiota did not amplify the withdrawal syndrome's affective aspect, nor the somatic.

Conclusions: Analyzing the baseline videos recorded on the 27thday, we found that antibiotics by itself increased the number of signs, possibly because inducing visceral pain. In the presence of nicotine this elevation disappeared, could be due the calming properties of nicotine.

Support: Erasmus-scholarship

O/4 CFF-DNA NON-INVASIVE PRENATAL TESTING IN CLINICAL PRACTICE

Dorina Greff 1, Olga Török 2,

1 Faculty of Medicine, University of Debrecen 2 University of Debrecen, Department of Obstetrics and Gynecology

Keywords: non-invasive, NIPT, prenatal screening, cffDNA, trisomy

Aims: Introduction: Non-invasive prenatal tests (NIPTs) are based on detecting cell-free fetal DNA (cffDNA) in maternal plasma. NIPTs screen for certain chromosomal abnormalities as early as 10th week of pregnancy. The sensitivity and specificity of cffDNA based NIPTs proved to be more than 99% according to validation studies. The aim of this study was to determine the efficacy of the tests in everyday clinical practice.

Methods: In the database of Genetic Counselling at the Department of Obstetrics and Gynecology of the University of Debrecen those patients were identified whose cffDNA NIPT results had to be confirmed by invasive tests. The screening and confirmatory invasive test results were compared.

Results: Between November 2011 and December 2018 the total number of confirmatory invasive tests from amniotic fluid cells and chorionic villi was 51. NIPT results were not confirmed in 10 cases including one false negative case of Trisomy-18. The gender of the fetus was determined incorrectly in two cases. The NIPT presented false positive results altogether in 7 cases (1 Klinefelter-, 1 Jacob-, 1 Patau- syndrome, 1 triploidy, 1 Trisomy-16 and 2 Turner-syndrome cases). NIPT result was confirmed in 36 cases. In 5 more cases NIPT could not provide result because of the low fraction of fetal DNA.

Conclusion: The sensitivity and specificity of cffDNA based NIPTs might be lower in clinical practice than expected by the validation studies. Set up of a national database collecting data of false positive and false negative cases should be encouraged.

Support: Students' Scientific Association. Talent Management Program (Detep)

O/5 DIFFERENTIATING TISSUES AND ORGANS IN ENDOSCOPIC IMAGES USING A CONVOLUTIONAL NEURAL NETWORK

Zoltán Tándor

Obstetrics & Gynecology Department, University of Debrecen, Hungary

Keywords: tissue recognition, CNN, AI, laparoscopy, decision making

Aims: Minimally invasive interventions have become more widespread throughout the world. In addition to their minimal disadvantage (lack of tactile information), the method is being used by more and more surgeons because of their many benefits. In endoscopic studies differentiation of organs is based on visual information, which makes the process difficult compared to the open surgical situation due to the lack of tactile information. The use of digital imaging and the use of IT methods is another opportunity for discrimination. By using a convolutional neural network (CNN), it is possible to distinguish organs of tissues of different structure and structure by separating the special properties that are difficult to perceive by the human eyes.

Methods: We used 35 endoscopic videos for the analysis. In these pictures, we have drawn them manually, marking the arteries and ureter. Subsequently, along with the indicated formulas, the program placed 2500 usable sub-images. Of these, 2000 pieces of cut-out sub-images were used for the teaching process, and the trained system was tested using the remaining 500 sub-images.

Results: Our proposed approach has reached 94.2% final accuracy regarding this binary classification task. Our experience has shown that, in accordance with the criteria of deep learning, the increasing amount of data results in increasing hit accuracy.

Conclusions: It can be concluded that the high-precision, semi-automatic digital imaging system developed by us provides useful assistance in gynecological operation. In the case of experienced surgeons, it facilitates decision-making and helps novice surgeons learn anatomical knowledge and surgical procedures.

O/6 THE EFFECT OF SIGNAL INTENSITY ON THE RELIABILITY OF OCT ANGIOGRAPHY MEASUREMENTS IN PATIENTS WITH DIABETES

Trevor Logan, Cecília Czakó, Lilla István, Mónika Ecsedy, Zsuzsa Récsán, Hajnalka Horváth, Zoltán Zsolt Nagy, Illés Kovács

Semmelweis University Department of Ophthalmology

Keywords: OCTA, diabetes, diabetic retinopathy, retina, microangiopathy

Aims: Optical coherence tomography angiography (OCTA) is a sensitive new tool for early detection of diabetic retinopathy. Image quality impacts reliability of quantitative retinal blood-flow measurements used in patient follow-up. This study's goal was to evaluate effects of image quality on OCTA parameters in patients with non-proliferative diabetic retinopathy.

Methods: In total, 37 eyes without retinopathy and 63 with detectable retinopathy were studied, from 50 patients. Each subject underwent one imaging session, where three OCTA images were consecutively obtained using the AngioVue OCTA system. Image quality was described using the Signal Strength Index (SSI), with values ranging from 1-100. Central retinal thickness (CRT) and superficial vessel density (VD) at the 3x3 mm foveal and perifoveal area, as well as the foveal avascular zone (FAZ) area, were measured. OCTA parameters were compared and correlated with changes in corresponding SSI values.

Results: SSI values ranged from 26 to 86, with a mean of 61.41 ± 11.01 . The mean difference in SSI values between

the measurements was 3.83 ± 3.23 . The difference in SSI values was significantly correlated with the difference in corresponding superficial vessel density in the 3x3 mm area ($r=0.33$, $p<0.001$, $\beta=0.2$), and the perifoveal area ($r=0.31$, $p<0.001$, $\beta=0.2$) from consecutive measurements. CRT values and FAZ area were not affected by changes in image quality.

Conclusions: For the RTVue OCT instrument, we recommend a correction factor of 2% for each 10 unit increase in SSI vessel density measurements for image comparisons during follow-up. No such correction factor is needed for retinal thickness and non-flow measurements.

O/7 METABOLIC HORMONES IN BREAST MILK

Anna A. Kiss¹; Timea Takács¹; Réka A. Vass^{1, 2}; Gabriella Kiss³, Attila Miseta³; Tibor Ertl^{1, 2}

1 Neonatológiai Tanszék, Szülészeti és Nőgyógyászati Klinika, Pécsi Tudományegyetem, Pécs; 2 MTA-PTE Humán Reprodukciós Kutatócsoport, Pécsi Tudományegyetem, Pécs; 3 Laboratóriumi Medicina Intézet, Pécsi Tudományegyetem, Pécs

No English abstract available

O/8 WHY NOT TO USE THE HANDGRIP TEST IN THE ASSESSMENT OF CARDIOVASCULAR AUTONOMIC NEUROPATHY?

Magdolna Békeffy, Anna Körei, Zsuzsanna Putz, Ildikó Istenes, Miklós Kempler, Orsolya Vági, Katalin Keresztes, Péter Kempler, Vincenza Spallone

1st Department of Internal Medicine, Semmelweis University, Budapest, Hungary

Keywords: cardiovascular autonomic reflex test, cardiovascular autonomic neuropathy, diabetes, hypertension

Introduction: The cardiovascular autonomic reflex tests (CARTs) have been considered as gold standard in the assessment of cardiovascular autonomic neuropathy among diabetic patients. However, only four of the five tests have been currently suggested to be performed- sympathetic function should be evaluated by the orthostatic hypotension test while measuring diastolic blood pressure response to sustained handgrip is omitted in recent guidelines.

Aim: Aim of our study was to assess the relationship of handgrip test with the other test results in detecting cardiovascular autonomic neuropathy as well as to determine the factors having impact on abnormal result of the handgrip test in diabetic patients.

Methods: Our study involved 353 diabetic patients (mean age: 60.2 ± 7.4 years; female: 57.2%; BMI: 29.3 ± 2.1 kg/m²; mean diabetes duration: 15.6 ± 9.9 years; mean HbA1c: $8.2 \pm 1.9\%$). Cardiovascular autonomic function was assessed by the five CARTs: the deep breathing test, Valsalva ratio, 30/15 ratio, handgrip and orthostatic hypotension test. Reflex tests detecting heart rate changes mainly reflect parasympathetic while blood pressure changes in response to manoeuvres characterize sympathetic function. Connection between results of the handgrip and the other reflex tests as well as parameters of the study population were analysed using Kendall monotony coefficient gamma (γ), Spearman's correlation. Dichotomous variables were analysed using χ^2 -test.

Results: Results of the handgrip test did not show any association with the results of the deep breathing test and 30/15 ratio ($p=0,897$; $p=0,357$), as they did not do with the results of the partially sympathetically controlled Valsalva ratio, either ($p=0,781$). The relationship between handgrip and the orthostatic hypotension could not be proven ($p=0,833$). The results of handgrip test did actually show a significant negative association with the presence of hypertension ($\gamma=-0,315$, $p=0,009$), whereas the diastolic blood pressure elevation during the manoeuvre was inversely related to the baseline diastolic blood pressure ($r=-0,283$, $p=0,013$). In multiple logistic regression analysis, the significant inverse association between abnormality of the handgrip test and hypertension was independent of age, gender, BMI, diabetes duration, type of antihypertensive medication, insulin treatment as well as presence of sensory loss and neuropathic pain medication.

Orthostatic hypotension was associated with the severity of the parasympathetic impairment ($\gamma=0,303$, $p<0,0001$) and with Valsalva ratio abnormality ($\gamma=0,342$, $p<0,0001$). Presence of hypertension had no effect on the results of orthostatic hypotension test ($p=0,97$).

Conclusions: Our data may provide evidence that the handgrip test should no longer be part of the cardiovascular autonomic evaluation being highly dependent of the hypertensive status and baseline blood pressure values. The putative mechanism for the inverse relation between abnormal result of the handgrip test and hypertension could be the exaggerated exercise pressor reflex associated with hypertension leading to augmented sympathetic cardiovascular response involving higher blood pressure elevations to sustained handgrip in diabetic patients with hypertension.

P. Multidisciplinary session IX.: RADIOLOGY session

P/1 HERITABLE EFFECTS ON THE DEVELOPMENT ON THE SIZE OF ADRENAL GLAND AND PANCREAS: A TWIN STUDY

Zsuzsa Incze¹, Pal Maurovich-Horvat², Adam Levente Jermendy², Gyorgy Jermendy³, Bela Merkely², David Laszlo Tarnoki¹, Adam Domonkos Tarnoki¹

1 Department of Radiology, Semmelweis University, Budapest, Hungary; 2 MTA-SE Cardiovascular Imaging Research Group, Heart and Vascular Center, Semmelweis University, Budapest, Hungary; 3 3rd Department of Internal Medicine, Bajcsy Zsilinszky Hospital, Budapest, Hungary

Keywords: pancreas, adrenal gland, twin study, heritable, size

Aims: Altered adrenal size can be present in adrenal insufficiency and chronic fatigue syndrome. Decreased pancreas size is seen in diabetes and chronic pancreatitis. However, the heritable effects on the aging dependent size change has not been investigated in healthy population. The purpose of the study was to determine whether the size of the adrenal glands and pancreas is heritable. Methods: 174 Hungarian twins (98 monozygotic, MZ; 72 dizygotic, DZ; 60% female, mean age 55.7 ± 9.2 years) underwent a cardiac CT using a 256-slice multidetector CT (Brilliance iCT). Using IntelliSpace program, the maximal cross-sectional area, density of the body of the adrenal glands were analyzed. The diameter of the pancreatic head and body as well as its density was measured. Raw heritability was calculated using Falconer formula.

Results: The cross-sectional area of left adrenal gland was increased ($r=0.235$, $p=0.005$) and the diameter of pancreatic head and body decreased ($r=-0.261$ and $r=-0.191$, $p<0.01$) with age. Age-adjusted MZ correlations were higher compared to DZ correlations, indicating a low (0.07) raw heritability for right adrenal cross-sectional area, and a high raw heritability for the density of right adrenal ($h^2=0.77$), the size (0.75) and density ($r=0.91$) of left

adrenal gland, and diameter of pancreatic head (1.0), and moderate raw heritability of the diameter of pancreatic body (0.36) and pancreatic density (0.35).

Conclusions: The aging dependent size and density of adrenal glands and pancreas is influenced by genetic effects. Our study might stimulate studies on the role of environmental effects on the maintenance of aging of these organs.

P/2 HIGH-RESOLUTION COMPUTED TOMOGRAPHY CHANGES IN THE DIFFERENTIATION OF CHRONIC HYPERSENSITIVITY PNEUMONITIS AND USUAL INTERSTITIAL PNEUMONIA

Christian Kadar¹, Kinga Karlinger¹, Veronika Müller², Noémi Eszes², Anikó Bohács², Dávid László Tárnoki¹, Ádám Domonkos Tárnoki¹

1 Department of Radiology, Semmelweis University, Budapest, 2 Department of Pulmonology, Semmelweis University, Budapest

Keywords: HRCT, HP, UIP, ILD, honeycombing

Aims: High resolution computed tomography (HRCT) proven was used to indicate usual interstitial pneumonia (UIP). However, recent radiopathologic observations suggest that honeycombing in different zonal distribution can occur in chronic hypersensitivity pneumonia (HP). In contrast to the dorsobasal distribution in UIP, apical and peribronchovascular distribution was referred in chronic HP. Our aim was to analyze retrospectively the HRCT images of patients who were referred as definitive UIP by the chest radiologist.

Methods: 31 patients (17 male, 14 female, mean age 69.7±10.5 years) who underwent HRCT at the Department of Radiology, Semmelweis University and referred in the interstitial lung disease (ILD) team as definitive UIP were analyzed retrospectively. The zonal distribution of honeycombing pattern was analyzed in 5 pre-selected levels (aortic arch, tracheal carina, supradiaphragmatic and two in-between) in the inspiratory scans to define the predominant zonal distribution.

Results: 8 of the 31 patients showed an apical and peribronchovascular honeycombing distribution suggesting chronic HP (25.8%) based on the imaging findings. The lower lobes were predominantly affected with a frequency of 74.2% suggesting a definitive UIP pattern. More male patients were affected by chronic HP pattern compared to definitive UIP (75% vs. 52%), however, the mean age of the two groups was identical (69.4±6.1 years for chronic HP and 68.4±11.8 years for UIP).

Conclusions: Chronic HP pattern was suggested in 1/4 of the cases defined originally as definitive UIP pattern in the ILD team which could argue for the lack of efficacy of antifibrotic drug therapy in a sizeable portion of UIP patients.

P/3 HERITABLE EFFECTS ON THE MORPHOLOGY OF HASHIMOTO THYROIDITIS: A TWIN STUDY

Gergely Szabó, Márton Fekete, Mercédesz Erdei, Marcell Szily, András Dienes, Alíz Persely, Ádám Domonkos Tárnoki, MD, PhD, Dávid László Tárnoki, MD, PhD

Department of Radiology, Semmelweis University, Budapest, Hungary

Keywords: Hashimoto, epidemiology, genetics, environment, elastography

Aims: Hashimoto thyroiditis (HT) is the most common cause of hypothyroidism after iodine deficiency worldwide affecting about 5% of the population. The initiative causes of HT is not yet fully understood but studies show a strong genetic component. Our aim was to identify if genetic or environmental factors have larger effects on the presence and stiffness of HT.

Methods: 106 twin pairs (mean age 52.8 ± 17.0 years, 60.5% female) from the Hungarian Twin Registry underwent thyroid ultrasound with elastography (ElastoScan and E-Thyroid applications, Samsung RS85) and body mass index (BMI) measurement. Pairwise concordance rates were estimated by a standardized formula.

Results: 4 concordant monozygotic (MZ), 2 discordant MZ, and 5 discordant dizygotic (DZ) twin pairs (9 female, 2 male) were identified whose ultrasound morphology suspected a HT, indicating a pairwise concordance of 0.67 for MZ and 0 for DZ twins suggesting a strong genetic influence. Parenchymal stiffness measured in hypoechogenic areas showed a tendency for higher values (0.85 vs. 0.75 for both sides, $p=ns$). Lower BMI was found in MZ twins with HT compared to the healthy twin. High intrapair correlation was found in HT concordant MZ twins ($r=0.992$, $p=0.008$ for both sides) compared to discordant DZ twins ($r=0.714$, $p=0.143$ for both sides) indicating a genetic component ($h^2=0.56$). HT concordant MZ twins had lower ΔBMI compared to discordant MZ twins (0.50 ± 0.22 vs. 3.30 ± 2.42 kg/m²).

Conclusions: HT as well as the parenchymal stiffness seems to be influenced by genetic factors, which is associated with lower BMI, possibly through genetic factors.

P/4 LATERALITY OF WHITE MATTER HYPERINTENSITY CORRELATES WITH BASILAR ARTERY-BENDING AND VERTEBRAL ARTERY DOMINANCE

1 Szalontai, L., 1 Jokkel, Zs., 2 Horvath, T., 1 Forgo, B., 3 Auyang P., 3 Zubair M., 1 Berczi, V., 1 Tarnoki, DL., 1 Tarnoki, AD.

1. Department of Radiology, Semmelweis University, 2. Department of Hydrodynamic Systems, Budapest University of Technology and Economics, 3. Department of Cardiovascular Surgery, Methodist De Bakey Heart & Vascular Center, Houston, TX, USA

Keywords: White matter hyperintensities, vertebro-basilar system,

Aims: Previous studies suggested that the morphology of the vertebrobasilar system contributes to the laterality of cerebral ischemic events. WMH has been shown to increase these events risk by 3-fold. Our first aim was to investigate whether BA geometry contributed to the existence and laterality of WMH. Since the BA branches from the confluence of the two VA, our second aim was to investigate the influence of the VA dominance on BA geometric indices.

Methods: In this retrospective study we analyzed 290 MRI scans of our patients who were admitted to our clinic between 2017-2018. WMH were counted, localized (supratentorial, brainstem, or cerebellar), grouped by sidedness (left or right dominant) and grouped based on WMH (control or WMH). We reconstructed 3D meshes of the posterior circulation, and subsequently analyzed the morphology of the VA and BA and their directional relationships with VMTK scripts and an in house written software in Python.

Results: Patients with WMH lesions were significantly older compared to the control group and the occurrence of hypertension and diabetes was also significant within the WMH group. We found significant correlations between

the morphological properties of the vertebro-basilar system and WMH in different brain structures. Furthermore, we found an opposite directional relationship between the dominant VA and BA laterality of bending. The dominant VA was more frequent on the left side.

Conclusions: Our findings indicate the unequal VA flow is an important hemodynamic contributor of the BA curvature. These posterior circulation morphological variations show correlation with the laterality development of the WMH.

Support: Erasmus+ program scholarship.

P/5 EFFECT OF PERCEIVED STRESS ON THE PRESENCE OF CAROTID AND FEMORAL ARTERY ATHEROSCLEROSIS

Zöldi Luca, Janositz Gréta, Gyulay Kata, Jokkel Zsófia, Zsupos Rebeka, Persely Alíz, Szabó Gergely, Bérczi Viktor, Szabó Helga, Hernyes Anita, Tárnoki Dávid László, Tárnoki Ádám Domonkos

Department of Radiology, Semmelweis University, Budapest, Hungary

Keywords: atherosclerosis, stress, ultrasound, plaque, twins

Aims: The role of perceived stress as environmental factor in carotid or femoral atherosclerosis has not been assessed yet. The aim of our study was to examine this relation.

Methods: 70 Hungarian twins (45 monozygotic, 25 dizygotic; 60% female, mean age $53,02 \pm 13,97$ years) completed the perceived stress scale (PSS) questionnaire. The twins underwent carotid and femoral ultrasound examination (Samsung RS85, 15MHz), blood pressure and arterial stiffness (TensioMed Arteriograph, Budapest, aortic pulse wave velocity, PWV) measurement. Carotid and femoral intima media thickness (IMT) was measured automatically.

Results: The PSS score showed weak correlation with the right maximal carotid IMT ($Rho: 0,293$, $p: 0,015$), and the right femoral stiffness values: compliance ($Rho: -0,297$), distensibility ($Rho: -0,265$), elastic modulus ($Rho: 0,259$), PWVfem ($Rho: 0,259$) $p < 0,05$. No significant correlation was found on the left side. The total carotid plaque volume showed a weak correlation ($Rho: 0,248$ $p: 0,038$), but not the femoral plaque volume and aortic PWV. The absence of daily moderate physical activity, however, showed stronger correlation ($Rho: 39,8\%$ $p = 0,001$).

Conclusions: The role of perceived stress in atherosclerosis development should not be separated from other lifestyle factors. Frequent sympathetic nervous system activation without simultaneous physical activity could raise atherosclerosis risk. Morphologically weak correlations could be found between PSS and carotid-femoral ultrasound atherosclerosis markers.

P/6 CT TEXTURE ANALYSIS IN LIVER FIBROSIS SHOWS STRONG CORRELATION WITH PORTAL PHASE ENHANCEMENT AND CAN PREDICT CIRRHOSIS IN DECISION TREE MODEL

Budai B1, Frank V1, Shariati S1, Folhoffer A2, Kaposi PN1

1 Department of Radiology, Semmelweis University, Budapest, Hungary 2 1st Department of Internal Medicine, Semmelweis University, Budapest, Hungary

Keywords: liver cirrhosis, radiomic analysis, CT texture analysis, machine

Aims: CT texture analysis (CTTA) has been successfully used to assess tissue heterogeneity and it may facilitate the diagnosis of liver cirrhosis when utilized in machine learning models.

Methods: CT scans were retrospectively collected from twenty-seven patients with chronic hepatitis. Examinations were performed with either a 16 (11 cases) or a 64 slice (16 cases) scanner (Philips Healthcare, the Netherlands). The stage of liver fibrosis was determined with shear-wave ultrasound elastography. Contrast-enhanced series in the portal venous phase (PVP) were reconstructed to 5 mm slice thickness with no gap. Anatomical liver segments were labeled manually, and 1112 texture parameters (TP) were calculated for each. TPs were used in a hierarchical cluster analysis (HCA), group comparisons, and in a binary tree prediction model (BTM).

Results: CTTA was performed on 319 anatomical liver segments. A comparison between the two scanners found a significant difference ($p < 0.05$) in 305 TPs. HCA revealed a uniform pattern, which divided segments into two groups. PVP densities showed a significant difference between the two groups in both the 16 (mean $\pm$ SEM= 108.9 $\pm$ 1.69 HU vs. 96.6 $\pm$ 1.16 HU, $p < 0.001$) and the 64 slice (mean $\pm$ SEM= 101.1 $\pm$ 1.24 HU vs. 85.2 $\pm$ 1.83 HU, $p < 0.001$) sets. Meanwhile, liver stiffness was not significantly different. A BTM was trained on the 64 slice set, and it could predict cirrhosis in segments of the 16 slice set with 92% accuracy.

Conclusions: Contrast enhancement and scanning parameters have a strong influence on TPs. CTTA based artificial intelligence may achieve success in the detection of liver cirrhosis.

Q. Highlighted topic: EDUCATION IN MEDICINE IN THE XXI. CENTURY: HUNGARY VS. USA VS. UK

Q/1 EDUCATION REFORM OF SEMMELWEIS UNIVERSITY

PROF. DR. MIKLÓS KELLERMAYER, DEAN OF SEMMELWEIS UNIVERSITY (BUDAPEST, HU)

No abstract available

Q/2 AMERICAN RESIDENCY PROGRAM: AMERIKAI REZIDENS KÉPZÉSRŐL/KUTATÁSRÓL/VÍZUMOKRÓL/LEHETŐSÉGEKRŐL

ANDREA HORVÁTH, MD, PHD (USA)

No abstract available

Q/3 INNOVATION IN HEALTHCARE PROVISION – KEY LEARNINGS FROM EUROPEAN PROVIDERS

ATTILA PETER VEGH, MD, PHD (PRESIDENT, HMAUK)

No abstract available

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All abstracts available to the Editorial Office as of August 7, 2018 are included in this edition of the Archives of the Hungarian Medical Association of America.

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With questions or suggestions, please contact the Editor at ssomkuti@abington-repromed.com.

*Thank you,
István Somkúti MD PhD*

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