

Background: Although exercise-induced cardiac hypertrophy has been intensively investigated, consecutive evaluation of its development and regression dynamics is not fully described. We aimed to characterize the effects of regular exercise training and detraining on myocardial mechanics by speckle-tracking echocardiography (STE) in a rat model.

Methods and results: Rats were divided into exercised and control groups ($n=12/\text{group}$). Trained rats swam 200min/day for 12 weeks. After completion of the training protocol, rats remained sedentary for 8 weeks (detraining period). Echocardiographic follow-up was performed regularly using a 13MHz linear transducer to obtain LV long- and short-axis recordings for STE analysis. Global longitudinal and circumferential strain and systolic strain rate (CSr, LSr) were measured. LV pressure-volume analysis was performed using also additional groups to obtain hemodynamic data.

Echocardiography showed the development of LV hypertrophy in the exercised group (exercised vs. control; LVmass index: 2.4 ± 0.1 vs $2.0 \pm 0.1 \text{ g/kg}$, $p < 0.05$), which was followed by improvement of systolic function. These differences disappeared during detraining (2.3 ± 0.1 vs $2.4 \pm 0.1 \text{ g/kg}$, n.s.). Strain and strain rate values were increased after the training period (exercised vs. control; CSr: -5.6 ± 0.3 vs $-4.0 \pm 0.31/\text{s}$; LSr: -4.6 ± 0.2 vs $-3.9 \pm 0.21/\text{s}$, $p < 0.05$), whereas supernormal values rapidly reversed to the control level after training cessation. Load-independent hemodynamic indices, e.g. preload recruitable stroke work, confirmed the exercise-induced systolic improvement and complete regression after detraining.

Conclusion: Our study provides the first comprehensive data to describe the development and regression dynamics of morphological and functional aspects of physiological myocardial hypertrophy in detail. Speckle-tracking echocardiography has been proven to be feasible to follow-up changes induced by exercise training and detraining.

Funding: Supported by the ÚNKP-17-4 New National Excellence Program of the Ministry of Human Capacities of Hungary to T.R.

doi:10.1016/j.yjmcc.2018.05.047

Poster session 1

Name of presenter: Mihály Ruppert

Abstract # 32

The role of gender in the regression of pressure overload-induced left ventricular myocardial hypertrophy

M. Ruppert, S. Korkmaz-Icöz, S. Loganathan, W. Jiang, L. Lehmann, A. Oláh, B.A. Barta, B. Merkely, M. Karck, G. Szabó, T. Radovits

Heart and Vascular Center, Semmelweis University

Background: Sex-related disparities were identified during the development of pressure overload (PO)-induced left ventricular (LV) myocardial hypertrophy (LVH). However, it is less clear whether gender also affects the regression of LVH after pressure unloading. Thus, we investigated the effect of sex on myocardial reverse remodeling in a rat model of banding and debanding of the abdominal aorta.

Methods and results: Abdominal aortic banding (AB) was performed to induce PO in male and female rats for 6 or 12 weeks. Sham operated animals served as controls. Pressure unloading was evoked by debanding the aorta at week 6. Cardiac morphology and function

were assessed by echocardiography and LV pressure-volume analysis. Additionally, molecular and histological markers of cardiac hypertrophy and fibrosis were measured.

In both genders, PO induced the development of LVH as confirmed by increased LV mass, heart weight-to-tibial length ratio (HW/TL), cardiomyocyte diameter and enhanced fetal gene expression. Similarly, enhanced myocardial collagen accumulation was observed in male and female AB groups as well. The extent of LVH was greater among females, while fibrosis was more severe in male animals. In both genders, LVH was associated with diastolic dysfunction. However, systolic function only impaired in males. Contrary to the sex-dependent differences in LVH, debanding the aorta resulted in morphological (decreased LV mass, HW/TL), histological (decreased cardiomyocyte diameter and fibrosis), molecular (decreased fetal genes) and functional (restored diastolic and systolic function) reverse remodeling in both genders.

Conclusion: Pressure unloading leads to myocardial reverse remodeling at a comparable degree in male and female rats.

Funding: New National Excellence Program of the Ministry of Human Capacities (ÚNKP-17-3-I-SE-6; to M. Ruppert), National Research, Development and Innovation Office of Hungary (NKFI; NVKP-16-1-2016- 0017)

doi:10.1016/j.yjmcc.2018.05.048

Poster session 1

Name of presenter: Marta Vigil-Garcia

Abstract # 33

Gene expression profiling of hypertrophic and failing cardiomyocytes identifies new players in pathological remodeling

M. Vigil-Garcia, C.J. Demkes, J.E.C. Eding, D. Versteeg, H. de Ruiter, M.M. Gladka, M. Harakalova, N. Liaw, A. Vink, W.H. Zimmerman, E. van Rooij

Molecular Cardiology, Hubrecht Institute

Background: Pathological cardiac remodeling induced by pressure overload triggers cardiomyocyte hypertrophy and fibroblast activation, and ultimately leads to heart failure. So far, to study the mechanisms behind these processes, genome wide expression analysis on full heart tissue led to the identification of molecular mechanisms at play. However, these data were based on signals derived from all cardiac cell types. To date, the progression from cardiomyocyte hypertrophy to failure remains insufficiently understood and as a result there is a lack of therapies to reverse maladaptive remodeling.

Methods and results: Here, we generated a cardiomyocyte-specific reporter mouse Myh6-Cre-tdTomato line which we exposed to pressure overload by transverse aortic banding (TAB). Using Fluorescence-activated Cell Sorting (FACS) we collected both hypertrophic (one week after TAB) and failing (eight weeks after TAB) cardiomyocytes. Using these cells we performed RNA sequencing and identified subsets of genes and pathways differentially regulated and specific for either the hypertrophic and failing stages, such as Col3a1 and Nppb, respectively. Moreover, we identified a group of genes that yet have not been linked to cardiomyocyte hypertrophy and failure. A subset of these novel genes, we also found to be upregulated during human end stage heart failure. To validate the