Abstract: **P1249**

**Correlation between myofilament Ca2+ sensitivity and left ventricular contractility parameters during the progression of pressure overload-induced left ventricular myocardial hypertrophy**

**Authors:**
M Ruppert\(^1\), B Bodi\(^2\), S Korkmaz-Icoz\(^3\), S Loganathan\(^3\), L Lehmann\(^4\), A Olah\(^1\), BA Barta\(^1\), A Sayour\(^1\), B Merkely\(^1\), M Karck\(^3\), Z Papp\(^2\), G Szabo\(^3\), T Radovits\(^1\), \(^1\)Semmelweis University Heart Center - Budapest - Hungary, \(^2\)University of Debrecen, Division of Clinical Physiology, Faculty of Medicine - Debrecen - Hungary, \(^3\)University of Heidelberg, Department of Cardiac Surgery - Heidelberg - Germany, \(^4\)University Hospital of Heidelberg, Department of Cardiology, Angiology and Pulmonology - Heidelberg - Germany,

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**Background:** During the development of pressure overload (PO)-induced pathological left ventricular (LV) myocardial hypertrophy (LVH) and its progression to heart failure distinct alterations could be observed both in LV contractility and myofilament function. However, whether the dynamic alterations on the two levels (contractility on the global ventricular level and myofilament function on the cellular level) correspond to each other has been not studied.

**Purpose:** Therefore, we aimed at investigating the relation between LV contractility and myofilament function in PO-induced LVH.

**Methods:** PO was evoked by abdominal aortic banding (AB) in male, Sprague-Dawley rats for 6, 12 and 18 weeks. Control animals underwent the same surgery without constricting the aorta (Sham). Characteristic PO-induced alterations were investigated by serial echocardiography, histology, quantitative real-time PCR and western blot. LV function was assessed by pressure-volume analysis. Force measurement was carried out in permeabilized cardiomyocytes.

**Results:** Sustained PO resulted in the development of pathological LVH in the AB groups as indicated by macroscopic (increased heart weight-to-tibial length ratio and LV mass index), microscopic (increased cardiomyocyte diameter) and molecular markers (reactivated fetal gene program: increased atrial natriuretic peptide and β-to-a myosin heavy chain expression). These alterations were already present at early stage of LVH (AB-week6). Furthermore, at more advanced stages (AB-week12, AB-week18), interstitial fibrosis and chamber dilatation were also observed. The detailed analysis of the pressure-volume loops revealed that the AB-wk6 group was associated with increased LV contractility (as indicated by increased end-systolic elastance [ESPVR]: 1.74±0.22 vs. 3.28±0.36 mmHg/µl, preload-recruitable stroke work [PRSW]: 104±8 vs. 140±8 mmHg and preload-adjusted maximal slope of systolic pressure increment [dP/dtmax-EDV]: 33±2 vs. 53±6 (mmHg/s)/µl Sham-week6 vs. AB-week6, P<0.05), maintained ventriculo-arterial coupling (VAC) and preserved systolic function. In the same experimental group, increased myofilament Ca2+ sensitivity (pCa50) and hyperphosphorylation of cardiac troponin-I (cTnI) at Threonin-144 was detected. In contrast, in the AB-wk12 and AB-wk18 groups, the initial augmentation of LV contractility, as well as the increased myofilament Ca2+ sensitivity and cTnI (Threonin-144) hyperphosphorylation diminished, resulting in impaired VAC and reduced systolic performance. Strong correlation was found between LV contractility parameters (ESPVR, PRSW and dP/dtmax-EDV) and myofilament Ca2+ sensitivity (pCa50) among the study groups.

**Conclusion:** Changes in myofilament Ca2+ sensitivity might underlie the alterations in LV contractility during the...
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1 Semmelweis University Heart Center - Budapest - Hungary, 2 University of Debrecen, Division of Clinical Physiology, Faculty of Medicine - Debrecen - Hungary, 3 University of Heidelberg, Department of Cardiac Surgery - Heidelberg - Germany, 4 University Hospital of Heidelberg, Department of Cardiology, Angiology and Pulmonology - Heidelberg - Germany.

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Conclusion: Changes in myofilament Ca2+ sensitivity might underlie the alterations in LV contractility during the development and progression of PO-induced LVH.