

22. Myocardial reverse remodeling after pressure unloading is associated with restored cardiac contractility in a rat model of left ventricular hypertrophy

Mihály Ruppert
Dr. Tamás Radovits
Dr. Sevil Korkmaz-Icöz
Dr. Shiliang Li
Dr. Balázs Tamás Németh
Dr. Péter Hegedűs
Prof. Béla Merkely
Prof. Matthias Karck
Prof. Gábor Szabó

Introduction: Pressure unloading represents the only effective therapy in increased afterload-induced left ventricular hypertrophy (LVH) as it leads to myocardial reverse remodeling (reduction of increased left ventricular mass, attenuated myocardial fibrosis), decreased arrhythmogenicity and preserved cardiac function. However, it is still debated whether the maladaptive contractility augmentation associated with LVH regresses or not.

Purpose: Therefore, in the present study we aimed to provide a detailed hemodynamic characterization in a rat model of LVH undergoing pressure unloading.

Methods: Pressure overload was induced in Sprague-Dawley rats by abdominal aortic banding for 6 (AB 6th week) or 12 weeks (AB 12th week). Sham operated animals served as controls. Aortic debanding procedure was performed after the 6th experimental week (debanded 12th week) to induce myocardial reverse remodeling. Serial echocardiography and electrocardiography were carried out to investigate the development of LVH and its regression by pressure unloading. In addition, after the 12 week long experimental period, left ventricular pressure-volume analysis was performed in order to precisely assess in vivo cardiac function. Besides the functional experiments, histological and molecular biological measurements were also carried out.

Results: Pressure unloading resulted in significant reduction of LVH (heart weight/tibial length ratio: 0.38 ± 0.01 vs. 0.58 ± 0.02 g/mm, cardiomyocyte diameter: 18.32 ± 0.13 vs. 24.14 ± 0.76 μ m debanded 12th week vs. AB 12th week, $p < 0.05$), attenuated the extracellular matrix remodeling (Masson's score: 1.37 ± 0.13 vs. 1.73 ± 0.10 , debanded 12th week vs. AB 12th week, $p < 0.05$) and protected the heart from functional decompensation (ejection fraction: 68 ± 2 vs. $47 \pm 11\%$, fractional shortening: 40 ± 2 vs. $25 \pm 3\%$ debanded 12th week vs. AB 12th week, $p < 0.05$). In addition, the maladaptive contractility augmentation was reversed as reflected by the reduced sensitive, load-independent contractility parameters (slope of end-systolic pressure-volume relationship: 1.39 ± 0.24 vs. 2.04 ± 0.09 mmHg/ml, $p < 0.05$ debanded 12th week vs. AB 6th week, $p < 0.05$).

Conclusion: Our results provide evidence, that the regression of LVH is accompanied by the reduction of pathologically enhanced contractility.