Electrical reverse remodeling following pressure unloading in a rat model of left ventricular hypertrophy

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Introduction: Left ventricular hypertrophy (LVH) is the pathological response reaction of the heart to sustained pressure overload (hypertension, aortic stenosis) and it represents a major risk factor for the manifestation of malignant ventricular tachyarrhythmias and sudden cardiac death. On the other hand, pressure unloading often leads to myocardial reverse remodeling (reduction of increased left ventricular mass, attenuated myocardial fibrosis) which was previously reported to decrease LVH associated proarrhythmic vulnerability as well. However, the responsible mechanisms for the recovery of the adverse electrophysiological changes in LVH during reverse remodeling are still poorly explored.

Purpose: Therefore, we aimed at providing an electrocardiographic characterization of a rat model of LVH undergoing pressure unloading and in parallel indentify the underlying cellular and functional alterations.

Methods: Pressure overload was induced in rats by abdominal aortic banding for 6 or 12 weeks (AB 12th week), while sham operated animals served as controls. Pressure unloading was evoked by removing the aortic constriction after the 6th experimental week (debanded 12th week) to investigate the consequences of reverse remodeling. Serial echocardiography and electrocardiography were performed in order to investigate the development and the regression of LVH. Protein expression levels were detected by western blot technique. Myocardial fibrosis was assessed by Picrosirius red staining.

Results: Pressure unloading resulted in significant reduction of the prolonged QT interval (corrected QT interval: 69.9±2.0 vs. 91.5±1.6ms

debanded 12th week vs. AB 12th week, $p<0.05$), in correlation with the regression of LVH (left ventricular mass: 1.64±0.10 vs. 2.48±0.14mg debanded 12th week vs. AB 12th week, $p<0.05$), and in association with restored Kv4.3 and SERCA2 expression. Furthermore, pressure unloading prevented the functional decompensation of LVH (ejection fraction: 64±1 vs. 45±4% debanded 12th week vs. AB 12th week, $p<0.05$) and simultaneously preserved adequate atrioventricular conduction (PQ interval: 48.1±1.4 vs. 54.0±2.5ms debanded 12th week vs. AB 12th week, $p<0.05$). Finally, pressure unloading effectively preceded the broadening of the QRS complex (QRS complex: 22.2±0.6 vs. 26.0±0.9ms debanded 12th week vs. AB 12th week, $p<0.05$) in parallel with attenuated interstitial collagen accumulation (Picrosirius score: 1.163±0.08 vs. 1.60±0.12 debanded 12th week vs. AB 12th week, $p<0.05$).

Conclusion: Regression of LVH with restored expression of Kv4.3 and SERCA2, maintained cardiac function and decreased myocardial fibrosis contribute to pressure unloading induced electrical reverse remodeling.