

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

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Introduction: Pressure overload-induced left ventricular hypertrophy (LVH) is characterized by increased proarrhythmic vulnerability. In contrast, pressure unloading leads to reverse remodeling and decreases LVH associated arrhythmogenicity. However, the cellular changes during electrical reverse remodeling are less explored.

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

Methods: Pressure overload was induced in rats by abdominal aortic banding (AB) for 6 or 12 weeks, while sham operated animals served as controls. Pressure unloading was evoked by removing the aortic constriction after the 6th experimental week (debanded) 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 staining.

Results: Pressure unloading resulted in significant reduction of the prolonged QT interval (corrected QT interval: 69.9 ± 2.0 vs. 91.5 ± 1.6 ms 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 ± 0.14 mg 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. $45 \pm 4\%$ 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 ± 2.5 ms 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 ± 0.9 ms 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.