

Abstract

In adult heart, pressure overload leads to cardiac hypertrophy. Higher propensity of hypertrophied myocardium to life-threatening arrhythmia is attributed to structural, mechanical and electrical remodeling. Pro-arrhythmogenic remodeling comprise several factors depending on an experimental model and a stage of heart failure. This thesis aims to characterize the impact of these factors in our unique model of pressure overloaded neonatal rat heart.

The constriction of abdominal aorta was performed at postnatal day 2 in male Wistar rats. Decreased body weight, significant since week 6, was observed during development of cardiomegaly. At 12 weeks, the heart to body weight ratio was increased by 45 % and by 109 % in group with compensated (AC I) and decompensated (AC II) heart failure, respectively. At this age, the ECG was recorded and histological and immunohistochemical measurements were performed to analyze the pro-arrhythmogenic remodeling of working myocardium and cardiac conduction system.

The markers of pro-arrhythmogenic remodeling such as significant prolongation of QT and QTc intervals were observed in the ECG recordings of AC II animals. However, spontaneously occurring arrhythmias was not detected. Further analysis of working myocardium showed decrease in Cx43 expression and its phosphorylated form (p-Cx43^{S368}) by 15 % and by 23 %, respectively, compare with Sham animals. Moreover, the negative correlation between the p-Cx43^{S368} expression and severity of heart failure (basen on HW/BW) was observed. The fibrosis content increased 2.5 times compared to Sham operated rats. Analysis of the cardiac conduction system showed remodeling of Purkinje fibers and increase in their diameter by 75 %. All these changes create a pro-arrhythmogenic substrate well known from adult models of pressure overloaded hearts.

Key words: ventricular arrhythmias, neonatal heart, left ventricular hypertrophy, connexin 43, myocardial fibrosis