THE DECOMPENSATION OF SYSTOLIC FUNCTION IN PRESSURE OVERLOAD-INDUCED LEFT VENTRICULAR MYOCARDIAL HYPERTROPHY IS ASSOCIATED WITH UNIQUE MICRORNA EXPRESSION PROFILE

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MicroRNA (miRNA) expression is dysregulated in pressure overload (PO)-induced left ventricular (LV) myocardial hypertrophy (LVH). However, whether the altered miRNA expression might contribute to the decompensation of systolic function in PO-induced LVH is still debated. Thus, we aimed to characterize miRNA expression in PO-induced LVH with and without systolic heart failure (HF).

Aortic banding (AB) was performed in male rats to induce PO. Sham-operated animals served as controls. Functional and morphological alterations were assessed by echocardiography and histology. At the end of the experimental period, rats in the AB group were subcategorized based on ejection fraction [EF] into AB_{LVH} (EF>40%) and AB_{HF} groups (EF<40%). Global miRNA expression profiling was performed using next generation sequencing. Bioinformatic network analysis was carried out to predict miRNA-target interactions. Expression of selected target genes was measured by qRT-PCR.

Increased heart weight-to-tibial length, LV mass and fibrosis confirmed the development of pathological LVH in both AB_{LVH} and AB_{HF} groups. Nevertheless, increased lung weight-to-tibial length, chamber dilatation and impaired EF were noted only in the AB_{HF} group, when compared to controls. 50 miRNA showed different expression in the AB_{HF} compared to the AB_{LVH} group. Based on this altered expression profile, bioinformatic analysis predicted over 3000 target genes. 15 genes with high regulation strength were selected for target validation. Fmr1, Zfpm2, Wasl, Ets1 and Atg16l1 showed decreased mRNA expression levels in the AB_{HF} group versus AB_{LVH}.

Decompensation of systolic function in PO-induced LVH is associated with unique miRNA profile leading to differential gene regulation.

Keywords: heart failure; decompensation; pressure overload-induced left ventricular hypertrophy; microRNA; bioinformatic network analysis