A Small Animal Model of Cardiac Hypertrophy and Heart Failure with Preserved Systolic Function

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Background: Left ventricular hypertrophy (LVH) is a strong predictor of arrhythmias, heart failure (HF) and death. Current therapies for pathological hypertrophy are limited to anti-hypertensive therapy. However, despite these therapies, the incidence of HF is on rise. Furthermore, the underlying molecular and cellular mechanisms of LVH and HF with preserved systolic function remain poorly defined. Thus, we aimed to develop a small animal model of LVH and HF with preserved systolic function to investigate the pathobiology of LVH and HF and to test novel therapies.

Methods and Results: Male salt-sensitive (SBH/y) and salt-resistant (SBN/y) Sabra rats were obtained from colony at the Barzilai Medical Center. Animals received either normal diet (groups SBN/y and SBH/y) or were salt-loaded with deoxycorticosterone-acetate (DOCA) and 1% NaCl as drinking water for 8 weeks. Systolic blood pressure (SBP) was determined in rats by the tail-cuff method. Echo analysis and cardiac magnetic resonance imaging (CMR) and Pressure-volume (PV) loop recording were performed on all rats at weekly intervals, beginning at 4 weeks and continuing for a period of 2 month followed SBP elevation. Echo and CMR showed that although systolic function was preserved, LV mass tended to be higher in the SBH/y DOCA rats compared with SBN/y DOCA rats ($p=0.08$), anterior wall thickness was also higher in SBH/y DOCA rats compared with control ($p=0.01$), Tau, which represents the exponential decay of the ventricular pressure during isovolumic relaxation, was also higher in SBH/y rats with DOCA (Tau-w: $p=0.09$, Tau-g: $p=0.02$), as assessed by PV loop data analysis. Postmortem analysis showed a trend for greater muscle area in SBH/y DOCA rats ($p=0.12$).

Conclusions: The present study establishes a small animal model of LVH and HF with preserved systolic function that can be used to study the molecular and cellular mechanisms that distinguish it from systolic HF and to develop novel therapies against LVH.