



Sex Differences in Morphological and Functional Aspects of Exercise-Induced Cardiac Hypertrophy in a Rat Model

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Background: Recent evidences suggest that sex hormones may be involved in the regulation of exercise-induced left ventricular (LV) hypertrophy. However, the sex-specific functional consequences of exercise-induced myocardial hypertrophy is still not investigated in detail. We aimed at understanding the sex-specific functional and morphological alterations in the LV and the underlying molecular changes in a rat model of athlete's heart.

Methods: We divided our young, adult male and female rats into control and exercised groups. Athlete's heart was induced by a 12-week long swim training. Following the training period, we assessed LV hypertrophy with echocardiography, while pressure-volume analysis was performed to investigate *in vivo* LV function. After *in vivo* experiments, molecular biological studies and histological investigations were performed.

Results: Echocardiography and post-mortem measured heart weight data indicated LV hypertrophy in both genders, nevertheless it was more pronounced in females. Despite the more significant relative hypertrophy in females, characteristic functional parameters did not show notable differences between the genders. LV pressure-volume analysis showed increased stroke volume, improved contractility and stroke work and unaltered LV stiffness in both male and female exercised rats, while active relaxation was ameliorated solely in male animals. The induction of Akt signaling was more significant in females compared to males. There was also a characteristic difference in the mitogen-activated protein kinase pathway as suppressed phosphorylation of p44/42 MAPK (Erk) and mTOR was observed in female exercised rats, but not in male ones. Myosin heavy chain α (MHC)/ β -MHC ratio did not differ in males, but increased markedly in females.

Conclusion: Our results confirm that there is a more pronounced exercise-induced LV hypertrophy in females as compared to the males, however, there are only minor differences regarding LV function. There are characteristic molecular differences between male and female animals, that can explain different degrees of LV hypertrophy.

Keywords: athlete's heart, exercise-induced hypertrophy, pressure-volume analysis, left ventricular function, sex differences