

Exhaustive physical exercise induces myocardial oxidative damage and left ventricular functional impairment in a rat model

Authors:

A. Olah¹, B.T. Nemeth¹, C. Matyas¹, L. Hidi¹, E. Birtalan¹, D. Kellermayer¹, M. Ruppert¹, M. Torok¹, B. Merkely¹, T. Radovits¹, ¹Semmelweis University, Heart and Vascular Center - Budapest - Hungary,

Topic(s):

Exercise testing and training

Citation:

European Heart Journal (2014) 35 (Abstract Supplement), 733

Purpose: The role of physical exercise in the prevention and treatment of cardiovascular diseases has been well-described, even though elevations in cardioneurotic biomarkers after prolonged exercise (i.e. ultramarathon running) were observed. We aimed to establish and validate a rat model of acute exhaustive exercise and determine the biochemical, molecular biological, structural and functional alterations in the heart.

Methods: Rats of the exercise group were forced to swim for 3h with 5% body weight (workload) attached to the tail, control rats were taken into the water for 5min. 2 hours after completion of swimming we performed left ventricular (LV) pressure-volume analysis using a pressure-conductance microcatheter to investigate LV function and mechanoenergetics. Additionally, blood and myocardium samples were harvested for biochemical and histological examination. Alterations of gene expressions were detected using qRT-PCR.

Results: When compared to controls, elevated plasma levels of cardiac troponin T (0.131 ± 0.022 vs. 0.025 ± 0.006 ng/ml, $p < 0.001$), creatine kinase, transaminases and lactate dehydrogenase were detected after exhaustive exercise. Histological analysis showed sporadic fragmentation of myocardial structure, tissue edema and leukocyte infiltration. Myocardial gene expression analysis showed a significant increase of endogenous antioxidants (thioredoxin-1: 1.24 ± 0.07 vs. 1.01 ± 0.04 , $p < 0.05$) and dihydroethidium staining indicated robust generation of superoxide anions after exhaustive exercise. We found a markedly significant augmentation of Bax/Bcl-2 ratio (1.80 ± 0.18 vs. 1.04 ± 0.03 , $p < 0.01$) and the proapoptotic activity was confirmed by semiquantitative analysis of TUNEL staining. Dysregulation of the matrix metalloproteinase (MMP) system (MMP-2/TIMP-2 (tissue inhibitor of matrix metalloproteinase-2) ratio: 1.46 ± 0.08 vs. 1.05 ± 0.03 , $p < 0.01$) was observed after exhaustive swimming. We observed increased end-systolic volume, decreased ejection fraction (48 ± 5 vs. $59 \pm 3\%$, $p < 0.001$), impaired contractility (end-systolic elastance: 0.70 ± 0.07 vs. 0.95 ± 0.07 mmHg/ μ l, $p < 0.05$) and mechanoenergetics (mechanical efficiency: 48 ± 2 vs. $59 \pm 2\%$, $p < 0.001$) of LV in the exercise group.

Conclusions: Excessive physical activity has an adverse effect on the heart. Enhanced oxidative stress and apoptotic signalling as well as MMP dysregulation could underly the elevation of myocardial necrotic markers. The characteristic molecular and histological alterations are associated with impairment of LV systolic function, contractility and mechanoenergetics.