PPARA and NRF2 Polymorphisms are Associated with Exercise Capacity in Trained Heart Failure Patients

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Background: Peroxisome proliferator-activated receptors (PPARs) and nuclear respiratory factors (NRFs) are associated with abnormal substrate metabolism and oxidative phosphorylation in heart failure.

Aims: the aim of the present study was to investigate whether polymorphisms in the PPARA (rs1800206, rs4253778), PPARD (rs2016520) and NRF2 (rs12594956) genes have an impact on exercise tolerance at baseline and in response to exercise training in HF patients.

Methods: A total of 61 patients with HF completed a 6-month exercise-training programme. Exercise tolerance (METs) was assessed before and after exercise training. Polymorphisms were detected with restriction fragment length polymorphism analysis.

Results: At baseline, there were no differences between genotypes in exercise tolerance. In contrast, training-induced increase in exercise tolerance was more pronounced in PPARA 162Val carriers than in 162Leu homozygotes (0.88 ± 0.81 METs vs. 0.41 ± 0.51 METs, $P = 0.032$). Moreover, exercise training increased exercise tolerance in NRF2 AA (from 3.9 ± 1.3 to 4.5 ± 1.5 METs, $P<0.05$) and AC genotype carriers (from 4.0 ± 1.0 to 4.6 ± 1.3 METs, $P<0.05$), but not in G allele homozygotes (from 4.5 ± 0.7 to 4.7 ± 0.8 METs, n.s). No differences were found for the other polymorphisms.

Conclusions: This study suggests that PPARA Leu162Val and NRF2 A/C SNPs are associated with the training response in heart failure patients.