Effect of exercise training on vascular function and endothelial repair in heart failure with preserved ejection fraction: results from the OptimEx trial

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Background: Exercise training improves peak oxygen uptake (VO2) in heart failure with preserved ejection fraction (HFpEF), but the underlying mechanisms are unknown. In other cardiovascular diseases, exercise training improves vascular function and increases levels of circulating endothelium-repairing cells. We aimed to investigate the effects of moderate continuous training (MCT) and high intensity interval training (HIIT) on vascular function and cellular endothelial repair in HFpEF.

Methods: This was a prespecified subanalysis of the Optimizing Exercise Training in Prevention and Treatment of Diastolic Heart Failure randomized trial. HFpEF patients (n=180) were randomized to HIIT, MCT or attention control. At baseline and after 12 weeks, we measured peak VO2, fingertip arterial tonometry (n=109), brachial artery flow-mediated dilation (n=59), aortic pulse wave velocity (n=94), and flow cytometry (n=136) for endothelial progenitor cells (CD45dimCD34+VEGFR2+) and angiogenic T cells (CD3+CD31+CD184+). Changes in these parameters were compared between groups using linear mixed models. Parameters were correlated using Spearman's rho.

Results: At 3 months, we did not observe significant differences between HIIT, MCT and control group regarding changes in vascular function throughout the vascular tree (fingertip arterial tonometry, brachial artery flow-mediated dilation and central arterial stiffness, Table 1) or levels of circulating endothelium-repairing cells (endothelial progenitor cells and angiogenic T cells, Table 1). Results were similar at 12 months and when restricting analysis to patients with at least 70% adherence to training sessions. Patients with higher peak VO2 at baseline had lower numbers of circulating endothelial progenitor cells (rho=–0.22, p=0.011).

Conclusions: In patients with HFpEF, exercise training did not change vascular function or levels of endothelium-repairing cells. Thus, improved vascular function likely does not contribute to the change in peak VO2 after training. These findings are in contrast with the benefits of exercise on vascular function in heart failure with reduced ejection fraction and coronary artery disease.

Change from baseline to 3 months, mean (SD)	*HIIT*	*MCT*	*Control*	*P value time:group interaction*
Peak VO_2 (mL/kg/min)	+1.1 (3.0)	+1.6 (2.5)	-0.6 (3.3)	.001
Fingertip arterial tonometry (reactive hyperemia index)	+0.07 (0.92)	+0.08 (0.75)	+0.05 (0.77)	.902
Brachial artery flow-mediated dilation (%)	+1.2 (4.5)	-1.1 (2.3)	+0.5 (4.2)	.142
Aortic pulse wave velocity (m/s)	-0.4 (1.0)	-0.9 (2.6)	-0.5 (1.2)	.910
Endothelial progenitor cells (per 10^6 mononuclear cells)	-2 (43)	+14 (50)	0 (44)	.197
Angiogenic T cells (per 10^6 mononuclear cells)	-90 (2301)	+389 (2277)	-47 (2499)	.915

Table 1