Exercise intolerance in volume overload heart failure is associated with low carotid body mediated chemoreflex drive

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## Abstract

Mounting an appropriate ventilatory response to exercise is crucial to meeting metabolic demands, and abnormal ventilatory responses may contribute to exerciseintolerance (EX-inT) in heart failure (HF) patients. We sought to determine if abnormal ventilatory chemoreflex control contributes to EX-inT in volume-overload HF rats. Cardiac function, hypercapnic (HCVR) and hypoxic (HVR) ventilatory responses, and exercise tolerance were assessed at the end of a 6 week exercise training program. At the conclusion of the training program, exercise tolerant HF rats (HF + EX-T) exhibited improvements in cardiac systolic function and reductions in HCVR, sympathetic tone, and arrhythmias. In contrast, HF rats that were exercise intolerant (HF + EX-inT) exhibited worse diastolic dysfunction, and showed no improvements in cardiac systolic function, HCVR, sympathetic tone, or arrhythmias at the conclusion of the training program. In addition, HF + EX-inT rats had impaired HVR which was associated with increased arrhythmia susceptibility and mortality during hypoxic challenges (~ 60% survival). Finally, we observed that exercise tolerance in HF rats was related to carotid body (CB) function as CB ablation resulted in impaired exercise capacity in HF + EX-T rats. Our results indicate that: (i) exercise may have detrimental effects on cardiac function in HF-EX-inT, and (ii) loss of CB chemoreflex sensitivity contributes to EX-inT in HF. © 2021, The Author(s).