

CORRESPONDENCE

Letters to the Editor

Is Ventilation Efficiency an Additional Target of Exercise Training Benefits in Heart Failure With Preserved Ejection Fraction?

We read with interest the remarkable results by Edelmann et al. (1) on the case series of patients with heart failure (HF) with preserved ejection fraction (HFpEF) undergoing a program of exercise training (ET). The researchers should be congratulated for providing this unique demonstration of the benefits of a regular physical activity program in this setting.

Our interest primarily focuses on the improvement in symptom-limited exercise capacity assessed by gas exchange analysis, and we would like to ask for some informative notes about how and whether regular exercise may have prompted any potential improvement in the ventilatory response to maximal exercise. As stressed in the accompanying editorial, peak oxygen consumption (VO_2) is objective and provides a reliable level of overall exercise performance; however, the amount of information derived by cardiopulmonary testing is actually much broader (2). Specifically, an abnormal ventilatory efficiency (i.e., an increased slope of ventilation [VE] vs. CO_2 production rate [VCO_2]) rather than peak VO_2 has been identified as a peculiar feature of an abnormal physiology behind exercise limitation in HFpEF (3,4), and the degree of ventilation efficiency in diastolic HF is actually prognostic (5). There is some evidence on how ventilation efficiency may be positively modulated by ET programs in patients with systolic HF (6).

The researchers reported that maximal ventilatory exchange, although increased, did not significantly change after ET, but it would be helpful to know whether the VE versus VCO_2 slope was actually improved. Indeed, an improved VE versus VCO_2 slope, in the presence of no major changes in maximal ventilatory exchange, would suggest, for similar levels of increasing exercise load, a better matching between exercise catabolic products (CO_2) and their elimination.

A potential improvement in the pattern of ventilation efficiency might relate to the observed changes in left ventricular diastolic function, providing further progress on the level of evidence of benefits by ET interventions in HFpEF syndrome.

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Reply

In response to the comment by Drs. Guazzi and Vitelli regarding our paper (1), we provide further details of the multicenter Ex-DHF (Exercise Training in Diastolic Heart Failure) pilot study investigating exercise training in heart failure with preserved ejection fraction (HFpEF). We agree with Drs. Guazzi and Vitelli that cardiopulmonary testing even in a trial that is investigating exercise training allows collecting more information than changes in peak oxygen consumption (VO_2). Drs. Guazzi and Vitelli demonstrated that beyond reduced peak VO_2 , disturbed ventilatory efficiency measured as increased ventilation (VE)/carbon dioxide output (VCO_2) slope is of prognostic relevance also in patients with HFpEF (2). However, the extent of the decrease in ventilatory efficiency in HFpEF seems to also depend on disease severity (2). Despite the relevant decreased peak VO_2 in our HFpEF cohort, the mean baseline VE/ VCO_2 slope values (27.2 ± 2.9) were better than those reported by others (2–4). Of note, the values measured in our pilot trial suggested overall preserved ventilatory efficiency despite our patients fulfilling the strict criteria of the European Society of Cardiology guidelines for the diagnosis of HFpEF (1). After 3 months of follow-up, no significant changes in either group or changes between the 2 groups were observed (training group 27.6 vs. 27.6, $p = 0.98$; control group 26.3 vs. 27.0, $p = 0.17$; the difference between groups was adjusted for baseline values: $-0.5, -2.4$ to $+1.5, p = 0.63$). Similar results have been obtained also by others (3,4). Interestingly, like Kitzman et al. (4), we observed increased values of VCO_2 after exercise training (training group 1.78 vs. 1.90 l/min, $p = 0.06$; control group 1.82 vs. 1.68 l/min, $p = 0.13$; the difference between groups was adjusted for baseline values: $+0.26, +0.04$ to $+0.48, p = 0.02$), and we found that this increase was significantly correlated with a decrease in E/e' ($r = -0.29, p = 0.03$).