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INVITED EDITORIAL

Exercise training in heart failure with preserved ejection fraction patients: the importance of resistance training

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Chronic heart failure with preserved ejection fraction (HFpEF) is the dominant form of HF, with an increasing prevalence and until recently very limited management options (e.g. diuretics, gliflozins, and incretin therapies).[1] Exercise intolerance (EI) presents one of the most common symptoms of HFpEF and is associated with a decreased quality of life (QoL) and increased risk of HF-related hospitalization and mortality.[1] The pathophysiology of EI is however complex and consists of pulmonary, skeletal muscle, vascular, and cardiac abnormalities that can substantially impact cardiac output, oxygen transport, and utilization to the exercising muscles, thereby leading to a substantial reduction in peak oxygen consumption (peak VO_2) and muscle strength.[1] This multiorgan dysfunction cannot be remediated by cardiovascular pharmacotherapy or cardiac implantable electronic devices only; therefore, optimal lifestyle management strategies are needed as well to improve the EI-related symptoms and outcomes.[1]

Exercise training (ET), as part of cardiac rehabilitation (CR), may alleviate the symptoms of HFpEF and has been associated with superior improvements in (sub)maximal aerobic capacity, muscle strength, and QoL and decreases the risk of all-cause and HF hospitalization in HF patients.[2] Current evidence on ET in CR was established on mostly patients with HF with reduced EF (HFrEF),[2] while the evidence in HFpEF patients is growing. Recently completed studies have demonstrated superior effects of moderate-intensity continuous or high-intensity interval aerobic training (AT) alone or combined with resistance training (RT) on peak VO_2 over standard care alone.[3,4] While these studies have provided important information for improving exercise-based CR in HFpEF, there may be (emerging) ET approaches that should be adopted for this patient group. For example, recent evidence suggests that moderate-to-high load RT [MHL-RT; 55–80% of one repetition maximum (1-RM)] is safe and can provide greater benefits on peak VO_2 and maximal muscle strength, compared with AT alone in coronary artery disease (CAD) patients.[5] Therefore, it remains interesting to assess whether the implementation of MHL-RT may provide additional benefits on exercise performance in HFpEF patients.

In this issue of the *European Journal of Preventive Cardiology*, Palau *et al.*[6] sought to determine the effects of novel ET approaches on improving symptoms of EI in HFpEF patients, all with chronotropic incompetence (chronotropic index <0.62 or <0.80 for patients previous on or without β-blocker therapy, respectively). The novelty of this paper is that the authors for the first time targeted the chronotropic incompetence with supervised ET intervention. In the study, the authors randomized 80 HFpEF patients to *exercise counselling alone* (counselling on regular unsupervised aerobic and resistance exercise), *high-intensity AT alone* (twice weekly, intervals of 1 min of high-intensity aerobic exercise separated by 2 min of active recovery), *combination of inspiratory muscle training* (20 repetitions at 40–60% of maximal inspiratory pressure performed twice daily), *AT and low-load RT (LL-RT)* (3 sets of 20 repetitions at 30–50% of 1-RM performed twice weekly), or *MHL-RT* (3 sets of 12 repetitions at 55–75% of 1-RM performed twice weekly). The study assessed changes in peak VO_2 (mL/kg/min and %), QoL, chronotropic response, and safety of and adherence to exercise intervention. After 12 weeks of intervention, all three supervised ET groups improved peak VO_2max, health-related QoL, and chronotropic response to a greater extent when compared with exercise counselling alone. The combination of home-based inspiratory muscle training with supervised AT and MHL-RT was superior to AT alone on the improvement in peak VO_2, while all supervised ET interventions induced similar improvements in QoL and chronotropic response, with 38% of the patients in the ET groups restoring their chronotropic response. In addition, all ET interventions were safe, well tolerated (all patients completed more than 83% of prescribed ET sessions) with no adverse cardiovascular events.

This study elegantly presents several novel insights into the benefits of concurrent ET methods (e.g. combination of AT and RT) to tackle the highly prevalent EI symptoms of HFpEF patients. First, the study clearly shows that supervised ET should be offered for HFpEF patients instead of exercise counselling alone that showed no clinical benefits. Second, this study demonstrates the importance of combining AT

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with MHL-RT to additionally improve peak VO_2, compared with the traditionally used AT in HFpEF patients.[6] The high adherence to and safety of both types of combined AT with RT[6] indicate a successful translation of potent novel ET approaches previously used in CAD and HFrEF patients[7] to HFpEF patients, which expands the ET approaches in CR. Third, the present study is also one of the first that examined the effects of concurrent ET in subgroup of HFpEF with CI, which is one of the leading causes of EI.[1] Therefore, it was great to see the huge positive impact of different ET interventions used in the study[6] on improving such symptoms that can worsen exercise performance and impact QoL and daily functioning. This can allow clinicians to select different ET approaches (AT alone, AT and LL-RT, or AT and MHL-RT) in early stages of exercise-based CR to optimally alleviate EI symptoms in HFpEF patients according to their baseline physical abilities. Third, this study also highlights that the dose of RT in combination with AT matters in HFpEF patients. The study used the highest RT load to date (70% of 1-RM) in combination with high-intensity AT and demonstrated a greater improvement in peak VO_2 (2.3 vs. 1.3 mL/kg/min) compared with a recently published study that used lower RT load (60% of 1-RM) in combination with AT.[4] In addition, this study consisted of mostly female patients with HFpEF (58%)[6]; therefore, it was great to observe that the combination of AT and MHL-RT may provide similar improvement in females when compared with male patients who have more prevalent HFrEF (82%).[8] Therefore, the study findings present an additional step towards improving enrolment and adherence of females with HF in exercise-based CR and thus closing the gender gap.

While the study of Palau *et al.*[6] extended our knowledge on the effects of concurrent ET in HFpEF patients, there are also some limitations that can be addressed in the future randomized controlled trials. First, the cause of CI, and ET might affect this deserves deeper investigation in HFpEF patients, as this may lead to new therapeutic strategies (including pharmacotherapy). For example, it remains to be clarified how the chronotropic response can be improved after exercise intervention: is it the result of changes in sinus node function, changes in catecholamine release during exercise, changes in sympathetic and vagal tone during exercise, or changes in exercise pressor reflex? Second, when comparing different types of RT, it is vitally important to include assessments of body composition and (sub)maximal muscle strength to evaluate changes in muscle quality and quantify, especially with high prevalence of sarcopenic obesity in HFpEF patients.[9] Data on changes of muscle strength would allow clinicians to better differentiate between effects of LL-RT and MHL-RT in HFpEF, as was previously established in CAD and HFrEF patients.[7] Future studies should also consider improving progression and balancing of RT workload (total workload during RT = number of sets × number of repetitions × load at % of 1-RM)[5] between LL-RT and MHL-RT to exclude potential mismatch in cumulative RT load between both RT modalities that might impact the exercise performance outcomes. Furthermore, it is also important to test whether the translation from traditional AT prescription based on percentage of peak effort to prescription based on ventilatory or lactate thresholds may be more optimal AT option for HFpEF patients.[10]

In conclusion, the translation of multimodal ET interventions from CAD and HFrEF patients was associated with improvements of EI, maximal aerobic performance, and QoL over traditionally used AT alone in HFpEF patients. Future trials are warranted to explore the effects of multimodal ET modalities on (sub)maximal muscle strength, body composition, and blood biomarkers of cardiometabolic health and inflammation in order to further reduce the burden of HFpEF.

Author's contribution

All authors contributed to the conception or design of the work. T.K. drafted the manuscript. D.H. critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Data availability

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