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EDITORIAL COMMENT

Bringing Cardiac Rehabilitation and Exercise Training to a Higher Level in Heart Failure*

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Considerable evidence, including that recently reviewed in the *Journal* (1), indicates a very high prevalence of physical inactivity and sedentary behavior and lack of physical activity and exercise training (ET) in the United States and much of the world. Simply stated, many people move too little (i.e., prolonged sitting time, too few steps, and no ET program) throughout the day (2). Certainly, there are numerous benefits of physical activity and ET for primary and secondary prevention of cardiovascular disease (CVD) (1-4). Although cardiac rehabilitation and ET (CRET) have been the standard of care for patients with coronary heart disease (CHD) for decades (1,3,4), this intervention, which is supported by a Class IA indication, is still very underused. Only in recent years has CRET therapy reached the frontline in patients with heart failure (HF) (5); in the United States, HF is now typically a covered diagnosis for CRET services, but CRET remains drastically underused in HF patients.

The HF-ACTION (Exercise Training Program to Improve Clinical Outcomes in Individuals With Congestive Heart Failure) trial was a multicenter, randomized control trial involving 2,322 patients treated for HF in 82 clinical centers; the HF patients included in this study all had an ejection fraction (EF) 35% or lower (6). Over a median follow-up of 30 months, patients randomized to CRET had an 11% reduction in mortality or hospitalizations ($p = 0.03$), although these results were considerably less than predicted, likely due to the lower increase in peak oxygen consumption (V_{O_2}) than expected (only 4% improvement compared with the expected 10% to 15% improvement in peak V_{O_2}), which was likely due to suboptimal compliance with the ET prescription. However, this study demonstrated significantly greater improvements in those who were more compliant with the ET prescription and who had significantly greater increases in their peak V_{O_2} with the ET (7). In patients with CHD, improvements in prognosis and mortality are strongly related with improvements in exercise capacity (8,9), and this also seems to be the case in HF patients with reduced EF (HFrEF) (10).

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In the present study in this issue of the *Journal* from Taylor et al. (11), which includes many of the top ET and HF experts worldwide, investigators assessed the impact of CRET compared with a no ET control group in 13 trials of 3,990 patients with HF, predominantly (97%) with HFrEF. They demonstrated that CRET therapy resulted in significant increases in exercise capacity, assessed by peak V_{O_2}, 6-min walk test (6MWT), incremental shuttle walk test, or cycle ergometry (Watts), as well as health-related quality of life (HRQoL), thus confirming the benefits of CRET therapy on exercise capacity and HRQoL in HFrEF and supporting the idea that CRET should potentially be offered to all HF patients. Although the gold standard for assessing exercise capacity in HF is cardiopulmonary exercise testing, which includes ventilatory expired gas analysis and direct measurement of peak

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$\dot{V}O_2$, Forman et al. (12) previously suggested that the 6MWT predicted prognosis as well as cardiopulmonary exercise testing. Interestingly, 6MWT increased significantly in the mid-analysis, whereas peak $\dot{V}O_2$ did not. We have recently demonstrated in nearly 1,200 patients with CHD that 23% did not significantly improve their peak $\dot{V}O_2$ with CRET, and these patients, considered nonresponders, had a significantly higher mortality (9). Although the investigators stated that they do not have ET compliance data in their current study (11), it is likely that noncompliance to the ET prescription influenced the improvements in exercise capacity, including peak $\dot{V}O_2$, following ET. In non-HF populations, higher volume and intensity of ET markedly reduced the nonresponse phenomenon (13), and certainly high-intensity interval training may result in better improvement in exercise capacity and prognosis in various groups of patients, including those with HFrEF (14,15).

It should be emphasized that this was almost entirely (97%) a study of HFrEF, as only 3% of the population were diagnosed with HF with preserved EF (HFpEF). However, other studies clearly show significant effects of ET in patients with HFpEF (16,17), although the mechanisms by which fitness improves with ET in HFpEF (peripheral mechanisms) differ from HFrEF (peripheral and central) and is an area of interest that warrants further investigation (17). Additionally, compelling data have recently been presented demonstrating the additional effects of diet and ET to improve fitness and lean muscle mass in patients with HF (18), suggesting that a multidimensional lifestyle intervention may contribute to more robust health outcomes.

Although improvements in exercise capacity, major morbidity, and mortality are generally viewed as more desirable outcomes in clinical trials, improvements in psychological risk factors and HRQoL should not be overlooked as important endpoints in patients with CVD, including HF (19–21). Clearly, many CVD patients have psychological distress, including depression, which is associated with worse clinical outcomes, and these symptoms dramatically improve following CRET (19,21). In patients with HFrEF in the HF-ACTION study, CRET therapy was associated with modest reductions in depression (22). However, with more significant improvements in peak $\dot{V}O_2$, reductions in depression may be more dramatic and associated with significant reductions in depression-associated increased mortality rates (21).

A significant issue with ET studies, including CRET, is the issue of nonresponse (8–10,13). In the current report (11), older, male, and nonwhite patients had less of an improvement in exercise capacity following CRET. We have previously addressed this as a potential health disparity risk factor in African Americans, who typically have lower baseline levels of fitness and less response to ET programs (23–25). Certainly, further studies targeting nonresponders or under-responders to ET with higher volumes and intensity of ET, including high-intensity interval training, are needed in many groups of patients, including those with HF. Targeting high-risk ethnic groups, such as African Americans, is particularly needed in ET studies, including HFrEF and HFpEF. Also, it is likely that patients with HFpEF, who currently are not commonly covered for CRET therapy in the United States, will likely also benefit from this therapy regarding major morbidity, mortality, hospitalizations, exercise capacity, and HRQoL, but this requires further study. Additionally, the recent statement (26) on the importance of exercise progression throughout the CRET program should also be emphasized and, if followed, could improve overall CRET outcomes in HF. In closing, we applaud this world class group of ET and HF authors on increasing the awareness of the profound potential benefits of CRET therapy in HF, bringing the evidence base to a higher level in secondary HF prevention (11).

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