Formal Cardiac Rehabilitation and Exercise Training Programs in Heart Failure

EVIDENCE FOR SUBSTANTIAL CLINICAL BENEFITS

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Heart failure (HF) is a major cause of morbidity and mortality in the United States (US) and most of the world. In the US, there are nearly 650,000 new cases of HF diagnosed annually, with an incidence markedly increasing with age, and HF is a leading cause of hospitalizations and disability in our elderly population, who account for nearly 75% of this chronic disease population in the US.1

A hallmark of HF is reduced exercise tolerance, leading to significant reductions in physical function and quality of life (QOL).2 We applaud the recent work from the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) for their excellent and detailed update on Guidelines for the Management of HF.1 Of particular interest were the recommendations regarding exercise training (ET) and, specifically, formal cardiac rehabilitation (CR) programs for patients with HF.

Exercise and functional capacity are markedly reduced in HF, resulting in symptoms of exertional fatigue and dyspnea at an oftentimes low workload, as well as reduced QOL and increased depression.1,3 Although reductions in cardiac output were originally hypothesized as being the sole limiting factor to exercise performance in HF,1,4 secondary changes in skeletal muscle, vasculature, and pulmonary function also play critical roles in the pathogenesis of HF symptoms and represent a potential therapeutic target for benefits with ET programs.2

EXERCISE TRAINING IN HEART FAILURE

In patients with HF, especially with HF and reduced ejection fraction (HFrEF) or systolic dysfunction, ET has many potential benefits, including improvements in peak oxygen uptake (VO2), central hemodynamics, peripheral vascular and skeletal muscle function, autonomic nervous system function, and overall functional capacity.2 The majority of ET studies in HF have demonstrated approximately 15–17% improvements in peak VO2.6,7 Several trials have also suggested that ET produces...
significant impact on morbidity and mortality in HF. The ExTraMATCH meta-analysis of 9 studies in 801 patients with HF demonstrated a 35% reduction in mortality in those patients who underwent ET compared with non-ET controls during a nearly 2-year followup.\(^8\) A more recent Cochrane Review of 19 trials in 3647 participants, however, showed a nonsignificant trend toward mortality reduction in the trials with >1 year followup, and a significant (28%) reduction in hospitalization rates at 1 year was noted with the ET programs,\(^9\) suggesting that these programs would be quite cost-effective by reducing expensive hospital admissions.

Probably the most well-known study of ET in HF is the recent HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training), which was a multicenter, randomized controlled trial in 2333 class II-IV HF patients with systolic HF. Patients were randomized to either 36 sessions of supervised, moderate-intensity (60–70% of heart rate reserve) ET followed by home-based ET or usual care.\(^10\) After a median followup of 30 months, a nonsignificant 7% reduction in the combined endpoint of all-cause mortality or hospitalizations was noted, but after adjustment for prespecified predictors of mortality, this primary endpoint was significantly reduced by 11%. Unfortunately, the median improvement in peak VO\(_2\) was only 4%, reflecting a relatively low adherence to ET in the intervention group, where only approximately 30% exercised at their target training level minutes per week. This increase in peak VO\(_2\) was markedly lower than the expected 10–15% or greater improvement in peak VO\(_2\) noted in earlier studies and meta-analyses.\(^10,11\) Nevertheless, in HF-ACTION, the authors noted a close relationship between volume of ET and clinical prognosis, with a 30% reduction in mortality and hospitalizations noted in the subgroups who achieved their ET prescription guidelines.\(^11\) Numerous ET studies have also demonstrated clinical benefits in patients with HF and preserved ejection fraction (HFpEF).\(^2\) Based on this considerable body of data, ET was recommended by the ACCF/AHA as a class I level in 2005,\(^12\) which was confirmed in these latest guidelines.\(^1\)

### Cardiac Rehabilitation in Heart Failure

Although the hallmark of CR secondary prevention programs is ET, experts in this field recognize that CR represents a multidisciplinary approach to secondary prevention that goes well beyond simply ET and provides valuable counseling and education to patients with a goal of improving QOL, exercise capacity, mortality, and hospitalizations,\(^13\) well beyond that provided in primary ET studies such as HF-ACTION.

Clearly, CR programs have been extremely valuable in the management of patients with HF. In fact, in an analysis of over 600,000 Medicare beneficiaries, a subgroup analysis of patients with HF demonstrated a 15% lower mortality rate in those who attended CR compared to a matched cohort who did not attend CR.\(^14\) Moreover, there was a strong dose effect for CR, with those attending more sessions having a greater mortality reduction similar to that seen in HF-ACTION. Recently, Davidson et al\(^15\) conducted a randomized, control trial to assess a multidisciplinary CR program on hospitalizations, functional capacity, and self-care. The program was nurse-coordinated and included ET and coordination around self-management, which was directed at assessing and monitoring signs of decompensation in HF status. During followup, CR patients showed greater improvements in exercise capacity (as determined by the 6-Minute Walk Test, which has been shown to be a statistically significant surrogate for peak VO\(_2\) in predicting prognosis in advanced HF\(^16\)), and were more likely to be on evidence-based therapies. At 12-month followup, those randomized to CR had lower decompensation of HF (24% vs 55%, \(P = .001\)), hospitalizations (44% vs 69%, \(P = .01\)), and mortality (7% vs 21%, \(P = .03\)). These data support the value of comprehensive CR, beyond just ET, in the management of patients with HF.

Additionally, long-term supervised moderate ET programs performed twice weekly for 10 years were shown to maintain functional capacity and improve QOL in patients with HF.\(^17\) Moreover, these sustained improvements were associated with lower cardiac events, including reductions in hospitalization (~36%; \(P < .001\)) and cardiac mortality (~32%; \(P < .001\)), suggesting long-term benefits from ET in a supervised CR setting for patients with HF, similar to phase III CR.

### Major Heart Failure Recommendations

Although we were overall delighted with the very strong recommendation for ET in the recent HF guidelines (Ia recommendation) and the overall favorable ranking for CR (IIa-B), we were somewhat disappointed that this latter level of recommendation did not meet the Ia level or at least the IIa-A level (as there certainly are many studies supporting this therapy). In all likelihood, the less than ideal clinical event reduction noted in HF-ACTION may have tempered the level of recommendation provided. However, the lack of formal CR-type supervision and relatively low
adherence to ET guidelines, as well as the lack of non-ET education and counseling in HF-ACTION, which is quite different than formal CR, in our opinion, is not surprisingly led to far less benefits in HF-ACTION than that typically obtained with formal, phase II CR. Also, the improvement in peak VO2 in formal CR programs in HF patients would typically be in the 10–15% range, more consistent with the level of improvement associated with marked clinical event and mortality reductions.

In summary, substantial evidence supports ET and formal CR in patients with HF. In all likelihood, the benefits of formal CR in HF, with improvements in overall cardiorespiratory fitness and psychological risk factors, including depression,18–20 as well as the intensive education and counseling directed at HF management, will lead to marked reductions in cardiovascular events, mortality, and hospitalizations in HF, similar to that noted for decades in coronary heart disease.

References