Exercise Training for Heart Failure
Coming of Age

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We have known for many years of the benefits of an exercise component in cardiac rehabilitation. It was initially thought that significant left ventricular impairment was a contraindication to participation in such programs. In fact, in heart failure, there was a vogue for and reports of the beneficial effects of prolonged bed rest. It is against this background that a few challenging reports emerged in the early 1980s that selected patients with significant left ventricular impairment had in fact participated in exercise programs and had achieved training responses with increased exercise capacity. It was not until the late 1980s, however, that the first reports of training patients with a history of chronic heart failure (CHF) emerged. Pioneering work from Duke University showed a significant enhancement in exercise capacity and ancillary physiological benefits, including reduced lactate production, improved use of ventilatory reserve, and increased leg blood flow during progressive exercise. This was quickly followed by the first prospective controlled trial of exercise training in CHF, an 11-patient crossover study of home-based exercise training using a cycle ergometer for 8 weeks versus a similar period of activity restriction. The result was an improvement in exercise capacity and an improvement in questionnaire-based heart failure–related symptoms. The era of training as a treatment of heart failure had begun.

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In the decade following these first reports, there have been a profusion of small trials and a long list of impressive physiological gains that could be achieved. These included increased peak oxygen consumption, an increase in peak cardiac output (in some but not all trials), and improvement in the autonomic control of the circulation with a reduction in sympathetic nervous system activity and an enhancement in vagal activity. More recent reports have documented an increase in endothelial function and in skeletal muscle biochemical and histological characteristics and improvements in patients’ perceptions of their quality of life and symptom severity. These training benefits have been shown against a background of increasing interest in and realization of the importance of secondary peripheral manifestations of the syndrome of CHF. The importance of neurohormonal overactivity has been recognized for a decade, but the importance of other changes, such as altered and wasted skeletal muscle and a host of major metabolic disturbances in CHF, are only now being appreciated. These include insulin resistance, deficient insulin-like growth factor-1, immune activation and cytokine release, endothelial dysfunction, and baroreflex, chemoreflex, and muscle ergoreflex (metaboreflex) alterations, all of which have the capacity to worsen the symptoms and prognosis of the heart failure patient and all of which at least in theory might be improved by a customized training program. It is against this background that exercise training (given its diverse and metabolically powerful effects) is being viewed as an exciting potential therapy for stable CHF patients.

The results of training in heart failure, however, have not been uniform. In the setting of a recent myocardial infarction, in particular, early reports stressed caution. Early fears that training after an MI in those with large infarcts could worsen left ventricular asynergy have not been confirmed by later, better-designed studies, which showed that these patients could train safely and improve their exercise capacity, as shown by the EAMI study group. In a second study by this group (ELVD), in fact, they actually showed an improvement in the harmful process of left ventricular remodeling by participation in a structured exercise rehabilitation program. It is easy to see how the chronic reduction in sympathetic tone could improve the remodeling process, and this may be more important in the long term than the short durations of the exercise necessary to achieve this increased fitness.

Wilson et al described a proportion of his patients who either were unable to complete an exercise program or achieved no increase in exercise capacity from so doing. These patients seemed to be those with limiting cardiac output rather than those limited by secondary changes in the periphery, such as impaired peripheral vasodilatory capacity or impaired skeletal muscle function. This distinction is quite plausible, because training does appear to achieve the majority of its beneficial effects through peripheral mechanisms with little or no effect on resting left ventricular function. More recent reports have suggested that some patients with ischemic cardiomyopathy may be able to increase their collateral blood flow to the myocardium as measured by perfusion scanning. Similar results were also seen in the study by Belardinelli in this issue of Circulation, to which this editorial refers.

Three major questions remain unanswered by the predominantly single-center studies that have been published to date:
(1) whether the training effects could be maintained over the long term, (2) whether training is practicable in multiple medical settings outside of enthusiastic specialist clinics, and (3) whether training would have an effect on mortality or morbidity, either adverse or beneficial. We have published our own experience of training in multiple units across several European countries with different healthcare systems and found that these differences were of less importance than such factors as the duration of training or the setting (in-hospital only, out-of-hospital, or a combination). It would appear that the type of training and the combination of some supervised and some unsupervised is, superficially at least, most likely to be associated with the largest increase in exercise capacity and that none of the patient factors studied (pathogenesis, NYHA class, left ventricular ejection fraction, or medication) appeared to predict the training response reliably.

The literature to date includes only ~500 to 600 patients reported as having taken part in randomized trials of exercise training in the setting of CHF. Against this background, any single-center report of a randomized trial of 99 patients is to be heartily welcomed, especially if it contains, as this study does, some of the valuable longer-term follow-up data lacking in many of the earlier reports. Belardinelli and colleagues randomized 99 patients with moderate to severe CHF to supervised exercise rehabilitation or control for a period of 14 months. They found a highly significant 18% greater increase in exercise capacity (peak oxygen uptake) in the trained group than in the control group, associated with improved indices of myocardial thallium uptake and increased quality-of-life questionnaire scores. With this trial and the as yet unpublished EXERT trial from Canada, the experience on training in CHF is growing at a rapid pace. A similarly large trial from another unit in Italy has also been completed, with heartening results on clinical outcomes (M. Volterrani, MD, Brescia, Italy, personal communication). We are also aware of similar initiatives either completed or nearing completion in the United States. Experience in this mode of therapy for CHF is therefore accumulating at a fast rate, and what is sorely needed now is definitive information on the impact of this treatment option on mortality and worsening of heart failure. The present report from Belardinelli and coworkers from a rehabilitation unit in eastern Italy gives heartening results, showing as it does statistically significant reductions in total all-cause mortality (9 versus 20 deaths; risk reduction, −63%; 95% CIs, 16% to 83%; P<0.01) and a similar effect on hospital readmissions for heart failure (5 versus 14; risk reduction, 71%; 95% CIs, 12% to 89%; P<0.02). This is not proof of a mortality reduction, because the trial clearly was not designed to be, nor could it ever have been, powered to show these effects reliably. The results do, however, give encouragement that we may now have sufficient trial data on which to make estimates of possible mortality effects of training in similar groups of patients. Furthermore, it now appears that a mortality trial of this nature is not impossible, should sufficient funding be found. We have proposed such a trial, and 2 working-group meetings have taken place to mount the initiative within Europe. We hope that like-minded North American units will form with the European group to make a mortality trial of training in CHF a reality before the millennium. It would be ironic if the group of patients initially denied the benefits of participation in cardiac rehabilitation programs formed the patient group who finally offered the rehabilitation community their first opportunity to prove a beneficial effect on mortality in a single prospectively designed mortality and morbidity trial. Much remains to be done and many unanswered questions remain, but the excellent work of Belardinelli and colleagues gives us an incentive to put exercise rehabilitation for heart failure to the test.

References


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