Editorial

Can sedentary patients with heart failure achieve the beneficial effect of exercise training without moving?

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In the current issue of the journal Nuhr et al. report a beneficial effect of chronic low-frequency stimulation (CLFS) to thigh and calf musculature on exercise performance and skeletal muscle histopathology in patients with severe congestive heart failure (CHF).

Congestive heart failure is a clinical syndrome with a complex pathophysiology initiated by left ventricular dysfunction leading to systemic and pulmonary congestion and elevated peripheral vascular resistance. Fluid retention along with peripheral vasoconstriction and reduced skeletal muscle perfusion provides the pathophysiological basis for the symptoms. Coupled with inactivity the stage is set for deconditioning. Skeletal muscle atrophy, changes of fibre-composition (i.e. an increase of type II fibres which are mostly anaerobic, at the expense of aerobic type I fibres), reduced capillary density and reduced cytochrome oxidase activity characterize the condition. Cross-talk between neuro-humoral activation and the inflammatory response further aggravates the histopathology with redistribution and atrophy of muscle fibres. Metabolic abnormalities in the skeletal muscles with early acidosis and accumulation of catabolites during exercise may be the trigger for a shift in the sensitivity of muscle afferent sensory nerves resulting in increased ventilation in response to exercise in these patients. Elevated plasma levels and enhanced myocardial expression of proinflammatory cytokines have been documented in patients with CHF. The cytokines directly contribute to skeletal muscle wasting, myocardial depression, left ventricular dilatation, left ventricular remodelling and cardiomyopathy by various mechanisms including changes in β-adrenergic signal transduction. Reduced sympathetic nerve activity demonstrated after exercise training decreases peripheral vasoconstriction and may improve regional blood-flow reducing the hypoxia-induced production of reactive oxygen species which may be the stimulus for cytokine production.

Exercise training

Thirty years ago the Scientific Council on Cardiac Rehabilitation considered the presence of heart failure an absolute contraindication to exercise training. However, inactivity and deconditioning are now recognised to be major factors aggravating the underlying pathophysiology. Indeed these changes can also be seen in sedentary, healthy individuals. However, physical activity has been documented to reverse this negative process. Exercise training is now well-established as a supplemental treatment for heart failure patients in that it reduces symptoms, improves daily activity levels, and reduces or reverses the pathological skeletal muscle fibre distribution. However, this intervention is usually only an option for patients with mild or moderate symptoms, while patients with severe CHF often are excluded due to co-morbidity and extensive symptoms with dyspnoea during minimal physical activity.

Neuromuscular electrical stimulation

As an alternative to training neuromuscular electrical stimulation of thigh muscles have been reported to be effective by increasing muscle strength and bulk, improving quality of life and decreasing morbidity. The beneficial changes in muscle performance and exercise capacity observed in patients with CHF after neuromuscular electrical stimulation are similar to those observed following bicycle training. However, the previously used protocols often employed an electrical
stimulation level triggering tetanic muscle contractions, which patients found unpleasant.

Chronic low frequency muscle stimulation

In the present issue of the journal Nuhr et al. evaluated the effect of CLFS on the skeletal muscle pathology in 32 patients with severe CHF. Fifteen patients were randomized to CLFS and 17 to the control-group. CLFS was performed applying electrodes on calves and thighs, and the stimulation in the treatment group was adjusted to give a muscle contraction of 25% of maximal contraction. The therapy was applied 4 h a day for 10 weeks. The control subjects received sham therapy with electrical stimulation that did not elicit muscle contractions at all.

The aetiology of heart failure was ischaemic in 16 patients and idiopathic in 16 patients. The patients were on optimal medical therapy, and eight patients actually received additional intravenous support due to refractory advanced heart failure. The mean left ventricular ejection fraction (LVEF) was 22±5%, but only four patients were in NYHA class IV. Muscle biopsies were performed 4 days before and 1 day after the 10 weeks treatment period and analysed with regard to fast and slow myosin chains and for respiratory enzyme activity. Cardiopulmonary exercise testing (CPX) on a cycle ergometer and a 6-min walk test was performed to assess changes in exercise capacity.

The results of the study extend our knowledge regarding the effect of muscle stimulation in CHF in that it demonstrates the beneficial effects of CLFS in a randomized, controlled, prospective study in patients with severe heart failure. In the CLFS group there was a significant increase in maximal workload, oxygen uptake at the anaerobic threshold and distance covered during the 6-min walk test. However, the novel findings in this manuscript are the description of the changes in enzymatic activity and skeletal muscle composition after CLFS in patients with severe CHF. Citrate synthase activity increased, glyceraldehydephosphate dehydrogenase activity decreased, and the myosin heavy chain (MHC) isoforms were shifted in the slow direction with increases in MHCIIId/x (fast isofrom) at the expense of MHCIIId/x (slow isofrom). This suggests that the therapy partly reverses the pathological histochemical changes associated with the deconditioning typical for advanced heart failure and may improve symptoms in this population.

Although this is a controlled, prospective, randomized trial, it is small and the population is heterogeneous. The average LVEF (22%), and the average peak oxygen consumption were consistent with functional class III–IV symptoms and poor prognosis. However, there was no report of weight-loss or signs of cachexia in this population, which seems a bit puzzling when eight patients were reported to be on additional continuous intravenous medical therapy for refractory advanced chronic heart failure. The stimulation was apparently well-tolerated by the patients in that this protocol employed a low-frequency stimulation that was only strong enough to initiate a muscle contraction of 25–30% of maximal contractile force.

Exercise training has been shown to reduce both the elevated levels of neurohormones and cytokines in heart failure patients, but the effect on prognosis of this improvement in the neurohumoral and inflammatory profile remains to be seen. However, the current paper suggests that electrical muscle stimulation has beneficial effects on exercise performance, quality of life and skeletal muscle pathology. In that the patients in the control group who received electrical stimulation below the limit for eliciting the contractile muscle response did not show any beneficial effect of the treatment, the authors suggests that these beneficial effects are due to muscle contractions per se. However, there was no comparison with patients receiving no electrical stimulation at all. Do we know that electrical stimulation has no consequence even if there is no muscle contraction?

What did we learn?

The good news is that an isolated form of intervention alone is effective in contrast to an exercise training programme which usually represents a multidisciplinary approach which includes education, social contact and a powerful placebo effect. The single intervention in this study was the electrical stimulation initiating the muscle contractions. Thus, the results confirm what we all believe, namely that exercise training per se, i.e. using the large muscle groups daily for a prolonged period of time counteract the deconditioning seen in heart failure patients.

This encouraging report should initiate larger studies to evaluate if this relatively simple treatment represents an additional therapeutic option for patients with severe heart failure whose sedentary lifestyle aggravate the underlying pathophysiology. If so, how could we best identify the population most likely to profit from this intervention? CLFS is intuitively a very attractive concept.

References


