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Benefits of exercise training for the failing heart

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Abstract

Heart failure is the most common cause of hospitalization among adults over 65. Almost half of inpatients older than 65 years with chronic heart failure (CHF) are readmitted within 6 months of hospital discharge. Exercise training is a nonpharmacological therapy that determines important adaptations and potentiates the effects of some medications. The choice of an exercise training program should be based on the patient's preferences with the objective to maintain the program as long as possible. Recent trials have demonstrated that different exercise training programs have reached a similar result in terms of improvement in functional capacity after a few months or one or more years. The majority of exercise training programs are based on continuous mild-to-moderate aerobic activity at 40% to 70% of peak oxygen consumption (peak $\dot{V}O_2$) or peak heart rate, with an average improvement in aerobic capacity ranging from 10% to 25% after 2, 6, or 12 months. Intermittent high-intensity exercise has been recently proposed in stable CHF patients and has shown greater improvements in aerobic capacity than traditional endurance exercise programs of moderate intensity. Waltz dancing has also been used in stable CHF with a 14% improvement in peak $\dot{V}O_2$ at 8 weeks. Very recently, a 10-year exercise training program was able to maintain peak $\dot{V}O_2$ at more than 60% of the $\dot{V}O_2$max at each year of follow-up and was associated with a reduction in major cardiovascular events, including hospitalizations for CHF and cardiac mortality. The improvement in aerobic capacity has been associated with a reduction in cardiovascular events during a follow-up of 3 to 5 years, suggesting a positive effect on morbidity and mortality. ■ *Heart Metab*. 2014;64:18–22

Keywords: chronic heart failure; exercise training; outcome

In the last decade, the demonstration that exercise may improve functional capacity and quality of life in patients with chronic heart failure (CHF) has opened an interesting debate among cardiologists about the modality of exercise programs, the effects of exercise on the heart, and the clinical implications.[1-4] Although these preliminary results are encouraging, many questions are not yet answered and need to be clarified. We will briefly discuss the selection of patients, the methodology of exercise training, and the effects of exercise on coronary vessels and myocardial perfusion. Finally, we will introduce recent results on the outcome of exercise training.

Patient selection

The essential condition (sine qua non) to obtain benefits from exercise training is the patient's clinical stability. In all studies, enrolled patients did not have severe ventricular arrhythmias, unstable angina, or

Abbreviations

CHF: chronic heart failure; **HF-ACTION:** Heart Failure: A Controlled Trial Investigating Outcomes of exercise traiNing; **$\dot{V}O_2$:** oxygen consumption

signs and symptoms indicating heart failure deterioration in the last 3 months. Over this time, they were not hospitalized for worsening heart failure, nor did they need to modify the type or dosage of medications. Moreover, the majority of patients were in sinus rhythm, but atrial fibrillation did not represent a contraindication to exercise training.

Age

In a recent review, the mean age of patients studied was 59±14 years.[5] The average increase in peak oxygen consumption (peak $\dot{V}O_2$) after training was above 10% from the initial value in all decades. However, above the age of 70, the improvement in functional capacity was lower.

Sex

There were no differences in the results of physical training between women and men with the identical age and clinical picture; however, the proportion of women to men was much lower (1:4).

Medications

The combination of standard medications for heart failure with exercise did not influence the response to training programs. Patients involved in exercise training more frequently received angiotensin-converting enzyme inhibitors, nitrates, and diuretics, and less frequently received cardioselective β-blockers and antiarrhythmics.

Functional class

More than 60% of patients are in the NYHA functional class II, and 30% are in class III. Pretraining peak $\dot{V}O_2$ was between 15 and 17 mL/kg/min and was not correlated with left ventricular ejection fraction or the response to exercise training. This important issue should be taken into consideration when patients are referred for physical training. Patients with an ejection fraction <30% can have a normal functional capacity, and they can improve their peak $\dot{V}O_2$ more than 10% or 2 to 4 mL/kg/min from the initial value.

Left ventricular diastolic filling

An interesting finding is that the pattern of left ventricular diastolic filling can predict not only the response to exercise training, but also the outcome of patients with CHF.[6] Patients with an abnormal relaxation pattern (low early filling, high late filling, and prolonged deceleration time) generally have a greater increase in peak $\dot{V}O_2$ after training and a better prognosis. By contrast, patients with a restrictive left ventricular filling pattern do not improve functional capacity after training and have a worse prognosis after 3 years. A greater early diastolic filling is associated with a higher stroke volume and peak $\dot{V}O_2$ because of a lower left ventricular end-diastolic pressure and a lower transmitral gradient.

Etiology

As recently shown, almost two-thirds of patients had ischemic heart disease, 20% idiopathic dilated cardiomyopathy, and 10% valvular heart disease. Extensive coronary artery disease with left ventricular dysfunction and CHF are now considered as two new clinical indications to exercise training because potential risks of exercising are overwhelmed by a demonstration of the benefits.[1-5]

Methodology of exercise training

The results of exercise training programs are not only conditioned by patient selection, but also by the choice of the program. There is agreement in preferring aerobic exercise to isometric or eccentric exercise. The combination of an initial warm-up of calisthenics or stretching exercise with cycling on a stationary cycle ergometer is more effective in improving functional capacity than cycling alone.[5] Waltz dancing has been recently proposed as an alternative form of exercise training of moderate intensity in stable CHF, with a 14% improvement in peak $\dot{V}O_2$ at 8 weeks comparable with traditional continuous aerobic training.[7] ECG monitoring by telemetry is indicated in patients with arrhythmias or stable angina, and it is used in all patients during the initial 2 weeks of training. Blood pressure and heart

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rate are measured at rest before each session, at peak exercise, and during recovery. After a warm-up phase (10 to 15 minutes), patients exercise on a stationary cycle ergometer, treadmill, or both for 30 minutes. Before and after the work phase, a short (3 to 5 minutes) loadless exercise is recommended. The intensity of the work phase is selected based on a symptom-limited–exercise test.

Since peak $\dot{V}O_2$ is a more accurate indicator of work tolerance than heart rate, it is preferable to measure gas exchange during exercise and prescribe the intensity of the exercise regimen on the heart rate corresponding to 50% to 70% of peak $\dot{V}O_2$. There is evidence that major benefits are obtained with programs of aerobic exercise at 60% to 70% of peak $\dot{V}O_2$, 3 times a week for a minimum of 8 weeks. Long-term programs are more effective than short-term programs because benefits are maintained for a longer time.[8] The results of recent randomized controlled trials have shown that two exercise sessions per week for 1 year can determine a sustained improvement in peak $\dot{V}O_2$. Supervision by a cardiologist is preferable, especially in patients with severe CHF and psychological problems. However, unsupervised home-based programs, which are more popular in northern Europe and the USA, are also effective.[5] The occurrence of untoward cardiac events is very low (<3%). The most common events are premature contractions and posttraining hypotension. Studies are concordant in reporting high compliance to training. Supervised programs, however, have a higher compliance than home-based programs (85% to 90% vs 75% to 85%).

Coronary artery adaptations

Although an improvement in functional capacity after exercise training is mainly related to peripheral adaptations,[9,10] recent studies have demonstrated myocardial and coronary vessel changes that can contribute to clinical benefits.[8,11-15] In patients with ischemic cardiomyopathy, a common finding is the coexistence of epicardial coronary artery stenoses with different amounts of necrotic, ischemic, hibernating, and normal myocardial cells. After short-term moderate exercise training, an improvement in left ventricular contractility is correlated with increases in coronary collateralization and thallium uptake.[11] Since no changes in the morphology and severity of epicardial stenoses have been demonstrated, the improved myocardial perfusion seems to be mainly explained by functional and/or structural adaptations of small coronary vessels and by improved endothelium-dependent vasorelaxation.[12] This effect has been also described in peripheral arteries after short-term programs.[16]

Another explanation may be an angiogenic effect of exercise. In the presence of a significant stenosis, intermittent bouts of exercise stimulates the expression of vascular endothelial growth factor and nitric oxide genes through a hypoxia-related mechanism.[17,18] New microvessels are generated that, in part, organize into large collaterals, and, in part, potentiate myocardial microcirculation. Adenosine concentration in the myocardial interstitium also increases after chronic exercise and can contribute to coronary collateral and vessel growth.[19,20]

A unifying hypothesis may be that exercise training improves regional myocardial perfusion through an indirect effect of opening preexisting collaterals and a direct effect of neoformation of small vessels. The former is due to functional adaptations of major coronary arteries determining a pressure difference between stenotic and normal arteries, and the latter is related to two mechanisms where one is dependent on adenosine and another that may be related to growth factors. An improvement in capillary diffusion capacity is a hypothesis that should be confirmed in humans. At present, no direct demonstration exists to show that an improvement in flow-mediated dilation of conduit arteries can improve myocardial perfusion. This is an intriguing hypothesis that needs to be demonstrated. Moreover, the clinical significance of these adaptations requires larger studies.

Outcome

A recent trial has demonstrated, for the first time, that a long-term program of supervised exercise training improved the survival of patients with CHF.[8] Trained patients, after 1214±56 days of follow-up, had a 63% reduction in cardiac mortality and a 71% lower rate of hospital readmission for heart failure than untrained controls. Cost-effective analysis pointed out that a patient's life can be prolonged, on average, by an additional 1.82 years at the low cost-effectiveness ratio of $1773 per life-year saved.[21] An independent predictor of survival was posttraining thallium uptake, suggesting that the improvement in myocardial perfusion after exercise training is more important than the severity and the number of coronary artery stenoses.[11]

More recently, the HF-ACTION trial (Heart Failure: A Controlled Trial Investigating Outcomes of exercise traiNing), a multicenter randomized controlled trial enrolling 2331 medically stable outpatients with heart failure, demonstrated a smaller, but significant, improvement in peak $\dot{V}O_2$ at 3 months that still persisted at 12 months.[22] This improvement, however, was not associated with a reduced incidence of hard events. In contrast to our previous trial, patients that exercised with no supervision had a dropout rate of 33% at 12 months, suggesting that supervision may be crucial and may explain a better adherence to training in a long-term exercise training program. Very recently, a 10-year exercise training program was able to maintain peak $\dot{V}O_2$ at more than 60% of the $\dot{V}O_2$max at each year of the follow-up and was associated with a reduction in major cardiovascular events, including hospitalizations for CHF and cardiac mortality.[23]

Conclusions

There is mounting evidence that exercise is a nonpharmacologic form of cardiovascular therapy, which potentiates the effects of standard pharmacological interventions and determines important biological and clinical benefits in patients with chronic heart disease. Nowadays, interest is focusing on the methodology of exercise training, the mechanisms of clinical benefits, and their prognostic significance over both short-term and long-term periods. Exercise, if correctly designed and performed, can be considered an adjunctive therapeutic tool in the management of CHF as well as ischemic heart disease. The improvement in aerobic capacity has been associated with a reduction in cardiovascular events during a follow-up of 3 to 5 years, suggesting a positive effect on morbidity and mortality. Recently published guidelines recommend including exercise training in the therapeutic strategy of CHF patients; however, only a small percentage of patients are referred for exercise training. Other studies are needed in order to confirm long-term clinical benefits and the choice of the best protocol for any single patient. ■

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