Exercise training in heart failure improves quality of life and exercise capacity

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Aims Benefits from exercise training in heart failure has mainly been shown in men with ischaemic disease. We aimed to examine the effects of exercise training in heart failure patients ≤75 years old of both sexes and with various aetiology.

Methods and Results Fifty-four patients with stable mild-to-moderate heart failure were randomized to exercise or control, and 49 completed the study (49% ≥ 65 years; 29% women; 24% non-ischaemic aetiology; training, n=22; controls, n=27). The exercise programme consisted of bicycle training at 80% of maximal intensity over a period of 4 months.

Improvements vs controls were found regarding maximal exercise capacity (6 ± 12 vs −4 ± 12% [mean ± SD]; P <0.01) and global quality-of-life (2 [1] vs 0 [1] units [median (inter-quartile range)]; P <0.01), but not regarding maximal oxygen consumption or the dyspnoea-fatigue index. All of these four variables significantly improved in men with ischaemic aetiology compared with controls (n=11). However, none of these variables improved in women with ischaemic aetiology (n=5), or in patients with non-ischaemic aetiology (n=6). The training response was independent of age, left ventricular systolic function, and maximal oxygen consumption. No training-related adverse effects were reported.

Conclusion Supervised exercise training was safe and beneficial in heart failure patients ≤75 years, especially in men with ischaemic aetiology. The effects of exercise training in women and patients with non-ischaemic aetiology should be further examined.

Key Words: Exercise training, heart failure, benefit, patient categories.

Introduction

Patients with chronic heart failure have traditionally been recommended to avoid physical exercise, due to a general belief that physical strain might be harmful and aggravate the pre-existing cardiac condition. Lately this recommendation has been challenged and several studies have shown a beneficial effect from physical endurance training involving large muscle groups in patients with depressed left ventricular function and/or clinical heart failure[1–13]. Up to now, patients have been carefully selected; in particular, relatively young patients, men, and patients with ischaemic aetiology for heart failure have been included. Thus, an investigation into the effects of training in a broader heart failure population is needed before recommending it more generally. It should be noted that some studies have indicated that certain categories of patients may not benefit from physical endurance training[6,6], and it is not known whether training might be harmful in specific categories of heart failure patients.

The aim of this study was to examine whether physical endurance training, in an unselected sample of patients not older than 75 years with stable mild-to-moderate heart failure, is safe and has beneficial effects on maximal oxygen consumption (VO₂-max), maximal exercise capacity (EC_max), global quality of life (QoL), and symptoms from daily activities, as assessed by the dyspnoea-fatigue index. As pre-specified in the protocol, the aim was also to investigate whether the training response depends on age, sex, left ventricular systolic function, or VO₂-max, and whether men with ischaemic aetiology differ from other patients regarding the effects of training.

Methods

Patients Patients were recruited at Malmö University Hospital, which has a primary catchment area of 250 000 inhabitants. Inclusion criteria were (1) ≥ 8 points of the Boston...
heart failure criteria\textsuperscript{[14]}; (2) left ventricular ejection fraction \(\leq 0.45\) at the most recent (not exceeding a year) radionuclide or echocardiographic examination; and (3) \(\leq 75\) years of age. Exclusion criteria were: (1) change of clinical status and/or medication within 4 weeks prior to inclusion; (2) myocardial infarction, heart surgery, or coronary angioplasty within 3 months prior to inclusion; (3) inability to perform a bicycle test; (4) exercise-terminating angina pectoris, ST-depressions (\(>2\) mm in \(>1\) lead), blood pressure fall (\(>10\) mmHg), or arrhythmia (e.g. ventricular tachycardia/fibrillation, increasing frequency of ventricular extrasystoles, supraventricular tachycardia \(>170\) beats. min\(^{-1}\)) at the most recent maximal exercise test (including the baseline test); (5) pulmonary disease judged to be the main exercise-limiting factor and/or peak expiratory flow rate \(<50\%\) of the age- and sex-adjusted reference value; (6) New Y ork H eart A ssociation class IV; and (7) clinically significant aortic stenosis.

Eligible patients were identified from hospital records and invited to participate in the study. Of the invited patients, 40\% did not wish to participate. Of the 61 patients who accepted, seven were found to meet with one or more exclusion criteria. Thus, 54 patients were included and all gave informed consent to participate.

Four patients randomized to training were withdrawn before the start of the study due to withdrawn consent (\(n=2\)), myocardial infarction (\(n=1\)) and back pain (\(n=1\)) between the baseline examinations and study start. Fifty patients (27 controls, 23 training patients) entered the active phase of the study.

Study design

The study was performed between 1992 and 1996 at one centre, with inclusion of patients twice a year. Patients who agreed to participate in the study and who met the entry criteria performed the baseline examinations. Patients who were not excluded following the baseline examinations were randomized on a 1:1 basis, either to complete a 16-week programme of exercise training, or to serve as controls. Each patient’s physician was requested not to change medication throughout the study duration, unless absolutely necessary. The control patients agreed not to change their degree of physical activity during the study, and patient compliance with this request was assessed by the physical activity score at study end. All baseline examinations were repeated at study end. The echocardiographic examinations at baseline and at completion of the study were all carried out by one investigator, and the exercise tests by the same group of investigators. The interviews were done by two investigators, and each patient was interviewed on both occasions by the same investigator. The results of the baseline examinations were not known to the investigators when the second set of examinations were performed, and all data were blindly evaluated.

The variables used to assess the response to exercise training (effect variables) were prospectively defined as changes in \(V_{O2}\)-max, \(EC_{max}\), dyspnoea-fatigue index, and QoL from baseline to study end (\(\Delta\)). The response to training was examined by comparing the whole training group with controls. In addition, men and women as well as patients with and without ischaemic aetiology were separately compared with controls. In the past, most studies on the effects of exercise training have been in men with ischaemic aetiology; thus, this category was also separately compared with controls, as pre-specified in the protocol. The study was approved by the local Ethics Committee.

Exercise testing

Each patient had performed at least one exercise test prior to this study. The exercise tests comprised upright bicycle ergometry, and were always limited by exhaustion. They were performed at both baseline and study end, were always carried out in the morning, after an overnight fast, or at least 3 h after a light breakfast. The initial workload of 30 W was increased stepwise by 10 W every minute. A breath-by-breath analysis of total body oxygen consumption and carbon dioxide production was performed, using a MedGraphics Cardiopulmonary Gas Exchange System CPX/MAX model 762014-102 (St Paul, M N, U.S.A.). Calibration against gases of known concentrations, as well as adjustments for air humidity, temperature, and air pressure were made. Continuous 12-lead ECG registration with computerized ST analysis was performed, as well as blood pressure measurement, registration of eftort, chest pain, and dyospnea, according to the Borg scale every 2nd min.

Echocardiographic examination

Two-dimensional echocardiography and Doppler examinations were performed using a Hewlett-Packard (Andover, M A, U.S.A.) Sonos 1000 echocardiography system and a 2.5 MHz transducer. Pulsed, continuous and colour-flow Doppler examinations were performed with the same transducer. Parasternal and apical views were obtained with the patient in a left lateral recumbent position. Measurements were acquired during silent respiration or end-expiratory apnoea.

Left ventricular systolic function was assessed by determining the mean atrioventricular plane displacement\textsuperscript{[15-19]}, derived from four measurements (eight in patients with atrial fibrillation) at each of the anterior, septal, lateral, and posterior walls (in the four- and two-chamber views). Ejection fraction was computed using the regression equation from Alam et al.\textsuperscript{[16]}. The equation described the relationship between ejection fraction by radionuclide ventriculography and echocardiographically assessed atrioventricular plane displacement: ejection fraction=\((5.5 \times \text{mean atrioventricular plane displacement}) - 5\) (\(r=0.87\), SEE =6.2). Atrioventricular plane displacement is considered to be a...
function of contraction of subendocardial fibres along the left ventricular long axis, whereas ejection fraction is considered mainly to be a function of contraction along the short axis\[19\]. Although the two are not the same, left ventricular atrioventricular plane displacement and ejection fraction calculated by two-dimensional echocardiography using the area–length method correlate well (r=0.96, SEE=4.5)\[17\]. Atrioventricular plane displacement can be determined despite poor image quality and shows high reproducibility; in our laboratory, the mean variability between two investigations, performed immediately after one another in the same patient, was 4.8% (ejection fraction range 0.0-0.06) in a series of 53 consecutive patients with a mean ejection fraction of 0.38. This method is therefore particularly well suited for assessment of changes in left ventricular systolic function over time. Furthermore, atrioventricular plane displacement has a very strong prognostic value in patients with heart failure\[19\].

Cardiac dimensions were measured in the parasternal long axis view in two-dimensional mode\[21\].

**Dyspnoea–fatigue index, global quality of life, and physical activity score**

Symptoms from daily activities were assessed by the dyspnoea–fatigue index\[22\]. The dyspnoea–fatigue index addresses how much daily activity the patient can tolerate (part 1), how large a workload the patient can tolerate before symptoms arise (part 2), and how fast the patient can work (part 3). For each part, the patient can receive 0 (most severe symptoms) to 4 (no symptoms) points. Thus, patients were assigned between 0 (very pronounced symptoms from daily activities) and 12 points (no symptoms).

At study end, patients were asked to rate their QoL in comparison with baseline. No change was assigned the figure 0, deterioration was rated from −1 (mild) to −3 (severe), and improvement from 1 (little) to 3 (much).

The degree of habitual physical activity was assessed in each patient. Average time (minutes/week) spent on each physical activity was noted, and the intensity by which the activity was performed was classified as either low (1 point), moderate (2 points), or high (3 points). A physical activity score was calculated for each activity according to the formula: time × intensity/100. For each patient the activity scores were then added, resulting in a total activity score. At the second interview (study end), activity due to the exercise training programme was not included in the score.

**Exercise training protocol**

The patients performed ‘interval training’ on a cycle ergometer: 90 s exercise and 30 s rest. Patients in sinus rhythm exercised at a digitally displayed heart rate corresponding to 80% of $V_O_2$-max (at the baseline exercise test) ± 5 beats·min$^{-1}$, for as long as possible during each interval. In patients with atrial fibrillation, exercise intensity corresponded to exhaustion grade 15, according to the Borg scale (approximately 80% of maximum). Patients individually adjusted the speed and load in order to reach the adequate intensity. The training was performed as a group, supervised by a physiotherapist who ensured that the protocol was complied with. The exercise time was gradually increased from 15 min twice a week to 45 min three times a week from week 7, for a total of 16 weeks.

**Statistics**

The t-test was used to assess differences in normally distributed continuous variables between controls and training patients as well as between controls and training men with ischaemic aetiology. For non-normally distributed continuous variables and regarding groups containing <10 patients the Mann-Whitney U test was applied. Within-group changes were examined by the paired t-test (normally distributed variables). For analysis of the relationship between continuous variables, simple and multiple linear regression analyses were used. To assess between-group differences regarding nominal variables, Fisher’s exact test was performed and differences in continuous variables between more than two groups were examined by the Kruskal-Wallis test. Data are expressed as mean ± SD or median [inter-quartile range] (non-parametric tests). Two-tailed P-values <0.05 were considered significant.

**Results**

**Baseline variables**

One patient randomized to training developed rheumatoid arthritis and did not complete the study. Our results are based on the 49 patients who completed the study. Baseline variables are shown in Table 1. All but one patient had atrioventricular plane displacement corresponding to an ejection fraction less than 50% at inclusion. Seven (14%) patients had chronic atrial fibrillation. The aetiology for heart failure was ischaemic (documented myocardial infarction or angiographically verified coronary artery disease) in 37 patients (75%), and non-ischaemic in 12. The group of patients with non-ischaemic aetiology contained four with an undetermined cause. They exhibited no signs or symptoms of ischaemic heart disease, showed no signs of myocardial ischaemia on exercise test, and showed no regional wall motion differences on echocardiography.

There were no differences between training (n=22) and control (n=27) patients as regards baseline variables (Table 1). Patients who declined to participate in the study did not differ from the 49 that completed it with regard to age and sex, but in most of these patients...
other baseline variables were unknown since they did not participate in the baseline examinations. The five patients withdrawn after randomization were all men but otherwise did not differ from those who completed in regard to baseline variables.

### Compliance

Compliance with the exercise training (% sessions attended) was 74.5%, ranging from 54.5 to 97.7, with the exception of one patient with only 27.3%. Compliance was 74.5% in all training patients: 78.4% in men with ischaemic aetiology, 77.3% in patients with non-ischaemic aetiology, and 66.9% in women (P = ns). None of the effect variables — ΔEC_{max}, ΔVO_{2-max}, Δdyspnoea–fatigue index, and ΔQoL — correlated independently with compliance. Training and control patients did not differ significantly regarding change in the physical activity score (excluding the physical activity of the training programme). In only one patient (in the control group) was cardiovascular medication temporarily adjusted during the study.

### Safety

No adverse reactions to the training were reported. None of the training patients experienced any worsening of heart failure during the study, and none of them were hospitalized, whereas three of the control patients were. Four of the seven training patients with the largest left ventricles (end-diastolic diameter of >34 mm  m^{-2}) had an improved VO_{2-max}, and in five of them dyspnoea–fatigue index and QoL either improved or did not change. Four of the seven training patients with the most pronounced left ventricular systolic dysfunction (corresponding to ejection fraction <0.30) showed an improvement in at least two of the four effect variables.

### Changes in effect variables with exercise training

In those who trained there was a significant improvement in EC_{max} compared with controls, whereas VO_{2-max} did not significantly improve (Table 2). QoL was significantly improved compared with controls (2 [1] vs 0 [1], P < 0.01), but not dyspnoea–fatigue index. Compared with controls, there were no significant changes in maximal heart rate, resting heart rate, respiratory exchange ratio, or submaximal exercise capacity (heart rate and VO_{2} at submaximal workloads; workload and VO_{2} at respiratory exchange ratio 1:0).

Figure 1 shows Δ in the effect variables in controls, in all training patients, in training men and...
women with ischaemic aetiology, and in training men and women with non-ischaemic aetiology. Men with ischaemic aetiology significantly improved all four effect variables compared with controls. Women (n=6) and patients with non-ischaemic aetiology (n=6) did not improve any of these variables significantly. Table 1 shows that training men with ischaemic aetiology did not differ from the training patients as a whole regarding any of the baseline variables, with the obvious exception of the percentage of women and patients with ischaemic aetiology. Men with ischaemic aetiology did not improve submaximal exercise capacity or resting heart rate compared with controls.

Among the training patients, the only correlation found between Δ in the effect variables was between Δ dyspnoea–fatigue index and ΔQoL (r=0·44, P<0·05). Thus, decreased symptoms from daily activities (i.e. increased dyspnoea–fatigue index score) correlated weakly with improved QoL score. Δ maximal heart rate did not correlate with Δ in any of the effect variables.

Continuous baseline variables predicting improvement with exercise training

Eleven baseline variables were tested for correlations with Δ in the effect variables among training patients (Table 3). Variables showing a correlation with P-value <0·15 were included in multiple linear regression analyses. Independent correlations were found only between ECmax and Δdyspnoea–fatigue index (standard coefficient 0·50, P<0·05), and between left ventricular end-diastolic diameter \( m^{-2} \) and ΔECmax (−0·44, P<0·05).

Changes in echocardiographic variables with exercise training

With training, left ventricular systolic function did not change significantly within the group or compared with controls. However, with training, systolic function improved significantly within the group in men with ischaemic aetiology (ejection fraction 0·37±0·09 to 0·42±0·14, P<0·05). Left ventricular end-diastolic diameter increased significantly in men with ischaemic aetiology compared with controls (0·6±1·3 vs −0·6±1·8 mm, P<0·05).

Discussion

The effects of physical endurance training involving large muscle groups in heart failure patients have recently been examined in randomized and controlled studies\(^{[6,8,9,11–13]}\) and also in some non-randomized and/or non-controlled studies\(^{[1–4,7]}\). Previous studies have usually examined selected groups of patients. In the six previous randomized and controlled studies\(^{[6,8,9,11–13]}\), no women trained (one female was included and randomized to the control group)\(^{[9]}\), mean age was 62, 51, 52, 54, 51 and 53 years, respectively, and although patients with non-ischaemic aetiology were included in some of these studies\(^{[9,11–13]}\), only a few patients with non-ischaemic heart failure have been subjected to ‘whole body’ physical endurance training. Thus, the question of whether exercise training is safe and beneficial in the general heart failure population, or...
if there are differences in the response to training depending on age, sex, or aetiology, has been unanswered. Furthermore, previous studies have shown conflicting results regarding the impact of baseline V\textsubscript{O2}-max/EC\textsubscript{max} and left ventricular systolic function in this respect\cite{2,4,6,8}. There has also been some concern regarding potential damage from exercise training in patients with an enlarged left ventricle and/or severely depressed ejection fraction\cite{4,6,23}.

The present randomized and controlled study examined the effects of physical endurance training in a sample of heart failure patients including 49% patients \( \geq 65 \) years of age, 29% women, and 24% patients with non-ischaemic aetiology. Although a few patients were in NYHA class I at baseline all patients had been clearly symptomatic prior to study entry, since all patients met the Boston score entry criterion \(( \geq 8 \) points). It is likely that these patients were asymptomatic due to the effects of pharmacological treatment; all patients were on ACE inhibitor therapy.

### Compliance to the exercise protocol

Compliance to the exercise protocol was of the same magnitude as was reported by Coats et al\cite{8}. It did not differ between categories of patients and, thus, did not affect the results of the analyses by category. There were no correlations between compliance and improvement in QoL, dyspnoea-fatigue index, EC\textsubscript{max}, V\textsubscript{O2}-max. The latter is in contrast with some previous studies\cite{3,8} in which the response to exercise improved with compliance. Differences between patients regarding compliance may have been too small to affect the response to training significantly. This may also explain why none of the baseline variables correlated with compliance.

### Safety

There were no indication that training was harmful in our patients with heart failure. One patient developed rheumatoid arthritis during the training period, but there were no adverse events related to the training. This is well in agreement with some of the previous studies\cite{2,8}, but in contrast with others\cite{3,6}. In the study by Jette et al\cite{6} there were several complications, possibly because the large quantity of training and short intervals between the training sessions allowed for too little time for recovery. Nothing indicated that training was harmful in our patients with the most pronounced left ventricular dilatation or systolic dysfunction, in contrast to the findings of some prior studies\cite{4,6}. The number of women and patients with non-ischaemic aetiology in our study was small, patients older than 75 years were not included, and no patient had suffered a recent (within 3 months) myocardial infarction. Conclusions regarding safety cannot therefore be made for the general heart failure population.

### Response to exercise

Compared with controls, there were small but significant overall improvements in EC\textsubscript{max} and QoL with training, but no significant improvements in V\textsubscript{O2}-max or dyspnoea-fatigue index. This finding is in contrast to previous findings\cite{3,4,7,8,11-13}. However, men with
ischaemic aetiology, none of whom had a prior myocardial infarction less than 3 months old, demonstrated significant improvements in all four effect variables (\( V_{O2\max} \), \( E_C_{\max} \), dyspnoea-fatigue index, and QoL) compared with controls. All improvements were numerically greater than for the whole group of training patients. This category of heart failure patients has been well represented in previous studies showing benefit from exercise training. The \( V_{O2\max} \) increase with training found in men with ischaemic aetiology (1.9 ml . kg\(^{-1}\) . min\(^{-1}\)) is similar to that reported by others\([8,11]\). Thus, our results are well in agreement with prior studies showing benefit from exercise training in men with ischaemic aetiology, whereas an effect of exercise training in women with ischaemic aetiology as well as in men and women with non-ischaemic aetiology could not be demonstrated. Due to the small number of women and patients with non-ischaemic aetiology there was, however, not enough statistical power to preclude a response to training in these categories. Humbrecht et al. mostly included patients with non-ischaemic aetiology (‘dilated cardiomyopathy’) and found a significant increase in \( V_{O2\max} \) with training\([12]\). It was not stated, however, how ‘dilated cardiomyopathy’ was diagnosed, and it is possible that these patients did not have non-ischaemic cardiomyopathy. Thus, the results of that study do not necessarily prove a response to exercise training in patients with non-ischaemic aetiology. We have found no reports on exercise training in women with heart failure, and our results are, to the best of our knowledge, the first so far reported in this category of heart failure patients. Future investigations will have to focus on the effects of exercise training in women and patients with non-ischaemic aetiology.

A n important observation in our study is that the response to training was independent of baseline left ventricular systolic function and \( V_{O2\max} \), and the linear regression analyses showed that improvement in the effect variables was also independent of age. Since improvements in \( V_{O2\max} \) and/or \( E_C_{\max} \) were associated with improved dyspnoea-fatigue and/or QoL, the training effect was not confined to performance on a bicycle. This agrees well with prior findings\([8]\).

There were no significant improvements as a result of training regarding submaximal exercise capacity variables. This was unexpected and in contrast with some previous studies\([3,8]\), although in agreement with another\([6]\). The reasons for this lack of improvement in submaximal exercise capacity cannot be explained by our data. The workload used in our study has been used in several prior studies\([1,3,4,6,8]\), and thus seems unlikely as an explanation. There was no increase in maximal heart rate with training, and the response to training was, thus, not attributable to an increase in maximal heart rate, which is in contrast with the findings of Keteyian et al.\([11]\).

We have no obvious explanation as to why only men with ischaemic aetiology showed a clear benefit from exercise training. Patients with idiopathic cardiomyopathy have been suggested to have a generalized cardiac and skeletal myopathy\([26]\). Patients with such a myopathy seem unlikely to improve with exercise training. It is uncertain whether this explanation is applicable to our findings since we do not know how many (if any) of our patients with non-ischaemic aetiology actually had idiopathic cardiomyopathy. Wilson et al.\([27]\) suggested that patients with severe haemodynamic dysfunction during exercise do not improve with exercise training because they are primarily limited by circulatory factors. However, since we did not assess the haemodynamic response to exercise, we do not know if this explanation is valid in our patients. The lack of haemodynamic data is a limitation of our study.

**Changes in echocardiographic variables with exercise training**

In men with ischaemic aetiology there was an increase in left ventricular size and systolic function. The improvements in systolic function are in agreement with the findings of some prior studies\([2,6]\), but contradict others\([3,5]\). The increases in left ventricular size are in contrast with previous findings\([3,6]\). However, these changes may be the result of a physiological adaptation to training, as seen in healthy men\([24]\), resulting in an increased stroke volume and maximal cardiac output. These findings agree with the findings of A dachi et al.\([25]\), that high-intensity training in patients with prior myocardial infarction improved stroke volume at rest, and with the findings of Coats et al.\([18]\), of an increased cardiac output at submaximal and peak exercise with training in men with heart failure due to ischaemic heart disease.

**Conclusions**

Exercise training was safe and beneficial in heart failure patients not older than 75 years. The response to training was independent of left ventricular systolic function and \( V_{O2\max} \) at baseline. Men with heart failure due to ischaemic heart disease showed a clear benefit from exercise training. Further investigation is needed to define the effects of exercise training in women and in patients with non-ischaemic aetiology for heart failure. Investigations into the long-term effects of exercise training in heart failure is also necessary.

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**References**


