

Quality of life and cardiorespiratory function in chronic heart failure: effects of 12 months' aerobic training

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Abstract

Objective—To examine the long-term benefits and safety of aerobic training in patients with chronic heart failure.

Design—Non-randomised control trial with 52 weeks follow up.

Setting—Outpatient cardiac rehabilitation referral centre.

Patients—Patients with compensated chronic heart failure (mean (SD) age 62 (6) years, New York Heart Association stage III, initial resting ejection fraction 22 (7)%). Experimental group of 17 men, 4 women; control group 8 men, 1 woman.

Interventions—Experimental group: progressive, supervised aerobic walking programme for 52 weeks. Control group: standard medical treatment.

Main outcome measures—Six-minute walk distance, progressive cycle ergometer test to subjective exhaustion, disease-specific quality of life questionnaire, and standard gamble test, all measured at entry, 4, 8, 12, 16, 26, and 52 weeks.

Results—Control data showed no changes except a small trend to improved emotional function ($P = 0.02$ at 12 weeks only). Fifteen of the 21 patients completed all 52 weeks of aerobic training; two withdrew for non-cardiac reasons (16, 52 weeks). Three were withdrawn because of worsening cardiac failure unrelated to their exercise participation (4, 4, 8 weeks), and one had a non-fatal cardiac arrest while shopping (16 weeks). Gains in cardiorespiratory function plateaued at 16–26 weeks, with 10–15% improvement in six-minute walk, peak power output, and peak oxygen intake linked to gains in oxygen pulse and ventilatory threshold and reductions in resting heart rate. Marked improvements in quality of life followed a parallel course.

Conclusions—Aerobic training is safe and beneficial in compensated chronic heart failure. Gains in aerobic function and quality of life persisted over a programme lasting 52 weeks.

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Keywords: exercise rehabilitation, chronic heart failure, long-term response, quality of life.

Over the past 15 years several published reports have described the effects of a physical

training programme in patients with compensated chronic heart failure due to systolic ventricular dysfunction.¹⁻⁴ The reported benefits include improved exercise tolerance, an increased peak oxygen intake, and at least partial relief from the symptoms of breathlessness, undue fatigue, sleep disturbance, and muscle weakness. None of the exercise programmes have encountered any adverse occurrences. Nonetheless, consideration of such patients for referral to a cardiac rehabilitation exercise programme has not become a customary option, as it has in the case of patients recovering from myocardial infarction, aorto-coronary artery bypass surgery, percutaneous transluminal coronary angiography, and cardiac transplantation. There are a number of reasons for the reluctance to prescribe exercise. The ominous nature of the condition favours a cautious approach. From the Framingham Study⁵ we know that 50% of patients with chronic heart failure die within five years of the initial diagnosis. Two exercise training reports have also suggested that sub-sets of heart failure patients (those with low ejection fractions and ST segment depression on exercise testing⁶ and those with extensive anterior infarcts⁷) might not benefit from exercise training and might even be affected adversely. On the other hand, Giannuzzi and associates noted that although patients with poor left ventricular function after anterior myocardial infarction were prone to further global and regional dilatation, long-term exercise conferred a significant improvement in physical work capacity and did not have an additional negative effect.⁸

There remains the need for a large controlled prospective trial to assess the value of medically prescribed and supervised exercise training in this group of patients. In the meantime, however, some physicians find the existing evidence favouring exercise sufficiently persuasive to warrant referring their appropriately treated chronic heart failure patients for exercise training in the out-patient rehabilitation setting. The objectives of this non-randomised study, which included a control group, were (i) to examine the safety and efficacy of progressive aerobic training in chronic heart failure when treatment was sustained for a year, a much longer period of training than has been examined by other investigators; (ii) to explore associations between gains of cardiorespiratory function and improvements in perceived quality of life; and (iii) to plot the time course of such changes.

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Patients and methods

STUDY DESIGN

Eligible patients completed an initial quality of life and cardiorespiratory function assessment, and this was repeated two weeks later. The first test served to familiarise patients with procedures, and the second provided baseline data. Patients then entered a programme of individually prescribed, supervised aerobic training. Quality of life and cardiorespiratory function measurements were repeated after four, eight, 12, and 16 weeks of exercise training, and further evaluations were performed after 26 and 52 weeks.

Given the length of the study, and the poor prognosis in such patients, it was not considered feasible to maintain a comparable control group for 52 weeks. However, a sample of nine subjects were observed for a total of 12 weeks before entering the exercise programme. This enabled us to determine the stability of the measures that were used in the absence of an exercise training programme.

PATIENTS

All patients were recruited in accordance with Sunnybrook Health Science Centre guidelines for written informed consent. The experimental group comprised 21 patients (17 men and 4 women, aged 62 (6) years); the control subgroup sample comprised 8 men and 1 woman, aged 64.8 (5.6) years. Selection criteria included: age 21 to 70 years, New York Heart Association (NYHA) functional class II or III, disability related to symptoms of chronic heart failure, ability to perform a progressive symptom-limited treadmill test for at least 3 minutes (modified Naughton protocol, 3 METs or 10.5 ml/[kg.min]), and clinical stability for a period of at least one month. Maintenance doses of digoxin, frusemide, and angiotensin-converting-enzyme inhibitors, as well as con-

comitant treatment with antihypertensive drugs, nitrates, and calcium antagonists were permitted if dosages had remained unchanged for at least one month before the start of the study.

Reasons for exclusion from the study included a scintigraphic resting left ventricular ejection fraction greater than 40%, β blocker therapy, the presence of symptomatic angina sufficiently severe to limit even low level training, myocardial infarction or cardiac surgery within the previous three months, obstructive cardiomyopathy, reversible causes of chronic heart failure, pacemaker dependency, and any coexisting condition which would preclude the proposed aerobic training or seemed likely to limit survival to less than one year.

The aetiology of the chronic failure was ischaemic in 15 cases, valvar in 3, idiopathic in 2, and ethanol-related in 1 (table 1). Two of the 21 patients were in NYHA category II and the remaining 19 were in category III. The resting left ventricular ejection fraction was 21.4 (1.5)%. Fourteen patients had experienced exacerbation of their symptoms sufficiently severe to require hospital treatment at least once during the previous year.

Radiological evidence of chronic failure was seen in 18 of the 21 patients. The remaining three patients had a typical history of increasing dyspnoea and physical findings that were diagnostic of overt chronic heart failure.

CLINICAL OBSERVATIONS

Patients were seen by the study nurse and cardiologist weekly for 16 weeks and monthly thereafter. Adjustments of frusemide dosage were permitted to maintain a clinically stable chronic heart failure status but any serious deterioration in the clinical condition was set as an immediate criterion for withdrawal from the study.

SIX-MINUTE WALK

Patients were asked to walk as far as they could in six minutes.⁹ Previous evaluation of this procedure had demonstrated an adequate reliability¹⁰ and useful correlations with measures of functional status in patients with chronic heart failure.¹¹

EXERCISE TEST PROTOCOL

This has been described previously.¹² Essentially, cardiopulmonary function was tested on an Elema-Schonander cycle ergometer. The work rate was increased stepwise by 16.7 W (100 kpm.min⁻¹) every minute until voluntary exhaustion or the onset of adverse symptoms or signs requiring a halting of the test. The exercise electrocardiogram (leads V1, CM₅, and III) was recorded continuously, the original Borg rating of perceived exertion¹³ was recorded at every stage, and the blood pressure was measured at rest, during the final seconds of every second stage, and at the second and fourth minutes of recovery.

Measurements were also made of the respiratory rate, respiratory minute volume, ventilatory (anaerobic) threshold, and peak oxygen intake, using a SensorMedics Horizon

Table 1 Clinical characteristics of patients participating in training programme

Case	Age	Sex	Aetiology	NYHA class	LVEF (%) [*]	In hospital with CHF in previous year	CHF on x ray
1	65	M	Ischaemic	III	10	Yes	Yes
2	63	M	Ischaemic (withdrawal: painful spur developed at 52 wk)	III	20	Yes	Yes
3	59	M	Ischaemic	III	15	Yes	Yes
4	60	F	Idiopathic	III	28	No	Yes
5	49	M	Ischaemic	III	10	Yes	Yes
6	69	M	Ischaemic (withdrawal: hypothyroidism at 4 wk)	III	23	Yes	Yes
7	64	M	Ischaemic	III	14	Yes	Yes
8	51	M	Ischaemic	III	31	No	No
9	67	M	Valvar	III	19	No	Yes
10	69	M	Valvar	III	22	No	Yes
11	66	F	Ischaemic	III	25	Yes	Yes
12	65	M	Ischaemic (withdrawal: atrial fibrillation at 4 wk)	III	22	Yes	Yes
13	59	F	Valvar (withdrawal at 16 wks, non-compliant)	III	25	Yes	Yes
14	65	F	Ischaemic	II	40	No	No
15	67	M	Ischaemic (withdrawal: worsening CHF after 8 wk)	III	25	Yes	Yes
16	59	M	Ethanol	III	23	Yes	Yes
17	65	M	Ischaemic	III	20	Yes	Yes
18	65	M	Ischaemic (withdrawal: cardiac arrest shopping at 16 wk)	III	20	Yes	Yes
19	65	M	Ischaemic	III	20	Yes	Yes
20	64	M	Idiopathic	III	13	No	Yes
21	71	M	Ischaemic	II	21	No	No

^{*}Mean (SE) 21.4 (1.5).

CHF, chronic heart failure; NYHA, New York Heart Association; LVEF, resting left ventricular ejection fraction.

Metabolic Cart. Details of the ventilatory threshold determination have been described previously.¹⁴ In brief, the primary criterion of ventilatory threshold was the oxygen intake at which the ventilatory equivalent for oxygen began to increase, corroboration being sought from an increase in respiratory minute volume, a carbon dioxide output that was disproportionate to the increase of power output, and a rapid increase of respiratory gas exchange ratio. Data were expressed as the oxygen intake at the ventilatory threshold (millilitres per kilogram per minute, standard temperature and pressure, dry (STPD)) and the percentage of peak oxygen intake corresponding to these criteria.

Because of their low initial fitness levels, a significant proportion of patients with chronic heart failure did not meet our normal criterion of maximal oxygen intake (an oxygen consumption plateau, defined as an increment in oxygen consumption of less than 150 millilitres per minute from the penultimate to the final stage of the cycle ergometer test). Subsidiary criteria of peak effort were a heart rate close to the anticipated age-related maximum (220 minus the age in years), a respiratory gas exchange ratio greater than 1.10^{10 15 16} and a rating of perceived exertion of 19 or 20 units on the Borg scale.

Resting ventricular ejection fraction was measured by radionuclide ventriculography at entry to the programme and after 52 weeks. Other measurements included height and body mass; a skinfold estimate of percentage body fat based on triceps, subscapular, and suprailiac skinfolds, as measured by Harpenden Calipers¹⁷; and the maximal grip force of the dominant hand as measured by Stoelting handgrip dynamometer.

CHRONIC HEART FAILURE QUESTIONNAIRE

The Chronic Heart Failure Questionnaire¹⁸ is a disease-specific health-related quality of life questionnaire which assesses the patient's dyspnoea during day-to-day activities (5 questions), fatigue (4 questions), emotional function (7 questions), and coping with the illness ("mastery", 4 questions). Responses to each item are scored on a 7-point scale. The

designers of the instrument have reported that it is reliable in patients in stable condition, offering a sensitive estimate of the disease-specific quality of life.

STANDARD GAMBLE

The standard gamble has the advantage of fulfilling the fundamental axioms of utility theory.^{19 20} Patients are offered two alternatives: the status quo, with the prospect of living with the existing disability for life, or taking a gamble on treatment for which the outcome is uncertain. The patient is told that the proposed treatment will lead to perfect health with a probability of p , but a probability of $1 - p$ that it will cause certain death. The value of p is varied, using a coloured wheel, until the patient perceives no difference between the alternatives of the treatment and the status quo. The probability value chosen by an individual at any given assessment summarises their perceived quality of life on a single scale that ranges from 0 (death) to 1.0 (full health).

EXERCISE TRAINING REGIMEN

The individualised aerobic training prescription was based on progressive walking. It followed the general practice of the Toronto Rehabilitation Centre.¹¹ The initial intensity of training was based on the results of the laboratory exercise test, as indicated by the ventilatory threshold, 50–60% of peak oxygen intake, and a perception of 13–14 on the Borg scale of perceived exertion. During the first 16 weeks patients attended the Toronto Rehabilitation Centre five times per week, and carried out the walk accompanied by a rehabilitation therapist. Initially, the total weekly distance averaged 10 km (range 6–16 km) at an average pace of 13 minutes per km. Over the first 16 weeks the distance was increased progressively to 21 km (16–33 km), and the average pace was boosted to 11.5 minutes per km. Thereafter, the training programme continued for one year, with visits to the exercise classes at the rehabilitation centre once weekly for a further 20 weeks, and then once monthly for the final 16 weeks. Throughout the period of reduced visits, the patients carried out their prescribed walk away from the centre, for a total of five exercise sessions weekly. Compliance was excellent; on average, patients attended 95% of the supervised exercise sessions during the first 16 weeks of training, 86% of the sessions during the subsequent 36 weeks, and completed 78% of the required home sessions.

STATISTICAL ANALYSES

Descriptive data are presented as mean (SE) of the mean. Changes in cardiorespiratory function and quality of life measured over the period of the study were analysed using an ANOVA for repeated measures. Where statistical significance was established, individual differences from initial readings were tested using Fisher's protected least significance difference test, with P set at < 0.05 . All graphs indicate the significance of differences from initial values: a = $P < 0.05$, b = $P < 0.01$, c = $P < 0.0001$.

Figure 1 Distance covered during a six-minute test walk over the course of the programme of aerobic training (sample size 17 subjects 0–16 weeks, 15 subjects at 26 and 52 weeks). Initial pace 81 (13) metres/min (ANOVA, $P < 0.0035$) to 95 (13) metres/min. (b = $P < 0.01$, c = $P < 0.001$).

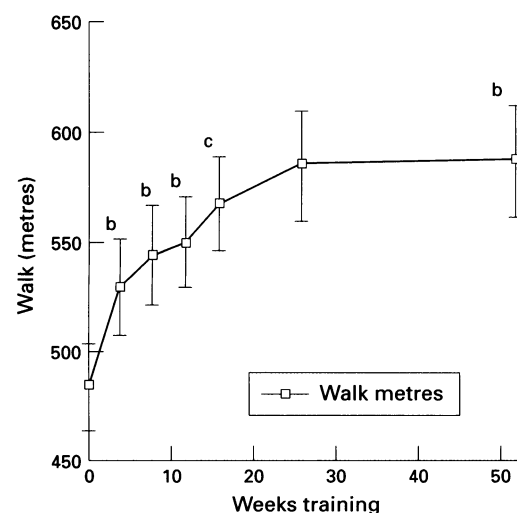


Table 2 Changes in physiological and cardiorespiratory variables in all patients: magnitude and timing of peak response, and response seen after 4 weeks of training (mean (SE)) (sample size 17 subjects at 0–16 weeks and 15 subjects at 26 and 52 weeks)

Variable	Initial	Peak Δ (weeks)	Δ at 2nd test (4 week)
LBM (kg)	58.7 (2.9)	-1.4 (0.7) at 26 weeks (NS)	-0.2 (0.3) (NS)
BMI (kg/m ²)	26.6 (1.0)	-0.7 (0.3) at 26 weeks (LSD P < 0.0062)	-0.2 (0.3) (NS)
Peak Power Output (W)	104.4 (34.9)	+12.3 (9.2) at 16 weeks (LSD P < 0.0001)	+6.3 (9.1) (LSD P < 0.015)
Peak O ₂ Intake (ml/[kg.min])	15.6 (3.5)	+2.6 (1.5) at 16 weeks (LSD P < 0.0001)	+1.0 (1.2) (LSD P < 0.044)
Ventilatory threshold (ml.kg)	11.9 (1.6)	+1.7 (0.5) at 52 weeks (LSD P < 0.0003)	+0.6 (1.3) (NS)
Ventilation (l/min)	56.6 (15.6)	+6.6 (10.5) at 52 weeks (LSD P < 0.05)	+4.3 (1.3) (NS)
O ₂ Pulse (ml.beat)	8.9 (2.9)	+0.9 (0.1) at 16 weeks (LSD P < 0.0013)	+0.3 (0.2) (NS)
\dot{V}_E/\dot{V}_{CO_2} (l/min)	40.3 (2.0)	-2.2 (0.6) at 16 weeks (NS)	+0.5 (0.5) (NS)
\dot{V}_E/\dot{V}_{O_2} (l/min)	46.3 (2.3)	-2.5 (1.0) at 16 weeks (NS)	+0.1 (1.2) (NS)
HRrest (beats.min ⁻¹)	80.4 (13.9)	-6.7 (7.8) at 26 weeks (LSD P < 0.0003)	-3.5 (6.0) (LSD P < 0.060)
HRmax (beats.min ⁻¹)	141 (17)	+7.8 (3.2) at 52 weeks (LSD P < 0.0011)	+0.9 (2.3) (NS)
Systolic BPmax (mm Hg)	161 (7.7)	+9.8 (3.2) at 26 weeks (LSD P < 0.055)	+5.1 (3.4) (NS)
RPPmax (beats \times mm Hg)	23 200 (1537)	+2010 (720) at 26 weeks (LSD P < 0.19)	+579 (609) (NS)

LBM, lean body mass; BMI, body mass index; RPP, rate-pressure product; \dot{V}_E/\dot{V}_{CO_2} , ventilatory equivalent for carbon dioxide; \dot{V}_E/\dot{V}_{O_2} , ventilatory equivalent for oxygen.

There were six patients who did not complete 52 weeks, and paired comparisons have been based on those who were still continuing to exercise at a given time point.

Results

CONTROL PATIENTS' OBSERVATIONS

During the 12 week period of control observations there were no significant changes in any

of the quality of life and physiological measurements, and the only change in the patients' perceptions was a trend to improved emotional function (significant at 12 weeks only). Mean (SEM) of initial and 12-week values for the components of the Chronic Heart Failure Questionnaire were: mastery (21.9 (1.2) and 22.0 (1.2)), fatigue (14.0 (1.3) and 15.1 (1.3)), dyspnoea (23.4 (2.9) and 24.2 (2.6)), and emotional function (28.3 (2.2) and 32.6 (2.4)). The mean value of the standard gamble test at baseline (0.68 (0.1)) was also unchanged at week 12 (0.66 (0.1)). There was no change in exercise performance or cardiorespiratory fitness: peak power output (103.7 (3.7) and 100.0 (4.4) W), peak oxygen intake (15.1 (0.5) and 15.3 (0.5) ml/[kg.min]), and ventilatory threshold (11.7 (0.3) and 11.4 (0.3) ml/[kg.min]).

CLINICAL STATUS

None of the patients showed any immediate adverse cardiac responses to either testing or training, with the exception of two individuals who developed short, self-limiting runs of asymptomatic ventricular tachycardia during their initial exercise test. The resting left ventricular ejection fraction increased from its initial value of 21.4 (1.5) to 27.3 (2.1)%; Δ 5.8 (1.3) (99% CI 0.3 to 11.3, P < 0.001) by the end of the programme. The New York Heart Association class improved from class II to class I in one patient, from III to II in nine, remained at class II in one, and remained at class III in four.

Fifteen of the 21 patients initially enrolled in the exercise programme completed all 52 weeks of the trial successfully. Three patients were withdrawn because of an apparent worsening of chronic failure, but in no instance did this appear related to the exercise programme. Patient 6 began experiencing extreme fatigue after 4 weeks of training—he was subsequently diagnosed as having developed hypothyroidism. Patient 12 developed atrial fibrillation with increasing chronic heart failure, and in consequence he was withdrawn from the study at 4 weeks. Patient 15 was removed from the study at 8 weeks because of worsening chronic heart failure. Patient 18 had a cardiac arrest while shopping for groceries at week 16 of the trial, and he was withdrawn from the study for this reason. He subsequently received an implantable defibrillator. Two other patients withdrew from the study for non-cardiac reasons; patient 13 became non-compliant after 16 weeks and refused to return for subsequent testing, and patient 2 was unable to walk at 52 weeks because of a painful spur in the right foot. In the remaining 15 patients, the clinical condition showed an early improvement that continued over the 52 weeks of observation.

The initial exercise prescription averaged a walking distance of 2.2 km per session, at a pace of 4.4 km/h, and this progressed over the first 16 weeks to an average of 5.3 km/session at a pace of 6.0 km/h; thereafter, pace and speed were maintained to 52 weeks. Compliance with the prescription was good, ranging from 82 to 100% of the required dose of exercise

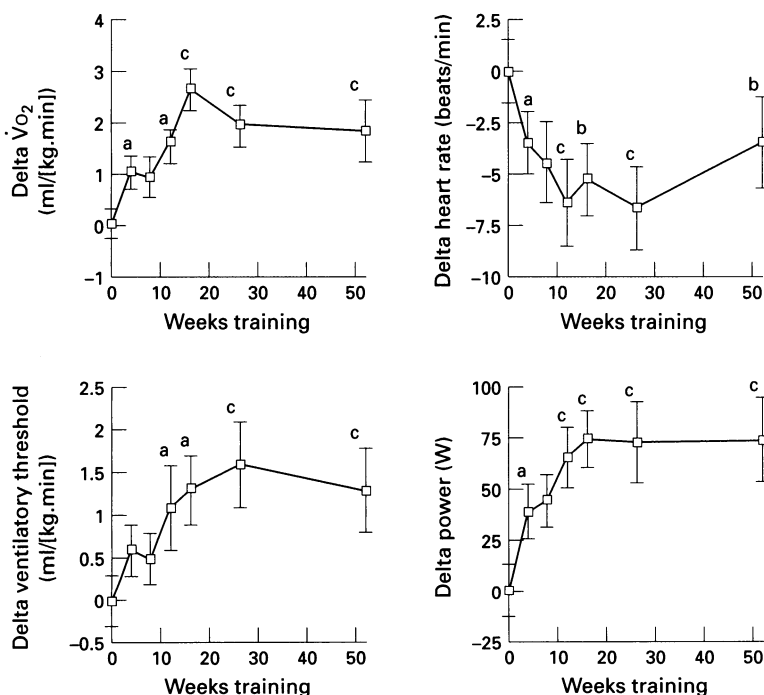


Figure 2 Changes induced by 52 weeks of aerobic training in patients with chronic heart failure. Values (delta (SE)) for peak oxygen intake (ml/[kg.min]), resting heart rate, ventilatory threshold, and peak power output on cycle ergometer. Sample size 17 subjects 0–16 weeks, 15 subjects at 26 and 52 weeks. (a = P < 0.05, b = P < 0.01, c = P < 0.001).

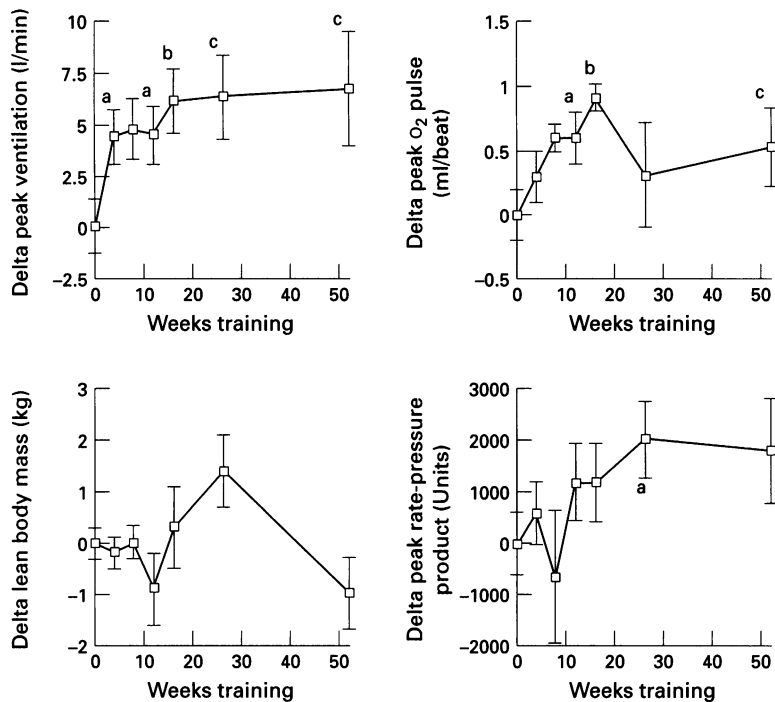


Figure 3 Changes in physiological variables over 52 weeks of aerobic training. Values (delta (SE)) in patients with chronic heart failure for peak ventilation, peak oxygen pulse, lean body mass, and peak rate pressure product. Sample size 17 subjects 0–16 weeks, 15 subjects at 26 and 52 weeks. (a = $P < 0.05$, b = $P < 0.01$, c = $P < 0.001$).

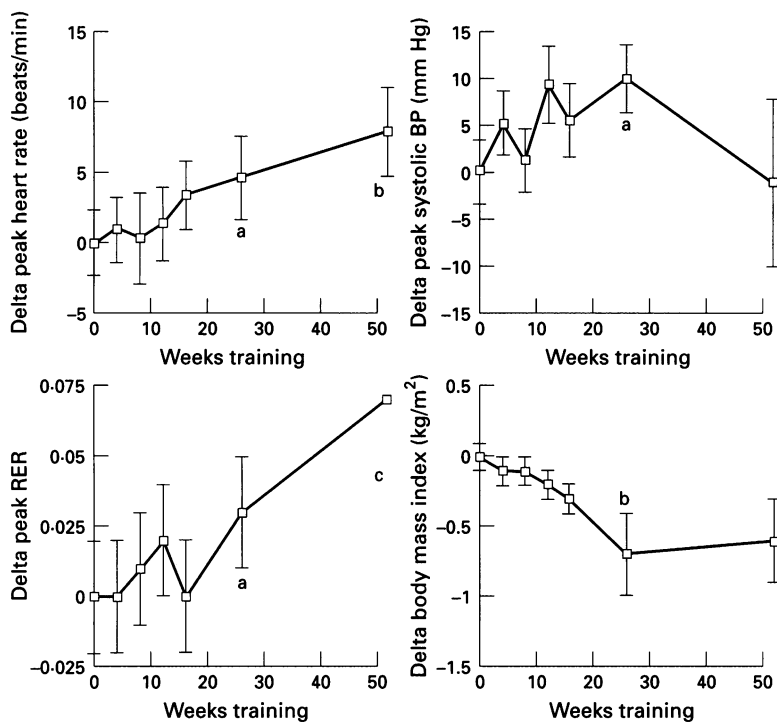


Figure 4 Changes in additional physiological variables over 52 weeks of aerobic training. Values (delta (SE)) in patients with chronic heart failure for: peak heart rate, peak systolic blood pressure, peak respiratory gas exchange ratio, and body mass index. Sample size 17 subjects 0–16 weeks, 15 subjects at 26 and 52 weeks. (a = $P < 0.05$, b = $P < 0.01$, c = $P < 0.001$).

(mean (SD), 93.4 (5.3)%). A qualitative measure of compliance was provided by the distance walked per week.

SIX-MINUTE WALK (FIG 1)

Significant improvements in the speed of the six-minute test walk continued throughout the trial. An initial pace of 81 (13) metres/min had risen (ANOVA, $P < 0.0035$) to 95 (13)

metres/min at 16 weeks, an improvement of some 18% (LSD $P < 0.0001$); thereafter, values were sustained at a plateau (98.8 ± 12.8 metres/min at 52 weeks). More than half of this response was already apparent at the 4-week test (pace = 88 (14) metres/min; least significant difference, $P < 0.009$).

CARDIORESPIRATORY FUNCTION (TABLE 2, FIG 2)

Gains of cardiorespiratory function, as indicated by peak oxygen intake (ANOVA, $P < 0.0003$), resting heart rate (ANOVA, $P < 0.007$), ventilatory (anaerobic) threshold (ANOVA, $P < 0.028$), and peak power output (ANOVA, $P < 0.0001$), tended to develop a little more slowly than the improvement in walking pace, with a suggestion of a plateau between the fourth and the eighth weeks of treatment, a peaking of gains at 16 weeks, and little deterioration of function thereafter. The peak oxygen intake increased progressively, with a peak gain at 16 weeks; the 4 week gain was 38% of this response. The resting heart rate decreased progressively, the largest decrease being seen at 26 weeks. The 4 week change in heart rate was 52% of this response. The ventilatory threshold showed its largest training response after 52 weeks of training; the 4 week response was only 35% of this. The peak power output showed a peak gain at 16 weeks of training; the 4 week response amounted to 51% of this change.

FACTORS ASSOCIATED WITH CARDIOVASCULAR RESPONSE (TABLE 2, FIGS 3 AND 4)

The gain in peak exercise performance was associated with an increase in minute ventilation (ANOVA, $P < 0.021$), the peak increase being seen at 52 weeks of training. There was also a small trend to an increase of oxygen pulse (ANOVA, $P < 0.066$); this response was maximal at 16 weeks of training, and at 4 weeks (NS) was only 33% of this. Lean body mass showed only minor and erratic changes over the period of observation. Handgrip force also failed to show significant changes. The maximum rate-pressure product tended to increase beyond the eighth week of training (ANOVA, $P < 0.19$), the peak gain at 26 weeks amounting to about 8.7%. This reflected a progressive and statistically significant augmentation of peak heart rate (ANOVA, $P < 0.037$), the peak gain being seen after 52 weeks of training. The peak systolic blood pressure also tended to increase over the study (ANOVA, $P < 0.085$), the maximum change being seen at 26 weeks of training. Changes in peak respiratory gas exchange ratio were erratic, but the body mass index tended to a small decline over the course of the experiment (ANOVA, $P < 0.091$); the largest decrease was seen at 26 weeks.

CHANGES IN THE QUALITY OF LIFE (FIGS 5 AND 6)

The chronic heart failure questionnaire showed a trend to improvement on all four perceptions of the quality of life. A decrease in fatigue (ANOVA, $P < 0.001$) and trends to

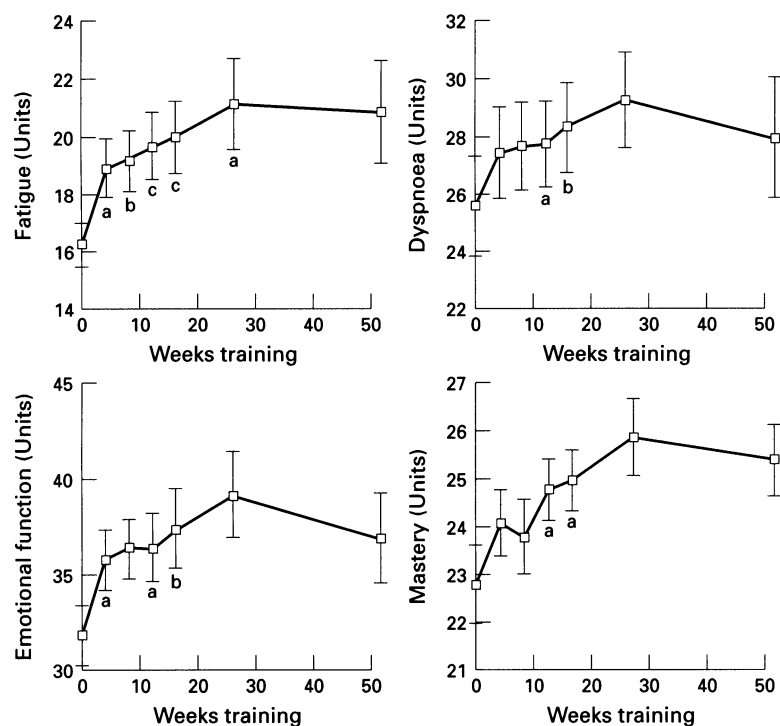


Figure 5 Changes in scores for symptom questionnaire over the course of 52 weeks of aerobic training. Values (delta (SE)) in patients with chronic heart failure for: fatigue, dyspnoea, emotional function, and mastery. Sample size 17 subjects 0–16 weeks, 15 subjects at 26 and 52 weeks. (a = $P < 0.05$, b = $P < 0.01$, c = $P < 0.001$).

decreased dyspnoea (ANOVA, $P < 0.115$), improved emotional function (ANOVA, $P < 0.132$), and increased mastery (ANOVA, $P < 0.149$) showed a general parallel to physiological gains, with improvement over the first four weeks of training, but continuing progress over at least 26 weeks of observation. The standard gamble showed a 14% improvement (ANOVA, $P < 0.0035$) from an initial assessment of 76 (18) (LSD, $P < 0.0001$), with 64% of this change occurring over the first four weeks of training (LSD, $P < 0.0085$); values peaked over the first 16 weeks of the programme, but the improvement was largely

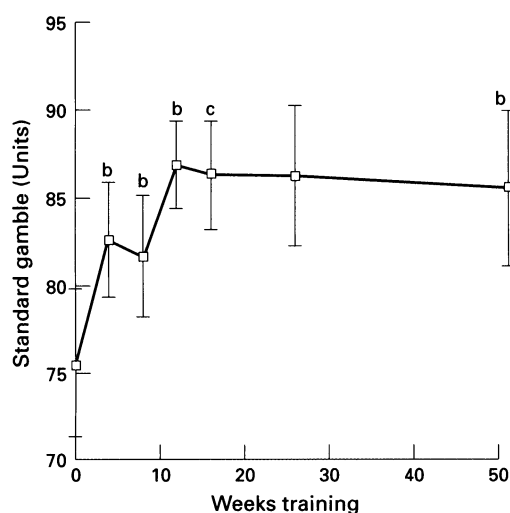


Figure 6 Changes in scores for standard gamble over the course of 52 weeks of aerobic training. Values (delta (SE)) in patients with chronic heart failure. Sample size 17 subjects 0–16 weeks, 15 patients at 26 and 52 weeks. (b = $P < 0.01$, c = $P < 0.001$).

sustained throughout the 52 weeks of observation.

Discussion

SUSTAINED BENEFIT

Previous authors have demonstrated that patients with chronic heart failure show short-term benefits in response to a programme of progressive aerobic exercise. However, this is the first investigation to provide detailed data showing that functional gains can be maintained over a year of continuing exercise and observation. Sustained improvements in physiological measures such as peak oxygen intake, peak power output, ventilatory threshold, and resting heart rate were associated with major improvements in the quality of life and functional ability as measured by habitual walking speed.

Demonstration that the functional gains persist is important, because an exercise programme cannot be administered in a double blind manner. Over the initial 12 weeks of control observations all measures, with the possible exception of emotional function, were unchanged, despite the fact that the patients were receiving close medical attention and observation throughout this period. It could be argued that the exercise programme itself could have induced an early placebo response. However, such a response would have waned as involvement in the programme continued, whereas the present results showed well-sustained physiological and psychological improvements.

MECHANISM OF BENEFIT

The hypotheses that have been invoked previously to explain the improved function of trained heart failure patients have included a correction of lean tissue loss associated with prolonged immobilisation,²¹ enhancement of oxidative metabolism in the leg muscles,^{22–24} and a decrease in respiratory minute volume at any given carbon dioxide output.²⁵

The present study sheds some additional light upon potential mechanisms of benefit. Given the training-related increases in peak heart rate, peak ventilation, peak systolic pressure, and peak respiratory gas exchange ratio, it is arguable that the extra medical attention increased the patients' confidence, allowing them to exercise to a higher level of peak effort with each successive test. However, the absence of change during 12 weeks of control observations that included participation in four maximal laboratory stress tests speaks against such a hypothesis, and the equally large gains in oxygen transport at the ventilatory threshold provide strong evidence that the programme did more than induce a simple increase in peak effort on the part of the patients.

There was a small trend to a decrease in body mass—1.1% at 16 weeks and 2.2% in 52 weeks. Other factors being equal, this would have increased the relative peak oxygen intake (expressed in ml/[kg.min]), but not the absolute peak oxygen intake. Thus the

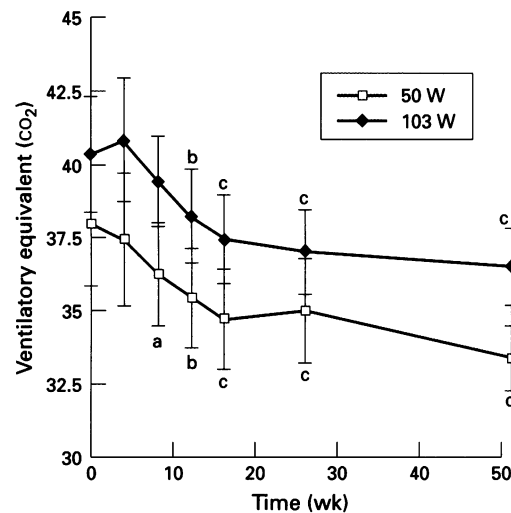


Figure 7 Changes in ventilatory equivalent for carbon dioxide over the course of 52 weeks of aerobic training. Values (mean (SE)) in patients with chronic heart failure at standard power output of 50 W and at highest power output consistently attained (average 103 W). Sample size 17 subjects 0 to 16 weeks, 15 patients at 26 and 52 weeks. (a = $P < 0.05$, b = $P < 0.01$, c = $P < 0.001$).

response cannot be attributed simply to a reduction of body mass over the period of exercise training.

Our programme did not contain any substantial muscle-strengthening component, and handgrip force did not change significantly over the 52 weeks of conditioning. Although some muscle wasting may already have occurred when the present study began, our estimate of lean tissue mass (initially 58.7 (11.6) kg, 3.43 g/m) was relatively high, and perhaps for this reason the functional gains developed in the absence of any change in lean body mass.

If the patients showed an excessive ventila-

tory response to exercise, this might reduce exercise capacity by diverting the available oxygen intake from the leg to the respiratory muscles.²⁶ Such a problem would not in itself alter the individual's peak oxygen intake (because the measurement does not identify where the oxygen is being used), but it would restrict the patient's peak power output. Over the course of the training period, the ventilatory equivalent for carbon dioxide showed a non-significant decrease at a fixed submaximal work rate (fig 7). The peak ventilatory equivalent for both carbon dioxide and oxygen also decreased slightly (table 2). However, the observed improvement, about 5% in both values, was smaller than the gain in either the absolute peak oxygen intake (15.0% at 16 weeks, 11.4% at 52 weeks) or the peak power output (11.3% at 16 weeks, 11.2% at 52 weeks). Moreover, there was not much of a discrepancy between the gains in peak power output and peak oxygen intake. Thus although the training programme tended to decrease the ventilatory equivalent for carbon dioxide and oxygen, probably by improving the aerobic enzyme activity of the muscles,^{22-24 27} it seems unlikely that this change made a major contribution to the observed increase of aerobic performance.

This leaves an improvement of cardiovascular function as the main probable source of benefit. Because of training-induced alterations of autonomic balance²⁷ and autonomic sensitivity of the heart, the cardiac stroke volume may have been increased and/or a larger fraction of the cardiac output may have been directed to the working tissues. This suggestion is supported by the improvement in resting left ventricular ejection fraction. At the onset of training, the peak oxygen pulse was also low (8.9 (2.9) ml/beat); a trend to a 10.3% increase was seen after 16 weeks of training, but a lesser response of 5.1% was seen at 52 weeks. Assuming that there was a parallel 10.3% gain of stroke volume at 16 weeks, this would explain most of the observed improvement in aerobic performance. Support for a shift of autonomic regulation and/or an increase of stroke volume is provided by the decrease of resting heart rate over the training period.

FUNCTIONAL CONSEQUENCES

The observed gains in aerobic power (fig 8) and performance of the 6-minute walk test (fig 9) correlated significantly with each of the four measures of subjective response (fatigue, dyspnoea, emotional function, and mastery). However, the gains in submaximal performance (the chosen speed of walking) showed a closer correlation with improvement in symptoms than did gains in aerobic power (respective significance of linear regression coefficients, $P = 0.0002$ to 0.0036 and $P = 0.026$ to 0.039). The explanation for this probably lies in the more subjective nature of the self-selected walking speed.

The response to exercise was substantially greater in those with a low initial quality of life, significantly so for dyspnoea ($r = 0.57$; $P =$

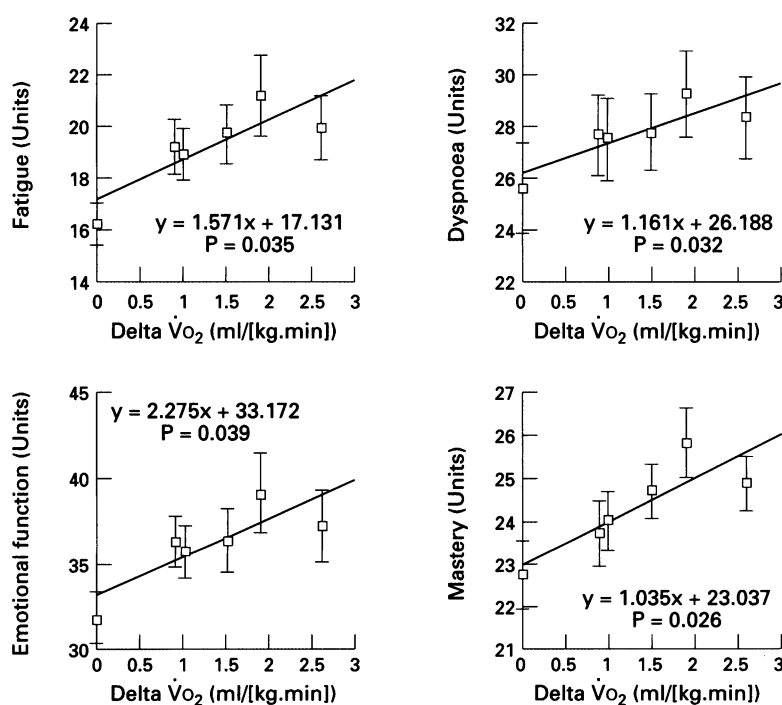


Figure 8 Relation between training-induced gain in $\dot{V}O_{2\max}$ (delta $\dot{V}O_2$ [ml/(kg.min)]) and symptom scores for fatigue, dyspnoea, emotional function, and mastery.

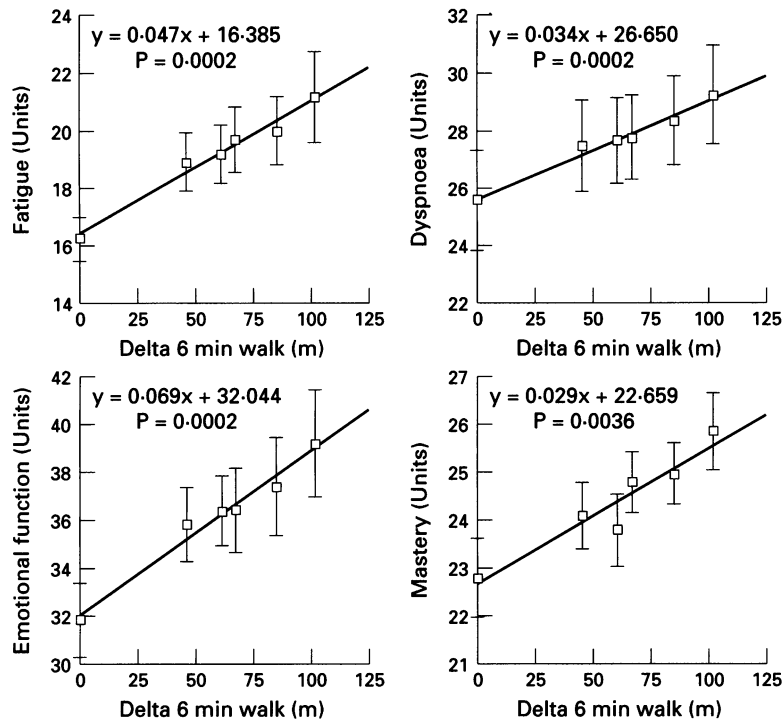


Figure 9 Relation between training-induced gain in distance walked over six minutes and symptom scores for fatigue, dyspnoea, emotional function, and mastery.

0.017), mastery ($r = 0.65$; $P = 0.005$), and the standard gamble ($r = 0.82$; $P = 0.0001$). There was a slight trend to an association between compliance and initial symptoms (greater compliance when score is high), but in no case was this statistically significant. Gains in quality of life also showed a trend to be greater when compliance was high, but again this was non-significant.

CONCLUSIONS

These observations show that in patients with stable chronic failure, the early gains of performance induced by an aerobic training programme are sustained over the course of at least 52 weeks, with parallel gains in functional capacity and mood state. Much of the observed benefit seems to be attributable to enhanced cardiovascular function, as shown by a slowing of resting pulse rate, a tendency to increase of peak oxygen pulse, an enhanced resting ejection fraction, and an increase of peak oxygen intake. Changes are independent of any alterations in body mass or lean tissue mass, and bear only a limited relation to a decreased ventilatory equivalent for carbon dioxide. Prolonged aerobic training seems safe, feasible, and effective, and should be commended to patients with stable chronic cardiac failure.

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