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Exercise capacity, physical activity patterns and outcomes six years after cardiac rehabilitation in patients with heart failure

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Objective: To determine the short- and long-term effects of an intensive, concentrated rehabilitation programme in patients with chronic heart failure.
Design: Randomized controlled trial, with one-month and six-year evaluations.
Setting: Residential rehabilitation centre in Switzerland.
Subjects: Fifty patients with chronic heart failure, randomized to exercise or control groups.
Interventions: A rehabilitation programme lasting one month, including educational sessions, a low-fat diet, and 2 hours of individually prescribed exercise daily.
Main measures: Exercise test responses, health outcomes and physical activity patterns.
Results: Peak $\dot{V}o_2$ increased 21.4% in the exercise group during the rehabilitation programme ($P<0.05$), whereas peak $\dot{V}o_2$ did not change among controls. After the six-year follow-up period, peak $\dot{V}o_2$ was only slightly higher than that at baseline in the trained group (7%, NS), while peak $\dot{V}o_2$ among controls was unchanged. During long-term follow-up, 9 and 12 patients died in the exercise and control groups, respectively ($P=0.63$). At six years, physical activity patterns tended to be higher in the exercise group; the mean energy expenditure values over the last year were 2704 ± 1970 and 2085 ± 1522 kcal/week during recreational activities for the exercise and control groups, respectively. However, both groups were more active compared to energy expenditure prior to their cardiac event ($P<0.001$).
Conclusions: Six years after participation in a residential rehabilitation programme, patients with chronic heart failure had slightly better outcomes than control subjects, maintained exercise capacity and engaged in activities that exceed the minimal amount recommended by guidelines for cardiovascular health.

Introduction

The benefits of exercise training for patients with chronic heart failure have been widely described in recent years. The physiologic benefits reported following varying periods of rehabilitation include improvements in exercise capacity, skeletal muscle

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metabolic adaptations, higher maximal cardiac output and improved endothelial function.[1,2] Recent meta-analyses have also demonstrated better survival and fewer cardiac events among chronic heart failure patients randomized to training programmes relative to usual care.[3,4] However, studies on the effects of training have generally been limited to the specific training period (e.g. 1–6 months), and little is known regarding the long-term effects of rehabilitation on the maintenance of physiologic adaptations, cardiac events and physical activity patterns.

We recently observed that in a heterogeneous group of post-myocardial infarction patients evaluated two years after participation in a residential rehabilitation programme, gains in exercise capacity were maintained and energy expenditure from daily physical activity patterns among patients in the exercise group were roughly three times that among control subjects.[5] While the benefits of rehabilitation after these two years were considerable, the effects of participation in the unique residential programmes common in central Europe over the longer term have not been explored, nor have these effects been studied in patients with chronic heart failure.

In the present study, we assessed exercise capacity, mortality, cardiac events and physical activity patterns in a group of patients with chronic heart failure a mean of six years after undergoing an intensive residential rehabilitation programme. Our objectives were: (1) to evaluate the effects of the training programme on long-term maintenance of exercise capacity and physical activity patterns; and (2) to compare long-term outcomes between exercise and control subjects following randomization to a residential rehabilitation programme or to a control group.

Methods

Fifty consecutive male patients with reduced ventricular function (mean age 55.0 ± 10) referred to a residential rehabilitation centre in Seewis, Switzerland participated in the study. Twenty-five were randomized to an exercise training group and 25 were randomized to a control group. A study flow diagram is presented in Figure 1. Subjects with ischaemic and non-ischaemic aetiologies were divided evenly between groups. Ischaemic aetiology was defined by history of myocardial infarction, angiographic coronary artery disease, or both at the time of randomization. Chronic heart failure was documented by clinical, angiographic or echocardiographic criteria, and a resting ejection fraction <40%. All subjects completed maximal exercise tests at baseline and one month following rehabilitation or usual care. A mean of 6.2 ± 1.4 years after randomization, subjects were asked to return for follow-up testing.

At baseline, 25 subjects (50%) had sustained a myocardial infarction, 3 (6%) had undergone percutaneous transluminal coronary angioplasty and 20 (40%) had undergone coronary artery bypass surgery (CABS). After the coronary event, patients were stabilized for approximately one month prior to beginning rehabilitation. Adjustments were made to medication regimens such that all patients had stable symptoms at baseline. All patients were limited by fatigue, dyspnoea or both on baseline exercise testing, and none had clinical evidence of pulmonary disease. After informed consent was obtained, baseline exercise testing was performed, and subjects were randomized into the exercise or control groups. Patients in the exercise group resided at the rehabilitation centre for one month. Control subjects received usual clinical care, including verbal encouragement to remain physically active.

Exercise training

Details of the rehabilitation programme have been described previously.[5,6] Five indoor cycling sessions were performed weekly for a duration of 30 min, and all subjects walked outdoors for 45 min twice daily. Training duration was one month. Exercise intensity was determined using both objective (heart rate reserve and work rate targeted to 60–80% of maximal), and subjective (Borg scale 12–14)[7] responses, and work rate was adjusted (manually) accordingly.

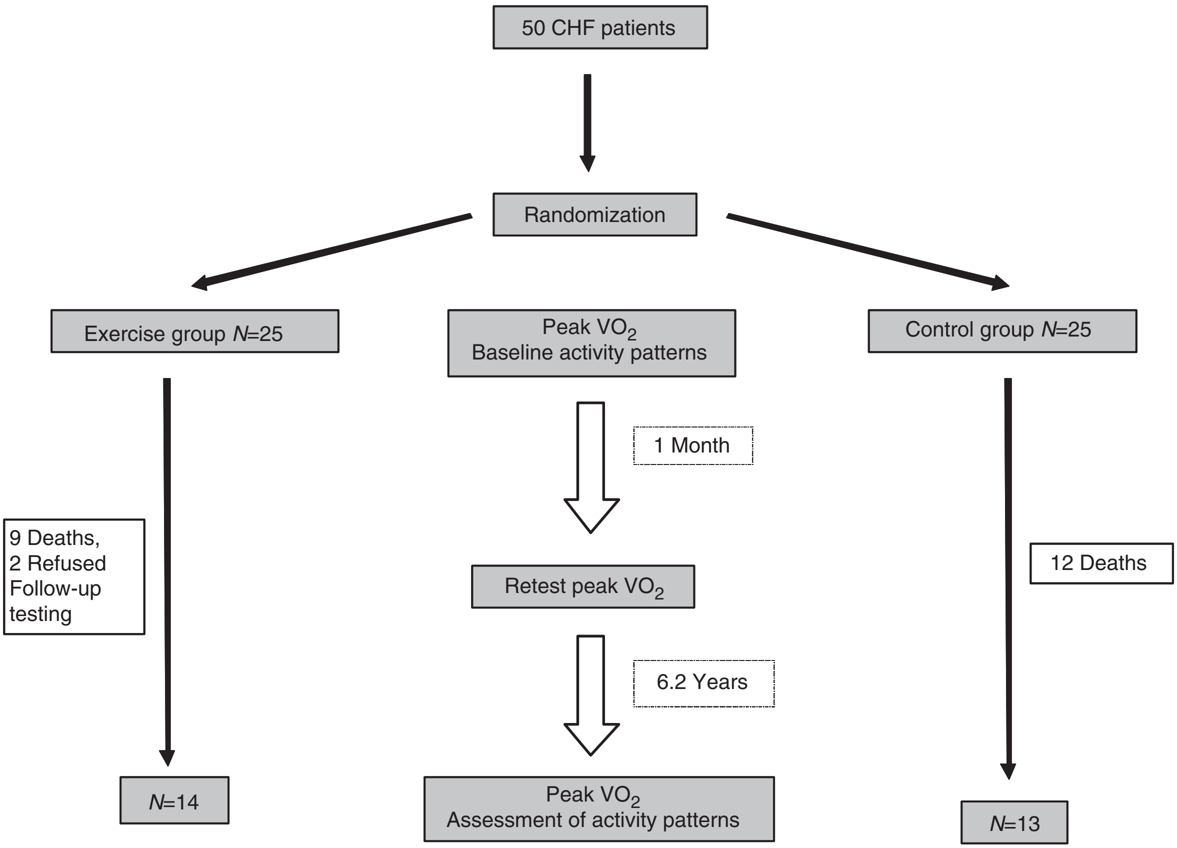

Figure 1 Study flow diagram.

Exercise testing

Maximal exercise testing was performed on an electrically braked cycle ergometer using an individualized ramp protocol,[8] which entailed choosing an individualized ramp rate to yield a test duration of ~10 min. The ramp rate chosen was the same for a given patient on the pre- and post-training test as well as the six-year follow-up test. A 12-lead electrocardiogram was monitored continuously, and blood pressure was measured manually every minute during exercise and throughout the recovery period. The patient's subjective level of exertion was quantified every minute using the Borg 6–20 scale.[7] All tests were continued to volitional fatigue/dyspnoea.

Assessment of physical activity

The quantification of physical activity was performed by interview using a questionnaire modeled after the Harvard Alumni studies of Paffenbarger and colleagues.[9] The questionnaire responses were entered into a Microsoft Access file, which computed metabolic costs of both occupational and recreational activities, and expressed the results as energy expenditure in kilocalories per week. Energy costs of activities were estimated from the compendium of activities developed by Ainsworth *et al*.[10] Energy costs of stairs climbed per week were calculated using the estimation of Basset *et al*.[11] Energy expenditure was expressed in terms of lifetime adulthood recreational activity, and separately as energy expended during the year prior to the evaluation.

Statistical analysis

NCSS software (Kayesville, Utah, USA) was used to perform all statistical analyses. Paired *t*-tests and chi-square procedures were used to compare differences between groups at baseline. Multivariate ANOVA procedures were used to compare exercise responses at baseline, after the rehabilitation programme, and at the six-year follow-up evaluation between groups. ANOVA was also used to compare current energy expenditure with that during adulthood within and between groups. Post-hoc procedures were performed using the Bonferroni method. Kaplan–Meier survival curves were constructed to compare survival between groups over the six-year follow-up; the log-rank test was used to assess differences between groups. Data are presented as mean ± SD.

Results

No differences were observed between the exercise and control groups initially in clinical or demographic data, including age, height, weight, pulmonary function or medication status. No untoward events occurred during any of the exercise testing or training procedures. Data from one patient in the control group was not available at the two-month evaluation due to refusal to complete testing. The mean follow-up period was 6.2 ± 1.4 years. Among subjects in the exercise group, 9 died, and 1 refused repeat testing. Among patients in the control group, 12 died and 2 refused repeat testing. Therefore, 14 and 13 patients performed six-year evaluations in the exercise and control groups, respectively.

Exercise testing responses

Exercise test responses before and after the rehabilitation period are presented in Table 1. For each evaluation, mean maximal perceived exertion levels were >19, suggesting that maximal

Table 1 Exercise test responses for baseline and post rehabilitation (one month) (mean ± SD)

	Exercise ($n=25$)		Control ($n=25$)		*P*-value between groups
	Baseline	Post training	Baseline	Post training	
At rest					
Heart rate, beats/min	78.5 ± 18	75.0 ± 14	82.5 ± 13	78.5 ± 11	0.92
Systolic BP, mmHg	136.9 ± 21	131.8 ± 23	137.6 ± 20	130.2 ± 19	0.79
Diastolic BP, mmHg	81.6 ± 14	77.8 ± 15	84.3 ± 15	79.4 ± 15	0.87
Peak exercise					
Heart rate, beats/min	148.7 ± 23	152.2 ± 19	146.4 ± 18	148.8 ± 19	0.89
Systolic BP, mmHg	183.4 ± 36	190.0 ± 35	181.6 ± 27	180.8 ± 27	0.55
Diastolic BP, mmHg	95.4 ± 19	90.3 ± 16	95.7 ± 12	90.8 ± 13	0.98
Vo_2, mL/min	1568.5 ± 325	1849.3 ± 435	1417.5 ± 342	1537.3 ± 478	0.28
Vo_2, mL/kg per min	20.7 ± 3.7	24.6** ± 5.1	19.1 ± 3.5	20.4 ± 3.6	0.09
Minute ventilation	60.4 ± 12.9	75.5** ± 17.2	54.4 ± 12.4	57.0 ± 13.2	0.03
CO_2 production, mL/min	1803.5 ± 390	2269.3** ± 547	1704.5 ± 387	1850.5 ± 448	0.08
Respiratory exchange ratio	1.15 ± 0.11	1.23 ± 0.09	1.21 ± 0.10	1.22 ± 0.14	0.14
Lactate max, mmol/L	3.49 ± 1.4	4.66 ± 1.5	3.45 ± 1.4	3.91 ± 1.4	0.24
Exercise time, s	589.6 ± 89	735.4** ± 124	560.3 ± 116	596.6 ± 117	0.02
Perceived exertion	19.1 ± 0.92	19.3 ± 0.56	19.3 ± 0.84	19.2 ± 0.69	0.20
Watts	131.8 ± 30	168.2** ± 42	122.0 ± 34	130.8 ± 33	0.05

*$P<0.05$ within group; **$P<0.01$ within group.
BP, blood pressure.

efforts were generally achieved. Training resulted in significant increases in peak Vo_2 (20.7 ± 3.7 to 24.6 ± 5.1 mL/kg per min, $P < 0.01$ within group), and concomitant increases in peak watts achieved ($P = 0.02$ between groups) and exercise time ($P = 0.05$ between groups). The training response was similar regardless of the presence or absence of an ischaemic aetiology.

Exercise test responses for the 27 subjects completing the six-year follow-up are presented for the exercise and control groups in Table 2. In the exercise group, peak Vo_2 increased significantly after training (from 22.0 ± 3.4 to 26.7 ± 4.3, $P < 0.05$), but was not significantly different from baseline at the six-year evaluation. Peak watts achieved and exercise time followed a similar pattern. No differences were observed among control subjects between the three tests.

Energy expenditure

Current recreational activity (encompassing the last year) did not differ between the exercise group control groups (2704 ± 1970 kcal/week versus 2085 ± 1522 kcal/week, $P = 0.40$). Within each group, current energy expenditure was higher than that reported for lifetime adulthood activity prior to their cardiac events (2137 ± 2021 and 1269 ± 1162 for exercise and control groups, respectively; $P < 0.001$ comparing current versus lifetime activity for both groups).

Outcomes

During the 6.2-year follow-up, 9 and 12 patients in the trained and control groups died, respectively. Kaplan–Meier survival curves depicting all-cause mortality in the two groups are illustrated in Figure 2. The difference between groups was not significant ($P = 0.63$). There were eight and five hospitalizations for cardiovascular reasons in the exercise and control groups respectively, during the follow-up. In the exercise group, the reasons for hospitalization were two instances of decompensated chronic heart failure, four pacemaker/ICD implantations, one bypass surgery, and one pulmonary embolism. In the control group, there were three instances of

Table 2 Exercise test responses for matching patients baseline, post rehabilitation and follow-up (mean ± SD)

	Exercise ($n = 14$)			Control ($n = 13$)			*P*-value between groups
	Baseline	Post training	Follow-up	Baseline	Post training	Follow-up	
Rest							
Heart rate, beats/min	75.6 ± 18	75.1 ± 13	70.0 ± 18	85.3 ± 12	77.1 ± 11	67.0* ± 11	0.26
Systolic BP, mmHg	137 ± 17	129 ± 16	118* ± 18	142 ± 18	141 ± 17	130 ± 15	0.59
Diastolic BP, mmHg	82 ± 11	78 ± 15	74 ± 9	89 ± 15	88 ± 13	84 ± 8	0.90
Peak exercise							
Heart rate, beats/min	151.2 ± 22	156.6 ± 16	140.5 ± 29	153.4 ± 19	153.0 ± 23	144.2 ± 17	0.81
Systolic BP, mmHg	183 ± 34	186 ± 31	169 ± 33	194 ± 26	191 ± 25	173 ± 12	0.90
Diastolic BP, mmHg	95 ± 15	89 ± 16	85 ± 14	99 ± 11	97 ± 11	90 ± 10	0.88
Vo_2, mL/min	1578 ± 360	1908 ± 449	1856 ± 563	1543 ± 306	1636 ± 351	1600 ± 389	0.15
Vo_2, mL/kg per min	22.0 ± 3.4	26.7* ± 4.3	23.6 ± 5.8	19.9 ± 2.7	20.9 ± 2.9	20.3 ± 4.5	0.25
Minute ventilation	59.4 ± 16	77.3 ± 19	67.6 ± 18	57.1 ± 12	58.1 ± 15	55.6 ± 13	0.16
CO_2 production, mL/min	1815 ± 475	2359 ± 577	2113 ± 655	1869 ± 332	1974 ± 367	1929 ± 511	0.29
Respiratory exchange ratio	1.14 ± 0.12	1.24 ± 0.10	1.17 ± 0.07	1.22 ± 0.11	1.22 ± 0.16	1.20 ± 0.12	0.36
Lactate max, mmol/L	3.16 ± 1.3	4.24 ± 1.2	6.35** ± 2.4	3.32 ± 1.4	3.71 ± 1.6	6.28** ± 1.9	0.77
Exercise time, s	591.4 ± 90	744.6* ± 124	570.0** ± 201	593.2 ± 90	623.8 ± 93	5100 ± 122	0.22
Perceived exertion	19.4 ± 0.51	19.4 ± 0.50	19.9 ± 0.27	19.2 ± 0.93	19.2 ± 0.72	19.8 ± 0.62	0.98
Peak watts	133.6 ± 36	172.9 ± 48	134.2 ± 45	133.0 ± 33	139.8 ± 32	115.2 ± 32	0.31

*$P < 0.05$ versus previous test within group; **$P < 0.01$ versus previous test within group.
BP, blood pressure.

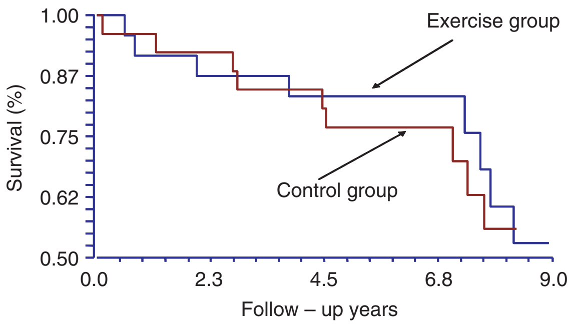

Figure 2 Kaplan–Meier survival curve comparing all-cause mortality between patients in the trained and control groups. The difference between groups was not significant ($P = 0.63$).

decompensated chronic heart failure and two hospitalizations for transient ischaemic attack.

Discussion

Although a significant body of data has been published over the last two decades on the long-term effects of rehabilitation in post-myocardial infarction patients, little is known regarding the effects of programmes of rehabilitation on long-term maintenance of exercise capacity and outcomes in patients with reduced ventricular function. Recent meta-analyses of randomized trials among patients with chronic heart failure have shown 25–30% reductions in cardiac events and all-cause mortality in patients randomized to exercise training compared with control subjects.[3,4] However, the duration of follow-up in these studies was largely limited to that of the training period, and few data are available regarding long-term maintenance of exercise capacity, physical activity patterns and outcomes in patients with chronic heart failure. Because of the reasonable proximity of our patients to the rehabilitation centre (representing one region of Switzerland), we felt it would be of interest to assess outcomes in a group of patients studied as part of a research protocol initiated 10 years earlier. In addition, we had as many patients as possible return to the hospital for follow-up testing, assessment of clinical status and evaluation of current physical activity patterns in order to determine the extent of sustained physical activity.

Exercise test responses

The exercise and control groups were divided equally between patients with ischaemic chronic heart failure and non-ischaemic dilated cardiomyopathy, and the responses to training were similar in the two groups. While data are comparatively sparse in patients with dilated cardiomyopathy, the present findings confirm previous results from our group[12] and others,[13,14] indicating that the response to training is similar between chronic heart failure patients with ischaemic and non-ischaemic aetiologies. We observed an overall 19% increase in peak $V\text{O}_2$, along with concomitant increases in exercise time and peak watts achieved (Table 1). These results provide further support for the use of exercise training in chronic heart failure,[1,2] and in particular add to the sparse body of data available in patients with dilated cardiomyopathy.[12–14]

Among patients in the exercise group who returned for exercise testing a mean of 6.2 years after completing the rehabilitation programme, peak $V\text{O}_2$ was reduced relative to that immediately following rehabilitation, though it remained slightly higher than the peak $V\text{O}_2$ measured before entry into rehabilitation. The decline in peak $V\text{O}_2$ after the six years is not surprising, given that: (1) the training period was intensive, and patients could not be expected to maintain this vigorous activity level following the rehabilitation period; and (2) the decline in peak $V\text{O}_2$ among healthy men during the fifth decade is estimated to be 15.6%.[15] Although to our knowledge there are no long-term studies on the expected decline in peak $V\text{O}_2$ with ageing in patients with chronic heart failure, one would expect that the decline in exercise tolerance would be significantly steeper with time relative to healthy individuals. Importantly, however, neither the exercise or control groups demonstrated the expected declines in peak $V\text{O}_2$ with time. This suggests that both rehabilitation (in those randomized to the exercise programme) and the recommendation to stay active (among controls) had at least some long-term favourable effect on maintaining exercise capacity.

Energy expenditure from physical activity

While subjects in the exercise group received intensive training and education for long-term exercise maintenance, as mentioned above, 'usual care' for the control subjects included instructions on home exercise and encouragement to remain physically active. This probably contributed to the comparatively high current (last year) recreational activity levels reported by the two groups (about 2700 and 2100 kcal/week for the exercise and control groups, respectively, Figure 1). These levels exceed the widely cited minimal recommendations for physical activity by various health organizations,[16–18] and are commensurate with a level that would maintain exercise tolerance for most individuals, particularly those with cardiovascular disease. In a heterogeneous group of post-myocardial infarction or bypass surgery patients assessed two years after completing rehabilitation, we recently observed that subjects in the exercise group were expending about 3100 kcal/week during leisure time, a value that was significantly higher than that expended during adulthood prior to their coronary event (about 900 kcal/week). In the present study, these estimates of energy expenditure from 'current' physical activity patterns were also significantly higher than those of 'lifetime' patterns (about 21 and 30% higher than lifetime activity in the exercise and control groups, respectively). These levels of energy expenditure would be considered physically active by most any standard, and confirm our previous observations suggesting that the rehabilitation programme has the effect of maintaining physical activity over an extended period.

These relatively high levels of activity in the current and previous study are partly explained by the fact that virtually all patients were retired, and that the country of Switzerland is more amenable than the US to activities such as hiking, farming and the like. The fact that control subjects were also comparatively active suggests that cultural factors contribute to an environment more conducive to physical activity. It might also be assumed that the education, exercise and peer support patients received while undergoing rehabilitation led to sustained participation in physical activity and this accounts for the maintenance of physical activity patterns and exercise tolerance after the lengthy follow-up period. However, a bias also probably exists such that those patients in the exercise and control groups who survived and returned for testing had the most stable chronic heart failure and therefore greater exercise tolerance.

Outcomes

While the present study was not originally designed to assess outcomes, nor was it powered sufficiently to do so, it is noteworthy that outcomes did not differ between the exercise and control groups (Figure 2). Although control subjects had slightly more deaths (12 versus 9), this difference was not significant between groups. Nevertheless, the 25% difference in outcomes favouring rehabilitation parallels that reported in two recent meta-analyses of exercise trials in patients with chronic heart failure.[3,4]

Previous studies

Few data are available regarding long-term effects of rehabilitation (e.g. beyond 1–2 years), and to our knowledge, no previous studies have performed objective measures of exercise capacity in the years subsequent to rehabilitation. In a three-year follow-up of 99 patients with chronic heart failure, Belardinelli *et al.*[19] reported significant reductions in mortality (relative risk 0.37) and hospitalization due to chronic heart failure (relative risk 0.29) among those randomized to one year of training. Two recent meta-analyses have evaluated outcomes in patients with chronic heart failure who participated in randomized trials of rehabilitation. A collaborative study of European centres that performed exercise training trials in patients with chronic heart failure during the 1990s was recently completed (termed the ExtraMATCH study).[3] Nine trials met the study inclusion criteria, comprising a total of 395 exercise intervention patients and 406 controls. After a mean follow-up period of 705 days, it was found

Clinical messages

- Exercise training is safe and effective for patients with chronic heart failure.
- The effects of rehabilitation programmes on long-term outcomes in chronic heart failure remain unclear; in the current study, outcomes did not differ between exercise and control groups.
- Six years after participation in a concentrated residential rehabilitation programme, physical activity patterns exceeded the minimal amount recommended for cardiovascular health, and tended to be greater in the group randomized to the exercise programme.

that exercise training reduced mortality in the order of 35%. Using death or hospital admission as an endpoint, training was associated with 28% fewer events versus controls. There was no evidence that any subgroup (elderly, severely reduced exercise capacity or ventricular function, type of chronic heart failure, duration of training or gender) would be less likely to benefit from training. Smart and Marwick[4] performed a similar but less restrictive analysis, including a search of the medical literature on exercise training in chronic heart failure between 1966 and 2003. A total of 81 studies were included in the analysis, which included aerobic training studies, strength training, inspiratory muscle training and combinations of these approaches. No significant differences were observed between the exercise and control groups in total adverse events. However, the mortality rate was 29% lower among subjects who participated in an exercise programme versus those randomized to a control group. While the current study was limited by small numbers, the 25% lower mortality rate in the exercise group parallels that in these meta-analyses.

Summary

Patients with reduced ventricular function due to either ischaemic heart failure or dilated cardiomyopathy respond favourably to a programme of exercise training. Six years after a cardiac event and participation in a concentrated residential rehabilitation programme, patients randomized to the exercise programme had slightly better outcomes than control subjects. However, both groups maintained their exercise capacity, and engaged in physical activities that exceed the amount recommended by guidelines for cardiovascular health. The current analysis was small, and larger prospective randomized trials are needed to assess the long-term effects of rehabilitation programmes in patients with chronic heart failure following a cardiac event.

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