Title

Effects of a home-based exercise program on clinical outcomes in heart failure

Journal

American Heart Journal, 154(5)

ISSN

0002-8703

Authors

Dracup, Kathleen
Evangelista, Lorraine S
Hamilton, Michele A
et al.

Publication Date

2007-11-01

DOI

10.1016/j.ahj.2007.07.019

Peer reviewed

Effects of a home-based exercise program on clinical outcomes in heart failure

Kathleen Dracup, RN, DNSc,[a] Lorraine S. Evangelista, RN, PhD,[b] Michele A. Hamilton, MD,[c] Virginia Erickson, RN, PhD,[c] Antoine Hage, MD,[c] Jamie Moriguchi, MD,[c] Cheryl Canary, RN, PhD,[d] W. Robb MacLellan, MD,[c] and Gregg C. Fonarow, MD[c] ***San Francisco and Los Angeles, CA***

Background The aim of this study was to determine the effects of a home-based exercise program on clinical outcomes. Exercise training improves exercise capacity in patients with heart failure (HF) but the long-term effects on clinical outcomes remain unknown.

Methods We randomized 173 patients with systolic HF to control (n = 87) or home-based exercise (n = 86). The primary end point was a composite of all-cause hospitalizations, emergency department admissions, urgent transplantation, and death at 12 months. Functional performance (as assessed by cardiopulmonary exercise testing and the 6-minute walk test), quality of life, and psychological states were measured at baseline, 3 months, and 6 months.

Results There was no significant difference between experimental and control groups in the combined clinical end point at 12 months and in functional status, quality of life, or psychological states over 6 months. Patients in the exercise group had a lower incidence of multiple (2 or more) hospitalizations compared with the control group: 12.8% versus 26.6%, respectively (P = .018).

Conclusions A home-based walking program that incorporated aerobic and resistance exercise did not result in improved clinical outcomes at 1-year follow-up in this cohort of patients with systolic HF. However, the exercise program resulted in reduced rehospitalization rates. (Am Heart J 2007;154:877-83.)

Controlled clinical trials have demonstrated that exercise training programs of various intensities induce favorable outcomes in patients with heart failure (HF) by significantly increasing aerobic capacity, delaying the onset of anaerobic metabolism, reducing sympathetic drive, and increasing vagal tone.[1-4] However, the effects of exercise training on clinical outcomes are not well identified. Moreover, only 3 studies to date have followed patients beyond 6 months,[3,5,6] leaving the role of exercise in HF unclear.[7]

Most exercise studies on HF have focused on laboratory-based or outpatient programs where patients exercise under controlled conditions. However, many patients are unable to access a formal program because they live in remote geographic locations, have difficulty with transportation, or do not have the financial resources to pay for a structured program. For these patients, a home-based exercise program is optimal. To date, only 5 studies[3,8-11] have tested a home-based walking program in patients with HF, and only 3 included a resistive component.[8,12,13] None tested the effects of the program on clinical outcomes, but rather focused on physiological training effects, symptom occurrence, and quality of life (QOL). Most importantly, almost all studies reported to date were conducted when β-blockers were contraindicated in the treatment of HF, and therefore results do not reflect current evidence-based recommendations for β-blockade.

Therefore, we conducted a randomized clinical trial to examine the effects of a home-based exercise program on combined clinical outcome (all-cause hospitalization, emergency department [ED] admission, urgent transplantation, and death) at 1 year and functional performance, QOL, and psychological states at 3 and 6 months in patients with HF. The training program involved both aerobic and resistive components. The primary hypothesis to be tested was that a low-level, home-based exercise program would result in improved clinical outcomes in patients with HF. Secondary hypotheses focused on functional performance, QOL, and the psychological states of anxiety, depression, and hostility.

From the [a]School of Nursing, University of California, San Francisco, CA, [b]School of Nursing, University of California, Los Angeles, CA, [c]Ahmanson-UCLA Cardiomyopathy Center, UCLA Medical Center, Los Angeles, CA, and [d]California State University Fullerton, Los Angeles, CA.

This study was supported by a grant from the American Heart Association Western Division (NCR, 133-09).

Submitted May 7, 2007; accepted July 24, 2007.

Reprint requests: Kathleen Dracup, RN, DNSc, UCSF School of Nursing N319C, 2 Kirkham Street, Box 0604, San Francisco, CA 94143-0604.

E-mail: kathy.dracup@nursing.ucsf.edu

0002-8703/$ - see front matter

doi:10.1016/j.ahj.2007.07.019

Methods

Study design

A randomized controlled trial was conducted with follow-up at 3, 6, and 12 months. The appropriate institutional review boards reviewed and approved the study and all patients gave written informed consent before randomization.

Patient population

Patients (N = 175) were recruited from 5 sites in Southern California: a university-based HF program, a university-based general cardiology practice, an HF clinic in a health maintenance organization, and 2 private cardiology practices. Inclusion criteria were as follows: English-speaking, aged between 18 and 80 years, HF (defined as New York Heart Association [NYHA] class II through IV) and left ventricular systolic dysfunction with a left ventricular ejection fraction ≤40% as documented by echocardiogram or radionuclide ventriculography within the previous 6 months, and sinus rhythm. Exclusion criteria included myocardial infarction or recurrent angina within the previous 3 months, orthopedic impediments to exercise, severe obstructive pulmonary disease with a forced expiratory volume <1 L in 1 second as measured by spirometry, stenotic valvular disease as measured by echocardiogram, history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiology study or 24-hour Holter monitor), or absence of an implantable cardioverter-defibrillator despite a history of sudden cardiac death. Patients were not enrolled until they were judged stable by their cardiologist. During the course of the study, medical regimens were relatively unchanged except for alterations in diuretic dosages and temporary medication changes during hospitalization or ED visits.

Two patients (one from the experimental and one from the control group) were lost to follow-up within the first 3 months of enrollment. One was incarcerated and the second left the geographic area with no forwarding information. The remaining 173 patients compose the final study.

Home-based exercise training intervention

After collection of baseline samples and measurements, patients fulfilling the recruitment criteria were randomized to an exercise group (n = 86) or a control group (n = 87). Patients assigned to the exercise group were asked to perform a graduated, low-level exercise protocol consisting of low-level aerobic exercise and resistive training. Aerobic training was initially 10 minutes at 40% maximal heart rate and progressively increased up to 45 minutes at 60% maximal heart rate for the remainder of the program. A research nurse walked the prescribed exercise course outside with the patient during the first home visit, using a measuring wheel to measure distance. Patients were given a written prescription to follow that included exercise sessions 4 times weekly with increasing session durations until they were walking a continuous 45 minutes. After 6 weeks for optimization of the aerobic portion of the protocol, a resistive training component was added that involved both upper and lower extremity strengthening. Resistance training was prescribed at 80% of one repetition maximum, which is the maximal weight lifted one time, for 2 sets of 10 repetitions using seated biceps curls to strengthen the arms and seated lateral raises to strengthen shoulders. A second set of 10 repetitions at 80% of one repetition maximum was also prescribed according to recommendations by the American College of Sports Medicine.[14] Lower body strengthening was accomplished by having the patient perform one set of 10 lunges (to strength the hip, thigh, and hamstring) or, in the case of more frail patients, to have the patients move from a sitting to a standing position 10 times. Patients in the experimental group were given hand weights and instructed to perform the resistance exercises 3 days/wk on the days they did not walk.

Patients in the control group maintained their usual level of daily activities, with no systematic exercise component. Patients in both treatment arms were given pedometers (Sportline Pedometer Model 330) and asked to wear them during waking hours as a check on internal validity.[15,16] The pedometers were sealed so that patients could not read the daily distance traveled and were only opened by the research nurses. Knowing that compliance to any home-based exercise program is a critical challenge,[17,18,23] 2 other approaches to measuring compliance with the research protocol were used. First, patients in both groups were asked to write the total number of minutes walked and distance traveled on a log sheet each day. Daily distance traveled in miles was recorded and used to compute weekly and monthly averages. Second, patients in both groups were asked once each month to report their average physical activity, including weekly distances walked, on an activity summary sheet.

Assessment of compliance to the intervention has been reported elsewhere[15] but will be briefly summarized here. Only 44% of the patients randomized to the experimental group (n = 38) had complete pedometer and daily diary data. Patients (n = 20) who demonstrated ≥10% increase in pedometer scores over the first 6 months of the trial had better functional status than patients (n = 18) who demonstrated ≤10% change in scores (6-minute walk distance 1718 ± 46 vs 1012 ± 25 m, F = 5.699, $P = .022$; peak oxygen consumption (Vo_2max) 17 ± 0.7 vs 10 ± 0.5 units, F = 7.162, $P = .011$), suggesting that pedometers, when used, were a valid and reliable measure of compliance. The correlation between pedometer distances and daily diaries was significant at $r = 0.60$, $P = .001$.

Research nurses made home visits weekly for the first 2 weeks and then monthly to assess protocol adherence, correct use of the pedometer, and tolerance to the exercise program. The home visits also served as a form of attention control in the care-as-usual group. All clinical questions were referred to the patient's cardiologist.

Measurements

Clinical events. The primary end point for the study was a combination of all-cause hospitalization, ED admission, urgent transplantation, and all-cause mortality over 12 months. A composite end point was selected over a single outcome (eg, death or rehospitalization alone) to increase the number of events over the 1-year period of follow-up and to reduce the need for a larger sample size or longer follow-up period. The 4 components were selected because of their clinical relevance and potential sensitivity to the exercise intervention. All-cause mortality and all-cause hospitalization was selected over HF mortality and HF hospitalizations to avoid missing events that were misdiagnosed as not related to HF. Given the clinical status of the patients, most events were expected to be related to HF in this population and therefore a loss of sensitivity was not expected.

All event data were obtained from the patients at each monthly visit and verified through the review of medical records. In those cases where patients died over the course of the study, cause of death was confirmed by official death certificates and interviews with the primary physician.

Functional performance

Functional performance was assessed at baseline, 3 months, and 6 months with the cardiopulmonary exercise test and 6-minute walk test. For the former, measurements obtained from the symptom-limited bicycle exercise test with gas analysis included peak $\dot{V}O_2$, minute ventilation, and anaerobic threshold. A standard 15-W ramp protocol was used and all cardiopulmonary exercise test personnel were blinded to patient assignment. Gas exchange measurements were obtained breath by breath using a metabolic cart. Peak $\dot{V}O_2$ was determined as the highest 10-second average value observed over the last 30 seconds of exercise. Earlier studies used peak $\dot{V}O_2$ to measure the effect of physical training.[5,19,20] However, changes in peak $\dot{V}O_2$ may underestimate the effect of therapeutic interventions on submaximal working capacity of patients with HF[19] and does not correlate as well with changes in QOL score as submaximal exercise capacity.[20]

Participants were also asked to do the 6-minute walk test to measure functional performance.[21] Although the 6-minute walk test gives only a rough estimate of the general functional status of the patient, it serves as a good reflection of capacity to undertake day-to-day activities and has acceptable reliability and validity.[21,22]

Quality of life

Quality of life was defined as the degree to which aspects of patients' physical, social, functional, and emotional well-being are impacted by health.[23] It was measured using the Minnesota Living with Heart Failure Questionnaire (LHFQ). The maximum scores are 105 for the total, 40 for physical health and 25 for emotional health; lower scores indicate better QOL.[24]

Psychological states

The Multiple Affect Adjective Checklist was used to measure psychological states at baseline, 3 months, and 6 months. Scores for anxiety, depression, and hostility range from 0 to 21 (norm 7), 0 to 40 (norm 11), and 0 to 28 (norm 7), respectively.[25] Higher scores reflect higher levels of dysphoria. The reliability and validity of the instrument have been demonstrated in patients with HF.[23]

Statistical analysis

Data were analyzed using the SPSS for Windows (version 14.0, SPSS, Inc, Chicago, Ill).[26] Sociodemographic and clinical data are presented as group means ± SD or percentages. To evaluate differences in baseline characteristics and individual clinical outcomes, χ^2 and the independent t test were used. A Kaplan-Meier survival curve was constructed using time-dependent all-cause hospitalization, ED admission, urgent transplantation, and death as a composite end point to test the primary hypothesis. The log-rank test was used to test differences in the number or timing of events between the groups. A sample size of 85 per group was identified as sufficient to allow detection of small to medium interaction effects and a small group (main) effect, with power of .80 at $\alpha = 05$.[27]

Table I. Sociodemographic characteristics at baseline

	Total (N = 173)	Control (n = 86)	Exercise (n = 87)	P
Age (mean years)	54 ± 12.5	54.6 ± 12.5	53.3 ± 12.7	.424
Male (%)	71.7	70.1	73.3	.210
Ethnicity (%)				.437
White	60.1	51.9	48.1	
Nonwhite	39.9	48.1	51.9	
Education (%)				.174
Less than high school	6.1	6.7	5.6	
High school	28.6	34.7	22.2	
Vocational school	13.6	17.3	9.7	
Junior college	22.4	16.0	29.2	
College	17.0	13.3	20.8	
Graduate school	12.2	12.0	12.5	
Income level (%)				.503
<$15000	21.0	26.4	15.5	
$15000-29999	18.2	18.1	18.3	
$30000-49999	23.1	19.4	26.8	
$50000-74,999	20.3	20.8	19.7	
$75000-100,000	9.1	9.7	8.5	
>$100000	8.4	5.6	11.3	
Relationship status (%)				.561
Single, in committed relationship	5.4	2.7	8.1	
Single, not in committed relationship	15.0	17.8	12.2	
Married	63.3	60.3	66.2	
Separated/divorced	8.8	9.5	8.1	
Widowed	7.5	9.6	5.4	
Employed (% yes)	30.1	54.5	45.5	.447

Functional performance, QOL, and psychological states were compared between exercise and control groups using a mixed models analysis as well as a repeated-measures analysis of variance. The results of both statistical approaches were similar, and therefore only the latter are reported here. Statistical significance was set at $P < .05$ for all analyses.

Results

Patients

Patients (N = 173) who had been randomly assigned to control (n = 87) or exercise (n = 86) were followed for 12 months. On average, the patients were aged 54 ± 12.5 years, male (71.7%), white (60.1%), married or in a committed living relationship (68.7%), and in NYHA class II or III (90.2%). Mean ejection fraction was 26.4% ± 6.8% and mean $\dot{V}O_2$max was 13.8 ± 3.6 mL kg^{-1} min^{-1}. Heart failure etiology was ischemic in 38% of patients. Seventy percent of patients were receiving β-blockers, whereas 92.4% were taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker.

There were no differences between the control and exercise groups at baseline with respect to sociodemographic variables (Table I) and most clinical characteristics (Table II). However, patients in the exercise group had a significantly higher likelihood of having a history of

Table II. Clinical characteristics at baseline

	Total (N = 173)	Control (n = 86)	Exercise (n = 87)	*P*
Ejection fraction , mean ± SD (%)	26.4 ± 6.8	26.1 ± 7.0	26.7 ± 6.7	.061
LVEDD, mean ± SD (mm)	66.5 ± 12.0	66.1 ± 10.5	66.9 ± 13.3	.125
Resting heart rate, mean ± SD (beat/min)	75.4 ± 13.4	75.3 ± 13.7	75.5± 13.2	.780
Peak V_{O_2}, mean ± SD (mL kg^{-1} min^{-1})	13.8 ± 3.6	13.3 ± 3.4	14.3 ± 3.7	.231
Anaerobic threshold, mean ± SD	10.3 ± 3.3	9.9 ± 3.3	10.7 ± 3.2	.276
6-min walk (distance in feet), mean ± SD	1351 ± 297	1324 ± 266	1375 ± 324	.167
Heart failure etiology (%)				.913
Ischemic	38.2	35.6	40.7	
Idiopathic	22.0	20.7	23.3	
Valvular	2.9	2.3	3.5	
Dilated	23.1	26.4	19.8	
Other	14.0	13.8	9.8	
NYHA class (%)				.272
II	27.2	21.8	32.6	
III	63.0	66.7	59.3	
IV	9.8	11.5	8.1	
Cardiac history (%)				
Hypertension	45.3	45.3	45.3	.561
Diabetes	25.6	19.8	31.4	.115
Insulin-dependent diabetes	8.0	9.9	6.1	.403
Dyslipidemia	49.4	43.0	55.8	.127
Former smoker	60.4	57.1	63.5	.434
Current smoker	8.7	8.1	9.3	.500
History of CAD	44.2	34.9	53.5	.021 *
Cardiac medications (%)				
ACE inhibitors	74.4	69.8	79.1	.221
Antiarrhythmics	19.2	19.8	18.6	.500
Anticoagulants	45.3	47.7	43.0	.646
Antiplatelets	40.1	31.4	48.8	.029 *
Angiotensin receptor blockers	18.0	20.9	15.1	.428
β-Blockers	69.8	66.3	73.3	.407
Diuretics	89.5	90.7	88.4	.804
Spironolactone	31.4	32.6	30.2	.870
Digitalis	68.0	72.1	64.0	.870
Lipid-lowering agents	47.7	43.0	52.3	.285
Nitrates	27.3	26.7	27.9	.500
Other vasodilators	5.8	7.0	4.7	.746

LVEDD, Left ventricular end-diastolic dimension; *CAD*, coronary artery disease.
*$P < .05$.

coronary heart disease and taking antiplatelet medication than in the control group.

Clinical events

We found no difference between the 2 groups in the combined end point of all-cause hospitalization, ED admission, urgent transplantation, and death ($P = .88$) (Table III). Kaplan-Meier product moment curves for the primary end point also showed no difference in patients assigned to exercise compared with control over 1 year of follow-up (odds ratio 1.228, 95% CI 0.780-1.933, $P = .374$ using the log rank [Mantel-Cox] test) (Figure 1).

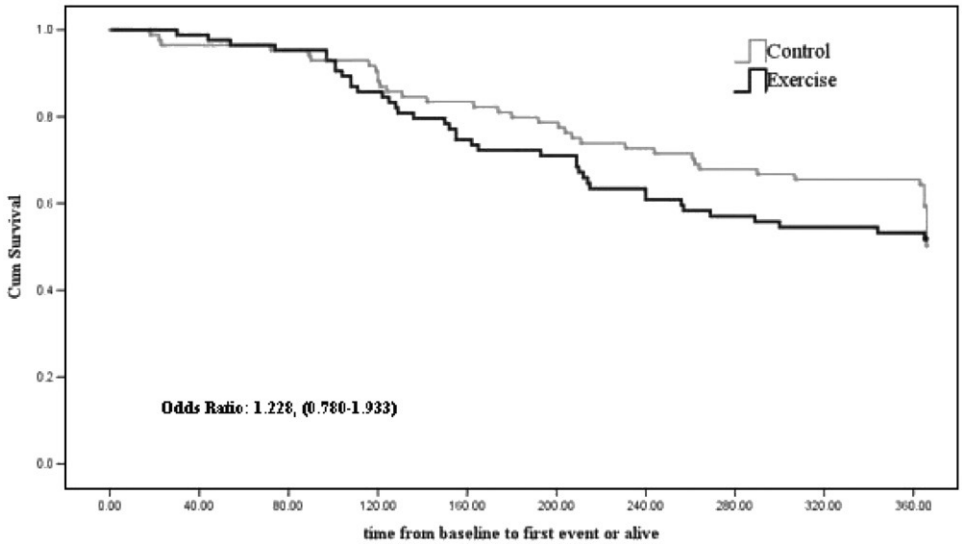
Table III. Differences in clinical outcomes between control and exercise groups at 1-year follow-up

	Total sample (N = 173)	Control (n = 86)	Exercise (n = 87)	*P*
Patients hospitalized during 1-year follow-up, n (%)	72 (41.6)	37 (43.0)	35 (40.2)	.752
Patients admitted to ED, n (%)	46 (26.4)	24 (27.6)	22 (25.6)	.864
Deaths/urgent transplantations, n (%)	17/6 (13.3)	8/3 (12.8)	9/3 (13.8)	.720
Hospitalizations per patient/1 y, mean ± SD	0.83 ± 1.3	0.99 ± 1.5	0.56 ± .8	.024
ED admissions per patient patient/1 y, mean ± SD	0.43 ± .85	0.46 ± .9	0.40 ± .8	.374
Total no. of hospitalizations in patients having ≥2 rehospitalizations, mean ± SD	0.83 ± 1.3	1.05 ± 1.5	0.60 ± .89	.002
Combined end point (% yes) *	75 (43.3)	37 (43.0)	38 (43.7)	.879

*Combined end point indicates hospital admission for HF, ED admission, urgent transplantation/death.

No deaths occurred while patients were exercising and there were no exercise-related injuries during the course of the study. When patients in the control and experimental group were compared on the individual clinical outcomes that made up the composite end point, only the number of hospitalizations was significantly different between groups (Table III). The mean number of hospitalizations in the 2 groups (0.99 ± 1.51 in the control group and 0.56 ± 0.88 in the experimental group) was significantly different ($F = 5.22$, $df = 1$, $P = .02$). There was also a significant difference between the 2 groups in the number of patients who had multiple (≥2) hospitalizations. In the control group, 26.6% (n = 24) had multiple admissions, whereas only 12.8% of patients (n = 11) in the experimental group had 2 or more hospital admissions ($\chi^2 = 7.99$, $df = 2$, $P = .02$). The range for multiple hospital admissions was 2 to 9 and the mean in the 2 groups of rehospitalized patients was 1.05 ± 1.5 versus text 0.64 ± .9, respectively ($P = .04$).

Figure 1



Kaplan-Meier curves illustrating time to first event.

Table IV. Comparison of functional performance, quality of life, and psychological states between groups at baseline, 3 months, and 6 months

	Exercise group (n = 86)			Control group (n = 87)				
Variable	**Baseline**	**3 mo**	**6 mo**	**Baseline**	**3 mo**	**6 mo**	**F**	***P***
Functional performance								
Peak Vo_2 (mL kg^{-1} min)	13.8 ± 3.6	14.1 ± 3.9	13.8 ± 4.1	13.3 ± 3.3	13.9 ± 4.4	13.4 ± 4.0	0.009	.781
Anaerobic threshold	10.3 ± 3.3	11.2 ± 2.6	10.3 ± 3.4	9.9 ± 3.3	10.8 ± 2.7	9.7 ± 3.7	1.29	.235
6-min walk test	1350.7 ± 297.4	1389.8 ± 322.0	1422.9 ± 354.3	1324.1 ± 265.8	1332.4 ± 293.5	1385.6 ± 317.3	1.32	.275
QOL (MLHFQ)								
Total score	46.7 ± 23.8	37.5 ± 23.9	35.7 ± 23.7	49.2 ± 22.4	46.7 ± 26.5	43.2 ± 27.3	0.20	.819
Physical score	19.7 ± 10.1	15.7 ± 10.0	16.1 ± 10.0	20.5 ± 10.8	21.1 ± 11.5	19.4 ± 11.3	0.53	.592
Mental score	10.3 ± 7.1	9.0 ± 6.8	7.8 ± 6.6	12.0 ± 6.9	10.9 ± 8.4	10.5 ± 7.4	0.40	.670
Psychological states (MAACL)								
Anxiety	7.0 ± 4.4	7.5 ± 4.5	7.0 ± 4.2	7.7 ± 4.6	7.3 ± 4.9	7.9 ± 4.4	1.61	.206
Depression	14.2 ± 6.7	8.5 ± 4.0	6.9 ± 3.2	15.0 ± 7.0	8.3 ± 4.7	8.6 ± 4.4	2.60	.081
Hostility	7.7 ± 4.0	14.9 ± 6.6	14.7 ± 6.4	7.6 ± 4.2	15.6 ± 8.0	16.3 ± 7.2	0.64	.533

Values are presented as mean ± SD. *MLHFQ,* Minnesota Living with Heart Failure Questionnaire; *MAACL,* Multiple Adjective Checklist.

Functional performance, QOL, and psychological states

Although the outcomes related to functional performance, QOL, and psychological states changed in the hypothesized direction, none of the changes between groups were statistically significant over time (Table IV). Depression decreased dramatically in the experimental group over 3 and 6 months, but similar decreases were noted in the control patients. In examining the data, the patterns of change were similar for both groups, with marked improvement over the first 3 months and a modulation of that improvement over the second 3 months.

Discussion

The primary hypothesis that a home-based exercise program with both resistive and aerobic components will improve the combined clinical end point of all-cause hospitalization, ED admission, urgent transplant, and all-cause death was not confirmed in this study of patients with systolic HF. To date, this is only the second study of a

systematic exercise program measuring these clinical outcomes in a population of patients with HF. The only other study to examine the effect of exercise on clinical outcomes in HF was conducted in Italy by Belardinelli et al.[5] They tested a hospital-based, outpatient exercise protocol using electronically braked cycle ergometers and found that exercise training resulted in fewer hospital readmissions and fewer cardiac deaths over 1 year. However, the 1-year cardiac mortality rate was significantly higher than in the current study (29.3% vs 13.2%, respectively), reflecting the major shift in treatment of patients with HF. Although approximately 90% of patients in both the earlier and current study were on an ACE inhibitor or angiotensin receptor blocker, the use of β-blockers between the 2 studies was very different; that is, none of the patients in the study by Belardinelli et al[5] were on β-blocker therapy, whereas 70% of the patients in the current study received β-blocker therapy. In addition, they tested a supervised exercise program using cycle ergometers. This type of program is not readily available or appropriate for many patients with HF because of transportation and cost issues.

In analyzing the components of the composite clinical end point, we found a difference in the total number of hospital admissions; patients in the control group required approximately twice as many hospitalizations over the 12 months of follow-up than patients in the exercise group. This may be an important finding given the high cost of frequent rehospitalizations. The difference in hospitalization rates between exercise and control was not related to the monthly home visits made by the research nurses, as these visits were made to patients in both groups. We hypothesize that patients in the exercise group may have become more compliant to the entire HF regimen as they became more active.

We were surprised that the exercise intervention did not result in significant changes in patients' functional performance, QOL, and psychological states, although it should be noted that the changes were in the hypothesized direction. We can offer 4 reasons as potential explanations. First, a degree of crossover may have occurred because of a lack of adherence to the exercise protocol in some of the experimental group patients and an increase in the activity level of the control group patients during the 12 months of the study. The challenge of continued adherence to a home-based exercise program was highlighted in a recent Canadian study[3] when peak oxygen uptake increased in the exercise group only during the 3 months of supervised exercise and not during the remaining 9 months of home-based exercise. Given the patterns of change, the trends seen in the experimental group on secondary outcomes may have reached statistical significance with higher levels of adherence to the study protocol by both groups.

Second, the attention nurses provided to participants in the monthly home visits may have acted as an intervention that muted the power of the exercise intervention to alter the psychosocial state of the patients. This explanation is supported by the results related to depression, because the levels of self-reported depression improved over time in both the experimental and control groups. Given the important predictive role that depression plays in mortality of patients with HF, any reduction in depressive symptoms is important.[28]

Third, the intervention was designed to be a low-level, inexpensive exercise program that could be implemented in any geographic setting. Numerous investigators[12,13] have demonstrated improvements in exercise capacity, and the lack of significant differences between groups in the current study suggests that the home-based exercise program may have been insufficient in intensity to achieve significant physical changes.

Fourth, 70% of all study patients were on β-blockers. Although β-blockers are now standard therapy for patients with HF, they can affect such psychological states as anxiety and depression and may have muted the potential effect of exercise on physical changes, QOL, and emotional states.

Despite 75 primary events and a 43% event rate over 1 year of follow-up, this trial may have been underpowered to detect a clinically meaningful difference in outcome. A large-scale, multicenter trial will be required to fully test this hypothesis. The National Institutes of Health is currently sponsoring a multisite clinical trial titled Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION) that has 3000 as an enrollment target.[29] For the first 3 months, participants exercise 3 times weekly at a participating institution and then continue their customized exercise regimen at home for up to 3 years using a treadmill or stationary bicycle. Although not equivalent to the trial reported here in that special exercise equipment is required, this large National Institutes of Health–sponsored trial is powered to answer definitively whether home-based exercise improves survival and reduces HF-related hospitalizations in this patient population.

Limitations

The limitation of using a composite end point was eloquently summarized by Neaton et al.[30] Composite end points are difficult to interpret if effects are not similar for all components, and this is indeed what occurred in the current study. Although there were twice as many hospitalizations in the control group compared with the exercise group over the year of the study, the number of deaths or urgent transplants and ED admissions were similar between the 2 groups. These differences in outcomes made it difficult to interpret the value of a home-based exercise program on the composite end point.

A second limitation is the difficulty of measuring compliance to exercise and control protocols in an outpatient, home-based setting. The daily diary and the

pedometers provided surrogate measures of exercise, but they were dependent on the fidelity of the patient to use them. Surveys of physical activity rank high on acceptability, cost, and low interference with usual habits, but again they are dependent on self-report and patient fidelity. Thus, we tested a protocol that had the advantage of being highly generalizable because it was convenient for patients and inexpensive, but the interpretation of our findings is limited by our inability to evaluate completely patient compliance to the protocol. Our findings are also limited by the age of our sample, which was considerably younger than the general population of patients with HF.

Clinical implications

The home-based, low-intensity aerobic exercise program combined with a resistive component did not have a significant impact on the combined end point of all-cause hospitalization, ED admission, urgent transplantation, and all-cause death. However, our findings demonstrate that this type of exercise appears to be safe and possibly effective in reducing rehospitalizations for patients with HF. While awaiting more definitive results of clinical trials, clinicians can consider recommending a home-based walking program with a resistance component for patients with HF who do not have access to cardiac rehabilitation programs or other supervised exercise programs.

References

1. Piepoli MF, Davos CH, Franc DP, et al. Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). BMJ 2004;328:189-95.
2. Braith RW, Welsch MA, Feigenbaum MS, et al. Neuroendocrine activation in heart failure is modified by endurance exercise training. J Am Coll Cardiol 1999;34:1170-5.
3. McKelvie R, Kroon KT, Roberts R, et al. Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). Am Heart J 2002;144:23-30.
4. Rees K, Taylor RS, Singh S, et al. Exercise based rehabilitation for heart failure. Cochrane Database Syst Rev 2004;3:CD003331.
5. Belardinelli R, Georgiou D, Cianci G, et al. Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life and clinical outcome. Circulation 1999;99:1173-82.
6. Kavanagh Y, Myers MG, Baigrie RS, et al. Quality of life and cardiorespiratory function in chronic heart failure: effects of 12 months' aerobic training. Heart 1996;76:42-9.
7. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol 2001;38:2101-13.
8. Oka RK, DeMarco T, Haskell WL. Impact of a home-based walking and resistance training program on quality of life in patients with heart failure. Am J Cardiol 2000;85:365-9.
9. Corvera-Tindel T, Doering L, Woo MA, et al. Effect of a home walking exercise program on functional status and symptoms in heart failure. Am Heart J 2004;147:339-46.
10. Smart F, Haluska B, Jeffriess L, et al. Predictors of a sustained response to exercise training in patients with chronic heart failure: a telemonitoring study. Am Heart J 2005;150:1240-7.
11. Hambrecht R, Gielen S, Linke A, et al. Effects of exercise training on left ventricular function and peripheral resistance in patients with chronic heart failure: a randomized trial. JAMA 2000;283:3095-101.
12. Maiorana A, O'Driscoll G, Cheetham C, et al. Combined aerobic and resistance exercise training improves functional capacity and strength in CHF. J Appl Physiol 2000;88:1565-70.
13. Tyni-Lenne RA, Dencker KE, Gordon AL, et al. Comprehensive local muscle training increases aerobic working capacity and quality of life and decreases neurohormonal activation in patients with chronic heart failure. Eur J Heart Fail 2001;3:47-52.
14. American College of Sports Medicine. American College of Sports Medicine position stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. Med Sci Sports Exerc 1990;22:265-74.
15. Evangelista LS, Dracup K, Erickson V, et al. Validity of pedometers for measuring exercise adherence in heart failure patients. J Card Fail 2005;11:366-71.
16. Bassey EJ, Dalloso HM, Fentem PH, et al. Validation of a simple mechanical accelerometer (pedometer) for the estimation of walking activity. Eur J Appl Physiol 1987;56:323-30.
17. Corvera-Tindel T, Doering L, Gomez T, et al. Predictors of noncompliance to exercise training in heart failure. J Cardiovasc Nurs 2004;19:269-77.
18. Clark DO. Issues of adherence, penetration, and measurement in physical activity effectiveness studies. Med Care 2001;39:409-12.
19. Willenheimer R, Rydberg E, Cline C, et al. Effects on quality of life, symptoms and daily activity 6 months after termination of an exercise training programme in heart failure patients. Int J Cardiol 2001;77:25-31.
20. Willenheimer R, Erhardt L, Cline C, et al. Exercise training in heart failure improves quality of life and exercise capacity. Eur Heart J 1998;19:774-81.
21. Guyatt G. Use of the 6-minute walk test as an outcome measure in clinical trials in chronic heart failure. Heart Fail 1987;3:211-7.
22. Cahalin LP, Mathier MA, Semigranm MJ, et al. The 6-minute walk test predicts peak oxygen uptake and survival in patients with heart failure. Chest 1996;110:325-32.
23. Dracup K, Walden J, Stevenson LW, et al. Quality of life in patients with heart failure. J Heart Lung Transplant 1992;11:273-9.
24. Rektor TS, Johnson G, Dunkman B. Evaluation by patients with heart failure of the effects of enalapril compared with hydralazine plus isosorbide dinitrate on quality of life, V-HeFT II. Circulation 1993;87:71-7.
25. Lubin B, Zuckerman M, Hanson PG, et al. Reliability and validity of the Multiple Affect Adjective Check List—Revised. J Psychopathol Behav Assess 1986;8:103-17.
26. SPSS user's guide. 3rd ed. Chicago (IL): SPSS Inc; 2001.
27. Elashoff JD. nQuery advisor. Boston (MA): Statistical Solutions; 1995.
28. Vaccarino V, Kasl SV, Abramson J, et al. Depressive symptoms and risk of functional decline and death in patients with heart failure. J Am Coll Cardiol 2001;38:199-205.
29. http://www.hfaction.org/index.html accessed June 5, 2007.
30. Neaton J, Gray G, Zuckerman B, et al. Key issues in end point selection for heart failure trials: composite end points. J Card Fail 2005;11:567-75.