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## Usefulness of a Home-Based Exercise Program for Overweight and Obese Patients With Advanced Heart Failure

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Exercise is an important behavior for long-term weight control in overweight and obese patients. However, little evidence exists confirming such findings in patients with advanced heart failure (HF). Using a prospective, experimental design, the effects of 24 weeks of a low-level, home-based walking program on weight loss were studied in overweight and obese (body mass index  $\geq 27$  kg/m<sup>2</sup>) patients with advanced HF who were randomized to exercise (n = 48) and control (n = 51) groups. Weight changes between the 2 groups at baseline and 6 months were compared using repeated-measures analysis of variance. Patients were on average aged  $53.3 \pm 10.1$ years and predominantly male (75%), Caucasian (57%), and married (55%). Most patients were in New York Heart Association class III or IV (67%), with a mean ejection fraction of 25%. Patients in the exercise group showed significant weight reduction from baseline to 6 months compared with those in the control group  $(-6.37 \pm 11.7 \text{ vs} - 0.33 \pm 9.3 \text{ kg}, \text{ p} = 0.002)$ . No significant differences were noted between the 2 groups in 6-minute walk distance or depression, although the changes were in the anticipated direction. Modest weight losses of >5% were associated with cardiopulmonary exercise test-documented workload levels at 6 months (r = 0.331, p = 0.006), as well as decreased depression (r = -0.315, p = 0.01) and hostility (r = -0.315) and hostility (r = -0.315, p = 0.01) and hostility (r = -0.315) and hostility -0.355, p = 0.005). The number of hospital admissions was significantly smaller for patients in the exercise group compared with those in the control group  $(0.63 \pm 0.94)$ vs 1.07  $\pm$  0.95, p <0.05). In conclusion, the findings demonstrate the beneficial effects of a low-level, home-based walking program on weight loss in overweight and obese patients with advanced HF. © 2006 Elsevier Inc. All rights reserved. (Am J Cardiol 2006;97:886-890)

The present randomized clinical trial investigation was designed to assess the effects of a 24-week, home-based exercise training program on weight loss, functional status, psychological state, and rehospitalization in patients with advanced heart failure (HF) and body mass indexes (BMIs)  $\geq 25 \text{ kg/m}^2$ . The overall aims of the study were to (1) compare the effect of a home-based exercise training program on weight loss over 6 months in an intervention group versus a control group; (2) examine the differences in functional status, psychological state, and rehospitalization in the exercise and control groups across time; and (3) determine whether weight loss is related to functional status and psychological state. We hypothesized that participants in the treatment arm would show significantly greater weight loss at 6 months, thus resulting in better functional status, psychological state, and clinical outcomes than patients in the control group.

### Methods

Setting and participants: The present study was a substudy of a larger prospective, controlled trial of patients with advanced HF who participated in a 6-month, supervised, home-based walking program designed to measure clinical outcomes, including mortality and rehospitalization events. Only data from overweight and obese patients (BMI  $\ge$ 27 kg/m<sup>2</sup>) who completed the 6-month follow-up (n = 99, or 57.2% of the 173 patients who enrolled in the parent study) were analyzed for this study. The participants were randomized to either the treatment group (n = 48) or the control group (n = 51) as part of the larger study design.

Additional inclusion criteria for the parent study and the substudy reported here were as follows: English speaking; aged from 18 to 80 years; advanced HF, defined as left ventricular systolic dysfunction with a left ventricular ejec-

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tion fraction  $\leq 40\%$  (documented by echocardiography or radionuclide ventriculography within the previous 6 months); and New York Heart Association class II to IV. Exclusion criteria for participation in the study included myocardial infarction or recurrent angina within the previous 3 months, orthopedic impediments to exercise, severe obstructive pulmonary disease with a forced expiratory volume in 1 second <1 L as measured by spirometry, stenotic valvular disease as measured by echocardiography, history of uncontrolled ventricular tachyarrhythmias (documented by electrophysiologic study or 24-hour Holter monitoring), or history of sudden cardiac death. Patients were excluded if they had implantable cardioverter-defibrillators or cognitive impairment as measured by the Mini-Mental Health Examination.

**Procedures:** Human subjects approval for the study was obtained through the appropriate institutional review board. Before study participation, potential participants completed an initial interview in which the requirements of the study were explained and informed consent was obtained. Cardiopulmonary exercise tests and 6-minute walk tests were scheduled for eligible participants <1 week after their initial visits. Patients were also given a questionnaire packet to assess their psychological states before study randomization. Questionnaire completion took 10 to 15 minutes, on average. Finally, hospitalization rates between the 2 groups were monitored through regular follow-up notes obtained from the research nurses and confirmed through chart reviews.

Patients assigned to the exercise group were asked to perform a graduated, low-level exercise protocol  $\geq$ 4 times weekly consisting of light aerobic exercise and resistive training. Aerobic training consisted of an individually tailored walking program of 45 minutes in duration designed to achieve 60% of maximal heart rate. After 6 weeks of optimization of the aerobic portion of the protocol, a light resistive training component was added to the exercise regimen, and the aerobic portion was maintained until the end of the study. Patients in the control group maintained their usual levels of daily activities, with no additional exercise components. All patients were monitored by monthly home visits conducted by a registered nurse, pedometers that were worn during waking hours, and questionnaires measuring daily activity.

**Measures:** Height and weight measurements were obtained from all participants during their baseline and 6-month visits. Height was measured to the nearest 0.5 cm using a stadiometer. Participants were weighed in clothing without shoes (to the nearest 0.1 kg) using a professional beam scale (model 402KLS, Health-o-Meter, Bridgeview, Illinois). The weighing scale was calibrated before each use following the calibration guidelines provided by the manufacturer. We used the documented height and weight to compute BMI, a convenient and increasingly accepted measure of adiposity and its relation to risk.<sup>1</sup> BMI assesses the amount of total body weight in relation to height and is calculated as a patient's weight in kilograms divided by the square of height in meters.<sup>2,3</sup>

Functional status was assessed at baseline and 6 months using 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 VO<sub>2</sub> (the greatest VO<sub>2</sub> observed during exercise), minute ventilation, and anaerobic threshold.<sup>4</sup> A standard 15-W ramp protocol was used. The 6-minute walk test was conducted by asking the patient to walk for 6 minutes at a comfortable pace in a corridor located adjacent to the HF clinic that was measured off in meters. The 6-minute walk distance served as an indicator of exercise tolerance and has been used in numerous clinical trials with high reliability and validity.<sup>5</sup>

Participants were also asked to complete the Multiple Affect Adjective Checklist to assess psychological state (specifically anxiety, depression, and hostility) at the 2 data collection points. The Multiple Affect Adjective Checklist is composed of 132 alphabetically arranged adjectives.<sup>6</sup> Scores for anxiety, depression, and hostility range from 0 to 21 (normal  $\leq$ 7), 0 to 40 (normal 11), and 0 to 28 (normal 7), respectively. Higher scores reflect greater levels of dysphoria. The reliability and validity of the Multiple Affect Adjective Checklist has been demonstrated in patients with HF.<sup>6</sup>

Demographic information was collected using a simple self-administered form. The form asked participants about their age, race, marital status, education, current employment status, and annual income. Information pertaining to medical histories (e.g., the cause of HF) was obtained through self-reports and verified by chart reviews. The results of diagnostic tests (e.g., echocardiography) and information related to the participants' current clinical status (e.g., the cause of HF, New York Heart Association class, the ejection fraction) was obtained from patients' medical records.

**Statistical analysis:** Data were analyzed using SPSS version 11.0 for Windows (SPSS, Inc., Chicago, Illinois).<sup>7</sup> The variables of interest are presented as group means  $\pm$  SDs or as chi-square statistics depending on their levels of measurement. For testing of aim 1, baseline and 6-month weights, psychological states, and functional status were compared between the exercise and control groups using repeated-measures analysis of variance.

General linear regressions were used to describe group differences and group and time differences in functional status and psychological states (aim 2). Univariate and multivariate regression analyses tested the independent association and contribution of sociodemographic and clinical characteristics to weight loss and the independent association and contribution of levels of age, gender, and weight loss to functional status and psychological states (aim 3). A p value <0.05 was considered significant for the univariate and multivariate analyses.

#### Table 1

Baseline demographic and clinical characteristics of the exercise and control groups (n = 99)

Characteristic	Exercise $(n = 48)$	Control $(n = 51)$	p Value
$A_{aa}$ (vm) (maan $\pm$ SD)	$53 \pm 13$	$55 \pm 12$	0.402
Age (yrs) (mean $\pm$ SD) Gender	55 ± 15	$33 \pm 12$	0.402
Men	37 (77%)	34 (67%)	0.230
Women	11 (23%)	17 (33%)	
Race	11 (23%)	17 (33%)	0.171
White	24 (50%)	32 (63%)	0.171
Nonwhite	24 (50%)		
Marital status	24 (30%)	19 (37%)	0.880
Married	27 (5601)	26(510)	0.880
	27 (56%)	26 (51%)	
Single, divorced, or widowed	21 (42%)	25 (49%)	0.712
Education	12 (250)	17 (220)	0.712
High school or less	12 (25%)	17 (33%)	
Vocational or junior college	17 (35%)	14 (27%)	
College or more	19 (40%)	20 (39%)	0.050
Employment status, employed			0.358
Employed	10 (21%)	15 (29%)	
Unemployed/retired	38 (79%)	36 (71%)	
New York Heart Association class			0.314
II	22 (46%)	15 (29%)	
III/IV	26 (54%)	36 (70%)	
HF cause			0.650
Ischemic	22 (45%)	19 (37%)	
Nonischemic	26 (54%)	32 (62%)	
Ejection fraction (%) (mean $\pm$ SD)	$27 \pm 6$	$27 \pm 7$	0.664
BMI category (kg/m <sup>2</sup> )*			0.078
25.1–29.9	22 (46%)	30 (60%)	
30.0-34.9	19 (40%)	13 (25%)	
35.0-39.9	5 (10%)	4 (8%)	
$\geq 40$	0 (0%)	4 (8%)	
Medications		. ,	
Diuretics	46 (96%)	47 (92%)	0.580
ACE inhibitors	37 (77%)	37 (73%)	0.860
Angiotensin II receptor blockers	9 (19%)	11 (22%)	0.645
Nitrates	18 (38%)	19 (38%)	0.870
β blockers	33 (69%)	38 (74%)	0.346
Digoxin	29 (60%)	27 (53%)	0.387
Risk factors/co-morbidities	2) (00%)	27 (3370)	0.507
Smoker	30 (64%)	27 (54%)	0.410
	. ,	27 (34%) 23 (45%)	
Hypertension Dichetes mellitus	20 (42%)	. ,	0.840
Diabetes mellitus	19 (40%)	11 (22%)	0.079
Hyperlipidemia <sup>†</sup>	26 (54%)	22 (43%)	0.317
Coronary artery disease <sup>‡</sup>	23 (48%)	17 (33%)	0.156

\* These groups are based on criteria specified by the American Heart Association guidelines for defining overweight.<sup>8</sup>

<sup>\*</sup> Includes hypercholesterolemia, hypertriglyceridemia, elevated lowdensity lipoprotein and low high-density lipoprotein cholesterol, and/or receiving any pharmacologic therapy for any of these conditions.

\* Defined as a history of myocardial infarction, angina, coronary bypass surgery, or coronary intervention (i.e., coronary stent placement, percutaneous transluminal coronary angioplasty).

### Results

A total of 110 participants in the parent study met the criteria for overweight and obesity (exercise group n = 53, control group n = 57), but only 99 patients (exercise group n = 48, control group n = 51) had complete baseline and 6-month follow-up data for the present analyses. However,

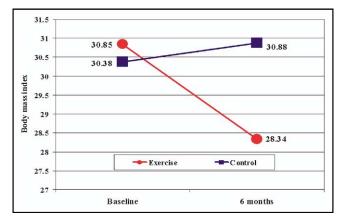


Figure 1. Comparison of weight changes as measured by BMI in the exercise (n = 48) and control (n = 51) groups. Baseline to 6-month comparison: p = 0.002; overall time and group interaction: p = 0.002.

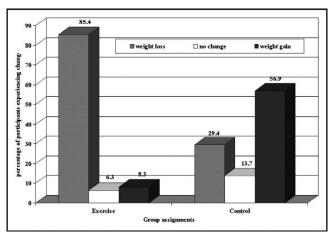


Figure 2. Changes in weight between baseline and 6 months in the exercise (n = 48) and control (n = 51) groups.

there were no differences in the baseline demographic and clinical characteristics of participants who were included or excluded for this substudy. The mean age of participants was 53.34  $\pm$  10.1 years, with no difference in mean age between the 2 groups. The average weight, height, and BMI of study participants were 92.8  $\pm$  13.5 kg, 170.1  $\pm$  10.3 cm, and  $30.5 \pm 4.2 \text{ kg/m}^2$ , respectively. Comparative analyses of sociodemographic and clinical characteristics of participants in the 2 groups at baseline are listed in Table 1. There were no significant differences in any of the baseline characteristics between the 2 groups. Baseline weights and BMIs were slightly greater in participants in the exercise group, although the differences were not statistically significant. Patients were categorized as overweight, mildly obese, moderately obese, and severely obese using the classification suggested by St. Jeor et al.<sup>8</sup> Comparable numbers of participants in the exercise and control groups were categorized in these 4 groups according to BMI. No significant differences in medical therapy and risk factors were noted between the 2 groups.

Changes in BMI between the exercise and control groups were significantly different over time (Figure 1). Eighty-five

Table 2					
Baseline and	6-month	outcomes	(n	=	99)

Variable	Exercise Group $(n = 48)$		Control Group $(n = 51)$		p Value (T $\times$ G
	Baseline	6 Months	Baseline	6 Months	
Clinical outcomes					
Peak VO <sub>2</sub> (ml/kg/min)	$14 \pm 3$	$14 \pm 4$	$13 \pm 3$	$13 \pm 4$	0.727
Workload (W)	$110 \pm 37$	$111 \pm 39$	$95 \pm 29$	$100 \pm 41$	0.631
6-minute walk test	$1,379 \pm 338$	$1,577 \pm 404$	$1,331 \pm 231$	$1,288 \pm 320$	0.514
Rehospitalizations	_	$0.6 \pm 0.9$	_	$1.1 \pm 0.9$	< 0.05
Mood states (MAACL)					
Anxiety	$7.0 \pm 4.1$	$7.2 \pm 4.2$	$8.6 \pm 4.0$	$8.5 \pm 4.1$	0.697
Depression	$14.0 \pm 7.6$	$7.2 \pm 3.4$	$16.2 \pm 5.3$	$9.0 \pm 3.9$	0.828
Hostility	$15.8 \pm 7.2$	$7.7 \pm 4.8$	$16.9 \pm 5.8$	$7.8 \pm 3.7$	0.322

Values are given as mean  $\pm$  SD.

MAACL = Multiple Affect Adjective Checklist;  $T \times G$  = time-by-group interaction.

percent of patients (n = 31) in the experimental group demonstrated >5% weight losses, whereas 57% of patients (n = 29) in the control group demonstrated >5% weight gains over the 6 months of the study. Approximately 1/2 of the patients randomized to the exercise group demonstrated weight losses of 5% to 10% (average 6.4 kg) over the 6 months of follow-up. The differences between groups are graphically represented in Figure 2.

To determine if age and gender played a role in weight loss, these 2 variables were used in a regression analysis along with group assignment. The only variable that was related to a modest weight loss of >5% was treatment group (r = 0.431, p <0.001); it accounted for 18% of the variance in weight loss ( $R^2 = 0.186$ , F change = 22.19, p = <0.001).

We found no differences in functional status (peak VO<sub>2</sub>, workload, and 6-minute walk distance) between the 2 weight groups over time (Table 2). However, we did note a trend toward longer 6-minute walk distances in participants in the exercise group. In addition, we noted no group differences in psychological state over time, but a trend for better scores was noted in the 2 groups across time. We also found that the number of hospital admissions was significantly smaller (F = 4.041, p <0.05) for participants in the exercise group (mean 0.63  $\pm$  0.94, range 0 to 4) compared with participants in the control group (mean 1.07  $\pm$  0.95, range 0 to 7).

Baseline clinical outcomes and mood states did not contribute to levels of weight loss over time. However, we did find that modest weight losses of >5% were associated with cardiopulmonary exercise test-documented workload levels at 6 months (r = 0.331, p = 0.006), as well as decreased levels of depression (r = -0.315, p = 0.01) and hostility (r = -0.355, p = 0.005). Multivariate analysis revealed that age, gender, and weight loss contributed independently to the variance in workloads and accounted for 27% of the variance.

### Discussion

Our findings are comparable with those of other studies examining overweight and obese but otherwise healthy adults that show that exercisers lose significantly more weight during treatment than nonexercisers.<sup>8</sup> Our findings confirm the beneficial effects of a low-level, home-based exercise program on weight loss in overweight and obese patients with systolic HF. These findings challenge the assumption that patients with relatively advanced HF who have the double burden of obesity have difficulty exercising at a level that could lead to weight loss.

In a study evaluating the impact of exercise on obese patients, researchers found that bicycle exercise significantly increased maximal oxygen consumption, arteriovenous oxygen difference, cardiac output, stroke volume, heart rate, mean arterial pressure, mean pulmonary artery pressure, and mean pulmonary wedge pressure.9 The safety and benefits of exercise training were been addressed in a systematic review of >1,500 patients with HF. The data showed that the average peak VO<sub>2</sub> increased from 14.7  $\pm$ 2.4 (i.e., approximately 4 METs) to 17.4  $\pm$  2.9 ml/kg/min (i.e., >5 METs) at the completion of training.<sup>10</sup> Counterintuitively, we did not observe improvements in maximal exercise capacity as measured by peak VO<sub>2</sub> in exercisers compared with nonexercisers in our study. It is likely that the walking exercise was not intensive enough to yield improvements in peak VO<sub>2</sub>. However, we did note higher submaximal exercise levels as measured by the 6-minute walk test in exercisers compared with nonexercisers over the 6 months of follow-up. Although the differences were not statistically significant, the positive trend for improved functional ability supports the potential benefits of weight loss in overweight and obese patients with HF. Clearly, additional research is needed to further understand the interaction between weight loss and cardiac performance and related risk factors.

Our findings showed no significant group differences in psychological states in exercisers and nonexercisers over time, but we did note that modest weight losses of >5% were associated with decreased levels of depression and hostility. Furthermore, our data support that weight loss was the only independent predictor of depression and hostility in

our model. Patients in the exercise group also showed an overall decrease in the number of hospitalizations compared with nonexercisers.

The results of this study are subject to limitations. Although patients with moderate co-morbidities such as asthma, mild arthritis, and non-insulin-dependent diabetes were allowed to enroll, patients were not eligible for inclusion if they had serious co-morbidities. The impact of serious but unfortunately common co-morbidities, such as insulin-dependent diabetes or chronic lung disease, was not measured in the study. Also, patients in our study were considerably younger than the average community-dwelling patient with advanced HF, so our findings may not be applicable to elderly patients with HF, although age did not seem to contribute to weight loss in our analyses. Weight loss was measured only at baseline and 6 months. It would have been more meaningful to track weight loss on a regular basis throughout the study to identify patterns of exercise and weight loss. Similarly, the nature of our data does not lend itself to an examination of a dose-response relation among the amount, frequency, intensity, and duration of exercise in which the participants actually engaged. However, data show that even when the amount of time spent exercising as part of a supervised program is small, exercise nonetheless is likely to lead to a more active lifestyle, so that the effective "dose" of exercise may be considerably greater than that actually prescribed.11 Finally, no study describing weight loss in patients with advanced HF is complete without some mention of the existing HF-obesity paradox that supports the association of greater, not lesser, weight with better outcomes. Chronic HF is a catabolic state, and the development of cachexia, characterized by the loss of all major tissue compartments (muscle, bone, and fat), is a marker of more severe disease.

Although weight reduction has shown positive effects on restoring systolic function and regressing eccentric hypertrophy in morbidly obese cardiac patients,12 recent studies have demonstrated an inverse relation between indexes of obesity and subsequent clinical outcomes in patients with advanced systolic HF.13-17 It has been speculated that moderately obese patients with HF may have greater metabolic reserves and may tolerate the metabolic stress of HF better than lean patients with HF. However, the current studies examining weight loss in patients with HF may not be generalizable, because they are small, conducted at single centers, and limited to patients with severe HF and left ventricular dysfunction. It has also been speculated that obese patients may present earlier; the functional limitations in such patients could be affected by noncardiac causes, and the longer survival in obese patients might indicate a bias toward being diagnosed early in the HF trajectory.<sup>14</sup> Thus, the causal relation between obesity, weight loss, and subsequent clinical outcomes is merely speculative, and evidence examining the impact of voluntary weight loss on outcomes is limited. Notwithstanding the limitations of published studies evaluating the prognostic significance of

weight loss in patients with HF, it is clear that involuntary weight loss of severe HF (cachexia) is a poor prognostic indicator, and overweight and mild to moderate obesity does not seem to be associated with worsening mortality in patients with chronic HF. In extremely obese patients with HF, weight reduction improves cardiac structure, systolic and diastolic ventricular function, and functional status. Evidence on the impact of voluntary weight loss on improvements in clinical outcomes, including survival, in overweight and obese HF patients, however, is limited. Hence, the risks and benefits of deliberate weight reduction are debatable.

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