Objectives
This study investigated the effect of a very long-term exercise training program is not known in chronic heart failure (CHF) patients.

Background
We previously showed that long-term moderate exercise training (ET) improves functional capacity and quality of life in New York Heart Association class II and III CHF patients.

Methods
We studied 123 patients with CHF whose condition was stable over the previous 3 months. After randomization, a trained group (T group, n = 63) underwent a supervised ET at 60% of peak oxygen consumption (VO2), 2 times weekly for 10 years, whereas a nontrained group (NT group, n = 60) did not exercise formally. The ET program was supervised and performed mostly at a coronary club with periodic control sessions twice yearly at the hospital’s gym.

Results
In the T group, peak VO2 was more than 60% of age- and gender-predicted maximum VO2 each year during the 10-year study (p < 0.05 vs. the NT group). In NT patients, peak VO2 decreased progressively with an average of 52 ± 8% of maximum VO2 predicted. Ventilation relative to carbon dioxide output (VE/VCO2) slope was significantly lower (35 ± 9) in T patients versus NT patients (42 ± 11, p < 0.01). Quality-of-life score was significantly better in the T group versus the NT group (43 ± 12 vs. 58 ± 14, p < 0.05). During the 10-year study, T patients had a significant lower rate of hospital readmission (hazard ratio: 0.64, p < 0.001) and cardiac mortality (hazard ratio: 0.68, p < 0.001) than controls. Multivariate analysis selected peak VO2 and resting heart rate as independent predictors of events.

Conclusions
Moderate supervised ET performed twice weekly for 10 years maintains functional capacity of more than 60% of maximum VO2 and confers a sustained improvement in quality of life compared with NT patients. These sustained improvements are associated with reduction in major cardiovascular events, including hospitalizations for CHF and cardiac mortality. (J Am Coll Cardiol 2012;60:1521–8) © 2012 by the American College of Cardiology Foundation

Chronic heart failure (CHF) is the major clinical and public health problem in the world. It is estimated that 23 million people have CHF worldwide. In the United States, 500,000 new cases are reported each year, and the age at diagnosis shifted from 65 ± 9 years from 1950 through 69 to 80 ± 10 years from 1990 through 1999 (1). A common finding in patients with CHF is exercise intolerance, which causes a progressive functional deterioration (2). Controlled clinical trials have shown that exercise training (ET) programs improve aerobic capacity, delay the onset of anaerobic metabolism, and improve the autonomic balance (3–5). Despite the encouraging results of randomized trials, some concerns still exist. One of them is whether ET must be supervised, partly supervised, or not supervised. Another is the duration of ET and its effect on clinical outcome. A previous report from our group demonstrated that a 12-month ET program at 60% of peak VO2 improved functional capacity by 18% at 2 months and was sustained at 1 year. This improvement was associated with lower mortality and hospital readmission for heart failure during a 5-year follow up (3). More recently, the HF-ACTION (Heart Failure: A Controlled Trial Investigating Outcomes of Exercise TraiNing) trial, a multicenter randomized controlled trial enrolling 2,331 medically stable outpatients with CHF, demonstrated a smaller but significant improvement...
in peak VO₂ at 3 months that persisted at 12 months (6). This improvement, however, was not associated with a reduced incidence of hard events. In contrast to our previous trial, patients exercised with no supervision, with a dropout rate of 33% at 12 months, suggesting that supervision may be crucial and may explain a better adherence to training in a long-term ET program. Moreover, we do not know whether the duration of ET is another important variable that may improve outcome.

The primary endpoint of the present study was to determine whether a 10-year supervised moderate ET program may produce a sustained improvement in functional capacity and quality of life in New York Heart Association (NYHA) class II and III CHF patients. We did not consider secondary endpoints. However, we determined whether a 10-year ET program is associated with improvement in clinical outcome compared to NT patients.

**Methods**

This was an independent study and no patients enrolled in the present study participated in the original study (3). Initially, 135 consecutive patients with CHF whose condition was stable were recruited. Of them, 123 decided to participate. Inclusion criteria were clinical stability for 3 months before enrollment, left ventricular ejection fraction (LVEF) of less than 40%, and ability to exercise. Exclusion criteria were hemodynamically significant valvular heart disease, uncontrolled diabetes mellitus and hypertension, orthopedic or neurological problems, and renal insufficiency (creatinine: >2.5 mg/dl). The clinical characteristics of the study population are summarized in Table 1. The cause of CHF was ischemic in 80% of the participants and nonischemic in 20% of the participants. Medications were adjusted according to the patient’s clinical needs in both groups. There were no changes in type and dosage in those patients whose conditions were clinically stable.

**Study design.** The protocol was approved by the local ethics committee. The study was longitudinal, randomized, controlled, and supervised by a cardiologist. All patients gave informed written consent. After the initial visit, patients were randomized into 2 homogeneous groups. The trained group (T group) underwent an ET program for 10 years (n = 63). The nontrained group (NT group) was not provided with a formal ET program (n = 60). On study entry and every 12 months, all patients underwent a cardiopulmonary exercise test (CPET), an echo-Doppler study, and quality of life (QOL) assessment. All studies were performed by skilled operators and were evaluated by 2 experienced observers blinded to each other. A third observer was asked to resolve differences when agreement was not possible. A consensus decision was obtained in all cases.

**Exercise training protocol.** Exercise sessions were performed under the supervision of a cardiologist and an exercise therapist, as previously described (3). The training program consisted of 3 sessions per week at the hospital for 2 months, then 2 supervised sessions the rest of the year. Every 6 months, patients exercised at the hospital, and then they returned to a coronary club, where they exercised the rest of the year. The coronary club is a nonprofit association of patients with cardiac disease promoting ET and healthy lifestyle changes. The intensity was chosen at 60% of peak VO₂ for the first 2 months, and thereafter at 70% of peak VO₂ for the following months until the end of the study. After each annual CPET evaluation, we calculated heart rate from peak VO₂ to maintain training intensity at 70% of peak VO₂. Trained patients were encouraged to exercise without supervision at home at least a third time, perform-

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**Abbreviations and Acronyms**

- CHF = chronic heart failure
- CI = confidence interval
- CPET = cardiopulmonary exercise test
- EF = ejection fraction
- ET = exercise training
- HR = hazard ratio
- LVEF = left ventricular ejection fraction
- NT group = nontrained group
- NYHA = New York Heart Association
- QOL = quality of life
- T group = trained group
- VO₂ = oxygen consumption
- VE/VO₂ = ventilation relative to carbon dioxide output
- VE/VCO₂ = carbon dioxide output
- VCO₂ = carbon dioxide

**Table 1: Clinical Characteristics**

<table>
<thead>
<tr>
<th>All</th>
<th>Group T</th>
<th>Group NT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (male/female)</td>
<td>123 (96/27)</td>
<td>63 (49/14)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>59 ± 14</td>
<td>60 ± 15</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>123</td>
<td>63</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>37 ± 8</td>
<td>38 ± 8</td>
</tr>
<tr>
<td>NYHA functional class II/III</td>
<td>72 (59)/51 (41)</td>
<td>38 (60)/25 (40)</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>98 (80)</td>
<td>50 (80)</td>
</tr>
<tr>
<td>Nonischemic</td>
<td>25 (20)</td>
<td>13 (20)</td>
</tr>
<tr>
<td>ICD</td>
<td>9 (7)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Medications</td>
<td>D 22, ACEI 89, AIIA 29, BB 56, DIU 64, ST 74</td>
<td>D 12, ACEI 45, BB 29, DIU 334, ST 39</td>
</tr>
</tbody>
</table>

Values are n, mean ± SD, or n (%).

ACEI = angiotensin-converting enzyme; AIIA = angiotensin II antagonist; BB = beta-blocker; DIU = diuretic; ICD = implantable cardioverter defibrillator; LV = left ventricle; NYHA = New York Heart Association; ST = statins.
ing aerobic activities at the same heart rate as the other 2 supervised sessions. Each session lasted approximately 1 h, beginning with a warm-up phase of calisthenics and stretching for 15 to 20 min, followed by 40 min of aerobic activity on a cycle ergometer, a treadmill, or both. Blood pressure was measured before the warm-up on a sitting position, at the middle of aerobic exercise, and at the fifth minute of recovery. Heart rate was monitored throughout the session. A written report of each session’s activities and the patient’s heart rate and blood pressure was completed by the supervisor. Patients also received counseling on smoking cessation, stress reduction, and diet. Before randomization, educational sessions were organized at the hospital with groups of patients to explain the objective of the study; the benefits of a healthy nutrition, physical activity, and smoking cessation; and the importance of medications prescribed to CHF patients. A printed summary of the session with examples of diet, exercise methodology, and calisthenics was given to all participants. Educational sessions were performed each year thereafter to participants in both groups until the end of the study.

Usual care. Patients in the NT group were not provided with a formal ET program. They were instructed to continue their usual home daily physical activities, avoiding ET in a supervised environment. All patients were recommended to take the usual medications and received counseling on nutrition, stress reduction, smoking cessation, and physical activity. They also were instructed to avoid high-intensity exercise. They were free to perform aerobic activities such as walking, cycling (home or outside), and swimming, avoiding a duration of longer than 30 min. We did not specify the intensity of exercise in the NT group, because of the potential of bias. However, we advised them to walk and to continue to perform usual physical activities. They were seen at the cardiology clinic every 3 months and were asked to call the supervisor every time they had a question or problem.

Cardiopulmonary exercise testing. After a familiarization test, all patients performed CPET at the Lancisi Hospital before the protocol was started and every 12 months thereafter until the end of the study (3). Briefly, work rate was increased 1 or 2 W every 5 s in a ramp fashion until volitional fatigue or symptoms such as dyspnea, chest discomfort, or dizziness emerged. Patients pedaled on an electronically braked cycle ergometer (Ergometrics 800, Sensormedics, Yorba Linda, California) at a constant rate of 60 rpm. During exercise, patients breathed room air through a Rudolph mask and ventilation and gas exchange were measured breath by breath on a metabolic cart (Cosmed Quark PFT, Rome, Italy). Peak VO₂ was the average oxygen uptake over the last 15 s of exercise. Maximum VO₂ automatically was provided by the system on the basis of age, height, weight, gender, and race. Percentage of peak VO₂ versus maximum VO₂ then was calculated for each comparison. Ventilation relative to carbon dioxide output (VE/VCO₂) slope was calculated as the slope between ventilation (y-axis) and VCO₂ (x-axis) by linear regression analysis. Gas exchange ratio was the ratio between VCO₂ and VO₂.

Echocardiography. M-mode and 2-dimensional echocardiographic studies were performed on study entry and every 12 months in all patients according to the recommendations of the American Society of Echocardiography (7). We used an ultrasound system with a phased-array 2.5-MHz transducer (Megas, ESAOTE, Rome, Italy). Details have been described previously (3,8).

Quality of life. QOL was assessed at baseline and every 12 months in both groups, as previously described (3). We used the Minnesota Living with Heart Failure Questionnaire, which is a patient self-assessment measure and consists of 21 items focused on patient perceptions concerning the effects of CHF on their physical, psychological, and socioeconomic lives (9).

Outcome measures. Outcome measures were defined prospectively as peak VO₂ and QOL change from baseline. We also considered all-cause mortality and cardiovascular morbidity, defined as acute heart decompensation requiring hospitalization and adjustment of medications, unstable angina, myocardial infarction, and cardiac revascularization procedures. Any of these adverse events ended a patient’s participation in the study. We did not consider secondary endpoints. Detailed information on medical history and clinical profile were collected at the time of enrollment and at every visit during the study period. A record was maintained on each patient’s clinical and functional status. Both the T and NT groups were subjected to the same scrutiny and management regimen apart from the exercise component.

Statistical analysis. The study was designed to have 90% power to detect a 10% improvement in functional capacity for patients randomized to ET compared with patients randomized to usual care, with an alpha level = 0.05. We considered a 10 ± 2% improvement in peak VO₂ in trained patients as a minimum value to detect a change on the basis of previous randomized controlled trials already published on the topic before 1994. The sample size was then calculated at 60 patients per arm, considering a dropout rate of 10% in the first year. All analyses were performed with an intention-to-treat principle, and probability values were 2-sided, as previously described (3). Briefly, chi-square analysis and unpaired t tests were used to evaluate differences in baseline parameters between the 2 groups. Multiple comparisons were assessed by repeated-measures analyses of variance. We used Bonferroni’s method to adjust for multiple comparisons. Univariate analysis of peak VO₂ with metabolic, clinical, and echocardiographic variables at baseline and every 12 months was performed until the end of the protocol by the use of change. Variables with significant correlations then were entered into a stepwise linear regression model to determine the strongest independent predictor(s) of change in peak VO₂ occurring after training. The baseline predictors of events were selected using a stepwise
variable selection based on treatment blinded data. Selected variables were entered into a Cox regression model for each endpoint. We also controlled for interactions between model variables. Selected variables were age, gender, cause of heart failure, baseline NYHA class, baseline LVEF, previous revascularization, history of myocardial infarction, beta-blockers at baseline, angiotensin-converting enzyme inhibitor use at baseline, peak VO2, VE/VCO2 slope, resting heart rate, and peak work rate. Only the most significant variables (p < 0.001) then were entered in the covariate-adjusted treatment comparisons. Covariates in the model were peak VO2, resting heart rate, peak work rate, and VE/VCO2 slope. Relative risks were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs) using the Cox proportional hazards model. We tested the proportional hazards assumption by modeling the interaction of follow-up time with changes in peak VO2 from baseline. We also applied this model for hard events, but this was not the primary objective of this study. Data were reported as mean ± SD. Statistical significance was assumed at p ≤ 0.05.

Results

Of 135 patients initially enrolled, 123 completed the protocol: 63 in the T group and 60 in the NT group. The protocol started in 1994 and was completed in 2005. Baseline characteristics of patients are shown in Table 1. The mean age was 59 ± 14 years, and 22% were women. LVEF was 37 ± 8% and 39 ± 7% in CHF patients with ischemic and nonischemic causes, respectively. Patients were in NYHA class II (59%) and III (41%). Medications were distributed similarly in the 2 groups: angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were given in 100% of patients (75% and 25%, respectively), aspirin was given in 75% of patients, beta-blockers were given in 46% of patients, diuretics were given in 52% of patients, and statins were given in 60% of patients. Medications were adjusted in 3 patients in the T group and in 12 patients in the NT group. In particular, beta-blockers were added in 7 NT group patients and in 1 T group patient, and diuretics were added in 10 NT group patients and 2 T group patients. The dropout rate was 3% on average in the T group. Two patients in the T group did not complete the protocol, one because of a car accident and the other for personal reasons. Three patients in the NT group decided to withdraw from the study for reasons unrelated to their clinical status. The adherence to the ET program was 88% over the study period, 100% in terms of minutes exercised, with an average annual rate of 137 ± 18 sessions per patient. Specifically, patients in the T group performed 39 ± 13 exercise sessions per year at home, whereas the NT group performed the following physical activities 2 ± 3 times a week: walking (100%), cycling (40%), and swimming (10%).

Functional capacity. On study entry, there was no difference in peak VO2 between the 2 groups (Fig. 1A). The gas exchange ratio was more than 1.05 in all CPET studies. After 12 months, peak VO2 improved by 14.7% in T patients, whereas it decreased by 2.5% in NT patients (p < 0.01). Peak VO2 was significantly higher in T patients compared with NT patients for each of the following years. At 2 years, the difference in peak VO2 between T and NT patients was 3.0 ml/kg per min, corresponding to a 24.6% difference (p < 0.01). At 5 years, the absolute difference in peak VO2 was 4.5 ml/kg per min (27.1%); at 7 years, the absolute difference in peak VO2 was 4.2 ml/kg per min (25.2%); and at 10 years, the absolute difference in peak VO2 was 3.6 ml/kg per min (21.8%; p < 0.01 for each comparison). In terms of percent of maximum VO2, peak VO2 was maintained at more than 60% throughout the 10 years (average: 65.3 ± 3%), whereas it was <55% in NT patients (52 ± 8%, p < 0.01) (Fig. 1B). A similar trend was noted in resting heart rate (Fig. 2A). We modeled the interaction of follow-up time with the strongest independent predictors of change in peak VO2 from baseline and observed that only exercise training interacted with it (p < 0.001).

Ventilation relative to carbon dioxide output slope. Changes in ventilatory efficiency were similar as in peak VO2 (Fig. 2B). In T patients, VE/VCO2 slope averaged 35 ± 9, whereas in the NT patients, it was 42 ± 11 (p < 0.01). Ejection fraction. Ejection fraction (EF) was not significantly different between the 2 groups at baseline and each
year until the fourth year (Fig. 3). At 5 years, there was a significant improvement in T patients (41% vs. 34%, $p < 0.01$) that was sustained until completion of the study. At 10 years, the difference in resting EF was 28% between T and NT patients ($p < 0.01$). There was no interaction between medications and LVEF. We modeled the interaction of follow-up time with medications and observed no significant deviations. Adjustments did not change statistical significance.

**Quality of life.** QOL average score was significantly better in the T group versus the NT group (43 ± 12 vs. 58 ± 14, $p < 0.05$), and it was sustained throughout the study for each comparison (Fig. 4).

**Safety of exercise training.** There were no important untoward events in T patients. During exercise sessions, hypotension at the end of exercise occurred in 4 patients over 10 years. Sporadic premature ventricular complexes occasionally were present during exercise sessions in 21 patients, and they did not require the interruption of any training sessions. In the T group, patients with an implantable cardioverter-defibrillator had no discharges.

**Clinical outcome.** Events were more frequent in NT than in T patients (35 vs. 12, HR: 0.55, 95% CI: 0.26 to 0.72, $p < 0.0001$) (Table 2). Hospital readmissions were 8 in the T group and 25 in the NT group (HR: 0.64, 95% CI: 0.34 to 0.81, $p < 0.001$). In particular, all of the 8 T patients were admitted for worsening heart failure, which was resolved with adjustment of medical therapy. In the NT group, 5 patients (20%) were readmitted for implantable cardioverter-defibrillator firing and 5 (20%) for atrial arrhythmias (fibrillation or flutter). Of the other 15 hospitalizations, 2 (8%) were the result of hip fracture, 2 (8%) were the result of ischemic stroke, 1 (4%) was the result of unstable angina, and 10 (40%) were the result of worsening heart failure. Cardiac deaths also were more frequent in NT patients (10 vs. 4, HR: 0.68, 95% CI: 0.30 to 0.82, $p < 0.001$). All deaths were cardiac. Multivariate analysis selected peak VO2 and resting heart rate as independent predictors of events (HR: 0.65, 95% CI: 0.37 to 0.79, and HR: 0.82, 95% CI: 0.45 to 0.93, respectively, $p < 0.0001$ for both). The survival model showed an overall effect of ET in predicting all cardiac events (log-rank: 7.29, $p = 0.001$) (Fig. 5), whereas cause and gender did not predict the outcome (Figs. 6 and 7).

**Discussion**

The results of the present investigation demonstrate that a 10-year supervised ET program of moderate intensity produces a sustained improvement in functional capacity and QOL in a group of patients with a NYHA class II and III CHF. These improvements are associated with a reduction in hospital readmission for acute heart failure and improved survival. Heart failure cause does not influence the response to training.

This is the first demonstration in humans that a long-term supervised moderate endurance ET program produced a sustained improvement in functional capacity and QOL. We measured functional capacity as peak VO2, which is preferable to NYHA classification because it represents an objective measure that is reproducible, accurate, and not
operator dependent. Functional capacity is a widely recognized independent predictor of survival in normal persons as well as in patients with cardiovascular disease (10,11). A 1-metabolic equivalent improvement in functional capacity from baseline has been associated with a 12.4% improvement in life expectancy in more than 7,000 middle-aged men with and without cardiovascular disease (10). The direct measurement of peak VO2 has been shown to be a more accurate predictor of survival than indirect derived peak VO2 (12). We found that peak VO2 was significantly higher after 12 months of ET of moderate intensity, and this improvement was maintained over 10 years in patients who performed the ET program. In contrast, NT patients had no change in peak VO2 evident already after 12 months. The sustained improvement in functional capacity was associated with a higher ventilatory efficiency (Fig. 2B). Previous reports have demonstrated that a higher ventilatory efficiency after training is obtained after a short-term ET program and is associated with improved functional capacity and outcome. (13) However, the efficacy of long-term exercise programs on ventilatory efficiency is not known. The remarkable increase in peak VO2 may account for the improvement in survival and reduction in hard events. However, conclusive statements cannot be made with certainty because the number of patients at risk in the survival curves was small. The low mortality in this study may be explained by the fact that patients were younger and mostly in NYHA class II.

Resting EF also was improved in our study, and it was statistically significant at 5 years. The improvement in EF was not evident until the fifth year and was sustained until the end of program, suggesting that a training-induced reverse remodeling effect requires a longer period to occur. The strongest independent predictors of higher functional capacity were resting heart rate and peak VO2. The improved functional capacity after training also may be explained by the lower resting heart rate as a result of improved autonomic balance (5).

Unlike the recently reported HF-ACTION trial (6), which showed no survival advantage in the ET group, our study demonstrated a significant reduction in mortality and cardiac events. There are several important differences between the 2 studies. The present study was supervised. We believe that supervision leads to good adherence and ensures exercise duration and intensity at the levels prescribed. In a nonsupervised study, the increase in peak VO2

### Table 2 Cardiac Events in the 2 Groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>T</th>
<th>NT</th>
<th>Absolute Difference %</th>
<th>HR (95%CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>12</td>
<td>35</td>
<td>41</td>
<td>0.55 (0.26–0.72)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hospital readmission for HF</td>
<td>8</td>
<td>25</td>
<td>29</td>
<td>0.64 (0.34–0.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>0.68 (0.30–0.82)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI = confidence interval; HF = heart failure; HR = hazard ratio.
achieved may not be sufficient to show a difference between the T and NT groups. In fact, the increase in peak VO2 in the HF-ACTION trial was rather modest, only 4%, suggesting less physical activity, and therefore, lower level of peak VO2. The HF-ACTION follow-up study lasted only 2.5 years. The present study lasted for 10 years. The adherence rate in our study was excellent (88%). A significant percentage of patients (55%) in the usual care of the HF-ACTION trial was dissatisfied and may have crossed over to the exercise group, thereby diminishing the study’s ability to detect a significant effect of ET on the primary outcome. In short, the several methodological differences noted above may explain the discordant results and lack of survival advantage. The differences between the present study and the HF-ACTION trial represent 2 different strategies rather than 2 different methodologies.

Although this is a small but well-studied cohort, the results of this study are unique, first, because the T group was supervised and ensured patients exercised at the levels prescribed; second, to our knowledge, the follow-up was the longest performed; and third, the coronary club played an important role in encouraging participation and compliance for the duration of the study. To our knowledge, this is the first long-term study to demonstrate a 32% relative risk reduction of cardiac mortality over 10 years in the T group of CHF patients compared with the NT group. Moreover, peak VO2 and resting heart rate were the most highly independent predictors of events. In contrast to the HF-ACTION trial, we did not find prognostic improvement in our model by adjusting for LVEF or history of atrial fibrillation (6).

On the basis of the results of the present investigation, supervision seems to be very important, because it contributes to lower dropout rate and maintains a higher adherence to exercise program. Previous studies reported higher dropout rates with unsupervised or partly supervised exercise programs (14). In the HF-ACTION trial, for the most part the exercise program was performed at home, and this in part may explain the small increase in functional capacity as compared with control patients. In the present investigation, the dropout rate was 3% on average in the T group and 5% in the NT group (15–19). Because of its social networking, the coronary club may represent an efficient model to follow for a large segment of CHF patients to participate in a long-term cardiac rehabilitation program.

**Study limitations.** The study was underpowered to demonstrate an effect of ET on outcome. Therefore, the significant reduction in cardiac events and improvement in survival should be confirmed in larger trials. This was a supervised study and the results may not be generalized to other parts of the world, where limited resources may not allow for medical supervision. We did not study nonwhite persons, and therefore our results are not applicable to them. Every effort was made to avoid bias. However, some bias cannot be completely eliminated. ET cannot be blinded. However, QOL assessment and CPET studies were performed in a blinded fashion by operators unaware of randomization. We tested the proportional hazards assumption by modeling the interaction of follow-up time with changes in peak VO2 from baseline. We also applied this model for hard events, but this was not the primary objective of this study. Our model was fitted for changes in peak VO2 from baseline. Both the mortality model and hospital readmission model have been adjusted for variables, such as LVEF, history of atrial fibrillation, baseline peak VO2, medications, age, and gender. The rate of beta-blocker therapy was relatively low, given that the study was initiated...
Chronic heart failure patients can maintain an advantage as a result of combining exercise therapy and standard care, because they demonstrate improved functional capacity and QOL compared with patients receiving standard medications who do not exercise regularly. ET was safe over 10 years and produced a significant improvement in functional capacity and QOL that were already evident after 12 months and were sustained for 10 years. Heart rate, ventilatory efficiency, and peak \( \text{VO}_2 \) were improved significantly after 12 months, whereas resting EF required a longer period of time to become significantly higher as compared with NT patients. These beneficial effects of aerobic exercise have been observed with moderate intensity, with 2 supervised sessions per week plus a third session without supervision. Supervision seems to be a crucial factor to reduce dropouts and increase adherence to long-term exercise sessions. The coronary club may be an efficient model to apply in cardiac rehabilitation in future studies.

Conclusions

Acknowledgments

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Key Words: cardiopulmonary exercise test • chronic heart failure • functional capacity • long-term exercise training • quality of life • supervision • survival.