(*Circulation.* 1997;96:1790-1797.)

Articles

Attenuation of Unfavorable Remodeling by Exercise Training in Postinfarction Patients With Left Ventricular Dysfunction

Results of the Exercise in Left Ventricular Dysfunction (ELVD) Trial*

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Abstract

Background Exercise is currently recommended for patients after myocardial infarction; however, the effects of regular exercise on the remodeling process remain to be defined. The aim of this multicenter, randomized study was to investigate whether a long-term physical training program influences left ventricular size and function in postinfarction patients with systolic dysfunction.

Methods and Results Consecutive patients with <40% ejection fraction after a first Q-wave myocardial infarction were randomly assigned to a 6-month exercise training program (n=39) or control group (n=38). After 6 months, a significant increase in work capacity was observed only in the training group (from 4.462±1.095 to 5.752±1.749 kilopond-meters [Kp-m], $P<.01$), not in the control group (from 4.375±1.143 to 4.388±1.199 Kp-m), whereas left ventricular volumes had increased in the control group (end-diastolic volume, from 94±26 to 99±27 mL/m^2, $P<.01$; end-systolic volume, from 62±20 to 67±23 mL/m^2, $P<.01$) but not in the training group (end-diastolic volume, from 93±28 to 92±28 mL/m^2, P=NS; end-systolic volume, from 61±22 to 57±23 mL/m^2, P=NS). Conversely, ejection fraction had improved in the training group (from 34±5% to 38±8%, $P<.01$) but not in the control group (from 34±5% to 33±7%, P=NS).

Conclusions In postinfarction patients with systolic dysfunction, long-term exercise training may attenuate the unfavorable remodeling response and even improve ventricular function over time.

Key Words: exercise • myocardial infarction • remodeling

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The beneficial effects of comprehensive cardiac rehabilitation and secondary prevention programs in patients with coronary artery disease are well documented.[1,2] Clinical benefits include improved exercise tolerance and quality of life, decreased mortality, and possibly lower costs due to lower rehospitalization rates.[1,2,3,4] The results of several uncontrolled, retrospective studies have also suggested that regular exercise may be effective in improving work capacity, even in patients with moderate or severe left ventricular dysfunction, without inducing any significant changes in global ventricular function or central hemodynamics.[5,6,7] During the past decade, however, questions have been raised about the possible detrimental effects of exercise training on left ventricular function and remodeling among patients with anterior Q-wave infarction.[8] A recent randomized, controlled study showed that patients with an initial left ventricular ejection fraction of <40% are prone to global and regional left ventricular dilatation and that physical training does not appear to worsen this anticipated effect.[9] Nevertheless, because the group of patients with low ejection fraction in this trial was not large enough to draw a definite conclusion, further studies were recommended to verify whether there are any specific subsets of the population with recent myocardial infarction in whom exercise training may be potentially harmful. To fill this information gap, the Exercise in Left Ventricular Dysfunction (ELVD) study was designed as a randomized, controlled trial to determine whether long-term physical training influences left ventricular size and remodeling in asymptomatic postinfarct patients with systolic dysfunction.

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Study Protocol and Organization

The ELVD trial was a multicenter, randomized, controlled study in postinfarction patients with left ventricular dysfunction, as defined by an echocardiographic ejection fraction of <40%, and no standard contraindication to exercise who were enrolled at 1 of 15 cardiac rehabilitation centers throughout Italy. All patients underwent functional evaluation both at entry (3 to 5 weeks after a first acute myocardial infarction) and at the end of the study, 6 months later. The functional evaluation included (1) physical examination and chest roentgenogram, (2) Doppler echocardiographic study, (3) standard upright exercise stress testing on a bicycle ergometer, (4) 24-hour ambulatory ECG monitoring, and (5) psychosocial and quality-of-life assessment. Cardioactive drugs were discontinued for ≥48 hours before each evaluation. Coronary artery angiography was also performed during the 6-month period of the study.

After the initial evaluation, patients were randomly allocated to physical training or a control group. All patients provided signed, informed consent before randomization. The principal investigator of the study at the coordinating center of Veruno was responsible for the overall execution of the trial. All data were collected and analyzed at the coordinating center. The study had been approved by the local scientific and ethics committees.

Study Patients

Statistical power calculations for the primary end point of left ventricular end-diastolic volume based on our previous data on the reproducibility of ventricular size by two-dimensional echocardiography in postinfarction patients with left ventricular dysfunction revealed a power of 0.8 to detect a 5% change at 5% significance level with 80 patients completing the trial.

Consecutive patients, survivors of a first acute myocardial infarction, in New York Heart Association functional class I or II were admitted into this prospective study if the following criteria were met: (1) history of a recent (3 to 5 weeks previously) first Q-wave acute myocardial infarction, (2) sinus rhythm and no atrioventricular or intraventricular conduction disturbances, (3) echocardiographic left ventricular ejection fraction of <40%, (4) no contraindications to exercise training, and (5) echocardiographic images of adequate quality for quantitative analysis. The diagnosis of acute myocardial infarction was supported by a typical history of chest pain (>30 minutes), evolutionary ECG changes with new abnormal Q waves (>30 ms), a typical pattern of elevated serum myocardial enzyme levels, and persistent left ventricular asynergy on two-dimensional echocardiography. Exclusion criteria were (1) systemic disease, (2) clinical instability (angina at rest and signs or symptoms of heart failure) at the time of the initial evaluation, (3) low-threshold ischemia (<50 W) or exertional angina uncontrolled by medical therapy, (4) low work capacity (<50 W), and (5) inability to participate in a prospective study for any logistic reason.

From January 1993 through June 1994, 108 patients were evaluated for possible enrollment. Twenty-eight patients were excluded because of recurrent angina at rest (n=5), angina or ST depression at low-level exercise (n=15), clinical heart failure (n=5), and low work capacity (n=3). The remaining 80 patients were enrolled and, after the initial evaluation, randomly allocated to a 6-month exercise training program (n=40) or control group (n=40). The patients were not told to

expect either training or restricted physical activity to be better for them, merely that we were trying to find out objectively which is better. During the study, they received follow-up at the participating centers that were responsible for the clinical evaluation and management of the exercise training program. Reinfarction, heart failure, angina at rest, reduction of effort angina threshold, exertional angina uncontrolled by medical therapy, coronary artery bypass graft surgery, and angioplasty were considered clinical end points and criteria for withdrawal of patients from the study.

Ergometric Test

A multistage symptom-limited bicycle ergometric test was used. Incremental loads of 25 W were given every 3 minutes. The ECG was monitored continuously from lead V_5 and recorded on paper from all leads every minute.

Sphygmomanometric blood pressure was also measured every 3 minutes. The criteria for stopping the test have been previously reported.[9] All tests were carried out by a neutral blinded observer who was unaware of the patient's study group (ie, training status). Heart rate was recorded from the ECG, and rate-pressure product was derived as systolic blood pressure multiplied by heart rate.

Echocardiography: Data Acquisition and Analysis

All patients underwent a complete resting echocardiographic study in multiple views (Hewlett-Packard 77020A) at both the initial and final evaluation; the position of the patient and transducer was noted for use in serial studies. Our methods of data acquisition and image digitalization and the computerized system for the automatic detection and quantification of regional wall motion, left ventricular function, and remodeling have been previously described.[9 10] In brief, the three apical (four- and two-chamber and apical long-axis) views were analyzed to assess left ventricular dimensions and function from three different planes and explore six different ventricular walls from the base to the apex of the heart. The endocardial contour of each view was divided by the computer into 23 segments of equal length, so the entire ventricular wall was represented by a total of 69 segments. By comparison with our reference data base of normal subjects, the presence of abnormal wall motion was automatically detected when the fractional shortening area from end diastole to end systole of each segment was <2 SDs of the mean normal values. The extent of wall motion abnormalities was then calculated as a percentage of the total endocardial length. Global ventricular enlargement and regional dilatation were also automatically identified when the total endocardial surface area and segmental areas at the end-diastolic frame exceeded 2 SDs of the mean values in healthy subjects. The extent of regional dilatation was calculated as the percentage of endocardial length of dilated segments to the total endocardial length. Left ventricular ejection fraction was obtained using the biplane area-length method. All measurements were derived in blinded fashion by a single experienced operator (Dr Giannuzzi) from three consecutive cardiac cycles, and the mean values were considered for analysis. Intraobserver variability in endocardial contouring and in the evaluation of end-diastolic and end-systolic endocardial surface areas by our quantitative analysis in both healthy subjects and patients with myocardial infarction in terms of mean of differences was 0.08±0.06 cm^2/m^2, with the coefficient of repeatability of 1.2 cm^2/m^2.[10]

Psychological and Quality-of-Life Assessment

Psychological evaluation was performed with the Cognitive Behavioural Assessment Hospital form (CBA II). CBA H is a standardized 152-item true/false questionnaire divided into four schedules that explore emotional state, vital exhaustion in the 3 months before evaluation, psychological and behavioral traits potentially related to ischemic heart disease, and behavioral lifestyle.[11 12] Validation analysis of the CBA H had been performed in 4888 Italian subjects, including healthy volunteers, patients with cardiac conditions, and patients with other diseases (lung disease, breast cancer, hypertension, duodenal ulcer) and had been used in the GISSI-2 population.[12] The questionnaire ranges from 0.84 to 0.87 on Cronbach's internal consistency and from 0.42 to 0.63 on retest at 6 months. Quality of life was assessed with modified Likert symptom questionnaires (graded on a six-point scale) on breathlessness, tiredness, chest pain, daily activity, and emotional status.[13]

Training Intervention

The exercise training program was designed in accordance with the rehabilitation centers taking part in the study. The target heart rate was 80% of that achieved at peak incremental exercise. Initially, patients randomized for physical training participated in a supervised, continuous session of 30-minute bicycle ergometry at least three times a week for 2 months. During each supervised session, intensity of exercise, heart rate (from ECG monitoring), and blood pressure were recorded. Thereafter, they continued the exercise program (30-minute bicycle ergometry three times a week) at home, reporting to the laboratory every 2 weeks when a new level of exercise could be tested and prescribed to maintain the target heart rate (80% of the previously determined maximum) for physical training. The intensity of home-based cycle ergometry was adjusted by using a pulse heart rate monitor (Polar Edge, Polar Electro Oly). In addition, patients were asked to take a brisk daily walk for >30 minutes as part of the home-based exercise program. They were instructed to fill in a diary, reporting the date, time, duration, and pulse heart rate at the end of each nonsupervised exercise session. Patients in the control group received educational and psychological support but no formal exercise program, and they

were invited to continue their usual lifestyle but to avoid any physical activity that caused breathlessness or fatigue.

Statistical Analysis

Baseline characteristics of the two groups were compared using the unpaired Student's *t* test for continuous variables and the χ^2 test for discrete variables. All data were analyzed through a comparison of the initial (at entry) with the final (after 6 months) study. Differences between the two groups and changes over time within each group, as well as any interaction (different trends between groups), were assessed by multivariate repeated measures ANOVA. Differences were considered significant at a value of $P<.05$. Results are expressed as mean±1 SD.

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A total of 80 patients (76 men and 4 women; mean age, 53±9 years) were enrolled in the study. The majority (78%) had had an anterior myocardial infarction. Mean ejection fraction was 34±4%; mean work capacity and total exercise time at entry were 4.418±1.115 Kp-m and 10.8±2 minutes, respectively. Two patients were withdrawn from the study: one in the training group because of hospitalization for congestive heart failure and one in the control group because of unstable angina requiring coronary artery bypass graft surgery. One patient in the control group died from refractory heart failure; therefore, 77 patients completed the study and represent the final study population. Of them, 39 were in the training group and 38 in the control group.

The initial data for the 77 patients who completed the study are reported in Table 1. Clinical data were similar in the two groups; infarct size appeared equivalent, and patients with exercise-induced ST depression, exertional angina, multivessel coronary disease, and patency of infarct-related vessel were equally distributed in the two groups. Furthermore, there was no difference between the two groups in the medications received during the 6-month study period (Table 2). Of note, the majority of patients in both groups were taking ACE inhibitors at the maximal tolerated dosage, which were usually initiated immediately after the initial evaluation.

View this table: **Table 1.** Initial Patient Data
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View this table: **Table 2.** Medications During the 6-Month Study Period
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Exercise Performance

Heart rate at rest was similar for the two groups at both entry and the final evaluation. Systolic blood pressure at rest decreased significantly after 6 months only in the training group, but the decrease in rate-pressure product observed in this group was not statistically significant. Peak heart rate decreased ($P<.01$) in both groups, whereas maximal systolic blood pressure and rate-pressure product did not change significantly after 6 months. Initially, total work capacity was similar in the two groups; after 6 months, it had not changed in the control group but had increased significantly ($P<.001$), by 20%, in the training group (Table 3). In a comparison of the initial with the final study at the same submaximal work load, heart rate, systolic blood pressure, and rate-pressure product did not change in the control group but decreased significantly ($P<.01$) in the training group (Table 3).

View this table: **Table 3. Ergometric Test**
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Data on Left Ventricular Function and Remodeling

Initial left ventricular volumes, ejection fraction, wall motion abnormalities, and regional dilatation were similar in the two groups (Table 4). After 6 months, end-diastolic volume, end-systolic volume, and regional dilatation had not changed in the training group, whereas they had increased significantly ($P<.01$) (by 5%, 8%, and 21%, respectively) in

the control group. Conversely, ejection fraction and wall motion abnormalities had not changed in the control group, whereas they had improved significantly ($P<.01$) (ie, ejection fraction increased by 12% and wall motion abnormalities decreased by 10%) in the training group (Table 4⊞).

View this table: **Table 4.** Left Ventricular Function and Remodeling
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Psychological and Quality-of-Life Assessment

All baseline factors examined were similar in the two groups. The most important changes during the study period are reported in Table 5⊞. At the final evaluation, both groups demonstrated a significant ($P<.01$) decrease in life stress perception and depressed mood; these changes, however, were more pronounced, although not significantly, in the training group. Furthermore, social anxiety, easy-goingness, symptoms perceived during daily physical activity, and general well-being significantly ($P<.001$) improved in the training group but not in the control group.

View this table: **Table 5.** Psychological and Quality-of-Life Assessment
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Physical training is currently recommended for patients after acute myocardial infarction, as well as for patients with other cardiac conditions.[1,2] The beneficial effect of cardiac rehabilitation exercise training on exercise tolerance and symptoms is one of the most clearly established favorable outcomes, even in patients with severely depressed ventricular function and compensated chronic heart failure, and particularly in those with decreased functional capacity.[5,6,7,8,9,14,15,16,17,18,19] No significant cardiovascular complications or other serious adverse events have been reported in these patients. Moreover, most studies on exercise training in patients with heart failure and moderate-to-severe left ventricular dysfunction do not demonstrate deterioration in left ventricular function and central hemodynamics[6,7,15,16]; the favorable training effect in these patients has been attributed predominantly to adaptations in the peripheral circulation and skeletal muscles rather than to adaptations in the cardiac performance.[6,15,16,18] Some studies have also suggested the possibility of improving ventricular function through physical training in selected patients with coronary disease.[9,20,21,22] However, the available data are limited and often contradictory. Furthermore, the effects of exercise training on ventricular function and remodeling in patients with left ventricular systolic dysfunction after myocardial infarction have still to be established.

Actually, during the past few years, questions have been raised about the possible detrimental effect of exercise training on left ventricular remodeling after myocardial infarction. Jugdutt et al[8] reported a significant deterioration in both global and regional function after anterior Q-wave myocardial infarction in a small group of exercised patients with reduced ejection fraction compared with a matched control group. Although this was not a randomized study and other major limitations were present (ie, standardization of timing of exercise training was lacking), the study had considerable impact on clinical practice, raising the cautionary note that the potential to adversely alter ventricular size and function exists in selected patients with anterior myocardial infarction. Recently, in a randomized, controlled trial, the EAMI Study,[9] we documented progressive ventricular enlargement in patients with left ventricular dysfunction after anterior Q-wave myocardial infarction, but exercise training did not appear to worsen this increasing deterioration. Postinfarction patients with reduced ejection fraction (<40%) showed a comparable spontaneous increase in left ventricular size, both with and without exercise rehabilitation. We concluded that patients with uncomplicated anterior myocardial infarction may benefit from a long-term exercise training program without additional deterioration of ventricular volumes and topography. Nevertheless, compared with the control group, patients with an initial ejection fraction of <40% who underwent exercise training demonstrated less ventricular enlargement (although not statistically significant) and a significant improvement in regional wall motion and global left ventricular function (ejection fraction increased from 35% to 39%). Thus, based on the results of the EAMI Study, we hypothesized that in patients with reduced ejection fraction, exercise training may even lessen the deterioration in left ventricular size and function over time. Further confirmation was obviously needed.

The present study is the first prospective, randomized, controlled trial specifically designed to address whether regular exercise influences the remodeling process and ventricular function in patients with left ventricular dysfunction after myocardial infarction. Our data confirm that a simple home-based exercise training program is feasible and effective in improving exercise tolerance and quality of life in these patients, without cardiovascular complications or other adverse outcomes. The major finding of the present study, however, was that in patients with decreased ejection fraction after myocardial infarction, long-term exercise training may attenuate the unfavorable remodeling process and even improve both global and regional function over time.

Mechanisms and Significance of Training Effect

Enhanced vasoconstrictor activity, decreased vagal tone, and impaired arterial baroreflex activity (ie, abnormalities in the autonomic control of circulation) have all been described in patients with left ventricular dysfunction with and without heart failure.[23] [24] [25] The endogenous release of vasoconstrictor neurohormones may eventually play a deleterious role in the progression of ventricular dysfunction and development of congestive heart failure by increasing the loading conditions of the dysfunctioning heart; worsening the remodeling process, particularly in patients with low ejection fraction; and favoring the development of complex arrhythmias.[26] Exercise training has been shown to increase functional work capacity, reduce catecholamines and vascular peripheral resistance, and enhance heart rate variability and baroreflex gain in subjects with normal ventricular function[27] [28] [29] as well as in patients with left ventricular dysfunction and heart failure.[15] The percentage increase in exercise performance in our study was similar to that observed in training programs in normal subjects and in patients with ischemic heart disease with preserved ejection fraction or without heart failure.[9] [20] [21] [22] [30] The features of the training response are consistent with a normal response to regular exercise, including reduction in resting heart rate (although this was not statistically significant in our study) and blood pressure and reduction in exercise heart rate and rate-pressure product. These findings may reflect beneficial changes in autonomic balance and/or baroreflex gain and are in agreement with the attenuation of the vasoconstrictor influences (mainly due to sympathetic activity) and the increased vagal tone described after training in animals with and without healed myocardial infarction[31] and in patients with hypertension[29] and heart failure.[15]

All patients in our study had a reduced ejection fraction and enlarged left ventricle at the time of the initial evaluation. In the control group, left ventricular volumes rose progressively during the 6-month period of the study, ejection fraction remained depressed, and indexes of regional function did not improve. Similar observations have been previously reported.[9] [32] These data confirm that patients with large infarct and left ventricular dysfunction are prone to progressive ventricular dilatation, which appears to be the major compensatory mechanism after loss of contractile myocardium to restore initially depressed stroke volume, despite unchanged, and still reduced ejection fraction.[32] In contrast, in our exercise patients, end-diastolic volume remained unchanged, end-systolic volume decreased, and ejection fraction improved. The improved ejection fraction we found after training is consistent with the training response in normal subjects,[33] as well as in selected patients with coronary artery disease,[20] [21] [22] but the mechanism of this has not yet been established. It may be due to enhanced diastolic recoil and/or a true increase in contractile performance. Because the resting heart rate slightly decreased after training, the possibility must be considered that the lengthened diastolic filling period with augmentation of stroke output through the Frank-Starling mechanism may have contributed to the increase in ejection fraction in these patients. However, compared with the control group, our exercise patients did not show a significant change in end-diastolic volume. This suggests that the small reduction in resting heart rate was not the cause of the increased ejection fraction after training. Instead, the decreases in regional wall motion abnormalities and end-systolic volume indicate that an enhanced contractile performance predominantly contributed to the improved ventricular function in our exercise patients. Therefore, the present study demonstrates that in addition to the well known peripheral adaptations,[6] [14] [15] [16] [18] [30] long-term exercise training in postinfarction patients with left ventricular dysfunction may result in direct cardiac adaptations characterized by more favorable remodeling and improved ventricular function.

Possible mechanisms of the training-induced attenuation of the remodeling process and improvement in ventricular performance are a lessened increase in ventricular wall tension, favorable adaptations in the coronary circulation, or both. The beneficial changes in autonomic balance (toward a vagal predominance with attenuation of vasoconstrictive forces) induced by physical training may limit the deleterious effects of sympathetic hyperactivity on left ventricular remodeling and function (antiadrenergic effect). The favorable control on left ventricular wall stress after training, as documented by the significant decrease in submaximal rate-pressure product in our exercise group, may attenuate the deterioration of left ventricular size and function over time and ultimately reverse the unfavorable remodeling process. On the other hand, regular exercise has been shown to favorably affect whole blood flow rheology, enhance vascular function and structure (collaterals and microvasculature), and thereby possibly be of benefit to peripheral and myocardial perfusion.[20] [34] Several reports have documented a reduction in exercise-induced ischemia, as manifested by ST-segment depression or thallium perfusion abnormalities at matched rate-pressure products after 1 year of exercise training.[20] [35] [36] Physical training may also retard progression of coronary artery disease, and patients participating in regular physical

exercise may achieve improvement in myocardial perfusion independently of regressive changes in coronary lesions.[36] The improvement in myocardial blood flow of the infarcted area, even late after acute infarction, may lead to a consistent recovery of both regional and global left ventricular function.[37] Although results of the present study cannot elucidate the possible effects of exercise training on myocardial perfusion (serial angiographic studies were not performed), we speculate that the decrease in ventricular wall stress, through peripheral adaptations, and possibly the improvement in myocardial perfusion may have facilitated functional recovery of dysfunctioning but still viable perinecrotic myocardial regions in our exercise patients. We have no data, however, to determine which of these or other factors are most operative in the training-induced attenuation of the remodeling response and improvement in contractile function. It should be noted that the majority of patients in both groups received ACE inhibitors as a common policy of treatment of their left ventricular dysfunction, and almost 50% of them were also receiving a ß-blocker, despite their reduced ejection fraction. Thus, postinfarction patients with left ventricular dysfunction undergoing regular exercise on "maximal" medical therapy, including ACE inhibitors, may well derive additional symptomatic and functional benefits from physical training. Similar observations have been reported recently in patients with heart failure.[17] Because there is a strong resemblance between the systemic and peripheral effects of ACE inhibition and physical training, the possibility should be considered that the long-term effects of a physical conditioning program may be mediated and even enhanced by these drugs, but also vice versa.

Study Limitations

Our patient groups were well matched in terms of initial ventricular volumes, ejection fraction, extent of wall motion abnormalities, and regional dilatation. Baseline clinical characteristics; residual exertional ischemia, as documented by electrocardiographic ST-segment changes; and medications during the 6-month period of the study were also similar between the two groups. Because exertional ischemia, detected by reversible (exercise-rest) perfusion defects on stress scintigraphic imaging, may contribute to progressive ventricular enlargement in patients with left ventricular dysfunction[38] and due to the low sensitivity of exercise electrocardiography (particularly in patients with anterior infarcts), one limitation could be that we did not use imaging techniques to explore the presence of exercise-induced myocardial ischemia. Nevertheless, because the proportion of patients with multivessel coronary artery disease and the TIMI flow grade of infarct-related vessel were similar between the two groups, exertional ischemia, even at scintigraphic studies (ie, supersilent), should have been equally distributed and thus should not have influenced our results.

We considered for this study patients with rest ejection fraction values of <40% after a recent first Q-wave myocardial infarction (3 to 5 weeks previously). Patients with unstable angina or low-threshold ischemia, as well as with exertional ischemia uncontrolled by medical therapy, and those with clinical heart failure were carefully screened out. Furthermore, patients who had extensive and unstable coronary artery disease requiring surgery and those who developed symptoms of congestive heart failure after randomization did not complete the serial evaluation. Thus, the observed results do not apply to all postinfarction patients with left ventricular dysfunction but only to a selected group of asymptomatic clinically stable patients with no contraindication to exercise.

Conclusions

We confirm that a simple home-based exercise training program is feasible and effective in improving exercise tolerance and quality of life in patients with left ventricular dysfunction after an uncomplicated myocardial infarction. These patients may benefit from physical training without any additional clinical deterioration or other adverse events. More importantly, our data indicate that in postinfarction patients with poor left ventricular function, long-term exercise training may attenuate the unfavorable remodeling process and even improve both regional and global left ventricular function over time. Thus, cardiac rehabilitation exercise training in postinfarction patients with left ventricular systolic dysfunction should be recommended as a useful adjunct to the existing medical therapy, not only to attain symptomatic and functional improvement but also to prevent the progression of left ventricular dysfunction and its attendant morbidity and mortality.

Acknowledgments

This study was supported in part by grant Ricerca Corrente 1994/95 from the Ministero della Sanità, Rome, Italy, and in part by the "S. Maugeri" Foundation, Pavia, Italy. We are grateful to Andrea Giordano, PhD, and Fabio Comazzi for computer and statistical help. We also thank Rosemary Allpress for English language assistance in preparation of the manuscript.

Footnotes

[1] Investigators and institutions participating in the ELVD Trial are listed in the "Appendix."

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ELVD Study Group

The following Investigators and Institutions participated in the ELVD Trial.

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Received February 4, 1997; revision received April 21, 1997; accepted April 28, 1997.

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Table 1. Initial Patient Data

	Training Group (n=39)	Control Group (n=38)
Age, y	54±8	53±9
History, n		
Hypertension	14 (36%)	15 (38%)
Diabetes	5 (13%)	6 (16%)
Hypercholesterolemia	17 (46%)	16 (42%)
Smoking habit	30 (77%)	27 (71%)
Thrombolytic therapy	29 (74%)	27 (71%)
Peak creatine kinase, IU/L	3469±988	3395±1055
Abnormal Q wave, n	5.0±2.0	4.9±1.5
Cardiothoracic ratio on chest radiograph	0.49±0.04	0.50±0.05
Exercise-induced ST depression, n	8 (21%)	9 (24%)
Exertional angina, n	2 (5%)	3 (8%)
Multivessel coronary artery disease, n	9/26 (35%)	8/25 (32%)
Patency of infarct-related vessel, n	16/26 (61.5)	16/25 (64)
TIMI flow grade of infarct-related vessel	1.9±1.3	2.1±1.2
Interval since infarction, wk	3.5±1	3.4±1.2

TIMI indicates Thrombolysis in Myocardial Infarction. Values are mean±SD or number (%) of patients. Twenty-six patients in the training group and 25 in the control group underwent coronary artery angiography. Differences between groups are not statistically significant.

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Table 2. Medications During the 6-Month Study Period

	Training Group (n=39)	Control Group (n=38)
ACE inhibitors	30 (77%)	30 (79%)
Nitrates	14 (36%)	17 (45%)
Digitalis	4 (10%)	4 (10%)
ß-Blockers	19 (49%)	17 (45%)
Diuretics	12 (31%)	13 (34%)
Calcium antagonists	3 (8%)	6 (16%)
Antiarrhythmic agents	3 (8%)	5 (13%)
Lipid-lowering drugs	5 (13%)	6 (16%)

Values are presented as number (%) of patients. Differences between groups are not statistically significant.

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Table 3. Ergometric Test

	Control Group (n=38)		Training Group (n=39)	
	Pre	Post	Pre	Post
Rest				
HR, bpm	70±7	69±11	70±9	67 ±12
SBP, mm Hg	120±10	120±12	124±12	117±12[1]
RPP	8.5±1.2	8.4±1.4	8.6±1.4	8.1±1.9
Peak				
HR, bpm	140±21	136±15	145±14	142±16[2]
SBP, mm Hg	173 ±25	178±27	172±20	180±15
RPP	24.2±4.8	24.1±3.9	24.9±5.7	25.5±4.0
Work capacity, Kp-m	4.375±1.143	4.388±1.199	4.462±1.095	5.752 ±1.749[3]
Exercise time, min	10.7±2.7	10.8±3	10.9 ±1.6	13.5±3.0[3]
Same submaximal workload				
HR, bpm	132±19	128±18	139±16	127±20[1]
SBP, mm Hg	168±16	167±11	172 ±10	165±17[1]
RPP	22.1±4.3	21.4±5.1	24.0 ±3.7	20.9±3.9[1]

Pre indicates initial study; Post, final study (after 6 mo); HR, heart rate; SBP, systolic blood pressure; and RPP, rate-pressure product (mm Hg · bpm · 10^3). Values are as mean±SD.

[1] $P<.01$ interaction.

[2] $P<.01$ within groups.

[3] $P<.001$ interaction.

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Table 4. Left Ventricular Function and Remodeling

		Training Group (n=39)	Control Group (n=38)
EDV, mL/m^2	Pre	93±28	94±26[1]
	Post	92±28	99±27
ESV, mL/m^2	Pre	61±22	62±20[1]
	Post	57±23	67±23
EF, %	Pre	34±5	34±5[1]
	Post	38±8	33±7
WMA, %	Pre	49±8	50±10[1]
	Post	44±10	51±12
Reg Dil, %	Pre	43±18	47±18[1]
	Post	45±26	57±22

Pre indicates initial study; Post, final study (after 6 mo); EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction; WMA, wall motion abnormalities; and Reg Dil, regional dilatation. Values are mean±SD.

[1] $P<.01$ interaction.

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Table 5. Psychological and Quality-of-Life Assessment

		Training Group (n=39)	Control Group (n=38)
Life stress perception	Pre	2.95±1.9	2.92±1.8[1]
	Post	0.95±1.3	1.53±1.6
Depressed mood	Pre	3.4±2.4	3.5±2.7[2]
	Post	1.9±1.7	2.7±2.8
Social anxiety	Pre	2.85±1.7	2.61±1.9[3]
	Post	1.6±1.7	2.69±2.0
Easy-goingness	Pre	2.5±0.9	2.7±0.2[4]
	Post	2.9±0.7	2.3±0.8
Symptoms perceived during	Pre	21.7±1.76	22.4±1.4[4]
daily physical activity	Post	24.1±2.1	21.8±2.0
General well-being	Pre	4.00 ±2.00	4.3±1.4[4]
	Post	5.3±1.4	4.3±1.8

Pre indicates initial study; Post, final study (after 6 mo). Values are mean±SD.

For life stress perception, depressed mood, and social anxiety, a low score is better; for easy-goingness, symptoms perceived during daily physical activity, and general well-being, a higher score is better.

[1] $P<.001$ within groups.

[2] $P<.03$ within groups.

[3] $P<.001$ interaction.

[4] $P<.05$ interaction.