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Original Contributions

A Randomized Trial of Exercise Training in Patients With Coronary Heart Disease

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• In order to determine whether or not regular exercise could alter myocardial perfusion or function, we randomized 146 male volunteers with stable coronary heart disease to either a supervised exercise program (n=72) or to a usual care program (n=74). Subjects underwent exercise tests initially and one year later. Significant differences between the two groups included improved aerobic capacity, thallium ischemia scores, and ventricular function in the exercise intervention group. It was not possible to classify the conditions of patients as to the likelihood of improvement or deterioration. This study demonstrated changes in myocardial perfusion and function in a select group of middle-aged men with coronary heart disease who underwent a medically appropriate exercise program lasting one year, but these changes were relatively modest.

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THE USE of exercise training in the treatment of patients with coronary heart disease has gained widespread acceptance because of the many potential beneficial physiological and psychological adaptations.[1] These include decreased symptoms, increased functional capacity, and improved psychological well-being. However, attempts to define the mechanisms of the physiological changes have yielded conflicting results. While many animal studies have shown favorable cardiac changes to be induced by exercise training,[2] studies in humans have attributed most of the beneficial changes in patients with coronary heart disease to peripheral adaptations.[3,4] In 1979, a National Heart, Lung, and Blood Institute workshop concluded that there existed a need for continued research using small randomized studies to further clarify the value of physical training[5] because larger trials using morbidity and mortality end points have been inconclusive.[6,7] In response to this, we proposed a program called "PERFEXT" (PERFusion, PERFormance, EXercise Trial), which was funded and has recently concluded.

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METHODS

The San Diego community was informed that we were recruiting male patients with coronary heart disease between the ages of 35 and 65 years for a free exercise program. The responding volunteers were a select group because they were highly motivated to be in an exercise program. During a telephone interview, potential subjects were screened to determine if they (1) had coronary heart disease, (2) were willing to be randomized and comply with either a low-level at-home walking program or a medically supervised exercise program at a university hospital, (3) could discontinue digoxin for two weeks and β-blockers for three days before testing, (4) had no complicating illnesses or locomotive limitations, (5) had not recently been in an exercise program, and (6) had the approval of their physician. Patients with symptomatic congestive heart failure, unstable dysrhythmias, diabetes mellitus, symptomatic pulmonary disease, systemic hypertension, severe claudication, or orthopedic problems were excluded.

During an initial interview, a history and physical examination were performed, and the patients were classified according to the following criteria: (1) history of myocardial infarction from record review, (2) stable exertional angina pectoris, or (3) coronary artery bypass surgery. Disease stability was assured by careful history taking and by not allowing the patient to enter the study until at least four months after a cardiac event, a change in symptoms, or surgery.

The patients were then scheduled for three entry-level exercise tests done on separate days, usually within a two-week period. For the one-year follow-up testing, the maximal oxygen-uptake test was done before the thallium treadmill test to enable matching the maximal double product achieved during the initial thallium test. Two did not complete initial testing because of a lack of motivation. Of the 159 who completed initial testing, two became unstable during this period and were referred to their physicians. Eleven had completely normal radionuclide test results and were excluded. Of the 146 patients randomized, 72 were in the training group and 74 in the control group.

Treadmill Exercise Testing

A modified Balke-Ware protocol was used for both the thallium scintigraphy and maximal oxygen-uptake procedures.[8] Continuous 12-lead and X,Y,Z recordings used throughout the test and recovery period were digitized on-line and later computer processed. Patients were in the fasting state and all exercise tests were symptom- or sign-limited maximal efforts.

However, the end point for the one-year thallium treadmill test was the maximal-rate pressure product achieved at the initial thallium study. Perceived levels of exertion were recorded using the Borg scale.[9]

The amount of horizontal or downward sloping ST depression was visually interpreted from the raw recordings. Horizontal or downsloping ST-segment depression of 1 mm (0.1 mV) or more was considered abnormal. The ST amplitude at 60 ms after the end of the QRS complex in the Frank leads and the displacement of the ST vector in space were calculated.[10]

Oxygen uptake, carbon dioxide production, and minute ventilation were measured using the open-circuit technique. Patients breathed through a mouth piece and expired gas was collected in meterologic balloons. Expired volumes were determined by evacuating the balloons at a fixed flow rate through a dry gas meter calibrated with a spirometer. Measured oxygen uptake was presented in liters so as not to be affected by weight changes. Estimated oxygen uptake was calculated from the treadmill work load based on the oxygen cost of normal persons performing the work load.[1,8]

Thallium Scintigraphy

Two millicuries of thallium 201 was introduced into an antecubital vein one minute before the maximal-exercise end point. Images were immediately performed, and at four hours after exercise in the following three views: anterior, 45°, and 70° left anterior oblique. All images were obtained for a preset information density (2,000 counts/sq cm) in the area of highest activity within the myocardium and recorded unprocessed on clear-base film. One year later, the exact same camera angles were used and an image with anatomic landmarks made during the initial test ensured identical camera placement.

The thallium images were interpreted by three independent readers who had no pertinent patient information. The three views were each divided into three separate segments. The segments were graded using a previously published scoring system based on both the size and intensity of defects ranging from 1 for normal to 10 for the most severe.[11] The scores of the readers were then averaged. Ischemia was defined as a score that decreased by two severity units if 5 or less on the immediate image or by three severity units if between 6 and 10 on the immediate image. A scar was a defect score of 3 or greater on the four-hour delay images. In addition, the immediate post treadmill scans for each patient were read side by side with the order randomized as to before or after and graded as either no change, 0; 1, a mild change; 2, a moderate change; or 3, a dramatic change.

Radionuclide Angiography

Radionuclide angiography was accomplished by the gated-equilibrium technique, with the subject in the supine position and the subject's legs horizontal and not elevated. A 20-mCi dose of technetium-labeled RBCs was administered intravenously. After equilibration, the activity within the blood pool was recorded in a left anterior oblique projection with a caudal tilt to optimally separate the chambers. With the axis of the pedals at the same level as the body, the patient performed three stages of supine bicycle exercise, each three minutes in duration. The work loads at the one-year retesting were the following: stage 1, matched to the previous year; stage 2, adjusted to obtain the same rate-pressure product as stage 2 on the initial test; and stage 3, maximal exercise.

Scintigraphic data were recorded using a single-crystal camera with a general purpose parallel-hole collimator and recorded simultaneously on videotape and on-line to the computer system.[2] All acquisitions were 2.5 minutes in duration and acquired with a spatial resolution of 64×64 pixels per full field. Ventricular volumes at end-diastole and end-systole were estimated from end-diastolic counts and end-systolic counts and the counts detected in 6 mL of blood taken during the corresponding rest and exercise periods.[12,13]

Exercise Program

The patients randomized to the exercise intervention group began training in a monitored class. The initial training intensity was set at a minimum of 60% of the estimated maximal oxygen uptake from the initial treadmill test. If the patient's physician wanted the patient to stay on β-blockers during training, a repeat test was done on the usual dosage for prescribing exercise. The intensity was usually progressively increased to 85% of the estimated maximal oxygen uptake by the eighth week of training. However, there was considerable variability because patients were not equally able or motivated to exercise. Aerobic training was carried out on arm, leg, and arm-plus-leg ergometers for 45 minutes three times each week. After completing eight weeks of monitored training, the participant was considered for graduation to either our gymnasium or outdoor walk-run programs. There were no episodes of cardiac arrest or other major complications during exercise sessions.

Control Group

Patients randomized to the control group were offered a low-intensity walking program. Two controls crossed over to a level of exercise comparable with the intervention group, but they were still considered controls.

Statistical Analysis

Differences between the control and exercise intervention groups were tested by standard statistical techniques such as the two-sample Student's t test, analysis of variance (ANOVA), and analysis of covariance (ANACOVA). The appropriateness of these methods was checked by visual inspection of histograms, normal probability plots, and residual plots.

The decision to use ANOVA (which subsumes the t test) or ANACOVA was based on the correlation between initial and one-year measurements in the control group. If this correlation was high, ANOVA was performed on the changes from initial measurement to one year. If the correlation was low, ANACOVA was run using the one-year value as the dependent variable and the initial value as a covariate. Multivariate stepwise regression was used to predict changes during the year in the exercise-intervention group.

Once randomized to a control or intervention group, a patient was always considered a member of that group regardless of his adherence to the protocol. There were 13 dropouts (six for medical reasons, and seven for motivational ones) in the exercise-intervention group, and, therefore, one-year data were not available for these patients. To examine the possibility of a self-selection bias, the data were analyzed twice, and the results compared for consistency. In the first analysis, dropouts were not considered and these are the results that are presented. In the second analysis, dropouts were included by considering their initial values to be their one-year values as well. This would tend to dilute any intervention effect if one existed, but bolster conclusions based on significant results. There were no important differences between the two analyses. The UCLA Biomedical Statistical package was used for all analysis. All reported P values are two-sided.

RESULTS

Entry Evaluation

The mean age was 53±8 years, and the mean weight was 84±13 kg. Of the patients without bypass surgery who had coronary angiography (n=43), 12 had one-vessel, 17 had two-vessel, and 11 had three-vessel disease, and three had left main coronary artery disease. Although three fourths of the patients had a history of angina pectoris at some time, only 35% had angina during the initial treadmill testing. No statistically sig-

Table 1.—Clinical Characteristics at Randomization

Clinical Variable	Controls, % (N=74)	Exercise-Intervention Group, % (N=72)
Currently smoking	8	14
Angina, documented by exercise testing	35	36
History of non-Q-wave myocardial infarction only	8	7
History of Q-wave myocardial infarction	68	68
Currently with		
Anterior Q waves	22	28
Inferior Q waves	39	30
Coronary artery bypass surgery	34	39
Medications taken before initial testing		
Digoxin	15	19
β-Blockers	57	42
Long-acting nitrates	43	31
Antidysrhythmics	15	14
Antihypertensives	9	17
History of congestive heart failure	9	10
Currently employed	65	56

Table 2.—Exercise Test Values at Randomization*

Test	Controls (N=74)	Exercise-Intervention Group (N=72)
Maximal oxygen-uptake treadmill		
Heart rate, supine, beats/min	66 (9)	70 (12)
Blood pressure, supine, mm Hg	128 (13)/86 (9)	129 (16)/85 (9)
Heart rate, maximal, beats/min	154 (19)	156 (21)
Blood pressure maximal, mm Hg	181 (26)/96 (10)	185 (29)/97 (11)
Vo_2 estimated, mL/kg/min	33 (8)	33 (9)
Vo_2 measured, mL/kg/min	26 (6)	26 (6)
Respiratory quotient	1.10 (.12)	1.13 (.11)
Maximal perceived exertion	17 (2)	17 (2)
% with abnormal ST depression	45 . . .	47 . . .
Radionuclide ventriculography		
Rest		
Ejection fraction	.52 (.13)	.52 (.15)
End-diastolic volume, mL	133 (61)	136 (60)
Stroke volume, mL	65 (28)	62 (21)
Cardiac output, L/min	4 (2)	4 (1)
Maximal exercise		
Heart rate, beats/min	139 (20)	137 (21)
Blood pressure, mm Hg	197 (26)/104 (11)	198 (30)/104 (13)
Ejection fraction	0.53 (0.15)	0.50 (0.16)
% change ejection fraction	1.5 (18)	−1.8 (16)
End-diastolic volume, mL	156 (59)	157 (68)
Stroke volume, mL	79 (30)	73 (26)
Cardiac output, L/min	9 (4)	8 (30)
Work load, kiloponds	769 (239)	739 (240)
Thallium 201 imaging		
% with fixed defects	71 . . .	68 . . .
Sum of ischemia scores		
4 hr minus immediate scores	3.4 (5)	4.5 (5)
Sum of immediate scores	16 (9)	16 (8)
% with reversible defects	50 . . .	51 . . .

*Exercise test parameters at randomization from the maximal oxygen-uptake treadmill test, supine bicycle radionuclide-ventriculography, and thallium tests. Column numbers and numbers in parentheses indicate mean (± 1 SD).

nificant differences were found between the groups. From Tables 1 and 2, it can be seen that randomization was successful in equally distributing the clinical, treadmill, radionuclide ventriculography, and thallium-imaging parameters between the two groups.

In Table 2, the discrepancy between measured and estimated oxygen uptake can be seen. Measured values are more accurate, but both are given to enable comparison with most previous studies that have only reported estimated values. Although the peak measurements were consistent with a maximal effort, all of the exercise-test end points were reviewed. Of the 146 patients randomized, 94 reached volitional fatigue during the initial treadmill test. Of the remaining 52, there were 32 stopped because of moderately severe angina, one each caused by shortness of breath and an excessive blood pressure rise, two because of atypical chest pain, two because of ST depression, seven because of systolic blood pressure drop, six because of leg pain, and one because of ventricular dysrhythmias.

Dropouts

During the course of the study year, there were five medical dropouts in the control group: two for coronary artery bypass surgery, one for myocardial infarction, one with both, and one death. There were six medical dropouts from the exercise intervention group: one for coronary artery bypass surgery, one for myocardial infarction, one for alcoholism, and three whose symptoms became unstable. Of the 66 remaining in the exercise group, seven dropped out because of job conflicts and/or lack of motivation and refused further testing. Repeat one-year testing was, therefore, performed on 59 of the 72 patients from the intervention group and on 69 of the 74 controls. The patient distribution is illustrated in the Figure.

Exercise Compliance

After the completion of the study, the exercise records of the 59 patients in the exercise-intervention group who had one-year testing were extensively reviewed. Average intensities for the entire year were as follows: percent maximal estimated oxygen uptake and heart rate by the Karvonen method was approximately 60% ± 10% (range, 40% to 100%). Percent of maximal heart rate and measured oxygen uptake was approximately 80%. The average caloric expenditure for each session was 319 ± 104 (130 to 719 calories). The mean attendance at exercise sessions was 76% ± 18% (23% to 97%).

Changes at One Year

During the year of study, one control and one exercise-trained patient gained both abnormal treadmill-induced ST depression by visual

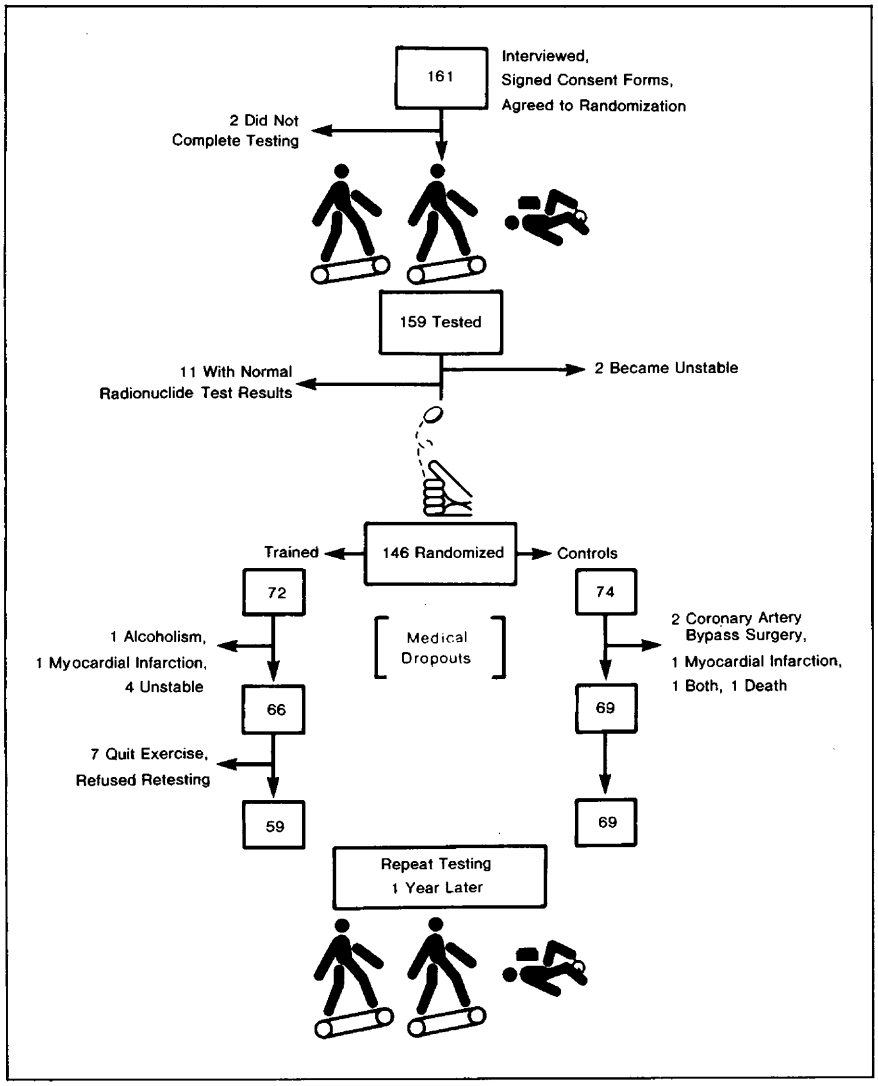

Illustration of patient distribution through course of study.

interpretation and angina, one exercise-trained patient lost both, and three controls and one exercise-trained patient gained angina but lost the criterion for abnormal ST depression. Nine controls and six exercise-trained patients lost abnormal ST depression and four controls and three exercise-trained patients gained it. Ten exercise-trained patients and four controls lost or decreased treadmill-induced angina and four controls and three exercise-trained patients gained it. Computer analysis of the ST amplitudes at 60 ms after the end of the QRS complex in lead X, or the length of the spatial vector at a double product and a heart rate matched at one year to the initial test, disclosed no significant differences between the groups.

As given in Table 3, a significant ($P<.05$) training effect in the intervention group is evidenced by the decrease in their resting and submaximal heart rates, as well as the significant ($P<.05$) increase in the measured and estimated maximal oxygen uptake. The control group showed a significant ($P<.05$) decrease in functional capacity at least partially caused by the lower maximal heart rate obtained at the one-year test. There was also a small but significant ($P<.05$) decline in the submaximal heart rate and rate-pressure product in the control group, probably caused by habituation. No changes were observed in maximal perceived exertion, respiratory quotient, or systolic blood pressure between the two groups initially or at one year, or between the initial and one-year tests.

Analysis of variance testing confirmed that the training effect, including an increase in measured oxygen uptake, occurred in subgroups of the exercise-intervention group relative to the control group. These subgroups included those with or without the following features: a history of a Q-wave myocardial infarction or bypass surgery, treadmill test-induced angina, an ejection fraction less than 0.40 or 0.50, abnormal exercise test-induced ST-segment depression, β-blocker administration, or a dropping ejection-fraction response. However, a three-way ANOVA showed that those with angina but without a Q-wave myocardial infarction in the intervention group did not increase their estimated oxygen uptake relative to the controls.

Radionuclide Ventriculography

Table 2 gives the initial measurements at rest and in response to supine bicycle exercise. There was an increase in both end-systolic and end-diastolic volume in response to supine exercise. In order to demonstrate reproducibility, correlations were performed in the controls between the initial and one-year data. The results were as follows: maximal heart rate .80; ejection fraction, .78 to .88; end-diastolic volume, .52 to .63; end-systolic volume, .70 to .78; stroke volume, .37 to .46; cardiac output, .25 to .42; and percent change ejection fraction, .49. Correlations of percent change in all volumes and cardiac output were all less than .33.

We examined the effect of intervention, relative to the controls, on the following variables: heart rate, ejection fraction, end-diastolic and end-systolic volumes, stroke volume and cardiac output at rest and at each of three stages, and percentage change of each from rest to each of three stages. The statistical method used was ANACOVA. The model employed the one-year value as the dependent variable, the initial value as the covariate, and allowed for effects caused by exercise intervention, angina, and Q-wave myocardial infarction. Differences caused by angina and/or Q-wave myocardial infarction alone are not reported.

Analysis of covariance showed a differential effect of the intervention on stroke volume and cardiac output in patients with and without angina as given in Table 4. For stroke volume

Table 3.—Initial and One-Year Measurements From the Maximal Oxygen-Uptake Treadmill Tests*

Test	Control (N=69)	Exercise-Intervention Group, (N=59)
Heart rate, beats/min		
Supine		
Initial	66 (9)	69 (12)
1 year	69 (11)	65 (11)
Mean difference	2.2 (10)	−3.8 (10)†‡
Submaximal, 3.3 mph/5%		
Initial	125 (15)	126 (16)
1 year	121 (16)	118 (15)
Mean difference	−3.1 (11)†	−9.3 (12)†‡
Maximal		
Initial	154 (19)	156 (22)
1 year	149 (23)	154 (22)
Mean difference	−5.2 (13)†	−2.2 (11)
Rate pressure product§		
Submaximal, 3.3 mph/5%		
Initial	209 (44)	215 (47)
1 year	199 (49)	196 (42)
Mean difference	−8 (35)†	−19 (34)†
Maximal		
Initial	279 (57)	286 (59)
1 year	273 (60)	289 (67)
Mean difference	−6 (46)	3 (50)†
Maximal oxygen uptake		
Estimated, mL/kg/min		
Initial	33 (8)	33 (9)
1 year	32 (8)	37 (9)
Mean difference	1.3 (5)	4.7 (6)†‡
% change	−3 (18)	18 (24)†‡
Measured, L/min		
Initial	2.1 (.5)	2.2 (.6)
1 year	2.0 (.5)	2.3 (.6)
Mean difference	−.1 (.3)†	.1 (.3)†‡
% change	−4 (17)†	8.5 (17)†‡

*Column numbers and numbers in parentheses indicate mean (± 1 SD).
†Significant ($P<.05$) change from initial value to one-year value within a group.
‡Significant ($P<.05$) difference between the groups.
§Heart rate×systolic blood pressure×10^{-2}.

Table 4.—Estimated Changes in Stroke Volume and Cardiac Ouptut During Supine Bicycle Exercise After One Year*

	Exercise-Intervention Group		
	With Angina (N=20)	Without Angina (N=39)	P Value
Resting supine stroke volume	−9.9 mL	7 mL	$P=.06$
Stroke volume, stage 2	−14.9 mL	11.9 mL	$P=.02$
Maximal stroke volume	−10.9 mL	10.3 mL	$P=.03$
Maximal cardiac output	−1.0 L/min	1.3 L/min	$P=.048$

*That was found by analysis of covariance adjusting for the controls. The values given are the differences between the adjusted means. The values are calculated as one-year test minus the initial test.

this was evident at stage 2, where rate-pressure product was matched to the initial test ($P=.02$), and at maximal exercise ($P=.03$), and suggested at rest ($P=.06$); for cardiac output, it was only evident at maximal exercise ($P=.048$). Exercise tended to increase stroke volume and cardiac output in patients without angina and to decrease them in patients with angina. Similar analysis for heart rate only detected a consistent exercise effect on all but maximal exercise.

There was no significant difference at rest, during the three stages of exercise, or in the percent change from rest to exercise between the control and exercise-trained groups at the one-year testing in the ejection fraction, end-diastolic volume, stroke volume, or cardiac output. However, Table 5 notes that the exercise intervention group, relative to the controls, had significantly lower percentage changes in end-systolic volume at all three work loads ($P=.02$, $P=.04$, and $P=.05$, respectively).

Thallium Perfusion Imaging

Correlations were computed between the initial thallium scores and the one-year values in the controls who completed the one-year testing (Table 6). For the sum of the scores of the immediate images the correlation coefficient was .89, and for the sum of the ischemia scores it was .67. The effect of exercise on the immediate postexercise thallium scores was examined by ANOVA. The ANOVA model contained terms allowing for effects caused by angina and Q-wave myocardial infarction, as well as the exercise intervention. The ANOVA results indicated a differential exercise effect, depending on the presence or absence of angina ($P=.008$). There was no indication of an exercise intervention effect in patients without angina relative to the controls ($P>.8$; with a mean change of −.26 in the controls, .05 in exercise-trained patients). There was a definite intervention effect relative to the controls in patients with angina ($P<.0005$; with a mean change of 1.52 in the controls, −3.90 in exercise-trained patients). Similar results were obtained when the difference between the immediate and four-hour scores was also examined.

When the immediate images were read side by side, blinded as to which was an initial or a final scan and to group, no significant difference was noted between the groups. Twelve patients (six exercise trained and six control) had a minor improvement (+1); two patients (one exercise trained and one control) had a major improvement (+2). A minor deterioration (−1) was apparent at one year in four controls and five exercise trained, while a major deterioration (−2) was seen in one control.

Stepwise multivariate linear regression to predict changes in the functional and radionuclide measurements from initial to one-year testing in the exercise-intervention group, using the initial variables, failed to explain a clinically important part of the variability.

COMMENT

Many favorable physiological changes have been documented in patients with coronary heart disease

Table 5.—Mean Values of Percent Change of Milliliters of End-Systolic Volume at One-Year Testing

	Total Study Group			Subgroup Without Q-Wave MI†			
				With Angina		Without Angina	
% CESV*	Control (N=45)	Exercise Intervention (N=41)	*P* Value	Control (N=8)	Exercise Intervention (N=5)	Control (N=10)	Exercise Intervention (N=7)
Stage 1	8	−3	*P*=.02	6	−21	15	−2
Stage 2	12	2	*P*=.04	17	−12	24	−3
Maximal	28	16	*P*=.05	46	5	33	14

*% CESV indicates percent change end-systolic volume from rest to exercise. At a given exercise stage, the one-year means within the various subgroups are statistically adjusted by analysis of covariance to a common value of % CESV at randomization.
†MI indicates myocardial infarction.

Table 6.—Initial and One-Year Measurements on Thallium Perfusion Images Using the Atwood Scores*

	Total Study Group		Subgroup With Angina			
			MI‡		No MI‡	
Scores Used†	Control (N=59)	Exercise Intervention (N=59)	Control (N=13)	Exercise Intervention (N=11)	Control (N=10)	Exercise Intervention (N=9)
Sum of immediate scores						
Initial	16.1 (9)	16.6 (8)	20 (8)	21 (8)	16 (11)	15 (4)
1 year	16.4 (9)	15.0 (7)	22 (7)	16 (6)	16 (11)	12 (5)
Mean difference	.3 (4)	−1.3 (6)§	2.2 (4)	−4.6 (6)§	7 (4)	−3.0 (9)§
Sum of ischemia scores						
Initial	3.5 (4)	4.1 (4)	5 (8)	6 (5)	6 (6)	6 (5)
1 year	3.9 (5)	3.1 (4)	7 (6)	4 (4)	7 (8)	3 (4)
Mean difference	.4 (4)	−1.0 (4)§‖	1.5 (5)	−1.6 (4)§	1.5 (4)§	−2.6 (5)§

*All units are the Atwood scores described in the "Methods" section. Mean difference between initial and one-year study (1 year−initial).
†Column numbers and numbers in parentheses indicate mean (±1 SD).
‡MI indicates myocardial infarction.
§Significant difference ($P<.05$) between exercise-trained and control groups.
‖Significant change ($P<.05$) from initial test to one-year test within a group.

who have undertaken an aerobic exercise program. Peripheral adaptations are at least partially responsible for these changes, and controversy still remains whether or not exercise training can promote coronary collaterals in the animal model subjected to chronic ischemia although a recent study supported this contention.[14] There have been a number of attempts to demonstrate the effects of exercise training on the hearts of patients with coronary heart disease.[15-17] Whether the negative findings can be explained by limitations in the techniques, patient selection, inadequate intensity, or length of training is uncertain.

Nuclear medicine procedures that noninvasively assess myocardial perfusion and performance have become important tools for the diagnosis of heart disease. They have also been used to evaluate the efficacy of coronary artery bypass surgery and angioplasty,[17-19] and more recently, they have been used to evaluate exercise programs.[20-24]

The one year of exercise training in our patients elicited the expected training response as given in Table 3. The significant increase in estimated (18%) and measured (8.5%) maximal oxygen uptake is similar to most studies as summarized by Hartung and Rangel.[25] We chose one year as the period of training because we were concerned that shorter periods might be inadequate in middle-aged cardiac patients.[26]

Our intervention group experienced a significant improvement in the thallium images after the year. The scoring done with the images side by side paired for a given patient did not show a statistical difference although there was a trend to agree with the Atwood score.[11] This may be explained by the greater gradations of the Atwood score and that it considered each area separately, while the side-by-side score required the readers to consider the entire scan. Therefore, comparing thallium scans side by side, which has been done effectively to evaluate surgical intervention, was not successful in our study. However, the improvement in the thallium scores, particularly in the patients with angina, is consistent with animal studies, suggesting that ischemia is the best inducer of collateral flow and that exercise can increase this stimulus. The ST-segment changes did not show an improvement nor did they agree with the thallium changes. These changes can only be assumed to represent relative, rather than absolute, changes in perfusion.

One of the only changes in ventricular function or volume of a consistent nature was the significantly ($P<.05$) lower percent change in end-systolic volume in the patients in the exercise-intervention group. There were no significant differences in blood pressure at any stage of bicycle exercise so there is no evidence that decreased afterload would explain this. Because there was a trend for decreases in end-diastolic volume as well, it seems that the exercise-trained heart has to use the Frank-Starling mechanism less than the exercise-untrained heart, probably because of lessened ischemia and/or improved contractility. The end-systolic volume changes were the only ones statistically significant because of the greater reproducibility of sys-

tolic (r=.78) v diastolic (r=.52) volumes.

The other significant ($P<.05$) change was the effect of the intervention on stroke volume and maximal cardiac output. Training is known to increase both, but the differential affect caused by angina was surprising. The decrease in stroke volume and cardiac output in the patients with angina accompanies a lessening of both ischemia and the end-systolic volume increase in response to supine exercise. This suggests that absolute volume changes had to occur that could not be detected because of the variability of the volume technique.

One criticism might be that our patients did not exercise hard enough and that if they had, more definite improvements might have been possible. However, even if we chose those that trained the most intensely or had the highest exercise class attendance, we did not find greater changes. Hagberg et al[27] have reported impressive cardiac changes in a highly selected group of cardiac patients with asymptomatic ST-segment depression exercised at very high levels. Hossack and Hartwick[28] have reported an increased risk for exercise-induced events in similar patients. The question remains whether the usual cardiac patient can be exercised safely at higher levels than we used and, if so, whether more definite cardiac changes can be demonstrated.

Further criticisms could be directed toward our sample size, the heterogenicity of the population (particularly because 40% were taking β-blockers and 35% had bypass surgery), and the techniques used. The population was heterogeneous and of this size in order to meet our recruitment needs in a reasonable time frame. Analysis of variance demonstrated that neither β-blocker administration nor previous bypass surgery affected their exercise intensity, compliance, or change in aerobic capacity.

We have demonstrated cardiac alterations caused by exercise training in middle-aged men with coronary heart disease, but these changes were subtle. Peripheral changes most likely are responsible for the increase in exercise capacity. Clinical or test responses other than angina did not predict who would show beneficial aerobic or radionuclide improvements; nor have we been able to identify those whose condition was likely to deteriorate. The probability of a given patient having a training effort was lower than expected, even for higher levels of intensity and frequency of training. We conclude that patients cannot be guaranteed benefits from exercise training and that recommendations to use this modality should be based more on the person's desires and needs than on particular test results. The radionuclide procedures are not necessary for screening patients for exercise programs nor can they be expected to reliably detect changes secondary to exercise in an individual patient.

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