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Use of Clinical Data in Predicting Improvement in Exercise Capacity After Cardiac Rehabilitation

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Fifty-nine men with coronary heart disease underwent 1 year of supervised aerobic exercise. They performed exercise tests for maximal oxygen uptake, ST segment analysis, thallium scintigraphy and radionuclide ventriculography before and after the year of exercise. A computerized data base that included clinical descriptors and exercise test results was retrospectively reviewed to determine whether initial features could predict the patient's response to the exercise intervention. Poor correlations were found between the initial measurements and change in maximal oxygen consumption and other indexes of training effect. Patients who initially were in the poorest state of fitness showed the most improvement with training. None of the initial features from the history and physical examination, treadmill study or radionuclide studies was a good predictor of a beneficial result from the exercise program. The usual measurements of work intensity during training were poor predictors of outcome. A significant decrease in the amount of ischemia measured by thallium perfusion scintigraphy was demonstrated after training.

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Exercise training is used to increase the functional capacity of patients after myocardial infarction and can result in a higher work load being performed before the onset of angina pectoris (1). Although favorable alterations in morbidity or mortality have not been documented, there is no doubt that work capacity can improve in most patients (2). However, cardiac rehabilitation programs are expensive and involve a risk (3). If a patient's likelihood of improving his or her work capacity could be predicted on the basis of initial data, much time and money could be saved. The present study is an analysis of data collected from men with coronary heart disease before and after a 1 year exercise program. Considering maximal oxygen consumption and other indicators of a training effect, we asked the following questions: 1) Can clinical features before training predict whether beneficial changes occur with training? 2) Do initial treadmill or radionuclide measurements, or both, contribute information to improve this prediction? 3) Does the intensity of training during the year predict beneficial changes?

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Methods

Study patients. Men with coronary heart disease between 35 and 65 years of age were recruited for a free exercise program through local physicians, hospitals, the American Heart Association and direct advertisement. During a telephone interview, potential subjects were screened to determine whether they: 1) had coronary heart disease; 2) could discontinue their medications for testing (digitalis preparations for 2 weeks and beta-adrenergic blocking agents for 3 days); 3) had no complicating illnesses or limitations on mobility; 4) had not recently been in an exercise program; and 5) had the approval of their physician. Patients with symptomatic congestive heart failure, unstable arrhythmias, diabetes mellitus, significant symptomatic pulmonary disease, systemic hypertension, severe claudication or orthopedic problems were excluded. Those accepted made their medical records, including data on hospitalizations, electrocardiograms, exercise tests and coronary angiography (performed in 70%), available for entry into our computerized data base.

During an initial interview with the principal investigator (V.F.F.), a history and physical examination were performed, and the patients were classified by the following criteria: 1) history of myocardial infarction from chart review with at least two of the following: typical prolonged chest pain, evolutionary electrocardiographic changes or an increase in creatine kinase (CK)-MB isoenzymes, or both; 2) stable ex-

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ertional angina pectoris confirmed by angiographic evidence of coronary heart disease or an abnormal exercise test; or 3) coronary artery bypass surgery. Disease stability was assured by careful recording of history and by not allowing the patient to enter the study until at least 4 months after a cardiac event, a change in symptoms or surgery. The patients were then scheduled for three entry exercise tests performed on separate days within a 2 week period.

Study group. The responding volunteers were randomized to a medically supervised exercise program (n = 72) or to usual community care (n = 74). The present study is a retrospective analysis of the exercise-trained group. There were six medical dropouts (one due to alcoholism, one to myocardial infarction and four to unstable angina) and seven who were noncompliant in the exercise group. These seven were not significantly different from the study group in terms of baseline variables. The 59 patients who completed 1 year of exercise had an attendance rate of 76 ± 18% (mean ± SD).

Treadmill exercise testing. A modified Balke-Ware protocol was used for both the thallium scintigraphic and maximal oxygen uptake procedures (4). Continuous 12 lead and Frank X, Y and Z recordings were obtained throughout the test and recovery periods. The electrocardiographic data were digitized on-line using Marquette Electronics Data Loggers and were computer-processed. Patients were in the fasting state and all exercise tests were symptom- or sign-limited maximal efforts. The test was terminated with the onset of 0.3 mV of horizontal or downsloping ST segment depression (in relation to the PR segment), severe angina, serious arrhythmias or a decrease in systolic blood pressure of more than 20 mm Hg. In patients without symptom or sign limitation, exercise was continued to volitional fatigue. However, the end point for the 1 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 (5), ranging from 6 (very, very light) to 20 (very, very hard).

The amount of horizontal or downsloping ST depression was visually interpreted from the raw recordings and entered into the data base. Horizontal or downsloping ST segment depression of 1 mm or greater was considered abnormal (6).

Oxygen uptake. Oxygen uptake, carbon dioxide production and minute ventilation were measured using the open circuit technique. Mixed expired oxygen and carbon dioxide were measured with an Applied Electrochemistry S-3A oxygen analyzer and a Gould Godard Mark IV Capnograph. Expired volumes were determined by evacuating meterologic balloons through a Singer dry gas meter calibrated with a tissot at a fixed flow rate. The maximal oxygen uptake was the average of the last two 30 second samples obtained at the sign- or symptom-limited end point. Because of technical difficulties, initial oxygen uptake could not be calculated in seven patients. Statistical analyses demonstrated no differences between the baseline characteristics of these seven patients and those of the study group. A regression analysis of measured maximal oxygen consumption against maximal treadmill time was performed (r = 0.92) and used to derive initial maximal oxygen uptake values for these seven patients. Estimated oxygen uptake was calculated from the treadmill grade and speed and time in stage on the basis of responses of normal men (4).

Thallium scintigraphy. Two mCi of thallium-201 were introduced into an antecubital vein 1 minute before the maximal exercise end point. Images were performed immediately and 4 hours after exercise in three views: anterior and 45° and 70° left anterior oblique. All images were obtained for a preset information density (2,000 counts/cm^2) in the area of highest activity within the myocardium and recorded unprocessed on transparent X-ray film. The same camera angles used in the initial study were used in each patient at 1 year. In addition, an image with anatomic landmarks made during the initial test was used to ensure identical camera placement.

The thallium images were graded by three independent readers who had no pertinent patient information and the results were averaged. Each of the three views was divided into three segments and graded on the size and intensity of defects ranging from 1 (normal) to 10 (most severe) (7). Ischemia was defined as an immediate image score of 5 or less that decreased by 2 severity units on the delayed image or an immediate image score of 6 to 10 that decreased by 3 severity units on the delayed image. A scar was defined as a defect score of 3 or greater on the 4 hour delayed image.

Radionuclide angiography. Radionuclide angiography was accomplished by the gated equilibrium technique with the subject in the supine position with the legs horizontal and not elevated. A 15 mCi dose of technetium-labeled red blood cells was administered intravenously. After equilibration, the activity within the blood pool was recorded in a modified left anterior oblique projection (angled between 30° to 45°) with a caudal tilt of 10° to 20° which permitted optimal chamber separation. With the axis of the pedals at the same level as the body, the patient performed three stages of supine bicycle exercise, each 3 minutes in duration, the last being maximal exercise. The work loads at the 1 year retesting were: stage 1, matched to the previous year; stage 2, adjusted to obtain the same rate-pressure product recorded in stage 2 of the initial test, and stage 3, maximal exercise. These loads represented 40, 60 and 80%, respectively, of maximal effort on upright treadmill walking.

Scintigraphic data were recorded using a single-crystal camera with a general purpose parallel-hole collimator (25% window) and recorded simultaneously on video tape and on-line to the MDS A^2 system. All acquisitions were 1.5 minutes in duration and were acquired with a spatial resolution of 64 × 64 bytes. Left ventricular ejection fraction was derived from a computer-generated, background-corrected time-activity curve using a variable region of interest. Ventricular volumes were estimated from end-diastolic and end-systolic counts and the counts detected in 6 ml of blood taken during the corresponding rest and exercise periods (8,9).

Exercise program. The patients randomized to the exercise intervention group began exercising with continuous electrocardiographic monitoring. The initial training intensity was set at a minimum of 60% of the estimated maximal oxygen uptake from the initial treadmill test. The intensity was usually progressively increased to 85% of the estimated maximal oxygen uptake by the eighth week of training. However, there was a considerable amount of variability because the patients were not equally able or motivated to exercise, although they were given an exercise prescription and encouraged to follow it.

Aerobic training was carried out on arm, leg and arm plus leg ergometers for 45 minutes three times a week. After completing 8 weeks of monitored exercise, the participant was considered for graduation to either our gymnasium or outdoor walk/run program after a review of his exercise responses, signs and symptoms. This program was conducted during both early morning and late evening hours and participation on Mondays, Wednesdays and Fridays was requested of all patients. An additional self-monitored session was recommended for all participants who could undertake it safely. An exercise intensity of 80 to 85% of maximal oxygen uptake was progressively reached after 1 to 2 weeks of training. In each session, a 10 minute warm-up period of progressive activity was followed by 30 to 45 minutes of continuous walking/running and a 10 to 15 minute cool-down activity period. Patients were taught pulse-counting techniques and given a target heart rate for training that corresponded to 80 to 85% of estimated maximal oxygen consumption. Staff members periodically checked counting accuracy by pulse counts. A stationary bicycle and rowing ergometer were made available to patients with orthopedic problems. The sessions were supervised by personnel trained in cardiopulmonary resuscitation. There were no episodes of cardiac arrest or other major complications during exercise training sessions.

Statistics. Five end points representing a training effect were used because each of these has been used in previous studies to denote a training effect. The hypotheses tested concerned correlations between baseline variables and the degree of improvement in these end points; thus, a nondichotomous approach was taken to test the major hypotheses.

Student's t test was used for comparisons between subgroups. Linear regression analysis used the method of least squares; the Pearson product-moment correlation coefficient (r) is reported as a measure of the strength of association between two variables. All statistics were obtained using the BMDP statistical Software package. The required level of significance was fixed at $p < 0.05$. Changes were calculated as absolute differences between the 1 year test results and the initial results.

Stepwise multivariate linear regression (BMDP-P6R) was used to evaluate whether the training effect could be predicted using groups of variables. Initially, predictions were made using variables from only the history and physical examination, only the treadmill studies, only the radionuclide studies or only the intensity of training measures. Subsequently, the variables from each area that proved the strongest predictors were combined and a final analysis was conducted. The variables used in each analysis are listed in the Appendix. Only the three variables with the highest partial correlation to a given measure of training effect were entered in each regression because using more variables is invalid with the number of patients in the study. Variables were required to have an F value of at least 1.0 to be entered into the equation.

Results

Table 1 shows the general features of the study patients. Sixty-four percent had a prior Q wave myocardial infarction, 34% had angina on treadmill testing and 42% had prior coronary artery bypass surgery. There was no significant weight change during the year. Table 2 shows the initial and 1 year measurements of the variables used to measure a training effect; each showed a statistically significant change. The ranges of the change were fairly large, demonstrating that a training effect occurred in some patients but not in others.

Table 1. Initial Characteristics of the Study Population (n = 59)

Age (yr ± 1 SD)	53 ± 8
Weight (kg ± 1 SD)	84 ± 13
History of congestive heart failure	7/59 (12%)
History of Q wave myocardial infarction	38/59 (64%)
History of a non-Q wave myocardial infarction only	3/59 (5%)
Prior coronary artery bypass surgery	25/59 (42%)
Angina (during treadmill testing)	20/59 (34%)
Abnormal ST depression on treadmill testing (> 1 mm)	28/59 (47%)
Abnormal exercise-induced ejection fraction (decrease in ejection fraction < 0)	29/59 (49%)
Number with thallium ischemia	34/59 (57%)
Thallium scar score (± 1 SD)	12.7 ± 6.5
Number with thallium scar	40/59 (68%)
Ejection fraction, supine (± 1 SD)	0.53 ± 0.16
Ejection fraction at maximal exercise (± 1 SD)	0.51 ± 0.17
Medications before initial testing	
Digitalis	10/59 (17%)
Beta-adrenergic blocking agents	24/59 (41%)
Nitrates	9/59 (15%)
Receiving beta-adrenergic blocking agents through the year	15/59 (26%)

Table 2. Initial and 1 Year Values of Indexes of a Training Effect

Variable	Initial (mean ± SD)	1 Year (mean ± SD)	Difference (mean ± SD)	Range of Change
HR at rest	69 ± 12	65 ± 11	−4 ± 10*	−20 to 29
HR 5% gd	126 ± 16	118 ± 5	−9 ± 12†	−10 to 43
$\dot{V}O_2$ est	33 ± 9	37 ± 9	5 ± 6†	−23 to 6
$\dot{V}O_2$ msd	26 ± 5	27 ± 7	1 ± 4‡	−13 to 7
Th isch	4 ± 4	3 ± 4	−1 ± 4‡	−3 to 2

*$p < 0.01$; †$p < 0.001$; ‡$p < 0.05$. est = estimated; HR = heart rate; HR 5% gd = submaximal heart rate on treadmill test; msd = measured; Th isch = thallium ischemia score (initial) (immediate sum − 4 hour sum); $\dot{V}O_2$ = oxygen consumption in ml/kg per min.

Training intensity. After 1 year, exercise and medication records were extensively reviewed on a month by month basis. Average training intensities for the entire year were used because intensities were consistent throughout the year. The averages and standard deviations were as follows: percent estimated oxygen uptake was 60 ± 12% (range 44 to 104), percent maximal heart rate reserve (Karvonen method) was 64 ± 9% (range 41 to 80), percent maximal heart rate was 80 ± 4% (range 69 to 87) and percent measured oxygen consumption was 77 ± 14% (range 42 to 109). The average caloric expenditure per session was 324 ± 106 calories (range 130 to 719). Mean attendance for the three times a week exercise sessions was 76 ± 18% (range 23 to 97). A patient was required to attend a minimum of 70% of the required exercise sessions to be classified as compliant with the exercise regimen. The compliance rate for the year was 81%. Dropouts were not included in the final analysis. Fifteen (26%) of the men were maintained on therapeutic doses of beta-adrenergic blocking agents during the year.

Markers of a training effect. Each marker of a training effect was regressed against its initial value (that is, initial heart rate at rest, submaximal heart rate, estimated oxygen consumption, measured oxygen consumption and ischemia on thallium scan) as well as against age, amount of myocardial scar on the thallium scan and the measures of intensity of training (Table 3). All but two relations showed correlation coefficients of less than 0.50. Correlation coef-

Table 3. Correlation Coefficients of the Usual Variables Associated With a Training Effect Regressed on a Variety of Initial Clinical, Treadmill and Radionuclide Variables, and on the Measures of Intensity of Training

	Variables Associated With Training Effect				
	dHR at rest	dHR 5% gd	d$\dot{V}O_2$ est	d$\dot{V}O_2$ msd	dTh isch
		Initial Variables			
Weight	−0.23	−0.23	+0.20	+0.11	+0.08
Age	+0.23	−0.02	+0.13	−0.24	+0.09
HR at rest	−0.56*	−0.13	+0.02	+0.21	+0.02
HR 5% gd	−0.24	−0.45*	+0.30*	+0.24	−0.06
$\dot{V}O_2$ est	−0.10	+0.29*	−0.26*	+0.12	+0.04
$\dot{V}O_2$ msd	−0.05	+0.16	−0.10	−0.04	−0.13
Th isch	+0.25	−0.05	−0.05	−0.18	−0.56*
Th scar	−0.03	+0.01	+0.10	+0.06	−0.14
EF at rest	−0.06	−0.22	0.00	−0.02	+0.06
		Training Intensity Variables			
%Karvonen	−0.05	+0.22	+0.01	+0.02	−0.21
%HR max	−0.22	+0.21	+0.08	+0.14	+0.19
%Tr $\dot{V}O_2$ est	+0.05	−0.22	+0.20	+0.08	+0.01
%Tr $\dot{V}O_2$ msd	+0.09	−0.01	−0.09	−0.01	+0.17
Calories	−0.04	+0.10	+0.09	+0.06	+0.09
% Attendance	−0.06	+0.02	−0.11	−0.11	+0.01

*$p < 0.05$. Calories = average number of calories per session; EF = ejection fraction; %HR max = percent of maximal heart rate achieved; %Karvonen = percent maximal heart rate reserve; %Tr $\dot{V}O_2$ est and msd = percent of estimated and measured maximal oxygen consumption achieved, respectively; Th scar = thallium scar score (initial) (sum of 4 hour scan scores); other abbreviations as in Table 2.

ficients of greater than 0.25 (absolute value) were associated with p values of less than 0.05 and therefore were considered related by more than chance.

The initial thallium ischemia score showed a correlation coefficient of -0.56 ($p < 0.001$) with change in thallium ischemia (patients whose initial ischemia score was highest showed the greatest decrease in ischemia with training). Similarly, those with the highest values for heart rate at rest showed the greatest decrease in heart rate at rest with training ($r = -0.56$, $p < 0.001$). For submaximal heart rate and estimated maximal oxygen consumption, patients with initial values consistent with the greatest deconditioning had the greatest improvement ($r = -0.45$, $p < 0.001$ for submaximal heart rate and $r = -0.26$, $p < 0.05$ for estimated oxygen consumption).

The percent of patients showing at least 5% improvement in a training response were: change in heart rate at rest, 44%; change in heart rate at 5% grade, 58%; change in estimated oxygen consumption, 66%; change in measured oxygen consumption, 52% and change in thallium ischemia, 44%. The percent of patients showing either no change or a worsening in the measurements of a training response were: change in heart rate at rest, 37%; change in heart rate at 5% grade, 27%; change in estimated oxygen consumption, 17%; change in measured oxygen consumption, 29% and change in thallium ischemia, 49%.

There were few significant interrelations among the variables. High initial submaximal heart rate correlated with a greater increase in estimated oxygen consumption ($r = 0.30$, $p < 0.05$). Low initial estimated oxygen consumption correlated with a greater decrease in submaximal heart rate ($r = 0.29$, $p < 0.05$).

There was no relation between initial measured oxygen consumption and the change in oxygen consumption ($\dot{V}O_2$) or the other variables after the 1 year period. The amount of thallium scar present did not correlate with any of the measures of training. Older patients had a smaller increase in measured oxygen uptake ($r = -0.24$) and a smaller decrease in heart rate at rest ($r = 0.23$), but neither of these relations was statistically significant.

The relations among the markers of a training effect were examined by linear regression. The changes in measured and estimated $\dot{V}O_2$ correlated significantly ($r = 0.52$) as did the change in heart rate at rest ($r = -0.43$), but they did not correlate with each other or with the change in thallium ischemia score.

Training intensity and outcome. The measures of intensity of training showed poor correlations with outcome. Most correlation coefficients were less than 0.20, none achieved statistical significance and trends were often conflicting. For instance, higher percent of maximal heart rate related to a greater decrease in heart rate at rest ($r = -0.22$) but to a smaller decrease in submaximal heart rate ($r = 0.21$).

Effects of ischemia or previous myocardial infarction. To test whether the presence of myocardial ischemia or scar was related to a lack of training effect, *t* tests were performed on the basis of the presence or absence of: 1) markers of exercise-induced ischemia (decrease in ejection fraction during the supine bicycle test, angina on treadmill testing or abnormal ST segment depression during the treadmill test); 2) historical features (prior coronary bypass surgery, transmural Q wave infarct or any infarct); and 3) features suggesting abnormal function (increased R wave amplitude at maximal exercise, ejection fraction at rest less than 0.50, initial estimated maximal oxygen consumption less than 10 METs or treatment with a beta-adrenergic blocking agent). In no case was there a significant difference in any measure of training effect between those who did or did not have a given characteristic.

Table 4 lists the variables selected as the best predictors of training in the stepwise regression analyses. The total list of variables from which these were selected are shown in the Appendix. In cases where no variables are listed, all partial F ratios were less than 1.0, indicating no significant relations. The number of cases in each analysis is slightly different because a few patients did not have data for every study.

Because 10 of our patients did not have volume or cardiac output data, these variables were not included in this analysis. A separate analysis on the study group with complete data did show small improvements in most predictions, although the percents remained small (change in measured $\dot{V}O_2$, 15%; change in estimated $\dot{V}O_2$, 0%; change in heart rate at rest, 11%; change in heart rate at 5% grade, 15% and change in thallium ischemia score, 11%).

The measurements based on heart rate (percent of maximal heart rate and percent of maximal heart rate reserve by the Karvonen method) could not be validly determined for the 15 patients receiving a beta-adrenergic blocking agent during training. To avoid this limitation of the study group, these variables were not included in the multivariate regression. A separate analysis was done including these variables (and thereby excluding the patients receiving a beta-adrenergic blocking agent). This improved the percent of variation in training effect explained, but the predictions were still poor (change in measured $\dot{V}O_2$, 14%; change in estimated $\dot{V}O_2$, 23%; change in heart rate at rest, 9%; change in heart rate at 5% grade, 26% and change in thallium ischemia score, 13%).

To test for the possibility that some patients who had an improved oxygen consumption in the second test were actually exerting more effort than in the initial test, correlations were performed between change in oxygen consumption after training and differences in respiratory quotient, maximal heart rate, ST segment depression and perceived exertion between the initial and final treadmill tests. These may represent differences in test end points. The following

Table 4. Variables Selected as the Best Predictors for Each of the Measures of Training Effect by the Regression Analyses

Measure of Training	Clinical Variables	Percent	Treadmill Variables	Percent	Radionuclide Variables	Percent	Intensity Variables	Percent	Combined Variables	Percent
d$\dot{V}O_2$ msd	Age	6	HR 5% gd	6	dEF	8	%Tr $\dot{V}O_2$ est	3	dEF	8
	DBP at rest	2	DBP max	5	Th isch	1			HR 5% gd	7
	HR at rest	5	$\dot{V}O_2$ est	4					%Tr $\dot{V}O_2$ est	5
	Total	13	Total	15	Total	9	Total	3	Total	21
d$\dot{V}O_2$ est	Weight	4	HR 5% gd	13			%Tr $\dot{V}O_2$ est	2	HR 5% gd	14
	Age	4	HR at rest	2			%Tr $\dot{V}O_2$ msd	2	Th immed	4
	CABG	2					Calories	3	HR at rest	5
	Total	10	Total	15	Total	0	Total	7		23
dHR at rest	HR at rest	31	HR at rest	37	Th isch	6			HR at rest	37
	Beta -blkrs	3	HR 5% gd	2					Beta-blkrs	3
	Weight	2	DBP max	2					EF max	2
	Total	36	Total	41	Total	6	Total	0	Total	42
dHR 5% gd	Weight	5	HR 5% gd	27	EF at rest	5	%Tr $\dot{V}O_2$ est	4	HR 5% gd	27
	Angina (hx)	4	Angina (tm)	2	Th immed	2	Calories	3	MI	5
	CABG	3	DBP 5% gd	1					Age	3
	Total	12	Total	30	Total	7	Total	7	Total	35
dTh isch	Ant MI	3	$\dot{V}O_2$ msd	4	Th isch	31			Th isch	35
			Angina (tm)	6	dEF	2			$\dot{V}O_2$ msd	3
			$\dot{V}O_2$ est	3					HR at rest	3
	Total	3	Total	13	Total	33	Total	0	Total	41

Angina (hx) = history of angina pectoris; Angina (tm) = angina during the treadmill test; Ant MI = history of anterior myocardial infarction; Beta-blkrs = patient was receiving a beta-adrenergic blocking agent before the training year; CABG = history of coronary artery bypass surgery; DBP = diastolic blood pressure; DBP 5% gd = diastolic blood pressure at 5% grade; DBP max = diastolic blood pressure at maximal stage; dEF = ejection fraction at maximal stage − ejection fraction at rest; dHR at rest = heart rate at rest at 1 year − initial heart rate at rest; dHR 5% gd = HR 5% gd at 1 year − initial HR 5% gd; dTh isch = Th isch at 1 year − initial Th isch (immediate sum − 4 hour sum); d$\dot{V}O_2$ est = $\dot{V}O_2$ est at 1 year − initial $\dot{V}O_2$ est; d$\dot{V}O_2$ msd = $\dot{V}O_2$ msd at 1 year − initial $\dot{V}O_2$ msd; MI = history of any myocardial infarction; Th immed = sum of the immediate thallium scores; other abbreviations as in Tables 2 and 3.

correlations were demonstrated: increase in maximal heart rate ($r = 0.43$, $p < 0.001$), increase in perceived exertion ($r = 0.36$, $p < 0.01$), increase in ST depression ($r = 0.28$, $p < 0.05$) and increase in respiratory quotient ($r = 0.16$, p = NS).

Discussion

The major finding of this study is that a patient's success or failure in improving aerobic capacity after a 1 year aerobic exercise program was poorly predicted from initial clinical, treadmill or radionuclide data. Correlations between initial variables and outcome were poor. Training intensity had little to do with outcome. Patients with evidence of ischemia (exercise test-induced angina, ST depression or decreasing ejection fraction) or evidence of myocardial damage did not differ in degree of training effect from patients without such evidence. History of coronary bypass surgery or myocardial infarction had no bearing on whether a patient's work capacity would improve after the training period.

Initial fitness and outcome. There was a trend for patients who initially showed evidence of the poorest state of fitness (high rest or submaximal heart rate, low estimated oxygen consumption or high thallium ischemia score) to have the most improvement in the respective measurement. However, initial measured oxygen consumption, the best index of aerobic capacity on entry, showed no relation to any measure of training effect at the end of the year of training. Older patients showed only slightly less benefit than younger ones. Those with characteristics suggesting larger amounts of scar or ischemia did not have significantly different results from those with less. Multivariate analysis did not greatly improve the ability to predict outcome.

Evidence of training response. The usual changes associated with a training response were observed after 1 year of exercising. Patients showed increased measured oxygen consumption (mean increase 1.3 ml/kg per min; $p < 0.05$) and decreased heart rate at rest and at submaximal work loads (4 and 8 beats/min, respectively; $p < 0.05$). Although these changes are small, other investigators (10) have found similar changes in training middle-aged men with coronary heart disease. In addition, the values exhibited a wide range of responses (Table 2) with many patients not showing any improvement in training measures.

Previous studies have found that those with the lowest initial measured oxygen consumption often have the largest improvement with an exercise program. In our study the correlation coefficient of initial measured oxygen consumption with any measure of training effect was always less than 0.20 (not significant) and it was never selected as a predictor in the multivariate analyses. Our range of initial values for measured oxygen consumption was narrow. Because a 4 month recovery period after a coronary event was required for entry into this study, the deconditioning associated with prolonged bed rest (12) was not a factor. Different findings in other studies may be due to an initial poorer degree of conditioning.

Training intensity and outcome. The lack of correlation between training intensity and change in oxygen uptake during the year is difficult to explain. In healthy men this relation is good ($r = 0.8$) (13); it is not clear from the present study why the correlations were so poor ($r < 0.2$, $p > 0.05$). Because oxygen consumption was not measured during training and heart rate was not continually monitored, the ability to assess training intensity was not ideal. However, the retrospective calculation of intensity and attendance from our research records was more accurate than what is possible in most situations. It may well be that setting exercise prescriptions using exercise tests limited by signs or symptoms gives too low of an exercise intensity. The analysis which excluded the 15 patients who were taking a beta-adrenergic blocking agent throughout training did show improved predictions. As discussed previously, there was no difference in mean training effect between the group on beta-adrenergic blocking agents and those not on beta blockers. Beta-adrenergic blocking agents may change the association between intensity and effect of training rather than having a bad effect on training.

Changes in oxygen uptake. There was relatively more change in estimated oxygen consumption than in measured oxygen consumption (mean increase 4.7 versus 1.3 ml/kg per min). Patients are even able to walk longer on a treadmill and perform the same submaximal work load at a lower rate-pressure product without a measurable improvement in aerobic capacity. Other studies (14,15) have found that patients can improve their exercise performance without showing any cardiac changes. This suggests that improved performance may be the result of peripheral adaptations (16) adding to the difficulty in predicting which patients will improve work capacity. However, there was a decrease in the amount of ischemia as measured by thallium scan after training. This implies that some central (cardiac) changes occurred.

The changes in test end points were moderately correlated with changes in oxygen uptake. This raises the question of what portion of the changes were due to the patients being encouraged to perform better on the 1 year tests by those administering the tests or by their own faith in the exercise program. Even maximal testing appears to be of questionable reliability and argues for using a different group of examiners for initial and final testing.

Limitations of study. Although the study design was a randomized, prospective study with a control group (15), the current analysis was conducted retrospectively on the training group only. It is possible that an analysis of a control group would have shown similar associations (or lack of them) between initial and 1 year measurements.

The relatively small increase in measured oxygen consumption in this group may have decreased the ability to predict improvement in this marker of a training effect, although this should not have affected the strength of association between initial and final measurements as reflected in the linear regression analyses. Finally, because multiple comparisons are made, 5% of them will be significant by chance alone. Because the emphasis of our study is the lack of correlations between initial and final measurements, this fact only strengthens our conclusions.

Conclusions. A very detailed initial evaluation did not allow accurate prediction of who would train and who would not. Even those patients whose characteristics suggested they had the most myocardial ischemia or scar showed as much improvement from training as patients without such characteristics. Thus, for instance, considering angina, a low ejection fraction at rest, ST segment depression or a decreasing ejection fraction with exercise as a contraindication to an exercise program is unjustified. Because many of the benefits obtained from an exercise program are intangible, it seems inappropriate to eliminate any stable patient from an exercise program on the basis of clinical, treadmill or radionuclide data.

In summary, we found that extensive clinical data gathered before an exercise program do not make it possible to predict the effect of training in men with coronary heart disease. Treadmill testing and radionuclide data do not greatly improve the ability to predict who will benefit the most from an exercise program.

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Appendix

Variables Used as Predictors in the Stepwise Regression Analyses

I. Clinical

Beta-adrenergic blocking agent
Digoxin

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Nitroglycerin
Angina (by history)
Coronary artery bypass surgery
Q wave myocardial infarction
Non-Q wave myocardial infarction
Either a Q wave or a non-Q wave myocardial infarction
Anterior Q wave myocardial infarction
History of congestive heart failure
Heart rate at rest
Systolic blood pressure at rest
Diastolic blood pressure at rest

II. Treadmill
Estimated maximal oxygen consumption (ml/kg per min)
Measured maximal oxygen consumption (ml/kg per min)
Submaximal (5% grade) heart rate
Maximal heart rate
Submaximal (5% grade) systolic blood pressure
Maximal systolic blood pressure
Submaximal (5% grade) diastolic blood pressure
Maximal diastolic blood pressure
ST depression (visually interpreted; V_5)
Angina (on treadmill)

III. Radionuclide
Ejection fraction at rest
Maximal ejection fraction
Change in ejection fraction during maximal supine exercise
Sum of thallium immediate scores
Sum of thallium ischemia scores
Sum of thallium scar scores

IV. Intensity
Percent estimated maximal oxygen consumption
Percent measured maximal oxygen consumption
Percent attendance
Calories (average expenditure per session)

V. Combined
Age
Weight
Angina (on treadmill)
Angina (by history)
Coronary artery bypass surgery
Beta-adrenergic blocking agent
Estimated maximal oxygen consumption
Measured maximal oxygen consumption
Heart rate at rest
Submaximal (5% grade) heart rate
Systolic blood pressure at rest
Diastolic blood pressure at rest
Submaximal (5% grade) diastolic blood pressure
Maximal diastolic blood pressure
Ejection fraction at rest
Maximal ejection fraction
Change in ejection fraction during maximal exercise
Sum of thallium immediate scores
Sum of thallium ischemia scores
Sum of thallium scar scores
Percent estimated maximal VO_2 during training
Percent measured maximal VO_2 during training
Percent attendance
Calories (average expenditure per exercise session)
History of any myocardial infarction

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