Comparison of High- and Low-Intensity Exercise Training Early After Acute Myocardial Infarction

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The effects of the intensity of exercise training on cardiorespiratory variables were investigated in a consecutive series of men with recent (median 6 weeks) acute myocardial infarction. Forty-five patients were randomly assigned either to a high- (65 to 75% maximum oxygen consumption rate \( [\text{VO}_2\text{max}] \)) or to a low-intensity (<45% \( [\text{VO}_2\text{max}] \)) exercise group. Patients engaged in medically supervised aerobic training 3 sessions a week for 12 weeks. With training, mean \( [\text{VO}_2\text{max}] \) significantly increased by 11% (2.09 to 2.31 liters/min) within the high group and by 14% (1.93 to 2.21 liters/min) within the low group. Differences between groups were not statistically significant. Both groups also had comparable changes in heart rate, blood pressure and double-product at submaximal and maximal workloads. Analysis of blood lipids revealed that both groups experienced a significant increase in high density lipoprotein cholesterol. There were no significant changes in total serum cholesterol or triglycerides. These findings suggest that within an unselected population of patients after acute myocardial infarction referred for cardiac rehabilitation, low- and high-intensity exercise training produces relatively similar changes in cardiorespiratory variables during the initial 3 months of exercise training.

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Exercise training of survivors of acute myocardial infarction (AMI) increases physical work capacity, and improves psychosocial functioning, decreases symptoms and may reduce risk for subsequent death or reinfarction. Although current standards for prescription of exercise to patients with coronary artery disease are based on the assumption that only strenuous activity (65% of maximal oxygen consumption \( [\text{VO}_2\text{max}] \)) is a sufficient stimulus to produce these beneficial effects, the scientific rationale for this assumption is based primarily on physiologic studies of healthy young adults, and the level of exercise intensity that is optimal for the general population of patients after AMI has not been subjected to rigorous empirical analysis. In 1 study that did examine the effects of different levels of exercise intensity in patients after AMI the exclusion of 25% of potential subjects because they were taking medication, too deconditioned or older than 54 years of age precluded any generalization of results to more representative populations of post-AMI patients participating in cardiac rehabilitation.

The assumption that strenuous activity is required to produce clinically significant physiologic effects in survivors of AMI has several important consequences for the management of this large population of patients. First, because strenuous activity after AMI is associated with a small but significant risk of ventricular fibrillation, many physicians are reluctant to recommend this potentially efficacious form of therapy, except under direct supervision of medical personnel trained and equipped to resuscitate patients of cardiac
arrest. Second, many patients experience subjective discomfort during exercise at high intensity and are therefore dissuaded from pursuing further training, despite its potential benefits.

The present study was designed as a systematic test of the hypothesis that low-intensity exercise (<45% VO_{2max}) may produce effects on physical work capacity that are substantially similar to those resulting from the strenuous exertion (>65% VO_{2max}) that is currently prescribed to patients after AMI. Because the risk of ventricular fibrillation during low-intensity exercise appears to be less than that associated with more strenuous effort,^{15} the potential benefits of low-intensity exercise should be investigated. Careful consideration of the relative risks and benefits of low-intensity exercise is necessary to make rational decisions when prescribing exercise therapy to patients recovering from AMI. Our patient sample was considered representative of most cardiac rehabilitation programs in that we included patients of all ages, many of whom were receiving cardiac medications, and who were not excluded by virtue of their having limited functional capacity.

Methods

This was a collaborative investigation by investigators from the Duke University Medical Center and Bowman Gray School of Medicine. Data were collected from both institutions using an identical protocol. Subjects were a consecutive series of male patients who had sustained an AMI documented by history, electrocardiographic changes and increases in serum enzyme levels. All subjects had the AMI no more than 1 year before participation in this study (median = 8 weeks), and none had previously participated in a formal exercise program. All subjects were randomly assigned either to a high-intensity (65 to 75% VO_{2max}) or to a low-intensity (<45% VO_{2max}) group. Of 54 potential subjects, 46 men completed the 3-month training program. Subjects ranged in age from 28 to 66 years (median 52). For purposes of this study, all electrocardiograms were rated for global AMI severity using a QRS scoring system^{16} (mean = 5 ± 4 standard deviation). Subjects taking cardiac medications were not excluded from the study, but were maintained on their prescribed pharmacologic regimens at the same dosage for the duration of the 3-month study. All subjects were given information on low-fat, low-cholesterol diets, but no closer dietary modification was attempted. Cardiac catheterization and radionuclide ventriculography were not performed routinely, but results of these additional diagnostic procedures were recorded when available.

Exercise testing: Exercise tests were performed in a thermoneutral (24 to 26°C) laboratory. Fasting subjects (12 hours) were extensively briefed about testing procedures before undergoing a graded exercise test. All subjects had at least 1 previous treadmill test before their participation in our study. Each subject performed a symptom-limited maximum test on a motor-driven treadmill (PaceSetter R-9). Criteria for termination included fatigue, weakness, chest pain, severe claudication, abnormal blood pressure response or marked ST-segment depression. The protocol consisted of 1-minute stages: minute 1: 2.0 mph, 0% grade; minute 2: 2.5 mph, 0% grade; minute 3: 2.5 mph, 20% grade and so on, so that each subsequent minute represented an approximate 1 MET (3.5 ml O_2/kg/min) increase.

Metabolic and respiratory measurements were obtained using a Beckman Metabolic Measurement Cart (model 040-301). Measurements of VO_{2} (liter/min and ml/kg/min), expired ventilation and respiratory exchange ratio were obtained every 15 seconds.

A standard 12-lead electrocardiogram was recorded at rest and at the end of each minute. Electrocardiographic tracings were also obtained during a 5-minute recovery period. Electrocardiographic recordings were displayed on a Marquette Electronics Exercise Module (series 6500). Heart rates were recorded at the end of each minute. Blood pressure was measured by cuff sphygmomanometry at 3-minute intervals.

Blood lipids: Plasma triglycerides, total serum cholesterol and high density lipoprotein cholesterol were determined on blood samples drawn between 7 and 9 A.M. after a 12- to 14-hour fast. Blood was withdrawn by 1-syringe 15 cc vacuum tube and anticoagulated with 3.5% sodium citrate (1:9, v/v), centrifuged at 6,000 X g for 15 minutes at 4°C and frozen at −20°C before analysis by a commercial laboratory.

Exercise training: Subjects exercised under medical supervision 3 times weekly for 12 consecutive weeks. Exercise sessions consisted of 10 minutes of warm-up exercises, followed by 30 to 45 minutes of continuous walking or jogging (approximately 3 miles) in their prescribed training range. A 10-minute cool-down period consisting of relaxation and light stretching exercises completed each exercise session.

The high-intensity subjects followed a regimen of increasing progressive aerobic exercise to a level of 65 to 75% of VO_{2max} determined at the time of their initial treadmill test using the Karvonen formula for determining maximum heart rate reserve. Their walking and jogging prescription progressed in intensity from 50% VO_{2max} for the first week to 75% VO_{2max} by the fourth week of training. The format for the low-intensity exercise program was identical, with the exception that subjects' exercise intensity was <45% VO_{2max} throughout the duration of study. All subjects had their heart rates checked at 10-minute intervals during each exercise session by trained nursing staff. Subjects also were continuously monitored by a heart rate monitor (Exersentry model III) at least once a week.

Data analyses: The primary mode of statistical analysis was a 2 by 2 multivariate analysis of variance (MANOVA). Time (before and after exercise training) served as a within-group variable and intensity (high and low) served as a between-group variable. We initially included site (Duke and Bowman Gray) as a between-group variable. Statistical analyses revealed an absence of a site main effect or any significant interactions. Consequently, all data were pooled in the 2 by 2
TABLE I Characteristics of Subjects

<table>
<thead>
<tr>
<th></th>
<th>High Intensity (n = 23)</th>
<th>Low Intensity (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>51 ± 8</td>
<td>52 ± 9</td>
</tr>
<tr>
<td>(24-63)</td>
<td>(28-66)</td>
<td></td>
</tr>
<tr>
<td>Body weight (lb)</td>
<td>194 ± 28</td>
<td>194 ± 27</td>
</tr>
<tr>
<td>(153-270)</td>
<td>(154-269)</td>
<td></td>
</tr>
<tr>
<td>Time since AMI (weeks)</td>
<td>13 ± 11</td>
<td>10 ± 11</td>
</tr>
<tr>
<td>(3-52)</td>
<td>(2-52)</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>47 ± 14</td>
<td>62 ± 13</td>
</tr>
<tr>
<td>(25-70)</td>
<td>(33-78)</td>
<td></td>
</tr>
<tr>
<td>QRS score</td>
<td>5 ± 4</td>
<td>6 ± 4</td>
</tr>
<tr>
<td>(0-16)</td>
<td>(0-15)</td>
<td></td>
</tr>
<tr>
<td>Number (%) having cardiac catheterization</td>
<td>16 (70%)</td>
<td>22 (95%)</td>
</tr>
<tr>
<td>Number (%) of patients with &gt;75% diameter stenosis in at least 1 coronary artery</td>
<td>16 (100%)</td>
<td>20 (91%)</td>
</tr>
</tbody>
</table>

Values are means ± standard deviations. Ranges are also included.

MANOVA. Separate MANOVAs were performed for resting and maximal treadmill data.

Results

Baseline characteristics: There were no differences among the high- and low-intensity groups in any of the initial demographic characteristics (Table I). Subjects were comparable with respect to age, weight, time since AMI, left ventricular ejection fraction and AMI severity. In addition, many patients had a previous cardiac catheterization, and the distribution of patients with significant 1-, 2-, and 3-vessel disease was generally equivalent.

Review of medication usage indicated that there were no group differences in the kind of cardiac medications prescribed. Seventy-eight percent of all patients were taking β-blocking drugs (70% selective; 30% nonselective), 57% were taking calcium channel blocking agents, and 37% were taking nitrates. Thus, the randomization procedure was successful in producing comparable initial characteristics in the high- and low-intensity exercise groups.

Exercise compliance: Careful assessment of patient participation indicated that participants of both the high and low groups were equally compliant with their respective exercise training protocols. Subjects assigned to the high-intensity condition exercised for a mean (± standard deviation) total of 32 ± 5 exercise sessions (out of a possible 36), and the low-intensity group exercised for a mean total of 33 ± 5 exercise sessions. Review of daily exercise logs indicated that the low-intensity subjects were within or below their prescribed training range 91% of the time, whereas the subjects in the high-intensity group were within or above their prescribed training range 86% of the time. Eight patients (15%) dropped out of the study before the completion of 3 months of exercise training, 4 patients from each group. The reasons for dropping out included recent diagnosis of cancer (n = 1), surgery (n = 2), refusal to be randomized (n = 1) and inconvenience with work schedule (n = 4).

Changes in cardiovascular functioning: A MANOVA performed for resting cardiovascular data revealed a significant main effect for time, F (4,40) = 3.31, p < 0.02. The main effect for intensity and the intensity by time interaction were not significant. Examination of the data listed in Table II reveal that a significant univariate main effect for time was obtained only for resting heart rate, with the low-intensity group experiencing a significant reduction in resting heart rate after the 3 months of exercise training.

A separate MANOVA for the maximal exercise treadmill data also revealed a main effect for time, F (3,35) = 12.02, p <0.0001. However, neither the intensity main effect (F <1) nor the intensity times time interaction [F = 1.05] was significant. Examination of the univariate main effects for time revealed that, averaged over exercise group, there were significant improvements in VO2max, F (1,37) = 28.09, p <0.0001, and in treadmill time, F (1,37) = 31.94, p <0.0001. The absence of an intensity time interaction indicates that the high and low groups showed comparable improvements in cardiorespiratory fitness. Examination of the data listed in Table II reveals that the average improvement in VO2max (liters/min) was 12%.

Out of program activity: Activity levels outside of the program were assessed by self-report and daily pedometer recordings for 1 week before and after training. The mean daily activity levels did not change for either the high- (mean 4.9 and 4.7 miles) or low- (mean 3.5 and 3.6 miles) exercise groups. Moreover, only 9 patients indicated that they had participated in any exercise activity on their own during the study period. Six patients assigned to the high group and 3
patients assigned to the low group reported walking, playing tennis or bowling. This minimal involvement is not considered physiologically significant.

**Lipids:** Because not all lipid values were expected to change with exercise, we performed a series of ANOVAs for each variable separately. Examination of these univariate analyses indicated that the time main effect was significant only for high density lipoprotein cholesterol, F (1,34) = 11.14, p < 0.01. Subjects in both the high- (28 ± 8 to 33 ± 10) and low- (27 ± 8 to 33 ± 10) intensity training programs increased their high density lipoprotein cholesterol. However, there were no significant changes in either total serum cholesterol (high: 209 ± 52 to 214 ± 54; low: 202 ± 33 to 201 ± 46) or triglycerides (high: 180 ± 98 to 185 ± 78; low: 201 ± 91 to 202 ± 128).

**Discussion**

The main finding of this study was that 3 months of low-intensity exercise training was equivalent to a comparable period of relatively high-intensity exercise in improving cardiorespiratory fitness. The 2 training regimens produced comparable improvements in functional capacity and had similar effects on blood lipids. Both groups increased their VO2max, and the improvement for the low group (14%) was not statistically different from the improvement for the high group (11%). These results appear to contrast with data from the Ontario Multicenter Exercise-Heart Collaborative Study, in which there were significant differences between 2 comparable exercise intensity regimens. However, the Ontario Study continued for 1 year, whereas the present study (and standard recommendations for many formal exercise programs for cardiac rehabilitation in this country) extended for only 3 months. Moreover, subjects in the Ontario study were younger (mean 45 years), were seen later after the myocardial infarction (mean 7 months) and 25% of the prospective participants were eliminated from the study because they were taking cardiac medications, were older than 54 or were "too deconditioned." It should be noted that the improvements in our high-intensity group were smaller than those reported in some, but not all studies of patients after AMI.

The fact that three-fourths of our patients were taking β-blocking drugs may have served to attenuate the magnitude of improvement in VO2max.

Subjects in our low-intensity condition increased their VO2max by an average of 14%. This level of improvement in the low-intensity group is consistent with other reports of improvement in aerobic capacity after AMI without formal exercise training. Moreover, in a study of 146 cardiac patients, those patients who trained the most intensely or who had the highest class attendance did not experience the most improvement. Thus, participation in routine daily activities alone may produce significant physiologic effects that may contribute to the improvement in VO2max observed during supervised exercise.

Taken together, these findings have important implications for the practice of cardiac rehabilitation. They suggest that the possibly increased risk of high-intensity training may not be justified by additional benefits in this population. This finding may be especially relevant for the sedentary patient in whom subjective discomfort during intense exercise may serve as a deterrent to long-term compliance with exercise therapy. We emphasize that these results should not be interpreted to exclude the possibility of additional cardiovascular benefits of high-intensity training pursued by certain patients who may exercise over longer durations of time. However, our data support the view that improvements in functional capacity for many patients after AMI may, at least in the short run, be relatively independent of the intensity of supervised exercise training.

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