Effects of 12 Months of Intense Exercise Training on Ischemic ST-segment Depression in Patients with Coronary Artery Disease


SUMMARY This study was undertaken to determine whether adaptation to 12 months of intense endurance exercise training could alter the relationship between the product of heart rate and systolic blood pressure (double product) and the extent of ischemic ST-segment depression during exercise in patients with coronary artery disease. True (i.e., not symptom-limited) maximum oxygen uptake capacity increased from 25.5 ± 4.2 ml/kg/min (mean ± SD) to 35.3 ± 4.4 ml/kg/min with training. The maximum degree of ST-segment depression during exercise averaged 0.20 ± 0.04 mV before and 0.16 ± 0.08 mV after training despite a 20% increase in maximum double product. The double product at which ST depression (0.1 mV) first appeared was 22% greater after training. The extent of ST-segment displacement at the same double product was less after training. These findings suggest that training, if sufficiently intense and prolonged, can result in a reduction in myocardial ischemia at the same or a higher double product.

EXERCISE is used widely in the rehabilitation of patients with coronary artery disease, and often results in major improvements in work capacity.1-3 Exercise training can induce an increase in the minimum work rate required to induce ST-segment depression4 or angina.5,6 in some patients with coronary artery disease. A decrease in the magnitude of ST displacement at a given submaximal level of exercise has also been reported.4,7 Among the adaptations to endurance exercise are a slower heart rate and a lower systolic blood pressure during submaximal exercise.8 As a consequence, myocardial oxygen consumption at the same submaximal work rate is reduced after training.8

However, in a group of patients with coronary artery disease studied by Detrny and Bruce,4 the quantitative relationship of ST depression to the product of heart rate and systolic blood pressure (double product) was unchanged by 3 months of training.4 If the degree of ST depression reflects the severity of myocardial ischemia, this finding argues against improved myocardial oxygen supply and favors the interpretation that the increased exercise threshold for ischemia after training is solely due to a reduction in myocardial oxygen requirement.

We speculated that the apparent failure of myocardial oxygenation to improve in response to training may have been due to an insufficient exercise stimulus. In studies on animals in which training appeared to improve myocardial blood supply, moderately strenuous exercise lasting 1-3 hours/day, 5 days/week was used.9-12 In contrast, the exercise used in studies in which training did not appear to improve myocardial ischemia in patients with coronary artery disease was generally mild, intermittent and brief.4,5,7,13 The present study was designed to evaluate the effect of a prolonged program of exercise of increasing intensity, duration and frequency on the relationship between the double product and the extent of ischemic ST-segment depression during exercise in patients with coronary artery disease. A small number of patients was included in this study because it is difficult to identify large numbers of persons who can participate with the prolonged commitment required to attain the level of exercise sought. Also, our purpose was to assess the efficacy of a successfully completed intense and prolonged exercise program rather than of conventional cardiac rehabilitation.

Methods

Patients

The 10 patients, ages 44-63 years, are the first group to complete 12 months of participation in the exercise program. Nine had sustained a single myocardial infarction, documented by characteristic chest pain, evolving electrocardiographic changes and increases in plasma enzyme levels. The interval between myocardial infarction and enrollment in the study ranged from 4 months to 5 years. One patient was asymptomatic but had type II hyperlipoproteinemia, a strong family history for coronary artery disease, frequent premature ventricular depolarizations, a positive exercise stress test and angiographically documented severe three-vessel coronary disease. Three patients were receiving modest doses of propranolol (40 mg daily). In two of these patients, propranolol was stopped during the study by their personal physicians. There were no other changes in medications during the study. We believe that inclusion of the results from the two patients with whom propranolol was discontinued is justified, because β-adrenergic blockers decrease rather than increase the

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magnitude of exercise-induced ST-segment displacement. Thus, discontinuation would not be expected to diminish the ischemic ST-segment response to exercise. Four patients were taking isosorbide dinitrate because of chest pain, which occurred only in the immediate weeks after acute myocardial infarction. However, none of the patients had effort angina at the time of admission to or during the study. In addition, none had clinical or electrocardiographic manifestations typical of variant angina with coronary artery spasm.

We also studied the ischemic ST-segment response at the beginning and end of a 12-month interval in eight additional men with coronary artery disease, who were suitable candidates for the training program in terms of exercise capacity and cardiac status, but who could not make the necessary time commitment for participation. Six of these men had sustained a well-documented myocardial infarction. The interval between myocardial infarction and the initial exercise test was 4, 5, 7, 22, 48 and 120 months. The other two patients had angiographically documented, severe, three-vessel coronary artery disease. These additional patients were studied to obtain information regarding the likelihood of spontaneous improvement in exercise-induced, ischemic ST-segment depression. Each patient gave written consent after being informed of the details, objectives and risks of the study.

Exercise Testing

Exercise testing was preceded by a history, physical examination and ECG at rest. The exercise tests were performed 2 hours after a light meal, and, in the five patients on medication, 3 hours after the last dose of medication. The exercise tests were performed in sequence, 1 week apart, before and after 12 months of participation in the exercise program. A maximal treadmill exercise test, using the Bruce protocol, was performed to evaluate work capacity and the heart rate, blood pressure, and ECG responses to exercise. A maximal treadmill test was performed to determine maximum oxygen uptake capacity (VO2max). After a 5-minute warmup, during which the subject walked on the treadmill at 2.5 mph up a 5% grade, the speed and grade were adjusted to match the next to the last stage attained in the preceding Bruce treadmill test. The work rate was then increased at 3-minute intervals using the Bruce protocol. A progressive, maximal exercise test on a bicycle ergometer (Quinton Model 845) was performed to obtain information regarding the heart rate, blood pressure, VO2 and ECG response to bicycle exercise. After a 5-minute warm-up at a work rate of 200 kg-m/min, the work rate was increased by 200 kg-m/min every 3 minutes to maximum. The end point for all exercise tests was exhaustion.

The patients in this study were not symptom-limited, so we could measure their true VO2max. The "leveling off" criterion, i.e., no further increase in VO2 with higher work rates, was used to establish that VO2max had been attained. To measure VO2, expired air was collected in Douglas bags and analyzed with a Perkin Elmer MGA 1100 mass spectrometer. The volume of expired air was measured with a Parkinson Cowan dry gas meter.

Before exercise testing, a standard 12-lead ECG and Frank X, Y and Z orthogonal leads were recorded with the subject recumbent. To determine the effect of the upright position on the ST segment, tracings from leads V4, V5 and V6 and Frank X, Y and Z leads were recorded also while the patients were standing on the treadmill before exercise. The ECG was monitored continuously during exercise. Throughout each exercise test, simultaneous tracings from leads V4, V5 and V6 and Frank X, Y and Z leads were recorded at 1-minute intervals. Blood pressure was measured with a mercury sphygmomanometer, 30 seconds before the end of each stage of the exercise tests and also at the time of appearance of ischemic ST-segment changes (0.1 mV depression). The double-product threshold for an ischemic ST-segment response was defined as the product of systolic blood pressure and heart rate at which ischemic ST-segment displacement first appeared. A horizontal or downward sloping ST-segment depression of 0.1 mV lasting for 0.08 second in three consecutive ECG complexes in a given lead was considered indicative of ischemia.

Echocardiographic Measurements

To assess the effect of endurance training on left ventricular size, M-mode echocardiographic examinations were undertaken using an Ekoline-20A ultrasonoscope (Smith-Kline) with a 2.25-MHz unfocused transducer, 1.25 cm in diameter, interfaced with a Cambridge multichannel strip-chart recorder as previously described. Echocardiograms were obtained after 15 minutes of rest with the subjects supine and during held expiration. The patients were instructed repeatedly to avoid the Valsalva maneuver. All echocardiograms were taken 3 hours after the last dose of medications and 24 hours after the last exercise session. The transducer was placed parasternally in the third or fourth left intercostal space with the ultrasonic beam passing through the left ventricle just distal to the tips of the mitral valve leaflets. Three to four cardiac cycles were averaged for each measurement. End-diastolic dimension was defined as the distance between the left side of the interventricular septum and the posterior wall endocardium at the onset of the QRS complex of the simultaneously recorded ECG. Left ventricular posterior wall thickness was measured as the distance from the posterior wall endocardium to the epicardium at the onset of the QRS. Left ventricular end-diastolic volume was estimated using the method described by Teichholz and left ventricular mass was estimated using the standard formula. To minimize variability in the serial echocardiographic examinations, special care was taken to use exactly the same body position and intercostal space in subsequent examinations as were used in the initial evaluation. To enhance the reproducibility, the tracings were examined carefully and the measurements were made using the same anatomic landmarks.
Exercise Program

The 12-month training program consisted of endurance exercise. Each exercise session began with 10 minutes of light calisthenics, stretching and walking. This was followed by a period of either alternate walking and jogging sequences, continuous jogging or bicycle ergometer exercise. During the first 3 months, the intensity of the exercise was adjusted to require 50–70% of the patient's VO₂ max. Thereafter, if the patient was adapting well to the training (i.e., increase in VO₂ max, decrease in heart rate), exercise intensity was increased to 70–80% of VO₂ max, with two to three intervals of exercise requiring 80–90% of VO₂ max, and lasting 2–5 minutes interspersed through the exercise session. The intensity of the exercise was related to the patients' VO₂ max by monitoring heart rate during the exercise sessions and adjusting running speed on the indoor track, or resistance on the bicycle ergometer, to elicit the heart rate equivalent to the desired percent of VO₂ max. Heart rate during the exercise sessions was measured initially by radiotelemetry and, when considered safe, by periodic ECG monitoring and palpation of the pulse. The relationship between heart rate and oxygen uptake was determined by measuring VO₂ and heart rate during the submaximal and maximal stages of the progressive treadmill and bicycle ergometer exercise tests, which were performed at 2–3-month intervals.

Patients were expected to exercise three times per week during the first 3 months, and four to five times per week for the next 9 months. The duration of the exercise sessions (not including the 10-minute warm-up period) was 30 minutes initially, and was progressively increased until after about 6 months the patients were exercising continuously for 50–60 minutes.

Statistical Analysis

The significance of differences between data obtained before and after the 12 months of training was assessed with the paired, two-tailed t-test. Least-squares linear regression analysis was used to evaluate the test-retest reliability for the determination of the double-product threshold for ischemic ST-segment changes. Values are as mean ± sd.

Results

Adherence to the exercise program was excellent for nine of the patients, with an average attendance of 4.5 days per week for the last 9 months of the program. However, patient 6 (tables 1–3) was irregular in his attendance after 6 months, and participated in an average of 2.5 exercise sessions per week during the last 6 months of the study. A weight loss from an average of 78.7 ± 11 kg to 73.9 ± 10 kg (p < 0.01) occurred over the 12-month period. Exercise performance progressively improved. During the last 3 months of the study, all the patients were running 4–5 miles continuously per exercise session or performing an equivalent amount of exercise on the bicycle ergometer. None of the patients had complications (angina, myocardial infarction, serious ventricular arrhythmias or cardiac arrest) during the study.

<table>
<thead>
<tr>
<th>Table 1. Effects of 12 Months of Training on Maximum Exercise Capacity and Maximum Exercise-induced Ischemic ST-segment Displacement</th>
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*Exercise time to exhaustion in the Bruce test.16
†Initial vs 12-month value: p < 0.001.
‡p < 0.01.

Abbreviations: VO₂ max = maximum oxygen uptake capacity; HR = heart rate; SBP = systolic blood pressure; max = maximum.
Table 2. Effects of 12 Months of Training on the Threshold for Ischemic ST-segment Displacement

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Period after MI (months)</th>
<th>Heart rate (beats/min)</th>
<th>Systolic blood pressure (mm Hg)</th>
<th>Double product (HR × SBP × 10⁻⁹)</th>
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<td>Mean</td>
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<tr>
<td>Mean</td>
<td>49.6</td>
<td>±7</td>
<td>125</td>
<td>119</td>
<td>164</td>
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*Initial vs 12 month: p < 0.01.
†Initial vs 12 month: p < 0.001.
‡See Methods section.

Abbreviations: MI = myocardial infarction; HR = heart rate; SBP = systolic blood pressure.

Maximal Oxygen Uptake Capacity

The VO₂max increased an average of 34%, from 2.01 ± 0.43 l/min to 2.69 ± 0.58 l/min (p < 0.001) in response to the 12 months of training. As a result of the decrease in body weight, VO₂max per kg body weight, which is considered a better indicator of aerobic exercise capacity, increased by an average of 38% (table 1).

Heart Rate

Resting heart rate decreased from 68 ± 9 to 58 ± 7 beats/min (p < 0.01), and maximum heart rate was 158 ± 17 beats/min initially and 165 ± 13 beats/min after 12 months of training. Because of large differences in response between individuals, the average increase in maximum heart rate was not statistically significant. After training, heart rate at the end of the first stage of the Bruce test was 12% lower (p < 0.05), and at the end of the second stage was 15% lower (p < 0.05) than before training.

Blood Pressure

Resting blood pressure did not change. Systolic pressure averaged 126 ± 15 mm Hg before and 121 ± 14 mm Hg after 12 months of training. Diastolic pressure was 80 ± 14 mm Hg before and 78 ± 7 mm Hg after training. Average systolic blood pressure at the end of the first stage of the Bruce test was significantly lower after training (153 ± 22 vs 129 ± 19 mm Hg; p < 0.001). A similar difference was seen after the second stage of the Bruce test. However, the systolic pressure attained at the time of maximal treadmill exercise was significantly higher (13%; p < 0.01) after 12 months of exercise training (fig. 1). The systolic blood pressure at maximum bicycle ergometer exercise increased from 179 ± 26 to 197 ± 17 mm Hg (p < 0.05) in response to training. The exercise program had no significant effect on the diastolic blood pressure response to exercise.

Double Product

As a consequence of the slower heart rate and lower systolic blood pressure, the double product was significantly lower at the same submaximal work rates after the 12-month exercise program (fig. 2). However, the average maximum double product attained during treadmill exercise increased by 20% (table 1). With bicycle exercise, it increased by 19% over the 12 months. The eight untrained patients had no significant change in maximum double product (table 1).

Ischemic ST-segment Changes

To determine the reproducibility of the double-product threshold for ST-segment depression, we performed Bruce treadmill exercise tests 4 weeks apart on seven of the patients, before admission to the exercise program, and again after 12 months of training, when they were on a constant maintenance exercise program. The double-product threshold for an ischemic ST-segment response was virtually identical in the tests performed 4 weeks apart, before and after training (fig. 3).
The double-product threshold for ischemic ST-segment depression (defined as the product of heart rate times systolic blood pressure required to induce 0.1 mV of ST-segment depression) increased by an average of 22% during the 12 months of training (table 2). The untrained group showed a small decrease in their double-product threshold for ST-segment depression (table 2).

The extent of ST-segment depression in response to a given submaximal work rate was smaller after training (fig. 2). This is not surprising; the double product was lower during the same work rates after the patients were trained. To control for this effect of training on the double product, we examined the relationship between extent of ischemic ST-segment depression and the double product at various work rates during the progressive bicycle exercise test. ST-segment displacement at the same double product was less after 12 months of training (fig. 4).

Although the maximum double product attained during exercise was 20% higher after 12 months of training, the maximum ST-segment depression decreased in six patients, did not change in three, and increased in only one, and the mean for the group did not change significantly (table 1). Over the same period, maximum ST-segment depression increased significantly in the untrained group, even though maximum double product did not change significantly (table 1).

**Resting ECG**

QRS voltage in the precordial leads was increased significantly after training (table 3). The sum of \( S_{V1} \) and \( R_{V5} \) increased by 15% during the 12 months of exercise training as a result of increases in both \( S_{V1} \) and \( R_{V5} \) voltage. The increase in QRS voltage was not associated with any repolarization changes.

**Changes in the Left Ventricular Dimensions**

To determine the reproducibility of the measurements, echocardiographic studies were performed 2 weeks apart on seven of the patients, both before enrollment in the exercise program and after 12 months of training. The differences between the two measurements made before or after training were small (table 4).
Good-quality echocardiograms were obtained in nine patients. Left ventricular end-diastolic dimension and posterior wall thickness were significantly increased after training (table 5). The estimated left ventricular end-diastolic volume index increased from 66 ± 17 to 83 ± 23 ml/m² (p < 0.01) and left ventricular mass index from 93 ± 17 to 135 ± 35 g/m² (p < 0.01).

Discussion

Sufficiently prolonged and intense exercise training can elicit the following cardiac responses in patients with antecedent myocardial ischemia, attributable to coronary artery disease, with or without associated spasm: elevation of the double-product threshold for ischemic ST-segment depression; decrease in the extent of ST-segment depression at the same double product; and a reduced or unchanged maximum ST-segment depression despite a large increase in maximum double product. These findings suggest that myocardial ischemia is reduced at the same, or a higher, double product as a result of the adaptation to exercise training. Coronary blood flow and myocardial oxygen consumption (MVO₂) have been shown to parallel closely the double product in normal persons and in patients with coronary artery disease during exercise. The decrease in electrocardiographic evidence of myocardial ischemia in our patients might be explained by an exercise-induced improvement in myocardial oxygenation. Alternatively, training could have induced a reduction in MVO₂ due to decreased left ventricular volume or decreased contractility associated with decreased sympathetic drive.

A reduction in left ventricular volume seems unlikely, considering our echocardiographic and electrocardiographic findings indicating that, as in young healthy subjects, the exercise training resulted in a volume overload hypertrophy of the left ventricle in our coronary patients. This increase in left ventricular size cannot be attributed solely to bradycardia, as left ventricular wall thickness and estimated mass were significantly increased. In contrast, slowing of the heart rate, by itself, results in an increase in left ventricular end-diastolic volume with a decrease in wall thickness. We could not measure left ventricular volume during exercise in this study. However, Hindman and Wallace found, using radionuclide angiography, that left ventricular end-diastolic and end-systolic volumes measured during submaximal and maximal exercise testing were significantly increased by 6 months of exercise training in a group of coronary patients. Decreased sympathetic drive also seems unlikely. Although plasma catecholamines increase less at the same absolute submaximal work rate, the plasma catecholamine response to maximum exercise is increased by training.

Studies in animals have provided data suggesting that exercise enhances myocardial blood supply. Training has been reported by others to raise the double- or triple-product threshold for exertional angina in some patients, suggesting an improvement in myocardial oxygenation. However, studies in which objective end points were used have not shown an improvement in myocardial blood supply or a decrease in myocardial ischemia in response to training in patients with coronary artery disease. Ferguson et al. measured coronary sinus blood flow and left ventricular oxygen consumption at various intensities of exercise in patients with coronary artery disease before and after 6 months of training. They found that coronary sinus blood flow and left ventricular oxygen consumption at the same double product were unchanged and that maximum coronary sinus blood flow and left ventricular oxygen consumption were unaffected by the training.

Nolewajka et al. evaluated the effects of a program of exercise on intercoronary collaterals in patients with coronary artery disease using coronary angiography and infusion of labeled microspheres. No
changes in the extent of collateralization or myocardial perfusion were evident after training. Detry and Bruce found that the double product and the magnitude of ST-segment depression at the same submaximal work rate were less after training, but the relationship between the magnitude of the ST-segment depression and the double product were unchanged. Maximum ST depression in Detry and Bruce's patients was actually greater after training, probably because they attained a higher double product.

These negative results suggested that the beneficial effects of training on exercise capacity and exertional angina threshold were mediated by adaptations in the skeletal muscles and autonomic nervous system, which result in a lower myocardial oxygen requirement during submaximal exercise and/or by an increase in arterial oxygen content. Despite such evidence that exercise training did not improve myocardial blood supply or ischemia at a given double product, the training programs were generally mild and of short duration. Typically, patients participated in 30–50 minute sessions of intermittent, mild exercise two to four times per week for 2–6 months. Because patients with coronary artery disease generally have a very low exercise tolerance when they begin training, exercise must initially be mild and intermittent. It usually takes 3–6 months before even highly motivated patients who are not symptom-limited, such as those in the present study, can perform moderately hard exercise (i.e., 65–85% of VO₂max) continually for an hour per day, 4–5 days/week. Therefore, the lack of improvement in myocardial ischemia in previous studies may have been due to termination of exercise training before a sufficient adaptive stimulus was attained.

This possibility motivated us to investigate the adaptive responses of patients with coronary artery disease to a more prolonged program of exercise of progressively increasing duration, frequency and intensity. This training program induced a large increase in VO₂max. The average increase in real VO₂max (these patients' VO₂max was not symptom-limited) of 38% is one of the largest reported with training in any group not initially limited by angio-

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Values are mean ± SD for seven patients.
Abbreviations: LVEDD = left ventricular end-diastolic dimension; LVPWT = left ventricular posterior wall thickness.
The large increase in VO₂max provides evidence that the training stimulus was substantial. Another adaptation to the training was a large increase in peak systolic blood pressure, which was statistically significant even if the two patients who discontinued propranolol therapy are excluded from the averages. The increase in the peak systolic blood pressure attained at the time of maximal exercise could reflect an improvement in left ventricular performance, since myocardial ischemia results in a lower peak systolic pressure during exercise. Exercise-induced hypertrophy (tables 3 and 5) of adequately oxygenated regions of the left ventricle might also have contributed to the increase in maximum systolic blood pressure by helping to compensate for loss of contracting myocardium as a consequence of previous myocardial infarction and scarring.

Our findings that prolonged and intense exercise training increases the double-product threshold for ST-segment depression, and results in a reduced or unchanged maximum ST depression despite a higher double product, are not necessarily in conflict with the report of Detry and Bruce\(^a\) that the relationship between the double product and ST-segment depression is unchanged after 3 months of training. Rather, our data probably reflect a later stage in the adaptive process or differences in the populations studied, as our patients were selected in part on the basis of being free from symptom-limited exercise. The available information is compatible with the view that adaptations in skeletal muscles and the autonomic nervous system occur rapidly in response to relatively mild exercise in patients with coronary artery disease and result in a lower double product during submaximal exercise as well as an improvement in exercise capacity. The present results indicate that if training is continued and increased in intensity, frequency and duration, additional cardiac adaptations can also occur in some patients with coronary artery disease, which result in an increase in the double-product threshold for myocardial ischemia.

### Acknowledgment

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### References

13. Nolewajka AJ, Kostuk WL, Rechnitzer PA, Cunningham DA:
Effects of 12 months of intense exercise training on ischemic ST-segment depression in patients with coronary artery disease.
A A Ehsani, G W Heath, J M Hagberg, B E Sobel and J O Holloszy

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