CARDIOVASCULAR RESPONSES TO REPEATED TREADMILL
EXERCISE TESTING SOON AFTER MYOCARDIAL INFARCTION

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SUMMARY To determine the response to repeated treadmill exercise testing soon after uncomplicated myocardial infarction, 24 males (mean age 54 ± 6 years) performed two symptom-limited tests several days apart 3, 7 and 11 weeks after the acute event. Significant within-week differences were noted for peak exercise tolerance (mets) and peak heart rate at 7 weeks (p < 0.05). Significant within-week differences in these variables were not noted for other weeks or for systolic blood pressure or heart rate-systolic blood pressure product for any of the three test periods. No significant within-week differences were noted for any variable recorded at a submaximal work load of 4 mets. The frequency of exercise-induced ischemic ST-segment depression, angina pectoris and premature ventricular complexes did not change from visit to visit and was highly reproducible (p < 0.01). All test variables measured at peak exercise increased significantly between 3 and 11 weeks after infarction. We conclude that cardiovascular responses to symptom-limited exercise testing are highly reproducible in the 3 months after uncomplicated myocardial infarction. Changes in the response to treadmill exercise tests performed several weeks apart reflect alterations in cardiovascular performance.

TREADMILL exercise testing has been used to document the natural history of cardiovascular function after myocardial infarction and to evaluate such therapies as exercise training, coronary artery bypass graft surgery and antianginal or antiarrhythmic drugs. The validity of exercise testing for such purposes depends on good test reproducibility - no significant variability in cardiovascular responses from one test to the next when the patient’s clinical status remains unchanged. In addition to factors that influence exercise test-retest variability in normal and stable coronary artery disease patients, soon after myocardial infarction the patient’s or clinician’s anxiety may lead to early termination of exercise, underestimation of exercise tolerance and poor test reproducibility. Also, since the functional capacity significantly increases between 3 and 11 weeks after infarction even in patients undergoing no formal exercise training, exercise test reproducibility during this time must be determined by exercise tests repeated within days instead of weeks or months.

Previous studies of exercise test reproducibility in patients with ischemic heart disease have not examined the early postinfarction period. The present study had two objectives: 1) to assess the reproducibility of cardiovascular variables measured during paired treadmill exercise testing performed 1 or more days apart, at 3, 7 and 11 weeks after uncomplicated myocardial infarction; and 2) to describe the natural history of the cardiovascular response to treadmill exercise 3, 7 and 11 weeks after infarction by comparing the results of the first of the paired tests performed on these occasions.

Methods

Subjects
Twenty-four males younger than 70 years of age who were free of major cardiovascular complications 3 weeks after myocardial infarction were evaluated. Myocardial infarction was documented in-hospital by a history of prolonged chest pain, the appearance of new Q waves or evolutionary ST-T changes and characteristic elevation of cardiac enzymes. Patients were discharged from the hospital between days 8 and 14. Patients with unstable or rest angina pectoris, clinical heart failure including an S1 gallop or any medical contraindication to vigorous exercise such as significant valvular heart disease, resting blood pressure greater than 180/100 mm Hg, pulmonary disease or musculoskeletal abnormalities 3 weeks after infarction were excluded from the study.

Mean age of the patients was 54 ± 6 years (sd). Infarction was inferior transmural in 17 patients (71%), anterior transmural in five (21%) and nontransmural in two (8%). Cardiac medications included procaainamide in three patients, quinidine in two, β blockers in two, long-acting nitrates in two and nitroglycerin in one patient. These and all other medications were withheld for 16-24 hours before testing. Doses of these medications were otherwise not altered during the 8 weeks of the study. None of the patients underwent formal exercise training, nor did any patient experience myocardial infarction or sudden death during the course of this study.

Testing Protocol

Patients visited the clinic twice during the third, seventh and eleventh weeks after infarction. Symptom-limited treadmill exercise testing was performed during the afternoons of nonconsecutive days in an air-conditioned laboratory. Informed consent was obtained and patients were examined before each treadmill exercise test, which was supervised by a physician and a specially trained cardiovascular nurse. A 12-lead resting ECG was recorded and indirect
brachial arterial blood pressure was measured by sphygmomanometry before exercise. The ECG was monitored for 3 minutes during rest to determine the frequency of any cardiac dysrhythmias.

The treadmill protocols were modifications of those recommended by Balke and Naughton.10 Three-minute work stages of increasing intensity were used. The specific work loads used at each phase of convalescence are depicted in table 1. The protocol was identical for all patients during a given week after infarction.

A 12-lead ECG was recorded at the end of each 3-minute stage of exercise, at peak effort and immediately after peak effort (standing) and at minutes 1, 2, 3, 5 and 10 of supine recovery. Leads V₄₋V₆ were continuously monitored during exercise and recovery. Systolic blood pressure was measured during the last 30 seconds of each work load and at peak effort. Test end points included limiting symptoms of angina pectoris (grade 3+); limiting fatigue or dysnea; abnormal blood pressure response, i.e., a fall in systolic blood pressure of 10 mm Hg or more from the peak value attained during an earlier phase of effort; or ventricular tachycardia i.e., three or more consecutive premature ventricular complexes (PVCs). Neither the magnitude of exercise-induced ischemic ST-segment depression nor attainment of an age-predicted maximal heart rate were used as end points. ST segments were defined as ischemic if they were flat or down-sloping and depressed 0.1 mV or more below the PQ baseline 0.08 second after the J point.

All tests were conducted by the same staff and the electrocardiographic response was interpreted by the same physician immediately after each test. Patients were not informed of their treadmill test duration and were encouraged to attain a symptom-limited performance on each test without respect to previous performances.

Data Analysis

The following variables were evaluated at peak effort and at a submaximal effort of 4 mets: 1) heart rate (HR), 2) systolic blood pressure (BPs), 3) HR × BPs/100 (double product). Analysis of variance was used to detect significant differences among the six tests. When analysis of variance detected a significant difference (p < 0.05), paired t tests were used to determine which tests were different from one another (p < 0.05; two-tailed t test). Pearson product-moment correlations were calculated for paired-test responses at peak exercise and 4 mets. Cochran's Q test was used to detect a change in the frequency of exercise-induced ischemic ST segment or PVCs between any of the six tests. The reproducibility of these responses from test to test was measured by the kappa coefficient.11

Results

No major cardiovascular complications were noted on any of the tests. Generalized fatigue, dysnea or leg fatigue were much more common end points than blood pressure abnormalities or angina pectoris (table 2). The frequency of these end points did not vary significantly among the six visits. Test end points were the same in 83%, 96% and 83% of patients who com-

<table>
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<th>Gradient (%)</th>
<th>Mets</th>
<th>Speed (mph)</th>
<th>Gradient (%)</th>
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<table>
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<th>Reason</th>
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<td>Test 1</td>
<td>Test 2</td>
<td>Test 1</td>
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<tr>
<td>Fatigue or dysnea</td>
<td>18</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Leg fatigue</td>
<td>4</td>
<td>5</td>
<td>2</td>
</tr>
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<td>BPs decrease</td>
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<tr>
<td>Angina</td>
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No tests were stopped for ventricular arrhythmias.

ST-segment depression or heart rate were not end points.

Abbreviation: BPs = systolic blood pressure.
completed both tests during weeks 3, 7 and 11, respectively. No test was terminated because of PVCs.

Within-week Comparisons

Peak cardiovascular responses are summarized in table 3. Peak heart rate and exercise tolerance were significantly higher on the second of two tests performed during week 7: 145 ± 21 vs 150 ± 18 beats/min and 8.8 ± 1.9 vs 9.4 ± 2.0 mets (p < 0.05). No other significant within-week differences in cardiovascular variables at peak effort were noted.

The test-retest correlations for peak cardiovascular responses measured within a single week were highly significant (p < 0.001) except for exercise tolerance (r = 0.28) at 3 weeks (p < 0.05). This lower correlation for mets at 3 weeks resulted from four patients who had a change in exercise capacity of 2 mets or greater from one test to the next. In each case the reason for test termination was different for the two tests: dyspnea vs leg fatigue with an increase of 2 mets, general fatigue vs leg fatigue with a decrease of 4 mets, decrease in systolic blood pressure vs general fatigue with an increase of 4 mets, and leg fatigue vs general fatigue with an increase of 2 mets. No other patient had a difference in exercise performance between these two tests of greater than 1 met.

Cardiovascular responses at a level of submaximal effort equivalent to 4 mets are depicted in table 4. No significant within-week differences for any of these variables were noted. The within-week test-retest correlations were highest at weeks 3 and 11 for heart rate, systolic blood pressure and double product at 4 mets, but even those for testing at 7 weeks were highly significant (p < 0.01).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week 3</th>
<th>Week 7</th>
<th>Week 11</th>
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<tbody>
<tr>
<td></td>
<td>Test 1</td>
<td>Test 2</td>
<td>Test 1</td>
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<tr>
<td>Heart rate (beats/min)</td>
<td>105 ± 14.8</td>
<td>102 ± 12.0</td>
<td>105 ± 11.5</td>
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<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>146 ± 18.5</td>
<td>141 ± 20.6</td>
<td>142 ± 16.5</td>
</tr>
<tr>
<td>Heart rate × systolic blood pressure/100</td>
<td>153 ± 33</td>
<td>144 ± 29</td>
<td>150 ± 24</td>
</tr>
</tbody>
</table>

p < 0.05 for following between-week comparisons: heart rate = 111, 112, 71, 72; systolic blood pressure = 31, 32, 71, 72. Values are means ± sd.
r = product-moment correlation for two tests during same week (all p < 0.01).
The frequency of ischemic ST-segment responses was not significantly different on any of the six tests (table 5). Ischemic responses within a single week were highly reproducible: 96%, 100% and 96% of the responses were the same on both tests performed during weeks 3, 7 and 11, respectively (p < 0.001). Treadmill exercise-induced angina pectoris was not frequent in these patients; only one patient reported it on both tests at week 3, two patients on both tests at week 7, and two and four patients reporting it on first and second test, respectively, at week 11. The frequency of exercise-induced PVCs was 29%, 37%, 37%, 42%, 54%, and 58% on the six tests, respectively, without significant differences in frequency among tests. We previously reported the frequency of exercise-induced PVCs soon after myocardial infarction and noted a similar increase in PVC frequency from week 3 to week 11.

**Between-week Comparisons**

Changes in cardiovascular responses between weeks were evaluated by comparing the first tests performed during each of the three weeks. Exercise tolerance at 3, 7 and 11 weeks was 7.0 ± 1.9, 8.8 ± 1.9 and 9.7 ± 1.8 mets; respectively, with all values significantly different (p < 0.05) from one another. Peak heart rate increased significantly between weeks 3 and 7: 135 ± 17 vs 145 ± 21 but not thereafter (147 ± 22 at week 11). Peak systolic blood pressure increased significantly between weeks 7 and 11, 166 ± 33 vs 178 ± 28, but not before this time. Peak double product demonstrated between-visit differences similar to those for heart rate: 7-week (241 ± 68) and 11-week (262 ± 62) values were higher than 3-week values (217 ± 46), without a significant difference between 7- and 11-week values. The correlation between the increase in peak heart rate and exercise tolerance between weeks 3 and 7 was 0.54 (p = 0.004), while the correlation for the same variables between weeks 7 and 11 was only 0.08 (p = 0.35).

Heart rate during submaximal effort declined significantly between the seventh and eleventh weeks: 105 ± 11.5 vs 96 ± 10.5, but not before this time (table 4). No significant interweek differences in systolic blood pressure or double product at 4 mets were noted.

**Discussion**

Exercise testing soon after myocardial infarction helps to establish guidelines for physical activity and permits evaluation of the response to therapy such as exercise training. If the results of such exercise testing are to be used to guide therapy, it is important that the cardiovascular response be reproducible, especially during early convalescence, when the cardiovascular response may change quickly as a result of myocardial healing and resumption of normal physical activity. Unless the testing methods are highly reproducible, changes in cardiovascular performance cannot be accurately determined and, conversely, a change in cardiovascular performance will lead to variability of test responses even if the reproducibility of the testing methods is excellent.

Previous studies of patients with chronic ischemic heart disease have documented excellent test-retest reproducibility for exercise tolerance, heart rate and systolic blood pressure, but none of these studies have evaluated the reproducibility of test responses soon after myocardial infarction. We expected that patients would be afraid to exert themselves maximally as soon as 3 weeks after myocardial infarction, resulting in falsely low cardiovascular performance on the first of the two tests performed at this time. Others have demonstrated a higher reproducibility for the second and subsequent tests than for the first and second tests, probably reflecting a "learning effect." In fact, we found no significant within-week differences in cardiovascular performance at 3 weeks. The only significant intraweek differences occurred during the 7-week visits, when peak heart rate and exercise tolerance were higher on the second of the two tests. These differences, although statistically significant, are probably too small to have clinical significance. Cardiovascular responses on the two tests performed during each week were highly correlated, indicating good reproducibility. Thus, the reproducibility of exercise test responses during the early phase of convalescence — 3–11 weeks after infarction — appears to be comparable to that of the responses in patients with stable chronic ischemic heart disease.

We previously reported a substantial increase in exercise tolerance between 3 and 11 weeks after infarction, even in patients who underwent no formal exercise training. A similar increase in functional capacity between 3 and 12 weeks after infarction was reported by Wohl et al. What accounts for the increase in functional capacity soon after myocardial infarction? Our data suggest that an increase in maximal heart rate is responsible for much of the early increase in exercise tolerance that occurred between 3 and 7 weeks after infarction, while the increase between 7 and 11 weeks is due to other factors, probably including increases in stroke volume, arteriovenous oxygen difference or mechanical efficiency. The increase in exercise tolerance was closely related to an increase in peak heart rate.

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**Table 5. Frequency of Ischemic ST Responses for First vs Second Tests 3, 7 and 11 Weeks After Infarction**

<table>
<thead>
<tr>
<th>Week</th>
<th>1st test of week</th>
<th>2nd test of week</th>
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<tr>
<td></td>
<td>No</td>
<td>1</td>
<td>18</td>
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</table>

*p < 0.001.
between weeks 3 and 7 ($r = 0.54$) but not between weeks 7 and 11 ($r = 0.08$). Thus, an increase in peak heart rate and a commensurate increase in peak cardiac output appear to contribute substantially to the early return of exercise tolerance. The increase in maximal heart rate between 3 and 7 weeks after infarction may reflect the gradual waning of a reflex arising from dyskinetic myocardial segments, a mechanism studied by Thoren in animals.\(^1\)

The fall in submaximal heart rate observed between 7 and 11 weeks after infarction may have been produced by an increase in mechanical efficiency due to a learning effect resulting from repeated treadmill testing,\(^2\) an increase in stroke volume thus maintaining a reasonably constant cardiac output for the same work,\(^3\) an increase in arteriovenous oxygen difference contributed to by enhanced metabolic capacity of skeletal muscle\(^4\) or some combination of these effects. If the heart rate decrease at submaximal exercise is due to an increased stroke volume, it most likely is due to myocardial healing, since the low-intensity physical activity regularly performed by these patients is unlikely to increase stroke volume in cardiac patients. If an increase in arteriovenous oxygen difference contributed to the decrease in submaximal heart rate and increased exercise tolerance from 7 to 11 weeks, it may be due to a “training effect” produced by ambulation. Although our patients received no formal guidelines for exercise training between 3 and 11 weeks, many reported walking regularly during this interval. This activity may have been sufficient to produce two classic effects of exercise training, i.e., an increase in exercise tolerance and a decrease in heart rate response to submaximal effort.

**Conclusions**

1) Cardiovascular responses to symptom-limited treadmill exercise testing are highly reproducible during a single week in the 2 months after uncomplicated myocardial infarction. Thus, a single treadmill exercise test during any one week reliably reflects cardiovascular performance soon after infarction.

2) Exercise tolerance increases significantly between weeks 3 and 11 after infarction, even in patients who undergo no formal exercise training. This increase in exercise tolerance is due in part to an increase in maximal heart rate during the early, but not the later, phase of convalescence. Factors contributing to the increase in exercise tolerance during the 3 months after infarction other than an increase in heart rate must be determined.

**Acknowledgment**

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**References**

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