Cardiovascular Responses to Repeated Treadmill Exercise Testing Soon After Myocardial Infarction

WILLIAM L. HASKELL, PH.D. AND ROBERT DEBUSK, M.D.

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 infarction1 and to evaluate such therapies as exercise training,2 coronary artery bypass graft surgery3 and antianginal or antiarrhythmic drugs.4-6 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,6 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.7-9 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.

方法

主题

24名年龄小于70岁、无重大心血管并发症的男性患者在心肌梗死后3周接受了心肌梗死评估。心肌梗死被记录为医院病史，出现新Q波或ST-T段变化，以及心脏酶的特征性上升。患者被从医院在第8和14天出院。有不稳定或心悸、心律失常、急性心力衰竭、或任何医疗禁忌的患者被排除在研究之外。

平均年龄为54 ± 6岁(标准差)。心肌梗死发生在17名患者(71%)的前间壁，3名患者(13%)的前间壁在5(21%)和非前间壁在2(8%)。心脏药物包括普罗布考在3名患者, 喹尼丁在2, β受体阻滞在2, 长效硝酸甘油在2和硝酸异山梨醇酯在1。这些和所有药物在16-24小时后使用。这些药物的使用在8周内不发生改变。没有患者在研究期间经历过正式的锻炼训练，也没有任何患者的心肌梗死或心脏骤停发生。

测试协议

患者在第三, 第七和第十一周期间每次到访医院。症状限制性跑步机运动测试是在下午非连续的日子在空调实验室进行的。知情同意书获得，并在进行跑步机运动测试前对患者进行了检查。这是一个12导联静息心电图被记录和间接
brachial arterial blood pressure was measured by sphygmonanometry 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. The 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 V1-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 dyspnea; 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 downsloping 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.

Results

No major cardiovascular complications were noted on any of the tests. Generalized fatigue, dyspnea 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 1. Treadmill Exercise Test Protocols Used at 3, 7, and 11 Weeks After Myocardial Infarction**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Minutes</th>
<th>Speed (mph)</th>
<th>Gradient (%)</th>
<th>Mets</th>
<th>7 and 11 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Speed (mph)</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1 (1 min)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 (2 min)</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3.5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2</td>
<td>7.0</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>2</td>
<td>10.5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>2</td>
<td>14.0</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>2</td>
<td>17.5</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Primary Reasons for Stopping Symptom-limited Treadmill Tests at 3, 7, and 11 Weeks After Infarction in 24 Patients**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Week 3 Test 1</th>
<th>Test 2</th>
<th>Week 7 Test 1</th>
<th>Test 2</th>
<th>Week 11 Test 1</th>
<th>Test 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue or dyspnea</td>
<td>18</td>
<td>17</td>
<td>19</td>
<td>17</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Leg fatigue</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>BPs decrease</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Angina</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

No tests were stopped for ventricular arrhythmias.
ST-segment depression or heart rate were not end points.
Abbreviation: BPs = systolic blood pressure.
TABLE 3. Cardiovascular Variables at Peak Exercise 3, 7 and 11 Weeks After Infarction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week 3</th>
<th>Week 7</th>
<th>Week 11</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test 1</td>
<td>Test 2</td>
<td>Test 1</td>
<td>Test 2</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>135 ± 17</td>
<td>138 ± 16</td>
<td>145 ± 21</td>
<td>150 ± 18*</td>
</tr>
<tr>
<td></td>
<td>r = 0.71</td>
<td>r = 0.91</td>
<td>r = 0.94</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>160 ± 22</td>
<td>164 ± 25</td>
<td>166 ± 33</td>
<td>167 ± 28</td>
</tr>
<tr>
<td></td>
<td>r = 0.88</td>
<td>r = 0.83</td>
<td>r = 0.76</td>
<td></td>
</tr>
<tr>
<td>Heart rate × systolic blood pressure/100</td>
<td>217 ± 46</td>
<td>229 ± 51</td>
<td>241 ± 68</td>
<td>253 ± 63</td>
</tr>
<tr>
<td></td>
<td>r = 0.84</td>
<td>r = 0.89</td>
<td>r = 0.93</td>
<td></td>
</tr>
<tr>
<td>Exercise tolerance (mets)</td>
<td>7.0 ± 1.9</td>
<td>7.1 ± 1.3</td>
<td>8.8 ± 1.9</td>
<td>9.4 ± 2.0*</td>
</tr>
<tr>
<td></td>
<td>r = 0.28</td>
<td>r = 0.87</td>
<td>r = 0.94</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 for within-week comparison.
*p < 0.05 for following between-week comparisons: heart rate (HR) = 31 vs 71, 75, 111, 115; 32 vs 71, 75, 111, 115;
systolic blood pressure (BPs) = 111 vs 31, 32, 71, 75; HR × BPs = 31 vs 71, 75, 111, 115; 32 vs 75, 111, 115;
mets = 31 vs 71, 75, 111, 115; 32 vs 71, 75, 111, 115;
Values are means ± sd.
r = product-moment correlation for two tests during same week.

Table 3 completes 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 4. Cardiovascular Variables during Submaximal Exercise 3, 7 and 11 Weeks After Infarction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week 3</th>
<th>Week 7</th>
<th>Week 11</th>
<th>F value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test 1</td>
<td>Test 2</td>
<td>Test 1</td>
<td>Test 2</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>105 ± 14.8</td>
<td>102 ± 12.0</td>
<td>105 ± 11.5</td>
<td>105 ± 17.0</td>
</tr>
<tr>
<td></td>
<td>r = 0.76</td>
<td>r = 0.43</td>
<td>r = 0.72</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>146 ± 18.5</td>
<td>141 ± 20.6</td>
<td>142 ± 16.5</td>
<td>135 ± 23.9</td>
</tr>
<tr>
<td></td>
<td>r = 0.75</td>
<td>r = 0.46</td>
<td>r = 0.69</td>
<td></td>
</tr>
<tr>
<td>Heart rate × systolic blood pressure/100</td>
<td>153 ± 33</td>
<td>144 ± 29</td>
<td>150 ± 24</td>
<td>141 ± 35</td>
</tr>
<tr>
<td></td>
<td>r = 0.76</td>
<td>r = 0.46</td>
<td>r = 0.80</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 for following between-week comparisons: heart rate = 111 vs 31, 32, 71, 75; 115 vs 31, 32, 71, 75;
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 11.12

**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 \( (147 ± 22 \text{ at week 11}) \). 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- 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 activity13 and permits evaluation of the response to therapy such as exercise training.2 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,1 heart rate6 and systolic blood pressure,9 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,8,14 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.15,16

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.17 A similar increase in functional capacity between 3 and 12 weeks after infarction was reported by Wohl et al.18 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.
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.18

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,20 an increase in stroke volume thus maintaining a reasonably constant cardiac output for the same work,21 an increase in arteriovenous oxygen difference contributed to by enhanced metabolic capacity of skeletal muscle22 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

Cardiovascular responses to repeated treadmill exercise testing soon after myocardial infarction.

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