The Exercise Test in Variant Angina: Results in 114 Patients

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SUMMARY One hundred fourteen patients with variant angina performed bicycle exercise stress tests, and were divided into three groups. Group 1 included 37 patients with a normal exercise test. Coronary arteriography revealed absence of significant coronary stenoses in 18 patients, one-vessel disease in 17 and involvement of two or more vessels in two. Group 2 consisted of 40 patients who had ST-segment elevation during or just after exercise. Coronary arteriography in these cases revealed absence of significant coronary stenoses in nine patients, one-vessel disease in 18 and disease of two or more vessels in 13. Group 3 included 37 patients who had ST-segment depression during exercise. Absence of coronary artery disease was found in only two patients, one-vessel disease was found in 19 and disease of two or more vessels was found in 16. Sixty-one patients repeated the exercise test after a mean of 18 months after hospital discharge. Exercise-induced ST-segment elevation was no longer present in surgically or medically treated patients; ST-segment depression was still evident in all the medically treated patients, but was absent in eight of 13 patients who underwent aortocoronary bypass surgery. Exercise testing can be useful in the follow-up of patients with variant angina and in selecting patients most likely to be helped by bypass surgery.

NO REPORTS in the literature describe the results of exercise testing in a large number of patients with variant angina. In a recent review of the literature, Weiner et al. concluded that half of the patients with variant angina have exercise-induced electrocardiographic changes diagnostic of ischemia; this conclusion challenges the prevailing belief that exercise tolerance is generally preserved in these patients. In this report, we present the results of exercise testing in 114 patients with variant angina.

Materials and Methods

Between January 1970 and April 1980, we observed 175 patients with Prinzmetal’s variant angina. All patients presented with typical chest pain occurring at rest associated with transient ST-segment elevation. In the presence of an old myocardial infarction, as determined by the presence of Q waves on the ECG, the ST elevations were observed not in the leads showing signs of infarction, but in those leads not altered by the infarct.

One hundred fourteen patients could perform a bicycle exercise test in the supine position. Patients
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with recurrent episodes of chest pain and severe ventricular arrhythmias or left ventricular failure during anginal attacks and those who did not undergo coronary arteriography were excluded from study. Through November 1975, 46 patients performed the bicycle exercise test by completing a predetermined work load (generally 150 W for 3 minutes). From December 1975, 68 patients performed a multistage bicycle exercise test with an initial work load of 50 W and subsequent increments of 25 W every 3 minutes. The exercise tests were all executed in the morning between 8:30 and 11:00. A12-lead ECG was obtained before and at the end of exercise and at 1-minute intervals during recovery. Leads V1 to V6 were monitored during exercise and recorded on paper at 30-second intervals. End points were typical anginal pain, dyspnea, exhaustion, and ST-segment elevation ≥ 2 mm or ST-segment depression > 3 mm compared with the resting tracing. The criteria for a positive exercise test were a horizontal or downsloping ST-segment depression ≥ 1 mm for 0.08 second compared with the resting tracing and ST-segment elevation ≥ 1 mm at 0.04 second after the J point compared with the baseline ECG.

Sixty-one patients (28 surgical and 33 medical) repeated a multistage exercise test at a mean of 18 months after hospital discharge. Drug therapy was suspended 12 hours before exercise tests were performed. Drug therapy in most of the patients consisted of nitrates and calcium antagonists. When we withheld the administration of the drug we did not observe any manifestation of withdrawal phenomena, such as accelerated angina or other coronary events. No patient was taking digitalis.

All patients underwent coronary arteriography performed by the Sones technique. Multiple views of each vessel were filmed. Significant coronary artery disease was thought to be present when there was more than 50% narrowing of the luminal diameter of one or more coronary arteries. When a lesion was noted, the vessel was filmed again in multiple views after administration of sublingual nitroglycerin. The left ventricle was opacified in the 30° right anterior oblique projection before coronary arteriography. Informed consent was obtained from each patient before coronary arteriography and exercise testing.

### Results

The 114 patients were divided into three groups according to the response to the exercise test. Group 1 included 37 patients who had a negative exercise test. The 40 patients who had ST-segment elevation during or just after exercise were placed in group 2. The 37 patients who had ST-segment depression during exercise were classified as group 3 (table 1).

#### Group 1

Of the 37 patients in group 1, 34 were male and three were female. The mean age was 44.4 years. Thirty-four of the patients had angina only at rest, while three had anginal attacks both at rest and with exertion. None of the patients had a history of myocardial infarction. Control ECGs were normal in 27 of the patients, and showed inverted T waves in 10. During the episodes of spontaneous chest pain, the ECGs showed ST elevation in the anterior leads in 20 patients and in the inferior leads in 17 patients.

Seventeen patients were tested at a predetermined work load, whereas 20 had a multistage test. The end points were completion of the test or exhaustion. The work load achieved by the 20 patients who had a multistage test was 130 ± 26 W. In this group we included three patients who had a reversal of originally negative T waves during the test. This reversal was not accompanied by chest pain. No patient had ventricular arrhythmias or conduction defects during the exercise test. Coronary arteriography showed normal or nearly normal coronary arteries in 18 patients, one-vessel disease in 17 and involvement of two or more vessels in two (table 1).

Nineteen patients repeated the exercise test after they were discharged from the hospital. The 15 medically treated patients had a negative test; three of the four surgically treated patients had a negative test and one developed ST-segment depression during exercise (table 2).

#### Group 2

Group 2 consisted of 39 men and one woman, mean age 46.5 years. Nineteen of the patients had chest pain

### Table 1. Electrocardiographic Changes at Rest and During Exercise, and Arteriographic Findings in 114 Patients with Variant Angina

<table>
<thead>
<tr>
<th>Group 1</th>
<th>ST during angina at rest</th>
<th>Exercise-induced ST abnormalities</th>
<th>Normal coronary arteries*</th>
<th>One-vessel disease</th>
<th>Two or more diseased vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 37)</td>
<td>Ant</td>
<td>20</td>
<td>18</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Inf</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>Ant</td>
<td>20</td>
<td>9</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>(n = 40)</td>
<td>Inf</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ant &amp; Inf</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td>Ant</td>
<td>23</td>
<td>2</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>(n = 37)</td>
<td>Inf</td>
<td>10</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ant &amp; Inf</td>
<td>4</td>
<td>Diff</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Also includes nearly normal coronary arteries.

Abbreviations: Ant = ST changes in anterior leads; Inf = ST changes in inferior leads; Diff = diffuse subendocardial ischemia; ST = ST-segment elevation.
at rest and the remaining 21 also had exertional angina. The ECGs taken under control conditions were normal in 30 patients and showed inverted T waves in eight; two patients had signs of old myocardial infarction. ECGs taken during episodes of spontaneous chest pain showed ST-segment elevation in the anterior leads in 20 patients and in the inferior leads in 17. The three remaining patients showed ST elevation in both inferior and anterior leads, though never simultaneously.

Eighteen patients exercised at a predetermined work load and 22 had a multistage exercise test. The reasons for terminating the test were chest pain in 26 patients, ST-segment elevation without chest pain in six patients and exhaustion in eight patients who later showed ST elevation (accompanied by chest pain in four) during the recovery period. In the 22 patients who had a multistage exercise test, the work load at the end of exercise was 101 ± 38 W. In all patients, ST-segment elevation occurred in the same leads as those during spontaneous attacks. The three patients who had ST-segment elevation either in anterior or in inferior leads showed ST elevation in the inferior leads during exercise. ST elevation developed during exercise in 25 patients and just after exercise (from 30 seconds to 3 minutes) in 15 patients. ST-segment depression preceded the appearance of ST-segment elevation in six patients. One patient developed a supraventricular tachycardia that disappeared spontaneously. Two patients developed ventricular fibrillation that required electrical defibrillation. During exercise, four patients had ventricular ectopic beats (≥ 6/min), six had left anterior hemiblock and 10 had left posterior hemiblock.7

Left ventriculography excluded the presence of ventricular aneurysm in those areas of the myocardium in which the ECG revealed ST-segment elevation. Coronary arteriography revealed a normal coronary tree or only minor atherosclerotic changes in nine

patients, one-vessel disease in 18 and involvement of two or more vessels in 13 (table 1).

Twenty-two of these patients repeated exercise testing after hospital discharge. The 11 patients who had undergone coronary bypass surgery had negative exercise tests. Six of the 11 medically treated patients had negative tests and five showed ST-segment depression during exercise (table 2).

Group 3

Group 3 consisted of 36 men and one woman, mean age 50.1 years. Twenty of the patients had spontaneous angina only, and the remaining 17 had both exertional and spontaneous angina. Control ECGs were normal in 31 patients and showed negative T waves in five; one patient had evidence of an old myocardial infarction. During anginal attacks at rest, ST-segment elevation occurred in the anterior leads in 23 patients, in the inferior leads in 10 and in either the anterior or the inferior leads in different ischemic episodes in four. Eleven patients exercised at a predetermined work load and 26 had a multistage test. The reasons for terminating the test were chest pain in 26 patients, ST-segment depression > 3 mm in four patients and exhaustion in seven patients. Eleven patients did not experience chest pain during the test. In the 26 patients who had a multistage exercise test, the work load at the end of exercise was 95 ± 29 W. Exercise-induced ST-segment depression occurred in the anterior leads in 18 patients, in the inferior leads in eight and was diffuse in 11 patients. Ventricular ectopic complexes (≥ 6/min) were observed in three patients, left anterior hemiblock in three patients and left posterior hemiblock in two patients.

 Coronary arteriography showed absence of significant coronary stenoses in two patients, one-vessel disease in 19 and involvement of two or more vessels in 16 patients (table 2).

Exercise testing was repeated in 20 patients after

<table>
<thead>
<tr>
<th>Group 1 (n = 19)</th>
<th>4 surgically treated</th>
<th>3 negative tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 medically treated</td>
<td>1 positive test with i ST</td>
<td></td>
</tr>
<tr>
<td>11 surgically treated</td>
<td>15 negative tests</td>
<td></td>
</tr>
<tr>
<td>Group 2 (n = 22)</td>
<td>11 surgically treated</td>
<td>6 negative tests</td>
</tr>
<tr>
<td>11 medically treated</td>
<td>5 positive tests with i ST</td>
<td></td>
</tr>
<tr>
<td>Group 3 (n = 20)</td>
<td>13 surgically treated</td>
<td>8 negative tests</td>
</tr>
<tr>
<td>7 medically treated</td>
<td>5 positive tests with i ST</td>
<td></td>
</tr>
</tbody>
</table>

The patients are divided in groups according to the results of exercise test during hospitalization (see table 1).

Abbreviation: i ST = ST-segment depression.

<table>
<thead>
<tr>
<th>Table 2. Results of Exercise Test in 61 Patients Who Repeated Exercise Test at a Mean of 18 Months After Discharge</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n = 19)</td>
<td></td>
</tr>
<tr>
<td>4 surgically treated</td>
<td>3 negative tests</td>
</tr>
<tr>
<td>15 medically treated</td>
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</tbody>
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hospital discharge. Eight of 13 surgically treated patients had a negative test and five developed ST-segment depression during exercise. In the seven medically treated patients, the exercise test again induced ST-segment depression (table 2).

Discussion

Not enough information is available to establish the diagnostic role\(^8\) and the prognostic value\(^9\) of exercise testing in patients with variant angina. Of 81 cases reported in the literature and recently reviewed by Weiner et al.,\(^8\) 26 had ST-segment elevation, 20 had ST-segment depression and 35 had a normal exercise test. We obtained similar results in our 114 patients: 37 had a normal exercise test, 40 had ST-segment elevation and 37 had ST-segment depression. The first 46 patients were exercised at a predetermined work load, as was our practice at the time. It has been shown that patients with variant angina frequently show the warm-up phenomenon,\(^9\) and positive tests can be obtained when the initial work load is high, whereas negative tests can be obtained when the initial work load is low even if the peak work load may be high. However, our study does not reveal marked differences in the frequency of positive tests in these patients.

Three patients showed reversal of negative T waves during exercise. Such electrocardiographic change may be the only abnormality related to myocardial ischemia in patients with variant angina.\(^10\) It is difficult, however, to establish the significance of T-waves reversal induced by exertion. Because this finding is not a classic criterion for a positive exercise test\(^11\) and because none of the three patients had pain or other significant electrocardiographic changes, we concluded that these three patients the exercise test was indeed negative.

In two patients, the exercise test was complicated by ventricular fibrillation that required electrical defibrillation. Although the occurrence of dangerous ventricular arrhythmias seems less frequent than has been reported,\(^12\) the risk of these rhythm disturbances should be considered and appropriate resuscitative equipment should be readily available.

Significance of Exercise-induced Electrocardiographic Changes

Exercise-induced ST-segment elevation does not predict coronary anatomy. Nine of 40 patients who had ST elevation during or just after exercise had no significant coronary lesions. Our data are in keeping with the observations of other investigators who have described the occurrence of exercise-induced ST-segment elevation in patients with normal coronary arteries.\(^5,\)\(^13\)\(-\)\(^17\) ST-segment depression is, however, generally recorded in patients with fixed coronary obstructions. Only two of the 37 patients who had ST depression had no significant coronary lesions. The different incidence of coronary artery disease in patients showing ST-segment depression and in those showing ST-segment elevation during exercise suggests a different pathogenetic mechanism for these abnormalities. It has been shown\(^18\)\(-\)\(^21\) that exercise-induced ST-segment elevation in patients with normal coronary arteries and in those with severe, fixed stenoses of the coronary tree\(^19\) is caused by a spasm occluding a coronary vessel. The significance of ST-segment depression during anginal attacks is still unclear. Whereas coronary spasm can cause chest pain at rest associated with subendocardial ischemia,\(^22\)\(-\)\(^25\) exercise-induced ST-segment depression is generally believed to be caused by an increase of myocardial metabolic demands exceeding the available supply.\(^26\)

We showed angiographically that this mechanism is operative during exercise even in patients in whom coronary spasm is responsible for chest pain occurring at rest.\(^27\) However, one cannot exclude the possibility that, in a few cases, coronary spasm could precipitate anginal attacks during exercise associated with ST-segment depression, as shown by Yasue et al.\(^28\)

The fact that ST-segment elevation and ST-segment depression probably have different underlying pathogenetic mechanisms helps to explain the results obtained in the exercise tests performed after hospital discharge. In fact, in both surgically and medically treated patients, exercise-induced ST-segment elevation was no longer observed, indicating that its occurrence and disappearance might be due to the fluctuating nature of the disease.\(^6,\)\(^9,\)\(^10,\)\(^29\) In contrast, exercise-induced ST-segment depression was still evident in all the medically treated patients, but was absent in eight of the 13 surgically treated patients, which suggests that the improved exercise performance in these patients was secondary to the successful bypass operation that resulted in improved coronary blood flow.

Implications

Exercise testing can provide follow-up data on patients with variant angina.\(^2\) In patients who have exercise-induced ST-segment elevation due to coronary artery spasm, repeated exercise testing can give important information about the spontaneous fluctuations of the disease and the efficacy of medical therapy.\(^29\) For this purpose, exercise testing can be considered a practical and valid alternative to the ergonovine test.\(^30\) Further studies must be conducted to establish the safety of these tests.\(^31\) Exercise testing may also prove useful in selecting patients with variant angina for aortocoronary bypass surgery. Although the role of surgery in variant angina\(^32,\)\(^33\) is controversial,\(^24,\)\(^25\) the surgical approach should be seriously considered when hemodynamically important atherosclerotic narrowings are associated with reduced exercise capacity. In addition, long-term results in surgically treated patients can be periodically assessed by postoperative exercise tests.

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