Postexercise Electrocardiogram in Patients With Abnormal Resting Electrocardiograms

By Peter F. Cohn, M.D., Pantel S. Vokonas, M.D., Michael V. Herman, M.D., and Richard Gorlin, M.D.

SUMMARY
One hundred and ten patients with chest pain syndromes and resting electrocardiograms demonstrating ST-T abnormalities and/or prior transmural myocardial infarctions were studied by means of the Master's two-step exercise test and selective coronary cine arteriography. Criteria for negativity were modified so that subjects with postexercise heart rates less than 110 beats/min, who did not develop significant ST-segment changes, were excluded from evaluation. Eighty-six per cent of the coronary artery disease group and 27% of the normal coronary artery group had positive postexercise electrocardiograms. Conversely, of the patients with positive results, 88% had anatomic coronary artery disease. With this degree of stress, positive responses \( \geq 2 \text{ mm} \) were invariably associated with multi-vessel disease. The type of pre-existing ECG abnormality did not influence either the frequency or severity of positive responses. False-negative subjects had no distinctive features relating to type of abnormal electrocardiogram, or location of vessel involvement, although most of these patients had significant disease of only one major coronary artery.

Additional Indexing Words:
Pre-exercise electrocardiogram Two-step test Coronary arteriography

SUBMAXIMAL exercise tests are widely used in the diagnosis of coronary artery disease, particularly in those subjects who have normal resting electrocardiograms. Relatively little has been written about the testing of individuals with abnormal electrocardiograms. This has been due to concern over the safety of the procedure, especially when there is evidence of prior myocardial infarction, and doubt that additional interpretable information can be obtained if the resting ECG is abnormal. The present study was undertaken to re-examine these objections, utilizing selective arteriography to demonstrate the presence and extent of coronary atherosclerosis.

Materials and Methods

Selection of Patients
Over 300 patients have been studied by means of both coronary arteriography and the two-step exercise electrocardiogram in our laboratory. From this larger group, 150 patients with abnormal pre-exercise electrocardiograms were selected for this study on the basis of specific criteria. These subjects had neither electrolyte abnormalities, nor disease entities known to influence either the resting or postexercise electrocardiogram (thyroid disease, anemia, alcoholism, valvular heart disease, severe hypertension, primary myocardial or pericardial disease), nor were they receiving drugs that also have...
modifying effects (digitalis, propranolol, quinidine).

The 150 patients thus selected were suspected clinically of having uncomplicated coronary artery disease. Because of the previously mentioned criteria for selection, they do not represent a consecutive series. All patients presented with a chest pain syndrome. A comparison of the results of the postexercise ECG was made between patients with arteriographically proven disease and those with normal coronary arteriograms.

Electrocardiograms were arbitrarily divided into four groups (fig. 1): type 1(A)—minor ST-T abnormalities (reduced or flattened T waves and/or ST-segment depression <0.5 mm); type 1(B)—major ST abnormalities (inverted T waves and/or ST depression ≥0.5 mm); type 2(A)—evidence of both a prior transmural myocardial infarction and ST-T abnormalities (though not necessarily in the same leads); and type 2(B)—evidence of a prior infarction but without ST-T changes. Because of their relative infrequency in our patient population, subjects whose electrocardiograms exhibited conduction defects were not included in the present study. No patient had had a myocardial infarction within three months, nor evidence of an impending infarction.

Exercise Test

Patients performed a standard double Master’s two-step test1-3 with a physician in attendance, and with both emergency resuscitative equipment and a syringe with 50–100 mg of lidocaine available. The test end-point was either chest pain, or completion of the required number of steps within 3 min. Twelve-lead electrocardiograms or leads II, V₄, V₅, and V₆ were recorded before, immediately after, 3 min after, and 8 min after the exercise.

Postexercise Electrocardiographic Criteria

Failure to achieve at least a minimal tachycardia after exercise testing raises doubts as to the adequacy of the stress. It also diminishes the frequency of positive results.4,5 In the present series, therefore, the level of immediate postexercise heart rate was one of the criteria used to interpret postexercise electrocardiograms. Complete criteria were as follows. Positive tests (fig. 1) were those in which horizontal or downward sloping R-ST-segment depression of at least 0.5 mm6 occurred at any postexercise heart rate or time interval. This group was further subdivided according to the degree of ST depression: ≥1.0 mm and ≥2.0 mm. If a lead exhibited pre-exercise R-ST depression, then any further R-ST depression had to be at least 0.5 mm. R-ST elevations were regarded as positive only if they exceeded 1 mm. T-wave changes and ventricular premature contractions were not regarded as positive criteria for purposes of this study. Negative tests (fig. 1) were those in which a postexercise heart rate of at least 110 beats/min was attained, and neither ST-segment depression ≥0.5 mm, nor ST-segment elevation ≥1.0 mm occurred. In 40 patients (24 with and 16 without coronary artery disease), postexercise heart rate did not reach 110 beats/min, there were no ST changes, and the test was considered uninterpretable.
In the present study, only the 110 patients with postexercise electrocardiograms that could be interpreted according to the above criteria will be discussed.

Coronary Arteriography

High quality selective coronary cine arteriograms were obtained on 16 mm Ilford Pan F film with either General Electric or Siemens 6-inch or dual field X-ray image intensification. Stenosis of greater than 75% of a vessel lumen was considered significant. Patients with lesser degrees of intramural disease or discrete stenosis less than 50% of the vessel lumen were included under the classification of "normal coronary arteriogram." Over 95% of patients in this category, however, including eight of nine with positive exercise tests, had completely normal coronary arteries.

Results

Coronary Arteriograms

The distribution of patients with and without coronary artery disease is seen in figure 2.

Abnormal Resting Electrocardiograms

Examples of the four sub-types are illustrated in figure 1. The overall relation between electrocardiographic and arteriographic abnormalities is depicted in table 1. Only four patients with electrocardiographic evidence of a transmural myocardial infarction had normal coronary arteriograms; there was a statistically significant correlation (P < 0.01) between this electrocardiographic finding and anatomic coronary artery disease. This was not true of pre-exercise ST-T abnormalities, since almost half of the patients with these findings had normal coronary arteriograms. In table 2, the extent and location of arterial lesions within the various electrocardiographic subgroups is examined in detail. No specific pattern was present. The most frequently involved vessel was the left anterior descending artery, the least frequently involved the left circumflex artery.

Exercise Tests

There was no significant difference between patients with coronary artery disease and patients with normal coronary arteries in the time of onset of postexercise ST changes. However, the greater the initial ST depression the longer it took for these abnormalities to revert to normal. Figures 3 and 4 demonstrate several points: (1) 86% of the patients with coronary artery disease had positive results compared with 27% of the patients with normal coronary arteries; (2) the number of abnormal responses tended to increase with

Table 1

Interrelationships Between Abnormal Resting Electrocardiograms and the Frequency and Severity of Positive Exercise Tests in 110 Patients with Chest Pain Syndromes

<table>
<thead>
<tr>
<th>Coronary artery disease</th>
<th>Total</th>
<th>Positive test*</th>
<th>Normal coronary arteriogram</th>
<th>Total</th>
<th>Positive test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG Type 1 (no MI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Minor ST-T abnormalities</td>
<td>38</td>
<td>34(18)</td>
<td>29</td>
<td>9(0)</td>
<td></td>
</tr>
<tr>
<td>B. Major ST-T abnormalities</td>
<td>13</td>
<td>11(6)</td>
<td>14</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>23(12)</td>
<td>15</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>ECG Type 2 (MI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. With ST-T abnormalities</td>
<td>39</td>
<td>32(13)</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>B. Without ST-T abnormalities</td>
<td>29</td>
<td>24(10)</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>8(3)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers in parentheses indicate patients with ≥ 2 mm post exercise ST depression.
MI = transmural myocardial infarction.
increasing vessel involvement; and (3) all 31 of the patients with ST depression \( \geq 2 \) mm had multi-vessel disease, and 24 of the 31 had three-vessel disease. (The only two patients in our study with significant ST elevation were also included in the \( \geq 2 \) mm category.)

Table 1 demonstrates a statistically significant correlation \((P < 0.01)\) between postexercise ST changes and anatomic evidence of coronary artery disease. As noted earlier such a correlation did not exist for pre-exercise ST-T abnormalities.

Table 1 also shows that the number of cases with positive tests was about the same in each of the four ECG subgroups. Patients with the more severe ST depression \((\geq 2\) mm) also had no particular distribution. Similarly, the patients with coronary artery disease who had negative responses exhibited no specific electrocardio-

graphic or vascular pattern (table 3). However (as already inferred by the data in fig. 4), the number of subjects with one-vessel disease and a negative postexercise ECG is higher than in the coronary artery disease group as a whole. Table 4 relates the postexercise ST changes to pre-existent abnormalities. Only six of 66 coronary artery disease patients, and two of nine noncoronary artery disease patients, exhibited positive postexercise changes confined solely to the inferior zonal leads. (The relative insensitivity of inferior zone leads has been discussed at length by Most et al.\(^{17}\)) In addition, patients with pre-existing anterior zonal abnormalities had the greatest frequency of ST depression \( \geq 2 \) mm.

In this study, T-wave changes were not regarded as positive results. Ten patients with pre-exercise T-wave inversions developed upright T waves after exercise. This occurred irrespective of the presence of coronary artery disease, and was not related to the development of ischemic ST abnormalities.

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### Table 2

**Relationship Between Extent and Location of Arteriographic Lesions and Types of Abnormal Resting Electrocardiograms in 77 Patients with Coronary Artery Disease**

<table>
<thead>
<tr>
<th>Arteriographic findings</th>
<th>Total</th>
<th>3VD</th>
<th>2VD</th>
<th>1VD</th>
<th>RCA</th>
<th>LAD</th>
<th>LCF</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG Type 1 (no MI)</td>
<td>38</td>
<td>26</td>
<td>7</td>
<td>5</td>
<td>31</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>A. Minor ST-T abnormalities</td>
<td>13</td>
<td>7</td>
<td>2</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>B. Major ST-T abnormalities</td>
<td>25</td>
<td>19</td>
<td>5</td>
<td>1</td>
<td>22</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>ECG Type 2 (MI)</td>
<td>39</td>
<td>17</td>
<td>16</td>
<td>6</td>
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<td>35</td>
<td>24</td>
</tr>
<tr>
<td>A. With ST-T abnormalities</td>
<td>29</td>
<td>14</td>
<td>12</td>
<td>3</td>
<td>22</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>B. Without ST-T abnormalities</td>
<td>10</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>13</td>
<td>11</td>
</tr>
</tbody>
</table>

Abbreviations: MI = transmural myocardial infarction; 3VD, 2VD, 1VD = three-, two-, and one-vessel disease; RCA = right coronary artery; LAD = left anterior descending artery; LCF = left circumflex artery.

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**Figure 3**

Results of exercise tests in 77 patients with coronary artery disease (CAD) and 33 patients with normal coronary arteriograms (NL. COR. ART.) \((P < 0.001)\). Positive tests are subdivided by degree of ST depression.

**Figure 4**

Results of exercise tests in patients with three-, two-, and one-vessel disease (3VD, 2VD, 1VD). Positive tests are subdivided by degree of ST depression.
No serious complications were observed during the performance of these tests. Ventricular premature beats were common, but no instances of ventricular tachycardia or fibrillation were noted.

Discussion

In his initial report on the two-step test, Master cautioned against its use in patients with abnormal resting electrocardiograms. He repeated this admonition as recently as 1961. Although in his latest review he states that such abnormalities are not a contraindication to exercise testing, the effect of his earlier writing, and that of others, was to discourage such testing.

Reports of deaths following exercise tests reinforced this cautionary attitude, although opinion was not unanimous. Mattingly stated that patients with prior myocardial infarctions had been safely tested; Friedberg questioned the exclusion of patients with only ST-T abnormalities, citing their diverse etiologies; and, perhaps most importantly, Robb and Marks, in their classic life insurance studies, reported that they had exercised many patients with resting electrocardiographic abnormalities without serious complications.

Unfortunately, in these and other studies reported sporadically throughout the 1950s (dealing with Q-wave abnormalities, conduction disturbances, and ST-T abnormalities) there was no way of knowing which of the positive responses (by any of the criteria used) were actually false-positive, and conversely, which of the negative responses were in patients truly free of coronary atherosclerosis. Clinical impressions and (rarely) autopsy evidence were the investigator’s main tools.

The advent of coronary arteriography has allowed a morphologically and temporally accurate evaluation of the anatomical lesions. Despite this diagnostic breakthrough, there is

Table 3

<table>
<thead>
<tr>
<th>Arteriographic Findings</th>
<th>Arteriographic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>ECG Type 1 (no MI)</td>
<td>4</td>
</tr>
<tr>
<td>ECG Type 2 (MI)</td>
<td>7</td>
</tr>
</tbody>
</table>

Abbreviations: see table 2.

Table 4

<table>
<thead>
<tr>
<th>Abnormalities of resting ECG</th>
<th>Postexercise ST depression*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>A. 77 Patients with Coronary Artery Disease</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>28</td>
</tr>
<tr>
<td>Confined to ant. zone</td>
<td>32</td>
</tr>
<tr>
<td>Confined to inf. zone</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
</tr>
<tr>
<td>B. 33 Patients with Normal Coronary Arteriograms</td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>14</td>
</tr>
<tr>
<td>Confined to ant. zone</td>
<td>8</td>
</tr>
<tr>
<td>Confined to inf. zone</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
</tr>
</tbody>
</table>

*Numbers in parentheses indicate patients with ≥ 2 mm postexercise ST depression.

Abbreviations: Ant. zone = ECG leads I, aVL, V1 - V6; Inf. zone = ECG leads II, III, aVF; Diffuse = combination of ant. and inf. leads.
still a paucity of specific information concerning patients with abnormal resting electrocardiograms. In the series of 1,000 patients reported by Proudfit, Shirey, and Sones,14 only "a few" of the patients whom they exercised had other than normal resting electrocardiograms. The studies of Demaney,15 Kattus,16 and, recently, Most17 from this laboratory, included patients with ECG abnormalities, but the findings were not selectively analyzed in this regard. Hultgren et al.18 did comment on 17 patients with various resting ECG abnormalities, half of whom had normal arteriograms, and found no significant inter-relationship between electrocardiographic and arteriographic findings.

In a recent angiographic study, Roitman et al.19 reported the results of sub-maximal treadmill testing in 100 patients with chest pain, 49 of whom had either pre-exercise R-ST abnormalities and/or QRS abnormalities (including infarct patterns and conduction defects). Twelve of these 49 patients had valvular heart disease and a lesser number were receiving digitalis. The authors concluded that the development of further post-exercise ST depression in such a group was not helpful in diagnosing coronary artery disease. In an earlier study, prior to the advent of coronary arteriography, Lepeschkin and Surawicz20 also found postexercise electrocardiograms difficult to interpret in the presence of valvular and myocardial disease, or during the administration of cardiac drugs.

Utilizing more stringent criteria for selection of patients for exercise testing, the present study has demonstrated that the two-step test can be of clinical value in patients with chest pain and abnormal resting ECGs. When patients with negative responses with postexercise heart rates less than 110 beats/min were excluded, 86% of the remaining patients with coronary artery disease had positive exercise tests. Twenty-seven per cent of patients with chest pain and a normal coronary arteriogram also had positive tests. (The nature of cardiac disease, if any, in such patients remains ill-defined.)

Because of the greater preponderance of patients with angiographically proven disease, the finding of a positive test by our criteria implied an almost 90% probability of diagnosing coronary atherosclerosis in subjects with abnormal resting electrocardiograms. This yield was 15% higher than that found in a similar number of patients with normal resting electrocardiograms.21 With the degree of stress provided by the two-step test, all patients in our series with ST depression ≥2 mm had coronary atherosclerosis, usually involving all three major coronary arteries. (As table 1 illustrates, the type of pre-existing electrocardiographic abnormality was not helpful in predicting which patients would develop such responses.) Prognostically, the degree of ST depression has been previously correlated, by Robb and Marks, with subsequent increased mortality from coronary artery disease.22

All patients with electrocardiographic evidence of a prior transmural infarction and a positive exercise test had coronary artery disease. It is of interest that of the small number of patients (four) with normal coronary arteriograms who presented with electrocardiographic and historical evidence of past myocardial infarction, all had negative exercise electrocardiograms. Although the etiology of such episodes remains unknown, these patients may well have an entirely different pathological process responsible for infarction, and therefore a different prognosis from those individuals whose infarctions are secondary to coronary atherosclerosis.23 Exercise tests are a potentially useful tool in the diagnosis of these patients, as well as in others whose histories and electrocardiograms are suspicious, but not diagnostic, of prior infarctions.

Patients with coronary artery disease and negative postexercise electrocardiograms demonstrated no specific electrocardiographic or vascular findings, although most of these patients had single vessel disease (table 3). As in other exercise studies, these patients remain an enigma. The relative insensitivity of the inferior zone electrocardiographic leads17 may
account for some of these false negative responses. This study demonstrates that there is no valid objection to assessing the patient with an abnormal resting electrocardiogram by means of the two-step test. The results have clinical relevance, and if appropriate precautions are considered, the test is safe.

Acknowledgment

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References

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