The Two-Step Exercise Electrocardiogram
A Double-Blind Evaluation of Its Use in the Diagnosis of Angina Pectoris

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In an effort to confirm the diagnosis of angina pectoris by objective evidence, Master devised a standardized two-step exercise electrocardiographic test that has become widely employed, especially in the presence of a normal resting electrocardiogram. A number of other investigators have pointed out various limitations of the test and have questioned its validity, criteria, and diagnostic reliability.1-3 On the other hand, Master has reported numerous studies over the past 20 years on the basis of which he has consistently claimed an accuracy of 95 per cent for the two-step exercise electrocardiogram in detecting or excluding angina pectoris caused by ischemic heart disease.4-6 As a result of these reports, many physicians have come to place such faith in the diagnostic accuracy of the test that a negative test has been interpreted to exclude angina pectoris and a positive test to indicate the presence of significant coronary disease, regardless of the clinical diagnosis.

If such a degree of reliability could be established, the two-step exercise test should virtually eliminate any diagnostic problem in regard to angina pectoris. We have been surprised, however, by the frequency with which patients without angina pectoris have shown a positive two-step test, according to Master's criteria, whereas others with unequivocal angina pectoris have presented negative tests. In our experience the test has sometimes been negative at one performance and positive several days later, although the technic was unaltered and there was no discernible cause for this change. We have also noted the failure of published reports to emphasize the frequency of borderline findings, of uncertainties or difficulties in reading and interpreting the test, and of differences of opinion among several observers concerning the same test. Our experience with the two-step exercise electrocardiogram has indicated that prior knowledge of the clinical history often influences the interpretation, and that clinical prejudice may be decisive in the many doubtful and borderline tests.

Because of all these problems it appeared to us important to undertake, for the first time to our knowledge, a double-blind study in which the test would be interpreted independently by two or three physicians with a long experience with the test, and without any knowledge of the patient or the clinical history. Since the two-step test is utilized in clinical practice when the diagnosis of angina pectoris is in question, it seemed desirable to carry out this double-blind study only in patients with chest pain. A decision as to the clinical diagnosis of angina pectoris was made independently by two or three physicians on the basis of the history alone before the test was performed. By taking these precautions, we hoped to arrive at an unprejudiced evaluation of the two-step test.

In this study, the accuracy of the two-step exercise electrocardiogram, that is, whether a positive test was true or false-positive, or whether a negative test was true or false-negative, was assessed by relating the result of the test to the independent unequivocal clinical diagnosis of angina pectoris or of non-cardiac pain. Different methods of evaluation may be employed when the test is given for other purposes. Although the diagnosis of angina pectoris is difficult to make or exclude clinically in some cases in which continued observation and therapeutic testing of the
patient may be required, in most cases the diagnosis is definite and unequivocal. In the latter cases one would anticipate an excellent correlation with the two-step test if the exercise is reliable.

Material and Method
A study was made of 100 consecutive patients referred from the Out-Patient Department or the wards, or by the hospital employees' physician, for investigation of the cause of their chest pain. Each patient was interviewed independently on one occasion by two or three physicians, with the aid of a detailed questionnaire specifically designed for the diagnosis of angina pectoris. Each physician recorded a specific diagnosis of angina pectoris or noncardiac pain, or occasionally, stated an uncertainty with recommendation of further observation and study. Later another physician, unfamiliar with the history, performed a double two-step test unless chest pain or other symptoms necessitated earlier discontinuation of the test. The test was carried out exactly as indicated by Master: two 9-inch steps were used and the number of trips shown in Master's tables was made. Leads V4, V5, V6, and II were recorded immediately, 2 minutes, and 6 minutes after completion of the exercise test. The electrocardiograms were interpreted independently by two or three physicians with specific recording of the presence and degree of depression of the ST segment and whether the ST-segment depression was of the J (junction) or ischemic type, of the duration of QX and QT, and the calculated QX/QT fraction and QT ratio.

Results
An unequivocal clinical diagnosis of angina pectoris or of nonanginal pain was made in 86 of the 100 patients (angina pectoris in 48 and nonanginal pain in 38). In the remaining 14 patients uncertainty was expressed as to diagnosis and in some of these the opinions disagreed. All 38 nonanginal patients were able to complete the double two-step test but only 33 of the 48 anginal patients did so (table 1).

The results of the two-step electrocardiograms were classified according to various criteria that have been proposed for a positive test. With the long-established criteria of Master, i.e., ST depression of 0.5 mm. or more, 39 per cent of the nonanginal patients had a positive, i.e., a false-positive, result, and 12 per cent of the anginal patients had a negative test, i.e., a false-negative result (table 2). When a positive test was based on ST depression of 0.75 mm. or more, the false positives were reduced to 21 per cent but the false negatives rose to 27 per cent. When 1-mm. ST depression was required for a positive result.

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**Table 1**

<table>
<thead>
<tr>
<th>Clinical diagnosis</th>
<th>Results</th>
<th>1/2 mm. or &gt;</th>
<th>'J'</th>
<th>'ST'</th>
<th>3/4 mm. or &gt;</th>
<th>'J'</th>
<th>'ST'</th>
<th>1 mm. or &gt;</th>
<th>'J'</th>
<th>'ST'</th>
<th>1-1/2 mm. or &gt;</th>
<th>'J'</th>
<th>'ST'</th>
<th>2 mm. or &gt;</th>
<th>'J'</th>
<th>'ST'</th>
<th>QX/QT positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double &quot;two-step&quot;'</td>
<td>Nonanginal pain</td>
<td>38</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Angina pectoris</td>
<td>33</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>4</td>
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<td></td>
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<tr>
<td></td>
<td>Equivocal</td>
<td>12</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Partial &quot;two-step&quot;'</td>
<td>Nonanginal pain</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
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<tr>
<td></td>
<td>Angina pectoris</td>
<td>15</td>
<td>1</td>
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<td>1</td>
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<tr>
<td></td>
<td>Equivocal</td>
<td>2</td>
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<tr>
<td>Totals</td>
<td>100</td>
<td>37</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>3</td>
<td>12</td>
<td>1</td>
<td>8</td>
<td>1</td>
<td>6</td>
<td>25</td>
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</tr>
</tbody>
</table>

"'ST'" junctional types of ST-segment depression; "'ST'" ischemic type of ST-segment depression; QX/QT positive indicates ratio is 50 per cent or greater.

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the false positives diminished to 8 per cent in the nonanginal cases but the false negatives rose to 43 per cent. At 1.5-mm. ST depression there were 5 per cent false positives but 70 per cent false negatives. There were no false positives only when a 2-mm. ST depression was required, but there were then 82 per cent false negatives.

Many authors have also based a positive test on the finding of an ischemic type of ST-segment depression, whereas a J (junction) type of ST depression is regarded as less significant. In the J type the ST segment is depressed at its origin or J joint (junction of S wave and ST segment) but ascends rapidly from the J point to the isoelectric line. The ischemic type of ST-segment depression extends horizontally for at least 0.08 second or sags below the J point. In the present study, however, the "ischemic type" of ST depression was actually more common than the J type in the nonanginal patients with a false-positive test: 9 of the 15 nonanginal patients with a false-positive test, based on ST-segment depression of 0.5 mm. or more, had the ischemic type of ST-segment depression (table 3). Of the 29 anginal patients with ST depression of 0.5 mm. or more, there were 10 with the junctional type of depression.

Lepeschkin and Surawicz found diagnostic value in measurement of \( \frac{QX}{QT} \) ratio, the QX representing the interval from the origin of the Q wave to the point of return (X) of the depressed ST segment to the isoelectric line. They regarded the two-step exercise electrocardiogram abnormal (positive) if the QX/QT ratio exceeded 50 per cent. According to this criterion alone, in our study 8 per cent of the nonanginal group showed a false-positive result and 58 per cent of the anginal patients showed a false-negative result.

Table 3

<table>
<thead>
<tr>
<th>Varying criteria for positive results: RS-T depression</th>
<th>38 Nonanginal cases with false-positive test (( J ) type)</th>
<th>33 Anginal cases with true-positive test (( J ) type)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2 mm. or more</td>
<td>6 9</td>
<td>10 19</td>
</tr>
<tr>
<td>3/4 mm. or more</td>
<td>4 4</td>
<td>7 17</td>
</tr>
<tr>
<td>1 mm. or more</td>
<td>1 2</td>
<td>3 16</td>
</tr>
<tr>
<td>11/2 mm. or more</td>
<td>0 2</td>
<td>2 8</td>
</tr>
<tr>
<td>2 mm. or more</td>
<td>0 0</td>
<td>1 5</td>
</tr>
<tr>
<td>Master's new criteria*</td>
<td>3 9</td>
<td>8 19</td>
</tr>
</tbody>
</table>

*(1) Any ischemic depression, or (2) "J" depression of 2 mm. or more or (3) "J" depression under 2 mm. with positive QX/QT fraction or positive QT ratio.
Recently Master and Rosenfeld\textsuperscript{10} proposed new criteria for a positive two-step exercise electrocardiogram: (1) an ischemic ST-segment depression of any depth; or (2) "J" depression of 2 mm. or more; or (3) "J" depression less than 2 mm. in association with an increased QX/QT fraction (more than 50 per cent) or an abnormal QT ratio (1.08 or more).\textsuperscript{*} Using these latest criteria, we found 32 per cent false positives among the nonanginal patients and 18 per cent false negatives among the patients with definite angina pectoris. It was also suggested by Master that the presence of an abnormal QT ratio could be used as the sole criterion of an abnormal test. When this criterion was applied to our cases, there were 42 per cent false positives among the nonanginal cases and 27 per cent false-negative tests among the anginal patients.

Discussion

The possible value of the two-step exercise electrocardiographic test in clinical practice depends on the reliability of the test and the frequency with which such a test is required in the diagnosis of angina pectoris. A review of the literature discloses not only critical analyses indicating theoretical shortcomings of the test and its interpretation, but also studies by careful observers who found a highly significant number of false-positive and false-negative results by various proposed criteria. For example, Davis et al.,\textsuperscript{11} employing the widely used test and criteria (0.5 mm. ST depression), found a false-positive result in 20.6 per cent of normal controls and 48.8 per cent false negatives in patients with coronary artery disease. Similarly, Thomas\textsuperscript{12} found false-positive tests in 15.8 or 18 per

\textsuperscript{*}The QT ratio (QTr) is the ratio of the actual, measured QT interval to the ideal QT interval. The ideal QT interval which takes into account the correction for heart rate is \(0.40 \sqrt{R-R}\) interval.

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\text{QT Ratio (QTr)} = \frac{\text{Actual QT}}{0.40 \sqrt{R-R}}
\]

The QTr may be easily obtained by using a rule calculator designed by Dr. William Welsh (The Bowen Company, Inc., Bethesda, Maryland.)
the ST joins the baseline may vary from beat to beat. Measurement of the QT ratio also offers difficulties for several reasons: the exact point where the T ends may not be definite, particularly if a "U" wave is present; the QT interval varies greatly with rate, which is often not constant in all leads.

The value of the two-step exercise electrocardiogram should be considered in terms of the purpose for which it is employed. Firstly, we are not concerned here with its use to measure functional capacity as a guide to work classification or recovery following an acute myocardial infarction. Secondly, our purpose was not to test asymptomatic and apparently healthy persons for possible subclinical coronary atherosclerosis. A third use of the two-step electrocardiogram, not pertinent to our present study, is in examinations for insurance, military service, and air pilots, when the clinical history may not be reliable. If the test proved to be negative in only a moderate majority of normal persons, and positive in only a moderate majority of anginal patients, the outlook for longevity would obviously be better in subjects with a negative test. Thus, the test would have a statistical value for the examinations mentioned even if there were many false positives and false negatives. Yet it would not be satisfactory as a diagnostic test of angina pectoris for the individual patient in clinical practice, which is precisely the concern of this study. Our observations indicate that the number of false positives or false negatives is too great to attribute great diagnostic value to the test whether the old or new criteria are used.

An essential problem in evaluating the two-step test is the determination whether a positive or negative test has been labeled correctly as true or false. Some authors have employed follow-up studies of subsequent longevity or myocardial infarction to prove the accuracy of the test in diagnosing the presence or absence of significant coronary disease. As indicated above, such follow-up studies only show the statistical prognostic value of the test for insurance purposes or for large-scale examinations in the Armed Forces or large industrial organizations. But such follow-up studies and statistical correlations are not valid for judging diagnostic accuracy in determining the presence or absence of angina pectoris at the time of the performance of the test. For purposes of this study it was decided that the best criterion of the accuracy of the two-step exercise electrocardiogram when used as an aid in the diagnosis of chest pain was the correlation of the test findings with the independent clinical judgment in cases regarded as being unequivocally anginal or nonanginal. Angina pectoris is, after all, a clinical syndrome and its diagnosis must in the final analysis be determined by the presence of typical features of that syndrome. A definite diagnosis was accepted only when two or more independent observers, without knowledge of any objective findings, were able to state definitely that the patient had angina pectoris. Similar negative statements were the basis of excluding that diagnosis; any expression of uncertainty or disagreement led to the exclusion of the case from either category. For control purposes it seemed desirable, as indicated above, not to use young, asymptomatic, and apparently healthy persons. Instead, and corresponding to the usual clinical situation in which anginal and nonanginal chest pain must be differentiated, those patients were chosen as controls whose pain was regarded by all the investigators as nonanginal and whose age range was similar to that of the patients with angina pectoris.

All patients submitted for this study presented a normal resting electrocardiogram, whether or not angina pectoris was present, in keeping with accepted procedure and to limit risk. There is merit in this restriction but it should be recognized that as a result half of all patients with angina pectoris, i.e., those with any abnormality in the resting electrocardiogram in whom there may be uncertainty as to the nature of chest pain, may not be subjected to this test for diagnostic confirmation. Because a resting electrocardiogram shows ST-segment depressions and T-wave inversions, or even definite evidence of old myocardial infarction, it should not be
inferred that the pain of which the patient complains at the time of the examination is necessarily caused by angina pectoris. Patients with such electrocardiographic changes may be asymptomatic or may have chest pain of diverse causes other than angina pectoris.

Our study confirms our previous clinical impression that, with few exceptions, angina pectoris can be definitely diagnosed or excluded on the basis of the clinical study alone, including the response to nitroglycerin. In this series, an unequivocal diagnosis of angina pectoris, or of nonanginal pain, agreed upon independently by two or three observers, was possible in 86 per cent of the patients, on the basis of a single interview. Undoubtedly further interviews, after the patient had been able to make careful observations as to the nature of the pain, the circumstances of its occurrence, the effect of walking rapidly, uphill, and after a meal, and especially the effect of sublingual nitroglycerin, would have increased the percentage of definite diagnoses. We believe that in private practice the percentage of definite diagnosis of angina pectoris or nonanginal pain after a few visits is not less than 95 per cent. This opinion takes into consideration an awareness that in many of the so-called problem cases of chest pain, there may be several kinds of chest pain of varying etiology. Such clinical experience tends to minimize the need for the two-step exercise electrocardiogram; the percentage of unequivocal clinical diagnoses indicates a higher degree of reliability in determining the presence or absence of angina pectoris in a given patient than does the two-step exercise electrocardiogram with any of the presently employed criteria.

Summary

A double-blind study was made to evaluate the two-step exercise electrocardiographic test (Master) as a means of differentiating between anginal and nonanginal chest pain in 100 consecutive patients.

A high percentage of false-positive results in nonanginal cases and a number of false negatives in anginal cases greatly impaired the usefulness of the test for this purpose. When Master's criterion of an ST depression of 0.5 mm. or more was employed, there were 39 per cent false positives and 12 per cent false negatives.

Stricter criteria progressively diminished the number of false positives, but resulted in increasing numbers of false negatives. Even if 1 mm. or more of ST depression was required, there were 8 per cent false positives and 43 per cent false negatives. There were no false positives only when the ST segment was depressed 2 mm. or more.

Although an ischemic type of ST depression may be more significant for angina pectoris than the J type, in our series ischemic ST depressions also occurred more frequently than the J type in false-positive tests in nonanginal patients.

The new criteria of Master and Rosenfeld were not more satisfactory than the previous criteria recommended.

There are relatively few cases in which an objective two-step test is necessary to aid in the differentiation of anginal and nonanginal pain, since an unequivocal diagnosis of angina pectoris or nonanginal pain was made in 86 per cent of cases independently by at least two observers, on the basis of a single interview, and since this percentage could undoubtedly have been increased by further interviews concerning the effect of effort and of nitroglycerin.

Insofar as confirmation of a clinical diagnosis of angina pectoris by an objective exercise test is desirable, an ST-segment depression of at least 1 mm. usually offers such confirmation. However, this degree of ST-segment depression is often absent in unequivocal cases of angina pectoris and conversely may be occasionally present in patients with nonanginal pain.

References

3. Mason, R. E.: The Master test in patients with

A Great Man's Opportunities

Hippocrates himself practised only in little towns, not one of which was of itself sufficient to support a single physician. Most of his observations were made in Thessaly and Thrace; and he names only small cities. Galen somewhere says that the smallest quarter in Rome contained more inhabitants than the largest town in which Hippocrates practised. It is, therefore, not the great number of patients, but the capacity for deriving all the possible information from each particular case, which tends to form the experienced physician.—Zimmermann (A Treatise on Experience in Physic, 1782). The Quiet Art: A Doctor's Anthology. Compiled by Dr. Robert Coope. Edinburgh & London, E. & S. Livingstone Ltd., 1952, p. 50.
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