Maximal Treadmill Exercise Electrocardiography
Correlations with Coronary Arteriography and Cardiac Hemodynamics

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SUMMARY
Electrocardiograms were recorded during and at 2-min intervals following maximal treadmill exercise in 100 patients and were correlated with coronary arteriograms, left ventricular cineangiograms, and resting and exercise cardiac hemodynamics. The incidence and extent of exercise-induced "ischemic" S-T segment depression increased significantly (P < 0.01) with increasing extent of coronary artery disease (CAD). A criterion of abnormality of 1.0 mm or greater S-T depression most accurately predicted the presence of CAD with a specificity (true negative) of 89% and a sensitivity (true positive) of 62%. Criteria of ≥0.75 and ≥0.5 mm S-T depression offered improved sensitivities (68 and 84%, respectively) but markedly reduced specificities (78 and 57%, respectively).

A significant correlation (P < 0.005) was found between increasing extent of exercise-induced S-T depression and the pulmonary artery wedge pressure during exercise. There were no correlations between the presence or extent of exercise-induced S-T depression and the resting or exercise pulmonary artery pressure, cardiac index, stroke-volume index, or exercise factor, or the resting left ventricular dp/dt, left ventricular end-diastolic pressure, left ventricular ejection fraction, or presence of asynergy on the left ventricular cineangiogram.

The maximal treadmill exercise test provided a noninvasive method for predicting the presence and extent of significant CAD in the individual patient with chest pain. Although a normal treadmill exercise test provided little insight into the underlying resting and exercise hemodynamics, an abnormal treadmill test (≥1.0 mm S-T depression) was associated with an abnormal increase in left ventricular filling pressure with exercise in 90% of the patients.

Additional Indexing Words:
Left ventricular function Left ventricular angiograms Coronary artery disease
Coronary collateral circulation

The diagnostic role of quantitative exercise electrocardiography has been placed into better perspective in recent years by the correlation of such studies with coronary arteriography.1-12 Graded submaximal or maximal treadmill exercise to the point of either limiting symptoms or an age-dependent maximal heart rate apparently offers significant advantages over the widely employed Master two-step test.2,12 The treadmill test permits increasingly strenuous exercise to a level dependent upon each patient's capacity in a mode familiar to all patients, e.g. upright walking on a flat surface. Furthermore, the test may be performed under continuous electrocardiographic surveillance so that significant S-T segment changes or arrhythmias may be immediately detected.
during the exercise. This improves not only the diagnostic sensitivity of the procedure but also patient safety.\textsuperscript{10-18}

The present study was designed to (1) assess prospectively the diagnostic usefulness of maximal treadmill exercise electrocardiography in the evaluation of patients with coronary artery disease, (2) to evaluate the sensitivity and specificity of certain criteria used in the interpretation of the exercise electrocardiogram, and (3) to correlate these results with the left ventricular cineangiogram, coronary arteriograms, and cardiac hemodynamics obtained at rest and during moderate supine exercise. The results are compared with data from a similar study by one of the authors (D.R.M.) which employed a double Master two-step test.\textsuperscript{1}

Methods

Data on 100 consecutive patients who had cardiac catheterization, left ventricular cineangiography, and selective coronary arteriography after completing a maximal treadmill exercise electrocardiographic test (MTE) are included in this report. There were 91 men and nine women, ranging in age from 23 to 51 years with a mean of 42 years. Patients with valvular heart disease, cardiac conduction defects, diastolic blood pressures greater than 100 mm Hg, or idiopathic myocardial infarction were excluded. Sixteen patients manifested a pattern consistent with an antecedent myocardial infarction on their control electrocardiogram. No patient had received any cardiac medication except sublingual nitroglycerin for a minimum of 1 week prior to study. Arteriographic examination was performed to establish or exclude the presence of significant coronary artery disease in cases of chest pain of uncertain origin (65 patients) or to define the location and extent of coronary artery disease in patients being considered for aortocoronary saphenous vein bypass surgery because of severe angina pectoris (35 patients).

Treadmill Exercise Test

All patients were exercised in a fasting state 1 day prior to cardiac catheterization. After a resting 12-lead electrocardiogram had been obtained, upright exercise on a motor-driven treadmill (Quinton Instrument Company, Model 18-49C) was initiated at a 0% grade and a speed of 3 mph. A modified precordial lead approximating lead V\textsubscript{5} was monitored continuously throughout the period of exercise and recorded at 30-sec intervals for subsequent analysis. Each patient exercised at a constant speed of 3 mph but the incline of the treadmill was elevated by 2½% increments every 2 min. In 95 of the 100 patients exercise was continued until the occurrence of symptoms of excessive fatigue, dyspnea, angina, dizziness, or “ischemic” S-T segment depression exceeding 2 mm. There were no instances of ventricular tachyarrhythmias necessitating termination of exercise in this study group. The stress was, therefore, considered “maximal” in these patients. In the remaining five patients exercise was continued until a heart rate exceeding 90% of the predicted maximal heart rate for age was obtained.\textsuperscript{19, 20} Electrocardiograms including all standard limb leads and the precordial leads V\textsubscript{4}, V\textsubscript{5}, and V\textsubscript{6} were then obtained in the recumbent position immediately after exercise and at 2-min intervals for a minimum of 8 min following exercise. The intracerebrogram and each lead of the postexercise ECG were then assessed for “ischemic” S-T segment depression, in which the S-T segment subtends an angle of at least 90° with the descending limb of the R wave for at least 0.08 sec. The maximal extent of such S-T depression below the baseline, as established by the P-R segment, was recorded for each lead. The exercise electrocardiograms were read independently by the authors, and any differences in interpretation were resolved prior to the cardiac catheterization.

Cardiac Catheterization Procedure

Right and left heart catheterizations with selective coronary arteriography were performed in a fasting state with meperidine (Demerol) (50 mg) and atropine (0.6 mg) premedication on the day following the maximal treadmill exercise test. Intracardiac pressures were recorded through fluid-filled catheters with Statham strain gauges on a photographic recorder (DR-12 Recorder, Electronics for Medicine) with the measured midchest position as the zero reference point. Mean pressures were derived by electrical integration. Mean pulmonary artery and pulmonary wedge pressures were obtained in a resting supine position after the feet had been placed in a bicycle ergometer (Collins Physiological Development Complex) for 5 min and at 1-min intervals for 5 min during supine leg exercise at a load of 75 w (400 kg-m/min). Wedge pressures were obtained with an end-hole catheter and the wedge position confirmed by determination of the O\textsubscript{2} saturation. The cardiac index (CI) as determined by the Fick principle using measured oxygen consumption and the stroke-volume index (SVI) were also measured at rest and during exercise. The exercise factor was calculated as the
exercise increase in cardiac output in cc/min for each 100-cc/min increase in oxygen consumption. Catheterization of the left ventricle was performed retrograde from the femoral artery using the Seldinger percutaneous technic. The maximal rate of rise of left ventricular pressure (LV dp/dt) using an electronic differentiator and the left ventricular end-diastolic pressure (LVEDP) at high sensitivity were obtained in the resting state only. All hemodynamic measurements were recorded before the use of contrast media. Data are not available regarding the incidence of angina pectoris or the extent of "ischemic" S-T segment depression occurring during the supine exercise, but complete hemodynamic data were obtained in 76 patients.

Left ventricular cineangiograms were recorded in the 30° right anterior oblique projection at 60 frames/sec using 40–60 cc of meglumine diatrizoate (Renografin-76%) injected through an 8-F preformed pigtail catheter (Cordis Ducor) at a pressure of 350–450 psi. Left ventricular ejection fraction (EF) was derived angiographically from a modification of the area-length method of Dodge. The left ventricular angiogram was also evaluated for abnormalities of myocardial contraction (asynery) using frame-by-frame analysis of the internal left ventricular outline.

Coronary arteriograms were then obtained in multiple projections using the technic as described by Judkins. Disease of a major coronary artery was considered to be functionally significant if its most severe narrowing exceeded 50% of the arterial luminal diameter.

Data were subjected to an analysis of variance, Duncan's multiple range test, and chi-square analysis using an Olivetti 101 Programma Computer and a General Electric 600 Digital Computer.

Results

Thirty-seven patients (32 men and five women, mean age of 40 years) were free of significant coronary artery disease, that is, they had no arterial occlusions exceeding 50% of the luminal diameter and were, therefore, considered to be "normal." Thirty-two patients in this group including one whose resting electrocardiogram showed a pattern of an inferior myocardial infarction were free of any luminal irregularity. Sixty-three patients (60 men and three women, mean age 43 years) had arteriographically documented coronary artery disease. Twenty-three cases had significant occlusive disease (more than 50% occlusion) limited to a single major coronary artery, 18 had disease affecting two major vessels, and 22 had diffuse disease involving all three major vessels. Fifteen of these patients with coronary artery disease had resting electrocardiographic evidence of an antecedent myocardial infarction.

Correlation of MTE with Coronary Arteriogram

The maximal "ischemic" S-T segment depression recorded during or following maximal treadmill exercise is correlated with the arteriographic extent of coronary artery disease in table 1.

False-Positive Exercise Tests

Twenty-one of the 37 arteriographically normal patients (57%) had maximal S-T segment depressions of less than 0.5 mm.

Table 1

<table>
<thead>
<tr>
<th>Max &quot;ischemic&quot; S-T seg depression in any lead (mm)</th>
<th>No. of pt (accoring to no. of vessels involved with CAD)</th>
<th>No. of pt with CAD (1-3 vessels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td></td>
<td>10 (16%)</td>
</tr>
<tr>
<td>0.5</td>
<td></td>
<td>53 (84%)*</td>
</tr>
<tr>
<td>≥0.75</td>
<td></td>
<td>43 (68%)*</td>
</tr>
<tr>
<td>1.0</td>
<td></td>
<td>39 (62%)*</td>
</tr>
<tr>
<td>1.5</td>
<td></td>
<td>30 (48%)*</td>
</tr>
<tr>
<td>2.0</td>
<td></td>
<td>24 (38%)*</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td>63 (100%)</td>
</tr>
</tbody>
</table>

*True-positive exercise ECG results using criterion in first column for abnormality.
†False-positive exercise ECG results using criterion in first column for abnormality.

Circulation, Volume XLVI, November 1972
Therefore, if an “ischemic” S-T depression of 0.5 mm or greater were considered abnormal, 43% of the normal subjects would have had a false-positive exercise study. If 1.0-mm “ischemic” S-T segment depression were considered abnormal, only 11% would have had a false-positive exercise test. No patient with an S-T depression of 1.5 mm or greater was free of significant coronary artery disease.

False-Negative Exercise Tests

As the extent of arteriographically determined coronary artery disease increased, both the frequency and extent of “ischemic” S-T segment depression significantly increased (P < 0.005), and the incidence of false-negative exercise tests diminished. If an “ischemic” S-T segment depression of 1.0 mm were considered abnormal, 65% of patients with single-vessel disease, 33% with double-vessel disease, and 14% with triple-vessel disease would have been considered falsely normal by exercise electrocardiography. Analyzing the patients with coronary artery disease as a group, 16% would be classified as normal (false negative) if a criterion for abnormality of 0.5-mm or greater S-T segment depression were used, 32% if 0.75 mm were used, 38% if 1.0 mm were used, and 52% if 1.5 mm were used as a criterion for a positive test. When the patients with an infarct pattern on their resting electrocardiogram were excluded from the above analysis, the results were not significantly altered.6

Yield from In-Exercise Monitoring

In 12 cases in this study (12%), the maximal “ischemic” S-T segment depression occurred during exercise. However, if an S-T segment depression of 1.0 mm or greater were used as the criterion of abnormality, seven of these cases would also have had abnormal postexercise electrograms. In-exercise monitoring thus yielded only five additional abnormal tests (5%) which would subsequently have gone undetected by the postexercise recordings. Only one of the 12 positive in-exercise tests (8.3%) was unassociated with significant coronary arteriographic disease. The incidence of false-positive exercise tests was therefore not increased by the inclusion of in-exercise results.

Effect of Collateral Vessels on Results of the Maximal Exercise Test

The incidence of collateral vessels as demonstrated by coronary arteriography increased significantly (P < 0.01) as the extent of coronary artery disease increased from zero to one- to two- or three-vessel disease (fig. 1). In the group of patients with single-vessel disease, the apparent tendency for patients with collateral vessels to exhibit less S-T segment depression compared with patients without collateral vessels was not statistically significant.

Correlation of Exercise Electrocardiogram with Cardiac Hemodynamics

Resting hemodynamic data were obtained in 89 patients and complete exercise data in 76.

In figure 2, the resting and exercise mean pulmonary artery wedge pressures (PAW) are related to the degree of “ischemic” S-T segment depression noted on the exercise electrocardiogram. No correlation existed between the resting PAW and the extent of S-T segment depression. However, an abnormal treadmill exercise electrocardiographic test

**Figure 1**

Incidence of collateral vessels with increasing extent of coronary artery disease. The groups are subdivided according to the extent of “ischemic” S-T segment depression. The numbers within the bar graphs represent the number of patients within each subgroup.
Correlation of resting and exercise mean pulmonary artery wedge pressures (in mm Hg) with extent of maximal “ischemic” S-T segment depression (in mm). Resting and exercise data are available for each patient.

Figure 2

provided a reliable clue to an associated abnormal increase in left ventricular filling pressure during exercise. The mean exercise PAW increased significantly (P < 0.005) as the maximal S-T depression increased from < 0.5 to 0.5-0.9 to ≥1.0 mm. Only 13 of 40 patients (32%) with less than 1.0-mm S-T depression had an exercise PAW of 15 mm or greater, whereas 28 of 36 patients (78%) with 1.0-mm or greater S-T depression had an exercise PAW of that magnitude. Thirty-two of these 36 patients (90%) with 1.0-mm or greater S-T depression compared with 17 of 40 patients (42%) with a lesser S-T depression had an exercise PAW exceeding 12 mm Hg.

No significant correlations were found between the extent of “ischemic” S-T segment depression on the exercise electrocardiogram and the CI, SVI, or mean pulmonary artery pressure at rest or exercise, or with the resting LVEDP, exercise factor, left ventricular ejection fraction, left ventricular dp/dt, or the presence of asynery on the left ventricular cineangiogram.

Comment

The advent of selective coronary arteriography has enabled the clinician to correlate in-vivo coronary artery anatomy with such noninvasive tests as exercise electrocardiography. Numerous recent reports using coronary arteriography have placed into better perspective the role of such stress testing in the evaluation and detection of patients with potential coronary artery disease.1-12, 23-31 However, many of these studies have interpreted the exercise electrocardiogram solely as normal or abnormal on the arbitrary basis of a predetermined extent of “ischemic” S-T segment depression. None of the methods of exercise stress testing permits a precise separation between the normal subject and the patient with coronary artery disease. Therefore, the present authors believe that the most valid diagnostic application of the exercise electrocardiogram would be to determine the probability of the maximal extent of S-T segment depression being associated with coronary artery disease in the individual patient presenting with chest pain.

Data enumerating the incidences of false-positive and false-negative responses for each level of S-T segment depression have been previously reported for the double Master two-step test.3, 4 The present study provides such information for the maximal treadmill exercise electrocardiographic test (MTE) (table 1). In this study 43% of the patients with normal coronary arteriograms had an exercise “ischemic” S-T segment depression of at least 0.5 mm, but only 11% of this normal group had an S-T depression of 1.0 mm or greater. None of the 37 arteriographically normal subjects had a maximal S-T depression of 1.5 mm or greater.

In contrast, 84% of the 63 patients with significant coronary arteriographic disease had S-T depressions of at least 0.5 mm, and 62% had depressions of at least 1.0 mm. Furthermore, as the extent of coronary arteriographic disease increased, the incidence of associated ST depression significantly increased at each level of S-T change. None of the patients with triple-vessel disease was free of at least some “ischemic” S-T segment depression on the MTE; 19 of 22 patients (86%) in this group with extensive coronary arteriographic disease.

Circulation, Volume XLVI, November 1972
had an exercise S-T depression of 1.0 mm or greater.

In table 2, criteria used in the interpretation of the double Master test are compared with criteria applied in the present study using the MTE. It was previously concluded that an "ischemic" S-T segment depression of 0.5 mm or greater was the optimal criterion for the double Master test. On the basis of data in the present report, a maximal "ischemic" S-T segment depression of 1.0 mm or greater apparently provides the best levels of specificity and sensitivity when a MTE is employed. If these optimal criteria for each test are compared (≥1.0-mm S-T depression for the MTE vs ≥0.5-mm S-T depression for the double Master test), it is apparent that the incidences of false-negative responses are similar (38% for MTE vs 37% for double Master). However, the incidence of false-positive responses is significantly less for the MTE (11% for MTE vs 17% for the double Master test). It is also apparent from table 2 that the different S-T segment criteria are not equally applicable to the different modes of exercise electrocardiography. At each level of S-T segment depression, the sensitivities and specificities vary between these different modes of stress testing.

Of the hemodynamic indices measured in this study, only the exercise pulmonary artery wedge pressure (PAW) correlated with the extent of exercise-induced S-T segment depression (fig. 2). This exercise PAW increased significantly \( P < 0.005 \) as the extent of S-T segment depression increased from <0.5 to 0.5–0.9 to ≥1.0 mm.

In the evaluation of patients with chest pain, an abnormal MTE (≥1.0-mm S-T depression) provides an imperfect, although diagnostically useful, method of separating normal subjects from those with coronary artery disease and offers slightly improved specificity compared with the double Master test when appropriate criteria are used. Such an abnormal treadmill test may also provide reliable indirect evidence of an abnormal rise in left ventricular filling pressure associated with exercise. Finally, the MTE provides an excellent opportunity to assess objectively a patient's exercise tolerance and any exercise-related symptoms during a monitored period of graduated exercise.

### References


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