Stress Testing 
with ST-Segment Depression at Rest

An Angiographic Correlation

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SUMMARY  Near maximal graded exercise tests and coronary angiograms were compared in 37 patients with a history of chest pain and with ST-segment depression at rest, who were free of obvious nonischemic causes of ST depression. Additional ST depression of 0.1 mV or more occurred with exercise in 26 patients and 23 of these had obstruction of one or more coronary arteries (sensitivity = 0.92). Eleven patients showed no additional ST-segment depression with exercise, and nine of these had normal coronary angiograms (specificity = 0.75). Patients with no increase in ST depression on exercise developed the highest heart rates; those with asymptomatic additional ST depression achieved intermediate rates; and those with anginal attacks during testing demonstrated the least heart rate acceleration. Those with less coronary obstruction exercised longer on the treadmill than those with more obstruction. Those showing added ST depression were predominantly men (18 of 26) and were older (mean 54 years) than those who did not (mean 44 years). No test complications were encountered. This study suggests that safe and effective stress testing may be accomplished not only in persons with normal resting ECGs but also in selected patients who have abnormal ST segments at rest.

THE EXERCISE TEST is of diagnostic and prognostic value in patients with ischemic heart disease who have normal resting ECGs. Its significance in patients with abnormal resting ECGs has been uncertain. Many investigators have hesitated to subject such patients to stress testing because of its possible hazards and questionable diagnostic value even if further ST-T changes took place during or after exercise. Robb1 in 1964, and Master2 in 1967 subjects some patients with abnormal resting ECGs to exercise. Hulgren3 in 1967, Proudfit4 in 1966, Mason5 in 1967, and Roitman6 in 1970 subjected some patients with abnormal resting ECG to submaximal stress tests and coronary cineangiograms, but no correlation was made between exercise ECG changes and coronary artery obstruction. Cohn et al.,7 Linhart’s group8 and Nasrallah9 have recently reported a high incidence of coronary artery obstruction in patients with non-specific ST-T changes in the resting ECG.

This study was undertaken to assess the significance of exercise-induced further ST-T changes in patients with non-specific ST-T changes in their resting ECGs, by comparing these changes with the degrees of coronary artery obstruction found by angiography.

Subjects and Methods

This is a study of 37 patients with chest pain who had abnormal resting ECGs manifesting ST-T depression of at least 0.5 mm, with or without Q waves characteristic of old myocardial infarction. Patients who had evidence of recent myocardial infarction, angina pectoris of recent onset, or with a pronounced change in the severity or frequency of angina were not tested. None of the 37 patients had electrocardiographic left ventricular hypertrophy, intraventricular conduction defect, hypokalemia, or were being treated with digitalis or any antiarrhythmic drugs. Most of them were receiving nitrates, and each of them had a sub-maximal graded exercise test and coronary angiograms. This study includes all patients satisfying the foregoing criteria who were tested between November 1970, when the present stress test protocol was adopted, and January 1975.

Graded Exercise Test Method

Patients were brought into the exercise laboratory two hours or more after their last meal. The exercise test procedure was explained to them and each patient then consented to be tested. A conventional 12-lead resting ECG was performed. Self-adhering, fluid-coupled electrodes were applied to each previously cleansed and abraded site to permit continuous recording of any three of the 15 conventional and Frank leads of the electrocardiogram. The ECG preamplifiers used had an input impedance of 5 megohms, a time constant of 3.4 sec and high frequency response linear to 1000 Hz. Visually, V6 or X, Y, and Z were monitored alternatively on a large screen oscilloscope, and heart rate was displayed on an adjacent cardio-tachometer. The electrocardiogram was recorded continuously on magnetic tape, and paper records of the above six leads were obtained in each three minute stage of exercise, at stop of exercise and every two minutes during the postexercise period for six minutes.

Patients exercised uninterrupted in three minute stages using the treadmill settings of Doan10 and colleagues. The test was considered complete if the subject attained an exercise heart rate within 8 beats/min of target heart rate (that is, 90% of predicted maximum heart rate according to Lester and co-workers) for that age.11 For athletically untrained men aged 40, 50 and 60 years, target heart rates are 170, 166 and 162 beats/min, respectively. This heart rate was reached and sustained for approximately two minutes, and then the exercise was concluded. The exercise was interrupted any time a patient developed chest pain, claudication, exaggerated fatigue, symptoms of cerebral insufficiency, intraventricular conduction defect, arrhythmias or unequivocal additional ST-T depression. Patients were not allowed to continue exercise to assess the maximum attainable ST-T depression even in the absence of other indications for stopping the test. Tests were judged incomplete if exercise did not continue until one of these indications for stopping oc-

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occurred, but rather was stopped because of mild fatigue or some noncardiac cause like leg pain. Such tests were excluded from the study.

ECG measurements were always made of three consecutive beats in which QRS-ST junction deviation was measured from a straight line connecting the onsets of QRS complexes. ST-T depression was defined as a horizontal or downsloping displacement lasting over 0.08 sec after the end of QRS. Its amplitude, to the nearest 0.5 mm, was measured 0.06 sec after the J point. Postexercise ECGs were studied immediately at the end of exercise and at 2, 4 and 6 minutes postexercise.

Coronary angiograms were obtained by conventional Judkin or Sones techniques with at least two clear views of each major vessel. They were interpreted independently by the catheterizing cardiologist and cardiac radiologist. Any differences were resolved by mutual agreement.

Coronary obstruction was graded as follows: no obstruction seen, 0; up to 50%, 1; > 50 - < 75%, 2; 75 - < 100%, 3; and complete obstruction, 4.

An obstruction score number was given separately for proximal, middle and distal parts of the left anterior descending (LAD), right (RCA) and circumflex (CCA) coronary arteries. Left main, right and left marginal and posterior descending arteries were given only one score. An index of the severity of obstructive disease was developed by adding obstruction scores of all vessels.

Results

Thirty-seven patients with satisfactory exercise tests and coronary angiograms were studied. Of this number, 26 patients had additional ST-segment depression with exercise. Eighteen were men and eight were women. The age range was 35-69 years with a mean of 53.6 years.

Patients with Further ST-segment Depression

The greatest degree of additional ST depression was 3 mm, found in one patient. Six of the 26 patients showing additional ST-T depression (23%) had some uniform or multiformal ventricular premature beats during exercise or in the postexercise period.

Coronary artery obstruction was present in 23 (88%) of these 26 patients, and 20 patients (77%) had coronary obstruction scores of more than six (fig. 1). The maximum score was 19 in a patient who had complete occlusion of middle parts of the RCA and CCA, with multiple scattered lesions in the other vessels. Evidence of old myocardial infarction was seen in the ECGs of five of these 26 patients. They were located inferiorty in three cases and were anteroseptal in two. All patients with old myocardial infarction had severe multivessel disease. Severity of further ST-T depression had no significant relation to the degree of coronary artery obstruction (fig. 2).

In 19 patients (73%) three vessels were involved, in four (15%) two vessel disease was seen, while in three (12%) of the patients no coronary artery obstruction was found. The LAD was most often affected (25, or 80% of cases), and the RCA and CCA were involved with equal frequency (18, or 70% of cases). Twenty-two patients (88%) had at least one vessel with greater than 75% obstruction. Proximal lesions were more common than distal.

Fifteen (58%) of the patients with additional ST depression were stopped from walking on the treadmill because they developed episodes of angina, and in no case was target heart rate achieved.

Patients who felt chest pain on exercise had a higher occlusion score than those who did not, but the difference was not statistically significant. Mean heart rate of all subjects at termination of exercise was 135 beats/minute, and the ratio of peak heart rate to target heart rate was 0.82. However, in the 15 patients who had angina while on the treadmill, the peak heart rate to target heart rate ratio was lower than in those who stopped for other reasons (0.78 and 0.92, respectively) and this difference was statistically significant (P < 0.005).

Patients without Further ST-segment Depression

Of the 11 patients who showed no further ST depression with exercise, ten were females. Their mean age was 43.8 years. In five patients reduction or complete disappearance of ST depression took place, and in an additional two patients T wave abnormality disappeared without appreciable effect on the ST segment. None of these 11 patients without further ST depression had evidence of healed myocardial infarction.
In these 11 patients coronary angiograms were normal in nine, while two subjects showed obstructive abnormality. In both cases it involved the LAD, in one instance amounting to 50% obstruction, and in the other, 95% (coronary artery obstruction scores were 2 and 3, respectively).

Peak heart rate to target heart rate ratio was 0.96 in these subjects without further ST depression. Their mean peak heart rate was 161/min. Exercise was not terminated due to chest pain in any of them. The commonest cause for stopping was fatigue, sometimes with shortness of breath. Patients without further ST depression all developed diagnostic exercise tachycardia (within 8 beats/min of target heart rate).

Thus it is seen that additional ST-segment depression with exercise identified 23 of a total of 25 patients with significant coronary arterial obstruction, yielding a sensitivity of 92%. Failure to develop additional ST-segment depression characterized nine of a total of 12 patients without significant coronary arterial obstruction, a specificity of 75%. The amount of additional ST-segment depression required to yield this sensitivity and specificity was only 1 mm. Among the persons who showed further ST depression with exercise there was a definite relationship between treadmill exercise time and coronary artery obstruction score \( (P = 0.0025) \); however, the variability of individual observations yields only a modest correlation coefficient \( (r = 0.57) \). Those persons not demonstrating additional ST depression showed no relationship at all between exercise time and obstruction score (fig. 3).

The longer mean exercise duration of those subjects with coronary artery obstruction (5.16 min) compared to those without (4.09 min) was not statistically significant.

Discussion

Many patients with the diagnostic problem of chest pain have resting ST-segment abnormalities. If ECG stress testing is not available to these individuals, accurate selection of therapy for them is hampered to an important degree. It is established that left ventricular hypertrophy, digitalis glycosides and intraventricular conduction defects seriously degrade the ability of the exercise ECG to indicate ischemia. However, patients without these equivocating conditions could be accurately tested if it were established that in these patients resting ST depression did not nullify sensitivity of the ST segment to exertional ischemia.

In 1968 Proudfit et al. studied 19 patients with abnormal resting electrocardiograms, and abnormal coronary arteriograms were found in six of them. Hultgren studied 17 patients with abnormal resting ECGs, half of whom had abnormal arteriograms, and found no correlation between ECG changes and coronary arteriograms. In 1970 Roitman et al. studied 10 patients with abnormal ST-T changes and found further ST-T depression in five of these. Three of these five (60%) had coronary artery disease. There were too few patients to draw any conclusions.

In 1971 Cohn and colleagues did two-step Master's tests on 110 patients with chest pain syndromes and with nonspecific ST-T changes in their resting ECGs. Though they used the step test rather than the treadmill, they eliminated from their study any test yielding a tachycardia \( <110/min \), in effect making theirs a post facto graded exercise test. This group correlated postexercise ECG changes with coronary cineangiograms and found 88% of the patients with further ST-T depression had anatomical coronary artery disease. They also commented that any additional ST depression \( \geq 2 \text{ mm} \) was invariably associated with multivessel disease. Our results are very similar. We found that any degree of further ST-T depression \( \geq 1 \text{ mm} \) yielded a diagnostic sensitivity of 92% although, not surprisingly, specificity was lower (75%) than Cohn's. Increasing the ST shift criterion to 2 mm would not have improved the diagnostic figures of merit in our study.

Linthart et al. did a similar study in 61 patients with repolarization abnormalities and found ST-T depression of \( \geq 1 \text{ mm} \) was of diagnostic value for the detection of myocardial ischemia (sensitivity 76%, specificity 79%). Their sensitivity is slightly lower than ours, perhaps due to the presence of intraventricular conduction defects and LVH in some of their patients.

Nasrallah et al. recently reported the diagnostic implication of further exertional ST-T depression in patients with resting ST-T abnormalities (sensitivity 63%, specificity 95%). It is difficult to account for the low sensitivity in this study. These authors have not mentioned the minimum tachycardia achieved on exercise which they accepted for a valid negative test although their criteria for a positive test are similar to our study.

The diagnostic sensitivity found in this study is higher than that reported by Likoff, \(^a\) Cohen \(^a\) or Roitman \(^a\) for patients with normal resting ST segments. However, considering the small number of subjects involved, the differences are probably not significant.

Although the occurrence of further ST-T depression with exercise was strongly correlated with the presence of coronary artery disease, the degree of ST-T depression was not correlated with the extent of coronary artery obstruction seen on angiography. This lack of quantitative correlation was also reported by Cohn. A possible reason for lack of correlation in our study is the fact that additional ST-segment depression was one of the indications for stopping the test, thus restricting the amount of ST depression which developed during exercise. Patients who developed \( \geq 1 \text{ mm} \) additional ST-T depression with exercise had a significantly lower ratio of peak heart rate to target heart rate than those who did not (0.82 and 0.95 respectively, \( P < 0.001 \)). Since peak heart rate is shown to be lower in the coronary artery obstruction patients, it follows that additional ST depression is closely correlated with the presence of coronary artery ob-

\[\text{FIGURE 3. Correlation of treadmill exercise time with degree of coronary artery occlusion.}\]
struction. Also as might be expected, these measurements were lower still in patients who developed chest pain during treadmill exercise. None of these patients had any complications of testing, and the incidence of arrhythmias was not higher than in patients with a normal resting ECG.¹⁰ The lack of a significant difference in exercise duration between the patients with coronary artery obstruction and those without would be paradoxical if the latter patients were known to be normal, but in fact they are not. They have both episodic chest pain and an abnormal resting ST segment, and certainly are not in the same category as normal volunteers. Among subjects with angiographically demonstrated coronary obstruction, exercise times were shorter in those with greater obstruction and longest in those with less. This is exactly what would be predicted by a disease model in which work capacity is dependent upon coronary artery flow reserve.

Three of our patients who showed further ST-T depression, yet had normal coronary angiograms, were females. On retrospective inquiry one of these patients was receiving digoxin until five days prior to the exercise test, which could account for a false positive additional ST-T depression of 2 mm on exercise. In another patient, although coronary angiograms showed no obstruction, there were high levels of lactate production when chest pain was induced during atrial pacing, suggesting that the ST depression did correspond with ischemia, albeit of unknown cause. Our three “false positive” responders were women, and others also have reported this phenomenon. Sketch¹⁶ and Cumming¹⁷ have reported a lower diagnostic value of postexercise ST-T changes in women than in men, when all patients’ resting ECGs were normal.

Remembering that all 37 patients herein reported had a history of chest pain, it is interesting that of those with advanced coronary occlusive disease men outnumbered women two to one, while of those with chest pain presumably not due to coronary disease, eight of nine were women.

Conclusions

1. Submaximal exercise testing is a safe and valuable aid in the diagnosis of coronary artery disease in patients with ST-T changes in their resting ECG provided LVH, intraventricular conduction defects and digitalis effect are absent. Further ST-T depression of ≥ 1 mm had a diagnostic sensitivity of 92% and specificity of 75% in this study. Its diagnostic value compares well with tests on patients who have normal resting ECGs.

2. Exercise duration and peak heart rate to target heart rate ratio were lower in patients manifesting additional ST-T depression than in those who did not.

3. Further ST-T depression in women with abnormal resting ECGs is probably of less diagnostic value than in men, and needs to be studied further.

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