

# The Effect of Resting ST Segment Depression on the Diagnostic Characteristics of the Exercise Treadmill Test

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- OBJECTIVES** The aim of this study is to demonstrate the effect of resting ST segment depression on the diagnostic characteristics of the exercise treadmill test.
- BACKGROUND** Previous studies evaluating the effect of resting ST segment depression on the diagnostic characteristics of exercise treadmill test have been conducted on relatively small patient groups and based only on visual electrocardiogram (ECG) analysis.
- METHODS** A retrospective analysis of data collected prospectively was performed on consecutive patients referred for evaluation of chest pain. One thousand two hundred eighty-two patients without a prior myocardial infarction underwent standard exercise treadmill tests followed by coronary angiography, with coronary artery disease defined as a 50% narrowing in at least one major epicardial coronary artery. Sensitivity, specificity, predictive accuracy and area under the curve of the receiver operating characteristic (ROC) plots were calculated for patients with and without resting ST segment depression as determined by visual or computerized analysis of the baseline ECG.
- RESULTS** Sensitivity of the exercise treadmill test increased in 206 patients with resting ST segment depression determined by visual ECG analysis compared with patients without resting ST segment depression ( $77 \pm 7\%$  vs.  $45 \pm 4\%$ ) and specificity decreased ( $48 \pm 12\%$  vs.  $84 \pm 3\%$ ). With computerized analysis, sensitivity of the treadmill test increased in 349 patients with resting ST segment depression compared with patients without resting ST segment depression ( $71 \pm 6\%$  vs.  $42 \pm 4\%$ ) and specificity decreased ( $52 \pm 9\%$  vs.  $87 \pm 3\%$ ) ( $p < 0.0001$  for all comparisons). There was no significant difference in the area under the curve of the ROC plots (0.66–0.69) or the predictive accuracy (62–68%) between the four subgroups.
- CONCLUSIONS** The diagnostic accuracy and high sensitivity of the exercise treadmill test in a large cohort of patients with resting ST segment depression and no prior myocardial infarction support the initial use of the test for diagnosis of coronary artery disease. The classification of resting ST segment depression by method of analysis (visual vs. computerized) did not affect the results. (J Am Coll Cardiol 2000;35:1206–11) © 2000 by the American College of Cardiology

The exercise treadmill test remains a useful test for diagnosing coronary artery disease (CAD) in patients with chest pain who are at intermediate risk for CAD (1). However, there is controversy regarding the utility of the exercise test in this patient population when ST segment depression is found on the resting electrocardiogram (ECG). Despite the recent American College of Cardiology/American Heart Association (ACC/AHA) guidelines which list exercise testing in patients with resting ST segment depression less than one mm as a Class I indication (2), many clinicians still

turn to more expensive stress-imaging modalities to diagnose CAD in this setting. This may be because most past studies have been performed on small patient groups and have generated conflicting results (3–7). Demonstration that the exercise treadmill test maintains its diagnostic accuracy in a large cohort of patients with resting ST segment depression could obviate the need for many stress-imaging studies.

Past studies evaluating the effect of resting ST segment depression on the accuracy of the exercise treadmill test have not utilized the now routinely available computerized analysis of the resting ECG (3–7). In this paper we examine the effect of resting ST segment depression, as classified by both visual and computerized analysis, on the diagnostic characteristics of the exercise treadmill test in a large cohort of patients without a prior myocardial infarction.

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#### Abbreviations and Acronyms

ACC/AHA	= American College of Cardiology/American Heart Association
CAD	= coronary artery disease
ECG	= electrocardiogram
LVH	= left ventricular hypertrophy
ROC	= receiver operating characteristic

## METHODS

**Patients.** Two thousand one hundred ninety-eight consecutive male patients with complete data underwent exercise treadmill testing at two Veterans Affairs Medical Centers between 1987 and 1998 to evaluate chest pain that was possibly due to coronary disease. All patients had coronary angiography within three months of the exercise treadmill test. Work-up bias could not be excluded, but we believe it was minimized because of the manner in which the sample was selected. Patients with valvular heart disease, previous cardiac surgery or angioplasty, or left bundle branch block, paced rhythms or Wolff-Parkinson-White on their resting ECG were excluded from the study. Prior cardiac surgery was the predominant reason for exclusion of patients who underwent exercise treadmill testing during this time period. In order to avoid falsely increasing the accuracy of the exercise treadmill test, patients with a previous myocardial infarction by history or by diagnostic Q wave were excluded from the diagnostic subgroup leaving a target population of 1,282 patients.

A complete clinical history was obtained at the time of exercise treadmill testing. While most of these data were gathered prospectively using computerized forms (8,9), some of the patients initially studied had incomplete data requiring retrospective chart review. Prognostic information is not available. Resting electrocardiographic abnormalities were classified by computerized analysis and by visual interpretation. Resting ST segment depression was defined as the amount of ST segment depression relative to the PQ interval.

**Exercise treadmill testing.** Patients underwent treadmill testing using the USAFSAM (10) or an individualized ramp treadmill protocol (11). Before ramp testing, the patients were given a questionnaire consisting of a list of activities presented in an increasing order according to metabolic equivalents. This questionnaire estimated the patient's exercise capacity before the test and thus allowed most patients to reach maximal exercise at approximately 10 min (12). Visual ST segment deviation was measured at the J junction and corrected for pre-exercise ST segment depression while standing; ST slope was measured over the following 60 ms and classified as upsloping, horizontal or downsloping. Slope was coded as 1 for horizontal, 2 for downsloping and 0 for normal slope (upsloping or ST segment depression < 0.5 mm). The ST response considered

was the most horizontal or downsloping ST segment depression in any lead except aVR during exercise or recovery. An abnormal response was defined as an additional one-millimeter or more of horizontal or downsloping ST segment depression.

No test was classified as indeterminate (13), medications were not withheld, and no maximal heart rate targets were applied (14). The exercise tests were performed, analyzed and reported per standard protocol utilizing a computerized database (Extra, Mosby Publishers, Chicago) (15). Decisions for cardiac catheterization were consistent with clinical practice. Analyses were performed with the investigators blinded to clinical and angiographic results.

**Computer analysis.** Microprocessor-based exercise ECG devices were used at the two sites to simultaneously record the electrocardiographic data at 500 samples/s (Mortara Electronics, Milwaukee, Wisconsin) on optical discs. Optical disc recordings were processed off-line using standard personal computers. Averaging of the raw data and determination of QRS onset and offset points were performed using software developed by Sunnyside Biomedical (Vista, California). The computer-chosen isoelectric line and QRS onset and offset points were confirmed visually for their accuracy. During the last two years of data collection at Palo Alto Health Care System, a QUEST treadmill system (Burdick, Milton, Wisconsin) was used. This system collected data on PCMCIA cards and utilized a 12-lead on-line version of the software.

**Coronary angiography.** Coronary artery narrowing was visually estimated and expressed as percent lumen diameter stenosis. Patients were considered to have significant angiographic CAD if they had a 50% narrowing in the left main coronary artery or in one or more of the following: left anterior descending, left circumflex or right coronary arteries or their major branches. The 50% criterion was chosen to be consistent with the cooperative trialists' choice (16).

**Statistical methods.** Sensitivity of the exercise treadmill test, defined as the number of patients with CAD and an abnormal exercise treadmill test divided by the total number of patients with CAD, was calculated for patients with and without resting ST segment depression. Specificity of the exercise treadmill test, defined as the number of patients without CAD and a normal exercise treadmill test divided by the total number of patients without CAD, was calculated for patients with and without resting ST segment depression. Predictive accuracy was calculated by dividing the number of true positive and true negative results by the number of true positive, false positive, true negative, and false negative results and then multiplying by 100%. Predictive accuracy and area under the curve of receiver operating characteristic (ROC) plots (using the entire range of ST segment depression for the ROC plots) were determined for patients with and without resting ST segment depression. All of the above calculations were then repeated for computerized classification of resting ST segment de-

**Table 1.** Clinical Characteristics in Patients With and Without Resting ST Segment Depression by Visual Analysis

Variable	No Resting ST Segment Depression (n = 1076)	Any Resting ST Segment Depression (n = 206)	p Value
Age (yrs)	58.3 ± 0.3	62.8 ± 0.6	< 0.0001
Body mass index (kg/m <sup>2</sup> )	28.0 ± 0.1	27.4 ± 0.3	0.09
Hypertension	556 (52%)	117 (57%)	NS
Diabetes	151 (14%)	39 (19%)	0.09
Family history of CAD	476 (44%)	76 (37%)	0.06
Smoking (current)	357 (33%)	62 (30%)	NS
Hypercholesterolemia	385 (36%)	80 (39%)	NS
Digoxin	16 (1.5%)	23 (11%)	< 0.0001
LVH	17 (1.6%)	21 (10%)	< 0.0001
Abnormal treadmill test	349 (32%)	142 (69%)	< 0.0001
CAD	619 (58%)	140 (68%)	0.005
Three-vessel disease	181 (17%)	51 (25%)	0.006

Data are presented as mean values ± standard deviation or number (percent) of subjects.  
CAD = coronary artery disease; LVH = left ventricular hypertrophy; NS = nonsignificant.

pression and compared to the results for visual classification of resting ST segment depression. A statistically significant difference between two proportions was defined as a p-value < 0.05 using the two-tailed Fischer's exact test. Statistical analysis was performed with the Number Crunching System Software™ (NCSS; Kaysville, Utah).

## RESULTS

**Population characteristics.** Of the 1,282 patients included in this study, 206 had evidence of resting ST segment depression based on visual analysis of their baseline ECG, with an average of 0.49 ± 0.02 mm, and 349 had resting ST segment depression based on computerized analysis of their baseline ECG, with an average of 0.39 ± 0.02 mm. Only 30 patients by visual analysis and 24 patients by computerized analysis had resting ST segment depression greater than one millimeter. Tables 1 and 2 compare clinical characteristics

of patients with and without resting ST segment depression based on visual or computerized classification of the resting ECG. More than twice as many patients with resting ST segment depression had abnormal exercise tests, and a significantly greater proportion of those with rest abnormalities were taking digoxin or had left ventricular hypertrophy (LVH). The presence of CAD and three-vessel disease was significantly greater in patients with resting ST segment depression.

**Sensitivity and specificity of treadmill testing.** The sensitivity of the treadmill test in patients with resting ST segment depression as determined by visual analysis of the resting ECG increased from 45 (41–49% 95% confidence limits) to 77 (69–84%) and specificity decreased from 84 (81–88%) to 48 (36–61%) when compared with patients without resting ST segment depression. In patients with resting ST segment depression as determined by comput-

**Table 2.** Clinical Characteristics in Patients With and Without Resting ST Segment Depression by Computerized Analysis

Variable	No Resting ST Segment Depression (n = 933)	Any Resting ST Segment Depression (n = 349)	p Value
Age (yrs)	57.5	63.3	< 0.0001
Body mass index (kg/m <sup>2</sup> )	28.0	27.4	0.0002
Hypertension	470 (50%)	203 (58%)	0.01
Diabetes	132 (14%)	58 (17%)	NS
Family history of CAD	416 (45%)	136 (39%)	0.08
Smoking (current)	329 (35%)	90 (26%)	0.001
Hypercholesterolemia	341 (37%)	124 (36%)	NS
Digoxin	7 (0.8%)	32 (9.2%)	< 0.0001
LVH	7 (0.8%)	31 (8.9%)	< 0.0001
Abnormal treadmill test	269 (29%)	222 (64%)	< 0.0001
CAD	519 (56%)	240 (69%)	< 0.0001
Three-vessel disease	134 (14%)	98 (28%)	< 0.0001

Data are presented as mean ± standard deviation or number (percent) of subjects.  
See Table 1 for abbreviations.

**Table 3.** Sensitivity and Specificity of the Exercise Treadmill Test Using the 1 mm ST Segment Depression Criterion

Subgroup	Sensitivity	Specificity
Visual analysis		
1.) No resting ST segment depression	45 ± 4% (278/619)	84 ± 3% (386/457)
2.) Resting ST segment depression	77 ± 7% (108/140)	48 ± 12% (32/66)
Computerized analysis		
3.) No resting ST segment depression	42 ± 4% (216/519)	87 ± 3% (361/414)
4.) Resting ST segment depression	71 ± 6% (170/240)	52 ± 11% (57/109)

P < .0001 for comparisons of sensitivity and specificity between subgroups 1 and 2 and between subgroups 3 and 4.  
 ±% = Lower and upper 95% confidence limit.  
 Numbers in parentheses are actual raw data.

erized analysis, the sensitivity of the treadmill test increased from 42 (37–46%) to 71 (65–77%) and specificity decreased from 87 (84–90%) to 52 (43–62%) when compared with those without resting ST segment depression (p < 0.0001 for all comparisons) (Table 3). In the 30 patients with more than one millimeter of resting ST segment depression by visual analysis, the sensitivity and specificity of exercise treadmill testing were 89 (65–99%) and 58 (28–85%), respectively.

Seventy-six patients with resting ST segment depression determined by visual analysis developed more than two millimeters of additional ST segment depression with exercise treadmill testing, while 120 patients with resting ST segment depression determined by computerized analysis did so. Using two millimeters of additional ST segment depression to define an abnormal exercise treadmill test, the sensitivity and specificity of the exercise treadmill test were 44 (36–53%) and 79 (67–88%), respectively, in patients with resting ST segment depression classified by visual analysis. In the group with resting ST segment depression classified by computerized analysis, the sensitivity and specificity were 43 (36–49%) and 84 (77–90%), respectively, when an additional two millimeters of ST segment depression was required for an abnormal exercise treadmill test. When these values were compared to the sensitivity and specificity of the exercise treadmill test in patients without resting ST segment depression (using one millimeter of ST segment depression to define an abnormal test) there were no significant differences (p = NS for all comparisons) (Table 4).

Sixty-six patients with resting ST segment depression classified by visual analysis developed between one and two millimeters of additional ST segment depression with exercise treadmill testing, while 102 patients with resting ST segment depression classified by computerized analysis did so. The sensitivity and specificity of exercise treadmill testing in the former group were 33 (25–41%) and 70 (59–80%), respectively, while in the later group they were 28 (23–34%) and 69 (60–78%), respectively.

**Predictive accuracy and area under the curve of ROC plots.** The predictive accuracy of the exercise treadmill test did not vary significantly between patients with and without resting ST segment depression. There was a trend suggesting that the predictive accuracy is higher in patients with resting ST segment depression as classified by visual analysis (Table 5). The area under the curve of the ROC plots was not significantly different between the four subgroups (patients with and without resting ST segment depression as classified by computerized analysis and patients with and without resting ST segment depression as classified by visual analysis) (Table 5).

**Effect of LVH or digoxin.** Although a significantly greater proportion of patients with resting ST segment depression were taking digoxin or had electrocardiographic evidence of LVH than those without resting ST segment depression, when patients on digoxin or with LVH were excluded from the data set, there was no significant difference in the results. The use of digoxin did not affect the diagnostic characteristics of the exercise treadmill test.

**Table 4.** Sensitivity and Specificity of the Exercise Treadmill Test in Patients With Resting ST Segment Depression When Using 2 mm or More of Additional ST Segment Depression to Define an Abnormal Exercise Treadmill Test

Subgroup	Sensitivity	Specificity
Resting ST segment depression		
Visual analysis	44 ± 8% (62/140)	79 ± 9% (52/66)
Computerized analysis	43 ± 6% (102/240)	84 ± 6% (91/109)

p = NS for comparison of each sensitivity and specificity with the corresponding sensitivity and specificity in patients without resting ST segment depression (using 1 mm of ST segment depression to define an abnormal test).  
 ±% = Lower and upper 95% confidence limit.  
 Numbers in parentheses represent actual raw data.  
 NS = nonsignificant.

**Table 5.** Area Under the Curve (AUC) of ROC Plots and Predictive Accuracy

Subgroup	AUC*	Predictive Accuracy
Visual analysis		
1.) No resting ST depression	0.66 ± .02	62 ± 3%†
2.) Resting ST depression	0.69 ± .04	68 ± 6%†
Computerized analysis		
3.) No resting ST depression	0.66 ± .03	62 ± 3%‡
4.) Resting ST depression	0.66 ± .02	65 ± 5%‡

\*p = NS for comparisons of AUC between all 4 subgroups. †p = 0.10 for comparison of predictive accuracy between subgroup 1 and 2. ‡p = NS for comparison of predictive accuracy between subgroup 3 and 4.

AUC = area under the curve; NS = nonsignificant; ROC = receiver operator characteristics.

## DISCUSSION

**Background.** For many years the use of exercise treadmill testing in patients with abnormal resting ECGs, in particular resting ST segment depression, has been controversial (3-7,17). Weiner *et al.* (17) evaluated the impact of resting ST segment and T wave abnormalities on results of stress testing in the Coronary Artery Surgery Study, and found that while the sensitivity did not change significantly, the specificity of stress testing was significantly lower in patients with these resting abnormalities. Indeterminate stress tests were excluded from this study, which may account for the high sensitivity of stress testing in patients without resting ECG abnormalities. On the other hand, in a meta-analysis of 150 studies of exercise treadmill testing, Detrano *et al.* (6) noted that the inclusion or exclusion of patients with resting ST segment depression did not significantly change the sensitivity and specificity of exercise testing. Miranda *et al.* (7) found that although resting ST segment depression decreased the specificity of the exercise treadmill test, the sensitivity was increased from 66% to 83%. Most recently, the prognostic capability of the Duke treadmill score was maintained in a large cohort of patients with nonspecific ST-T abnormalities on the resting ECG (18).

Based on these more recent studies, the ACC/AHA practice guidelines now list exercise treadmill testing as a Class I indication in patients with an intermediate pretest probability of CAD and less than one millimeter of resting ST segment depression (2). Despite this recommendation, however, many physicians continue to favor stress-imaging studies over exercise treadmill testing in this patient group. We evaluated the effect of resting ST segment depression on the diagnostic characteristics of the exercise test in a large cohort of patients without a prior myocardial infarction to add support to the ACC/AHA recommendations and perhaps discourage what may be unnecessary use of more expensive stress-imaging studies.

**Resting ST segment depression increases sensitivity.** We found that the sensitivity of the exercise treadmill test

significantly increased from 45% in the group without resting ST segment depression to 77% in the group with resting ST segment depression. The high sensitivity confirms that the exercise treadmill test can be used as an effective initial diagnostic test in patients with resting ST segment depression. Unfortunately, there was an equally significant decrease in specificity from 84% in patients without resting ST segment depression to 48% in those with resting ST segment depression (Table 3). The sensitivity and specificity of the exercise treadmill test changed in a similar fashion in the subgroup of patients with more than one millimeter of resting ST segment depression. However, because this subgroup is so small, we are unable to draw any firm conclusions.

Although there are significant changes in the sensitivity and specificity of the treadmill test when comparing patients with and without resting ST segment depression, the diagnostic accuracy of the test does not change significantly as demonstrated by the equal predictive accuracy and area under the curve for these two groups (Table 5). The similar ROC curves suggest that in patients with resting ST segment depression the position of the "cutoff" value for determining an abnormal treadmill test shifts to a different spot along the ROC curve. By using a higher "cutoff" value (2 mm of additional ST segment depression) in patients with resting ST segment depression, one can shift the point where the "cutoff" value is located on the ROC curve, resulting in little if any change in the sensitivity and specificity of the treadmill test between patients with and without resting ST segment depression (19) (Table 4).

The reason this shift in the position of the "cutoff" value occurs remains unclear. Our data show that more than twice as many patients with resting ST segment depression have abnormal exercise treadmill tests than do patients without ST segment depression, while only 10% more have CAD (Tables 1 and 2). This disproportionate increase in abnormal tests results in more sensitive and less specific testing characteristics, and may explain the shift in the position of the "cutoff" value on the ROC curve.

In conclusion, Tables 2 and 3 suggest that the exercise treadmill test has a high sensitivity in patients with resting ST segment depression when using the criterion of one millimeter of additional ST segment depression to define an abnormal test. Conversely, when using the criterion of two millimeters of additional ST segment depression, the exercise treadmill test has a high specificity in this population, as expected.

**Computerized versus visual analysis.** Computerized classification of resting ST segment depression tends to be more exact. This is because physicians round off and, for example, list patients with 0.1 mm of resting ST segment depression as having no ST segment depression, while the computer will not do so. Because of this difference, the impact of resting ST segment depression on the diagnostic accuracy of

the exercise treadmill test might vary depending on whether visual analysis or computerized analysis is used to classify patients with resting ST segment depression. Moreover, past studies evaluating the effect of resting ST segment depression on the sensitivity and specificity of the exercise treadmill test have not included computerized classification. Therefore, we included both computerized and visual analysis in an attempt to compare the two, as well as optimize our ability to detect any effect of resting ST segment depression on the diagnostic characteristics of the exercise treadmill test.

Computerized analysis of the baseline ECG did result in the classification of a significantly greater number of patients with resting ST segment depression than did visual analysis (349 vs. 206). This occurred because the computer is more exact in this setting. Despite this discrepancy, a similar increase in sensitivity and decrease in specificity was found when computerized analysis of the resting ECG was used to classify patients with resting ST segment depression (Table 3). Moreover, the area under the curve of ROC plots and the predictive accuracy of the exercise treadmill test were also equal between groups classified via computerized and visual analysis. In fact, there was a trend suggesting that the predictive accuracy was better when resting ST segment depression was present (Table 5). Thus, the overall diagnostic accuracy of the exercise treadmill test remains equal in all four subgroups.

**Study limitations.** Since there was no effort to eliminate work-up bias in this study, our results may be somewhat skewed. However, we and others have anecdotally noted that because more and more patients are undergoing coronary angiography irrespective of the exercise treadmill test result, the importance of eliminating work-up bias in this setting has lessened. Other major limitations include the lack of women and the retrospective design in this study.

**Conclusions.** We demonstrated in a large cohort of patients presenting with chest pain and no prior myocardial infarction that resting ST segment depression on the baseline ECG does not affect the overall diagnostic accuracy of the exercise treadmill test. In fact, the exercise treadmill test has a very high sensitivity in patients with resting ST segment depression, making it an effective initial diagnostic test, and perhaps obviating the need for many stress-imaging studies. These results were validated by both visual and computerized analysis of the resting ECG.

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