ANALYSIS METHODS TO IMPROVE THE DIAGNOSTIC POWER OF TREADMILL EXERCISE STRESS TESTING IN PATIENTS WITH SUSPECTED ANGINA PECTORIS

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ABSTRACT

To assess the ability of 3 established analysis methods in exercise stress electrocardiography to non-invasively detect the presence of coronary artery disease (CAD), 67 consecutive patients who had typical angina, positive exercise stress electrocardiography (ST segment depression ≥ 1 mm), and coronary arteriography were studied. Thirty-three patients had significant CAD, and 34 had normal coronary arteriograms. The results showed that the Treadmill Score Method, utilising both ST and non-ST segment variables, had the highest accuracy in predicting disease. The predictive power of all 3 methods was lower in females.

Keywords: *coronary artery disease, syndrome X, exercise stress electrocardiography*

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INTRODUCTION

Normal coronary arteriograms are found in about 20% of patients undergoing coronary arteriography for evaluation of chest pain[1]. Patients with typical angina pectoris, positive exercise stress electrocardiography, and angiographically normal coronary arteries have been labelled as having syndrome X[2]. In this study, we evaluated the ability of 3 different analysis methods in exercise electrocardiography to better discriminate patients with syndrome X from those with abnormal coronary arteries. They were the Treadmill Score Method, the Multivariate Method, and the ST Segment/Heart Rate Index (ST/HR Index) Method[3-7].

METHODS

The study population consisted of 67 consecutive patients who had typical angina pectoris, a positive treadmill exercise stress test (ST segment depression ≥1.0 mm), and had undergone coronary arteriography within 4 weeks of the exercise test. Thirty-three had significant CAD, and 34 were found to have normal coronary arteries.

Significant CAD was defined as the presence of at least one coronary stenosis with 50 percent or greater reduction of luminal diameter in a major epicardial coronary artery. Patients with normal or trivial (no stenosis greater than 25% diameter loss) coronary disease were categorised as having syndrome X[8-11]. None of the patients had valvular heart disease, cardiomyopathy, a previous myocardial infarction, or metabolic derangements such as hypokalemia.

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Exercise stress tests were done with anti-anginal medications withdrawn at least 3 days before the test. The standard Bruce protocol was used in every case, and the end-points used for terminating the test were progressive angina, marked dyspnea or fatigue, or ST depression of 3 mm or greater. The 12-lead electrocardiogram was monitored continuously throughout exercise, and for 6 minutes after exercise. Blood pressure was recorded every minute during and after exercise.

Selective coronary arteriograms were obtained in multiple routine and angled views using the standard Judkin's technique from the right femoral artery. The cine-angiograms were interpreted by two cardiologists.

All exercise stress test recordings and measurements were interpreted using all of the following methods of analysis: (1) the Treadmill Score Method, (2) the Multivariate Method, and (3) the ST/HR Index Method.

Treadmill Score Method

A score was given for each of the exercise variables shown in Table I. The scores obtained were then summed. A score of 7 or more was taken as indicative of the presence of CAD.

Multivariate Method

In this method, patients with 2 mm or greater ST segment depression were classified as having CAD. Patients with 1.0-1.9 mm ST segment depression were classified as having CAD if they had, in addition, 2 out of 3 of the following variables: (1) heart rate blood pressure product at peak exercise not greater than 23000 mmHg-beats/minute; (2) treadmill time less than 6 minutes, and (3) ST segment depression recovery time of 3 minutes or more.

ST/HR Index Method

The ST/HR Index was calculated by dividing the maximum ST segment depression (corrected for any pre-exercise resting ST segment deviation) at peak exercise by the exercise induced increase in heart rate. The criterion for an abnormal response indicating the presence of CAD was 0.016 mm/beat/minute or greater.

Table I - Treadmill Score Method

Exercise variables	Treadmill score
Males	
ST-T depression ≥1 mm	6
Age ≥55 years	5
Achieved heart rate <80% age-predicted maximum heart rate	9
Exercise duration <8 minutes	3
Females	
Achieved heart rate <90% age-predicted maximum heart rate	4
Exercise duration <6 minutes	3

For all methods, standard formulae for calculating sensitivity, specificity and predictive accuracy were used. A patient with CAD correctly predicted by an analytical method was considered a true positive, and a patient with syndrome X correctly predicted was considered a true negative.

Continuous data are presented as mean ± standard deviation, and analysed using the Student's t test for unpaired data. Differences between proportions were analysed with the chi square test. A p value of <0.05 was considered statistically significant.

RESULTS

The CAD group comprised 33 patients (27 male, 6 female), aged 35-78 (mean 57) years. Ten had single, 10 had double, and 13 had triple vessel disease. The syndrome X group comprised 34 patients (10 male, 24 female), aged 28-73 (mean 54) years. Table II tabulates the comparisons between the 2 groups.

Table II – Comparison of patients with CAD and syndrome X

Variables	CAD	syndrome X	p value
Age (years)	57.0 (10.6)	54.6 (11.2)	>0.50
Gender (% females)	18.2 (6/33)	70.6 (24/34)	<0.005 ••
Max ST depression (mm)	1.81 (0.59)	1.86 (0.68)	>0.50
Angina during test (%)	30.3 (10/33)	23.5 (8/34)	>0.50
Resting heart rate (beats/min)	71.6 (11.2)	76.2 (11.2)	>0.05
Resting systolic BP (mmHg)	146.3 (18.6)	142.9 (19.0)	>0.20
Peak heart rate (beats/min)	128.4 (21.0)	146.7 (16.2)	<0.01 ••
Peak systolic BP (mmHg)	187.2 (33.1)	203.5 (30.8)	<0.05 •
Peak RPP* (mmHg.bpm)	23372.7 (6279.6)	28494.1 (6615.3)	<0.01 ••
Exercise duration (min)	6.45 (2.76)	6.55 (2.00)	>0.50
ST recovery time (min)	7.51 (3.65)	5.03 (4.48)	<0.02 •

* RPP (Rate Pressure Product) is the product of the heart rate and the systolic blood pressure

• Significant (p<0.05); •• Highly Significant (p<0.01)

There were substantially more females with syndrome X, and substantially less females with CAD. Compared to those with CAD, patients with syndrome X had higher peak heart rate, peak systolic blood pressure and, consequently, higher peak RPP during exercise stress testing. Their ST segment depression recovery time was significantly shorter. Other variables were not significantly different.

There were no significant differences in sensitivity (to detect true positive) for detecting CAD between the 3 analysis methods (Table III). However, the specificities (to detect true negative, or syndrome X) of the 3 methods were considerably different, being very poor for the ST/HR Index. The Treadmill Score Method showed the highest predictive accuracy (67.2%), and correctly classified 45 of the 67 patients.

Table III – Comparison of analysis methods in exercise stress testing

Analysis methods	Sensitivity	Specificity	Predictive accuracy
Treadmill Score	81.8 (27/33)	52.9 (18/34)	67.2 (45/67)
Multivariate	78.8 (26/33)	38.3 (13/34)	58.2 (39/67)
ST/HR Index	81.8 (27/33)	5.9• (2/34)	43.3•• (29/67)
ST depression ≥1.0 mm*	100.0 (33/33)	0.0 (0/34)	49.3 (33/67)

* Applicable only for this study cohort and reflects study criteria

• p<0.005 (with Treadmill Score and Multivariate methods),

••p<0.01 (with Treadmill Score method)

Table IV – Differences in of predictive accuracy of the three methods by gender

Analysis method	Males	Females	p value
Treadmill Score	70.3	63.3	>0.50
Multivariate	70.3	43.3	<0.05•
ST/HR Index	59.5	23.3	<0.005••

DISCUSSION

Treadmill exercise stress testing, utilising only electrocardiographic and blood pressure monitoring, is a widely used non-invasive diagnostic technique for identifying patients with probable CAD, but suffers from limited sensitivity and specificity especially in females. In a usual treadmill population, the approximate sensitivity and specificity are 80-85% and 60-65% respectively.

In our study, all 67 patients had an "abnormal" treadmill by the standard criterion of ST segment depression of at least 1.0 mm, and all underwent coronary arteriography. Other standard clinical and electrocardiographic observations, such as provoked angina or maximal ST segment depression, did not distinguish patients with CAD from those with normal coronary arteries.

To improve on the performance of standard diagnostic criteria, we studied the value of 3 analysis methods that used the information obtained during routine exercise testing. The Treadmill Score Method had a sensitivity of 81.8% and a specificity of 52.9%. These percentages are not strictly comparable to those in the general treadmill population, as they represent the sensitivity and specificity in a treadmill population subset all of whom had at least 1.0 mm ST segment depression. The sensitivity and specificity of the other 2 analysis methods were inferior to those of the Treadmill Score Method.

If the Treadmill Score Method had been used to decide whether coronary arteriography should have been performed in those with simply 1.0 mm ST segment depression or more. it would have missed 18.2% of those who had CAD, but would have avoided coronary arteriography in 52.9% of those who had normal coronary arteries. The ST/HR Index would have missed the same number of CAD patients, but would have avoided coronary arteriography in only 5.9% of those with normal coronary arteries.

Using the analysis methods resulted in an improvement in predictive accuracy over the standard criterion for abnormality (ST depression ⩾1.0 mm) when the Treadmill Score or Multivariate methods were used. Quite surprisingly, the predictive accuracy of the ST/HR Index was lower than standard ST criteria which do not relate to ST changes to heart rate.

The improved accuracy of the Treadmill Score Method may be due to its inclusion of non-electrocardiographic criteria such as age, exercise duration and peak heart rate. By contrast, the other two methods which relied more heavily on ST segment changes were less predictive.

Patients with syndrome X are preponderantly female[12, 13]. The precise reasons for this are unclear. One likely explanation is that the prevalence of CAD in the female population is lower, and the predictive accuracy of any test is impaired when the disease prevalence is low. Others have speculated on the role of estrogens or a lower haematocrit in females[14].

Although syndrome X patients have, by definition, normal coronary arteries, it is by no means certain that they are normal. The chest pain may be due to pathophysiologic mechanisms other than stenosis of angiographically visible coronary vessels[15]. Some have speculated on the presence of microvascular coronary disease (involving vessels smaller than 200 microns in diameter), and others have shown that diastolic dysfunction is present in syndrome X.

The failure of the ST/HR Index in our study group to distinguish those with CAD from those with normal coronary arteries, rather than being a negative finding, provides some positive evidence that patients with syndrome X are not entirely normal. It has been shown that the ST/HR Index in CAD and syndrome X patients are similar, but different from the ST/HR Index in normal patients without chest pain[11,16].

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