EXERCISE TOLERANCE TEST: A COMPARISON BETWEEN TRUE POSITIVE AND FALSE POSITIVE TEST RESULTS

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Background: To study the factors which predetermine the coronary artery disease in patients having positive Exercise Tolerance Test (ETT) after comparing the ETT test results and coronary angiographic findings in true positive and false positive groups. **Methods:** This Cross-sectional study was conducted at Punjab Institute of Cardiology, Lahore from January 1, 2004 to December 31, 2004. All patients who had ETT done for chest pain diagnosis were studied. Patients were advised coronary angiography if ETT was positive for exercise induced ischaemia. One hundred and forty eight patients had coronary angiography done after positive ETT. Patients were divided into two groups depending upon the angiographic findings, i.e., true positive and false positive. Both groups were compared with each other. **Results:** Out of 148 patients, 126 (85.1%) patients had true positive ETT and 22 (14.9%) patients had false positive ETT. The mean age of patients in true positive group was 48.96±9.08 years and 50.9±7.85 years in false positive group. One hundred and eighteen (93.7%) male patients and 8 (6.3%) female patients had true positive ETT, whereas 14 (63.6%) males and 8 (36.4%) females had false positive ETT (p<0.0001). There was no statistically significant difference in the two groups in comparison of age and other conventional risk factors like diabetes mellitus, hypertension, smoking, family history and dyslipidemia. Abnormal resting ECG had a statistically significant difference between the groups (p<0.04), likewise is hypertensive haemodynamic response during ETT (p<0.003). The symptom limited ETT as compared to no symptoms during ETT also conferred a statistically significant difference between the groups (p<0.0001). Strongly positive ETT was also associated with true positive ETT (p<0.002). Amongst the vessels involved the most common was the LAD 113 (89.7%), followed by LCX 80 (63.5%) and the RCA 72 (57.1%). Most of the patients 51 (40.5%) had three vessel disease as compared to SVD 34 (27%). **Conclusion:** It can be concluded that amongst the patients who have positive ETT, females with abnormal resting ECG, who achieve target heart rate and have a hypertensive haemodynamic response with no symptoms are likely to have a false positive test result. Conversely male patients with normal resting ECG who do not achieve target heart rate, have a normotensive haemodynamic response and a strongly positive, symptom limited ETT are likely to have a true positive treadmill test result.

Keywords: Exercise tolerance test, Coronary artery disease, Coronary angiography, true positive, false positive.

INTRODUCTION

Exercise induced changes in electrocardiogram (ECG) have been used to identify coronary artery disease (CAD) for almost a century. It was Einthoven[1] in 1908 who documented changes in ST segment of ECG with exercise. It was not until 1932 that Goldhammer and Scherf[1] proposed exercise electrocardiography as a diagnostic tool for angina. Since then Exercise tolerance test (ETT) has played a central role in the diagnostic workup of CAD.

The sensitivity and specificity of ETT varies considerably. Gianrossi *et al*[2] investigated the diagnostic accuracy of ETT through a meta analysis including 147 published reports involving 24,074 patients who underwent both coronary angiography and ETT. There was a wide variability in sensitivity and specificity of ETT [sensitivity 68±16% (range 23–100%); specificity 77±17% (range: 17–100%)]. Another Meta analysis[3] showed sensitivity of 81±12% (range: 40–100%) and specificity of 66±16% (range: 17–100%). The ETT is still the least costly of all other non- invasive tests currently available. We can always improve the accuracy of treadmill test by applying various scoring systems or algorithms and eliminating the factors which can cause false positive test results.

In Pakistan, ETT has been studied previously for the diagnosis of coronary artery disease.[4,5] This study was conducted to study the factors which can predetermine the coronary artery disease in patients having positive ETT after comparing the ETT results and coronary angiographic findings in true positive and false positive groups.

MATERIALS AND METHODS

This cross-sectional study was conducted at Punjab Institute of Cardiology Lahore from January 1, 2004 till December 31, 2004. During this period all patients with positive ETT undergoing coronary angiography were included in the study.

All patient with known CAD (past history of Myocardial infarction, Angioplasty, coronary artery bypass surgery) were excluded. Similarly patients with valvular or congenital heart disease, patients with resting ECG abnormalities like left bundle branch block or Wolf Parkinson White (WPW) syndrome were excluded. Patients with borderline or inconclusive test result were also excluded from the study.

All patients underwent symptoms limited treadmill testing according to Bruce protocol. The drugs like beta blockers, Calcium channel blockers and nitrates were stopped a day before the test.

A relatively flat or depressed ST segment ≥0.1 mV 80 mSec after the J point (ST 80) in three consecutive beats in any lead except avR during exercise or recovery was considered to be an abnormal response. At a heart rate of ≥130 beats/min ST 60 measurement was used. In case of ST segment elevation, 0.1 mV (1 mm) or greater J point elevation 60 mSec after the J point in three consecutive beats with a stable baseline was considered to be an abnormal response.[6] The test results were reported as negative for ischemia (normal) or positive for exercise induced ischemia (abnormal). The positive test results were further classified into positive and strongly positive depending upon the following.[6] Duration of symptom-limiting exercise <5 Mets. Failure to increase systolic blood pressure ≥120 mm Hg, or a sustained decrease ≥10 mm Hg, or below rest levels during progressive exercise. ST segment depression ≥2 mm, downsloping ST segment, starting at less than 5 mets involving ≥5 leads, persisting ≥5 minutes into recovery. ST segment elevation, avR excluded. Angina pectoris at low exercise workload. Reproducible sustained (>30 sec) or symptomatic ventricular tachycardia.

After informed consent all patients who had positive ETT were included in the study and advised coronary angiography. Significant CAD was defined as luminal narrowing of 50% or more in any coronary artery with reference diameter of at least 1 mm.[7]

The study population was divided into true positive and false positive groups. Patients who had coronary artery disease proven on coronary angiography were taken as true positive while patients having normal or mild coronary artery disease were taken as false positive.

Baseline clinical characteristics, exercise tolerance test and angiographic data was entered prospectively into the pre-designed proforma, subsequently the data was entered into the computer.

The results were analysed by using SPSS (Statistical Package for Social Sciences) version 12 for windows. Descriptive statistics were generated with percentages for discrete variables and means and standard deviations for continuous variables. Categorical variables were analysed by using Chi Square test while continuous variables were analysed by using student's *t*-test. A *p* value of <0.05 was considered significant.

RESULTS

During the study period a total of 522 patients presenting with chest pain diagnosis had positive ETT. All patients were advised to undergo coronary angiography. Only 148 patients [132 (89.2%) males and 16 (10.8%) females] had coronary angiography done and were included in the study while the rest of patients were excluded from the study.

The mean age of study population was 49.25±8.91 years. Mean age of true positive group was 48.96±9.08 years while it was 50.9±7.85 years in false positive group (Table-1). Out of 148 patients, 126 (85.1%) patients had coronary artery disease, i.e., true positive, while 22 (14.9%) patients had normal or mild CAD, i.e., false positive. In the true positive group there were 118 (93.7%) males and 8 (6.3%) females, whereas 14 (63.6%) male patients and 8 (36.4%) female patients were in false positive group. More female patients were present in the false positive group as compared to true positive group (p<0.0001).

The conventional risk factors like diabetes mellitus, smoking, hypertension, dyslipidemia and family history of CAD had non-significant difference between the groups (Table-1).

Table-1: Epidemiological characteristics of the study population

Characteristics	True positive n=126	False positive n=22	*p* value
Age mean	48.96±9.08	50.9±7.85	0.217
Male **Female**	118 (93.7%) 8 (6.3%)	14 (63.6%) 8 (36.4%)	<0.0001
Diabetes Mellitus	34 (27%)	3 (13.6%)	<0.142
Smoking	37 (29.4%)	3 (13.6%)	<0.097
Hypertension	51 (40.5%)	12 (54.5%)	<0.159
Dyslipidemia	16 (12.7%)	3 (13.6%)	<0.564
Family History	58 (46%)	9 (40.9%)	<0.418

The baseline ECG was normal in 119 (94.4%) patients and abnormal in 7 (5.6%) in true positive group, whereas resting ECG was normal in 18 (81.8%) patients and abnormal in 4 (18.2%) patients in false positive group (p<0.04) (Table-2).

In true positive group 13 patients (10.31%) achieved their target heart rate, while 6 (27.27%) patients in false positive group achieved their target heart rate in false positive group (p<0.04) (Table-2). Normotensive response was observed more frequently 120 (95.2%) patients in true positive group as compared to false positive group while hypertensive response was more frequently observed 6 (27.3%) patients in false positive group (p<0.003).

The percentage of target heart rate achieved, mets achieved and exercise time had non-significant difference between the two groups (Table-2). Chest pain was most frequently observed 91 (72.2%) in true positive group while no symptoms occurred in 14 (63.6%) patients in false positive group (p<0.0001). Strongly positive ETT result was noted in 44 patients (34.9%) in true positive group as compared to 1 (4.5%) patient in false positive group (p<0.002), (Table-2)

Table-2: Exercise test comparison between true positive and false positive

Characteristics	True positive n=126	False positive n=22	*p* value
Resting ECG			
Normal	119 (94.4%)	18 (81.8%)	<0.04
Abnormal	7 (5.6%)	4 (18.2%)	
Target Heart rate achieved	13 (10.31%)	6 (27.27%)	<0.04
Percentage of target heart rate achieved	84.23±13.21	93.04±9.9	0.865
Mets achieved	7.56±2.69	8.7±2.44	0.968
Exercise time	5.74 ±2.69	6.93±1.99	0.12
Haemodynamic response	120 (95.2%)	16 (72.7%)	<0.003
Normotensive	6 (4.8%)	6 (27.3%)	
Hypertensive			
Symptoms			
None	16 (12.7%)	14 (63.6%)	<0.0001
Chest pain	91 (72.2%)	7 (31.8%)	
Shortness of Breath	19 (15.1%)	1 (4.5%)	
ECG changes			
ST depression	122 (97.7%)	22 (100%)	<0.637
ST elevation	1 (0.8%)	0	
None	3 (2.4%)	0	
Complications			
None	123 (97.6%)	22 (100%)	<0.698
Yes (MI, VT)	3 (2.4%)	0	
ETT results			
Positive	82 (65.1%)	21 (95.5%)	<0.002
Strongly positive	44 (34.9%)	1 (4.5%)	<0.002

Coronary angiography revealed that 34 (27%) patients had single vessel disease, 41 (32.5%) patients had two vessel disease and 51 (40.5%) had three vessel disease. The individual vessels involved included Left main stem 10 (8%), Left anterior descending (LAD) 113 (89.7%), Left circumflex (LCX) 80 (63.5%), Ramus Intermedius (RI) 4 (3.2%) and right Coronary artery (RCA) 72 (57%). Left ventricular angiogram showed a higher ejection fraction (EF) 62.7%±5.5% in false positive group as compared to the true positive group 56.04±8.39 (p<0.04), (Table-3).

One patient had ST-segment elevation Myocardial infarction and two patients had non-sustained ventricular tachycardia all in the true positive group. There was no death during the procedure.

Table-3: Angiographic findings

Characteristics	True positive n=126	False positive n=22	*p* value
Number of diseased vessels			<0.0001
None	0	22 (100%)	
Single	34 (27%)	0	
Two	41 (32.5%)	0	
Three	51 (40.5%)	0	
Individual vessel			
LMS	10 (8%)	0	<0.213
LAD	113 (89.7%)	0	<0.0001
LCx	80 (63.5%)	0	<0.0001
RI	4 (3.2%)	0	<0.684
RCA	72 (57.1%)	0	<0.0001
Ejection Fraction	56.04 ±8.39	62.7 ±5.5	<0.04

DISCUSSION

Exercise tolerance test has played a central role in the diagnostic workup of CAD for almost a century. But because of the limited sensitivity and specificity of the test, other expensive investigations are being increasingly used. The ETT is still the least costly of all other non-invasive tests currently available. The diagnostic accuracy of the treadmill test can be improved by identifying the factors which can cause false positive test results.

In this study one year data of patients undergoing ETT for chest pain diagnosis followed by coronary angiography if test result turned out to be positive has been presented.

The current study showed a higher percentage of false positive results among females with a significant gender difference between the two groups (p<0.0001). This finding is consistent with other studies which showed low specificity of ST segment depression on treadmill test in women compared with men.[8,9] Many investigators have attempted to improve the diagnostic accuracy of treadmill testing in women by creating new variables such as ST/Heart rate slope, computer generated algorithms and gender specific guidelines for interpretation.[10-12] Other investigators have suggested that initial testing strategies in women should be stress imaging rather than treadmill testing.[13-16] But the Duke Treadmill Score improves the diagnostic accuracy of ETT in women.[17]

It was noticed that changes in the resting ECG like ST-segment depression or T wave inversion also affect the test result. On comparison of abnormal resting ECG with normal resting ECG in the two groups, the difference was statistically significant (p<0.04). William et al have shown in their study that the specificity of the ETT decreases with resting ST-segment depression (48±12% versus 84±3%),[18] because of inclusion of more false positive test results

Sever systemic hypertension may interfere with the subendocardial perfusion and may lead to ST-segment depression even in the absence of atherosclerosis, thus resulting in false positive test results. The current study also showed a significant statistical difference in hypertensive haemodynamic response in the two groups ($p<0.003$).

In the current study chest pain was observed more frequently in the true positive group and a symptom limited ETT showed a significant difference between the groups ($p<0.0001$). Exercise induced chest discomfort without associated ECG changes may be the only signal that obstructive coronary artery disease is present.[6] Early onset of angina is an important parameter of adverse prognosis.

Strongly positive ETT was more commonly noted in the true positive group, this has been reported by other studies as well.[19-22] Fletcher et al have reported that the patients who have strongly positive ETT show adverse prognosis and a multi vessel coronary artery disease.[19-22] In patients with single vessel disease the sensitivity of ETT is 25–71%, whereas it is 81% in patients with multivessel CAD.[21] It was also observed that the most frequent coronary artery involved was LAD followed by RCA and than LCx. This has been reported previously by other investigators as well.[6]

This study had few limitations, i.e., the Study population was very small. Out of 522 only 148 patients underwent coronary angiography, because coronary angiography is an invasive procedure and the patients who were not symptomatic could not be compelled to go for the test.

CONCLUSIONS

It can be concluded that amongst the patients who have positive ETT, females with abnormal resting ECG, who achieve target heart rate and have a hypertensive haemodynamic response with no symptoms are likely to have a false positive test result. Conversely male patients with normal resting ECG who do not achieve target heart rate, have a normotensive haemodynamic response and a strongly positive, symptom limited ETT are likely to have a true positive treadmill test result.

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