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Angiographic Evaluation of ETT (Treadmill) Positive Patients in a Tertiary Care Hospital of Bangladesh

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Abstract**—**To evaluate the factors which predetermine the coronary artery disease in patients having positive Exercise Tolerance Test (ETT) that is treadmill results and coronary artery findings. This descriptive study was conducted at Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh from 1st January, 2014 to 31st August, 2014. All patients who had done ETT (treadmill) for chest pain diagnosis were studied. One hundred and four patients underwent coronary angiogram after positive treadmill result. Patients were divided into two groups depending upon the angiographic findings, i.e. true positive and false positive. Positive treadmill test patients who have coronary artery involvement these are called true positive and who have no involvement they are called false positive group. Both groups were compared with each other. Out of 104 patients, 81 (77.9%) patients had true positive ETT and 23 (22.1%) patients had false positive ETT. The mean age of patients in positive ETT was 53.46± 8.06 years and male mean age was 53.63±8.36 years and female was 52.87±7.0 years. Sixty nine (85.19%) male patients and twelve (14.81%) female patients had true positive ETT, whereas 15 (65.21%) males and 8 (34.79%) females had false positive ETT, this was statistically significant ($p<0.032$) in the two groups (sex) in comparison of true and false positive ETT. The risk factors of these patients like diabetes mellitus, hypertension, dyslipidemia, family history and smoking were seen among these patients. Hypertensive patients having true positive which were statistically significant ($p<0.004$) and diabetic, dyslipidemic patients having true positive which were statistically significant ($p<0.032$ & 0.030).True positive patients had family history were 68(83.95%) and smoking were 52 (64.20%), where family history patients had statistically significant ($p<0.017$) between two groups of patients and smokers were significant ($p<0.012$). 46 true positive patients achieved THR which was not statistically significant ($P<0.138$) and 79 true patients had abnormal resting ECG whether it was significant ($p<0.036$). Amongst the vessels involvement the most common was LAD 55 (67.90 %) followed by LCX 42 (51.85%), RCA 36 (44.44%), and the LMCA was 9 (11.11%). 40 patients (49.38%) had SVD, 26 (30.10%) had DVD, 15(18.52%) had TVD and 23 had normal coronary arteries. It can be concluded that among the female patients who have positive ETT with normal resting ECG, who had achieved target heart rate are likely to have a false positive test result. Conversely male patients, resting abnormal ECG who had not achieved THR, symptom limited ETT, have a hypertension, diabetes, dyslipidemia, family history and smoking are likely to have a true positive treadmill test result.

Keywords**—**Exercise tolerance test, Coronary artery disease, Coronary angiography, True positive, False positive.

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I. Introduction

EXERCISE TREADMILL TEST (ETT) is one of the used means in evaluation of coronary artery disease (CAD). Since the first medical treadmill designed to diagnose heart and lung disease was invented by Dr. Robert Bruce and Wayne Quinton at the University of Washington in 1952, it became the golden criteria in diagnosing CAD till coronary angiography (CAG) came out. However, it is still a very easy and comprehensive way in diagnosis of CAD. The position of ETT is going down these years by its high false positive and negative rates [1]. People are looking for more parameters that ETT can provide to increase its accuracy rate, like ST/HR slope, Duke treadmill score, QT dispersion and so on [2]-[5]. ST-segment depression and chest pain as the classic criteria for CAD diagnosis are well known and accepted. However, each has their own limitations. ST-segment depression is often modified by some other factors, like blood pressure, cigarette smoking, serum cholesterol level etc [6]. The sensitivity and specificity of ETT varies considerably. Gianrossi et al. [24] 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 showed sensitivity of 81± 12% (range: 40–100%) and specificity of 66± 16% (range: 17–100%) **[**3]. 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. Chest pain is a subjective complaint which maybe obscured by patients own feelings. Based on what mentioned above, the false positive and negative data is inevitable. Interestingly, we found that chest pain, which is considered subjective, seems more reliable than the objective one, ST-segment depression. The usefulness of ETT in male patients is much greater than that in female ones**.**

II. Materials and Methods

This cross-sectional study was conducted at invasive lab of department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh from January 1, 2014 to August 31, 2014. During this period all patients with positive ETT undergoing coronary angiography were included in the study. All patients with known CAD (history of STEMI, PCI, coronary artery bypass surgery(CABG) were excluded. Similarly patients with Aortic Stenosis or congenital heart

disease, patients with resting ECG abnormalities like left bundle branch block (LBBB) or Wolf Parkinson White (WPW) syndrome were excluded. After testing, a structured history and medical review were obtained to document symptoms, medical history, medication use, cardiac risk factors, and previous cardiac events and procedures. A questionnaire was designed to record patient's identification, weight, height, history of hypertension, diabetes, dyslipidemia, smoking, and chronic kidney disease. The questionnaire was filled after exercise testing. Patients were instructed to perform 12-lead-ECG exercise tolerance test according to the Bruce & Modified Bruce protocol. Hemodynamic, ECG and symptoms were recorded before and during each step of the test, and during recovery period. The 12-lead-ECG was recorded at rest, in each stage of the test, and after the test every minute up to five minute. After test completion, test result was assessed by a trained cardiologist. According to ETT interpretation, patients were categorized into negative or positive ETT but we included only positive treadmill result patients group. The classic criteria for positive stress test were used [J-point and ST80 (defined as the point that is 80ms from the J point) depression of 0.1 mV (1 mm) or more and/or an ST-segment slope within the range of ± 1 mV/s in 3 consecutive beats]. Patients with positive ETT results were advised to undergo coronary angiogram. After informed consent all patients who had positive ETT were included in the study and advised coronary angiogram. Significant CAD was defined as luminal narrowing of 50% or more in any coronary artery with reference diameter of at least 1mm [8]. Angiographic studies were performed in the catheterization laboratory of Ibrahim Cardiac Hospital & Research Institute by the attending cardiologist. The procedure was done using modified Seldinger technique through the femoral or radial artery by Judkins catheters using Iodixanol contrast. Variables in questionnaire and results of ETT and angiographic findings were entered in SPSS version 16 for windows statistical software and analyzed. Descriptive statistics were generated with percentages for discrete variables and means and standard deviations for continuous variables. Categorical variables were analyzed by using Chi Square test while continuous variables were analyzed by using student's *t*-test. A *p* value of <0.05 was considered significant. 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.

III. Results

During the study period a total of 104 patients presenting with chest pain diagnosis had positive ETT. All patients were advised to undergo coronary angiography. Out of 104 patients 80 (76.92%) males and 24 (23.08%) females had coronary angiography done and which were included in this study. The mean age of study population was 53.46±8.06 years. Mean age of male was 53.63±8.36 years and female was 52.87±7.0 years. Out of 80 true positive group male was 69 (85.19%) and female was 12 (14.81%). Out of 104 patients, 81 (77.88%) patients had coronary artery disease, i.e. true positive, while 23 (22.12%) patients had normal i.e. false positive.

In the true positive group there were 65 (80.24%) males and 16 (19.76%) females, whereas 15 (65.22%) male patients and 8 (34.78%) female patients were in false positive group. Female patients were present in the false positive group as compared to true positive group (p<0.131). The risk factors like hypertension, dyslipidemia had significant difference and diabetes, smoking history with family history were also statistically significant in true positive group (Table I).

TABLE I
Epidemiological Characteristics of the Population Study

Characteristics	True Positive (n=81)	False Positive (n=23)	p value
Mean age (53.46±8.06)			
Male	69(85.19%)	15(65.21%)	0.032
Female	12(14.81%)	8(34.79%)	
Diabetes Mellitus	61(75.31%)	12(52.17%)	0.032
Hypertension	66(81.48%)	12(52.17%)	0.004
Dyslipidemia	64(79.01%)	13(56.52%)	0.030
Smoking	52(64.20%)	8(34.78%)	0.012
Family History	68(83.95%)	14(60.87%)	0.017

Hypertensive patient was observed more frequently 66 (81.48%) in true positive group as compared to false positive group while hypertension was more frequently observed 12 (52.17%) patients in false positive group (p<0.004). Diabetic patients had true positive which were statistically significant (p<0.032). True positive patients had dyslipidemia, present family history and smoking were 64(79.01%), 52(83.95%) and 52 (64.20%), where dyslipidemia patients had statistically significant (p<0.030) between two groups of patients and Family history, smokers were significant (p<0.017,p<0.012). Out of 104 patients 55.77% patient's BMI range was 18.5-24.9, 38.46% had 25.0-29.9 and 5.7% had 30.0-34.9 (Fig. 1).

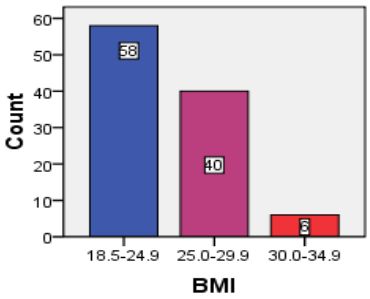

Fig. 1 Distribution of pts in different BMI range

TABLE II
Echocardiographic Characteristics between True and False Positive

Characteristics	True Positive (n=81)	False Positive (n=23)	p value
Diastolic dysfunction (DD)	39(48.15%)	4(17.39%)	0.008

All patients had no regional wall motion abnormality with good LV function. In case of diastolic dysfunction true positive 39 (48.15%) had DD and 4 (17.39%) false positive had DD and is statistically significant (p<0.008) (Table II).

TABLE III
EXERCISE TEST COMPARISON BETWEEN TRUE POSITIVE AND FALSE POSITIVE

Characteristics	True Positive (n=81)	False Positive (n=23)	p value
Resting ECG			
Normal	2(2.46%)	3(13.04%)	0.036
Abnormal	79(97.54%)	20(86.96%)	
Target Heart Rate achieved	46(56.79%)	17(73.91%)	0.138
Symptom during ETT	40(49.38%)	4(17.39%)	0.006
ECG change during recovery phase	59(72.83%)	21(91.30%)	0.024
Both (Symptom & ECG change during ETT)	40(48.38%)	3(13.04%)	0.002
METs achieved			
1-6.9	20(24.69%)	0	
7.0-10.0	42(51.85%)	15(65.22%)	0.028
10.10-12.0	19(23.46%)	8(34.78%)	

The baseline ECG was normal in 2 (2.46%) patients and abnormal in 79 (97.54%) in true positive group, whereas resting ECG was normal in 3(13.04%) patients and abnormal in 20 (86.96%) patients in false positive group (p<0.036). In true positive group 46 patients (56.79%) achieved their target heart rate, while 17 (73.91%) patients in false positive group achieved their target heart rate in false positive group (p<0.138) (Table III).

Other parameters like symptom occurred during ETT, ECG change during recovery phase of ETT and both symptom and ECG change during test of true positive are 40 (49.38%), 59 (72.83%), 40 (48.15%) and false positive pts. are 4 (17.39%), 21 (91.30%), 3 (13.04%) which was statistically significant (p<0.006, p<0.024 and p<0.002) .

TABLE IV
ANGIOGRAPHIC FINDINGS

Characteristics	True Positive (n=81)	False Positive (n=23)	p value
Individual vessel			
Left main(LM)	9(11.11%)	0	0.094
LAD	55(67.90%)	0	0.000
LCx	42(51.85%)	0	0.000
RCA	36(44.44%)	0	0.000
Number of diseased vessels			
Normal	0	23(100%)	0.000
SVD	40(49.38%)	0	
DVD	26(30.10%)	0	
TVD	15(18.52%)	0	

TABLE V
RECOMMENDATION AFTER CAG

Characteristics	True Positive (n=81)	False Positive (n=23)	p value
PCI	38(46.91%)	0	0.000
CABG	24(29.63%)	0	
Medical Management	19(23.46%)	0	
Primary Prevention	0	23(100%)	

Coronary angiography revealed that 40 (38.5%) patients had single vessel disease, 26 (25.0%) patients had double vessel disease and 15 (14.4%) had triple vessel disease (Table IV). The individual vessels involved included Left main stem 9 (8.7%), Left anterior descending (LAD) 55 (52.9%), Left circumflex (LCX) 42 (40.4%), and right Coronary artery (RCA) 36 (34.6%) (Table II). Out of 81 true positive patients 38 (46.91%) had recommended for PCI, 24 (29.63%) had recommended for CABG and 19 (23.46%) had recommended for medical management (Table V). There was no death during the procedure.

IV. 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 eight months data of patients undergoing ETT for chest pain diagnosis followed by coronary angiogram 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<0.032). This finding is consistent with other studies which showed low specificity of ST segment depression on treadmill test in women compared with men [9], [10]. 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 [11]-[13]. Other investigators have suggested that initial testing strategies in women should be stress imaging rather than treadmill testing [14]-[17] .But the Duke Treadmill Score improves the diagnostic accuracy of ETT in women [18]. 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<0.036). 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%) because of inclusion of more false positive test results [19]. Hypertension may interfere with the sub endocardial 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, diabetic, dyslipidaemia, present family history and smoker patients are in the two groups (p<0.004, p<0.032, p<0.030 ,p<0.017 and p<0.012). In the current study chest pain was observed frequently in the true positive group and a symptom limited ETT showed a significant difference between the groups (p<0.006). Exercise induced chest discomfort without associated ECG changes may be the only signal that obstructive coronary artery disease is present [7]. In recovery phase of tread mill test our study showed ECG change were statistically significant (p<0.024) between the two groups. 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 show adverse

prognosis and a multi vessel coronary artery disease [20]-[23]. In patients with single vessel disease the sensitivity of ETT is 25–71%, whereas it is 81% in patients with multivessel CAD [21]. In our study we found SVD are 49.38%, DVD are 30.10%, TVD are 18.52 and 23 cases are normal. It was also observed that the most frequent coronary artery involved was LAD followed by LCx and than RCA. This has been reported previously by other investigators as well [7]. This study had few limitations, i.e. the Study population was only 104 patients underwent coronary angiogram, because coronary angiogram is an invasive procedure and the patients who were not symptomatic or STEMI or NSTEMI or UA could not be compelled to go for the test.

V. Conclusions

It can be concluded that amongst the patients who have positive ETT, female patients with normal resting ECG, who achieve target heart rate (THR) are likely to have a false positive test result. Conversely male patients with abnormal resting ECG, both symptomatic & ECG change during treadmill test and ECG change during recovery period with risk factors like hypertension, diabetes, dyslipidemia, family history and smokers are likely to have a true positive treadmill test result.

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