

# Relying on ST Segment Depression alone to Predict Ischemic Heart Disease- How Far We can Go ?

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## Abstract:

**Introduction:** Ischemic heart disease (IHD) or coronary artery disease (CAD) has become predominant cause of death across the world and frequently stable angina, which is the most common presentation of this disease, gives hard time to reach a proper diagnosis due to duality of non-invasive testing. While Exercise Treadmill Test (ETT) is an inexpensive non-invasive modality which may have many output depending on method of interpretation, ST segment depression is much utilized but traditionally less perfect than available treadmill scores. We have compared its accuracy to Duke Treadmill Score (DTS), Simple Treadmill Score (STS) and Cleveland Clinic Score (CCS) among Bangladesh people to generate a local insight. **Objective:** To estimate and compare accuracy of ST segment response, DTS, Simple Treadmill Score and Cleveland Clinic Score to predict CAD. **Method:** In a cross-sectional study total 130 patients who had visited at a medical university with stable chest pain were selected according to predefined inclusion and exclusion criteria over one year. After taking proper history and physical examination their ETT report and Coronary Angiogram (CAG) finding, which were done according to indication defined by their consultants. ETT interpretation as ST segment response and treadmill scores were compared with gold standard test for CAD that is CAG. Accuracy of ST-depression and treadmill scores were calculated by the formula "Accuracy = TP+TN / Total Sample". **Result:** Among the total sample (n=130) male and female were 93 & 37, respectively. Nearly half of male sample fell into 5<sup>th</sup> decade and around same portion of female sample was in 4<sup>th</sup> decade. About 58%, 28% & 14% patients came with typical, atypical & non-cardiac chest pain. As calculated with above mentioned formula accuracy of ST segment response alone to diagnose IHD came about 68.4% (p value 0.004). Similarly DTS, STS and CCS had 83.3%, 83.9% and 77.2% accuracy, respectively (p value 0.000). **Conclusion:** During ETT relying on ST segment depression alone to diagnose CAD is significantly less accurate than treadmill scores namely, Duke Treadmill Score, Simple treadmill Score or Cleveland Clinic Score. Applying any of these treadmill scores during exercise test interpretation can identify ischemic heart disease patients with more accuracy.

**Key Words:** Exercise Treadmill Test, ST segment response, Duke Treadmill Score, Simple Treadmill Score, Cleveland Clinic Score, Treadmill Scores.

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## Introduction:

Ischemic heart disease or Coronary Artery Disease (CAD) is ahead of other illnesses that causes death worldwide.<sup>1</sup> Acute Coronary Syndrome (ACS) in the form of myocardial infarction as well as Unstable Angina (UA), and chronic clinical condition like Stable Ischemic Heart Disease (SIHD) or Chronic Stable Angina (CSA), all are included under the term Coronary Artery Disease (CAD). Stable chest pain is often the forerunner among other CAD presentations before a massive and dreadful one such as ST Elevated Myocardial Infarction (STEMI), Non-ST Elevated MI (NSTEMI) or UA takes place.

In this days of industrialization where lack of physical activities and stressful daily life, food adulteration and increased consumption of oily fast food have put the cardiovascular health at stake. Nonetheless, in recent days CAD has become an alarming health problem among Asian countries, leading to an increased burden of treatment cost and disability. CAD is the leading cause of mortality in Bangladesh as well. Like other South Asian ethnicity, Bangladeshi's are unduly prone to develop CAD, which is often premature in onset as well as involves multiple coronary arteries. As vast majority of our country people are economically broke and not under government

provided proper health service for cardiovascular health, we should rely on non-invasive tests to diagnose ischemic heart problems to meet the cost.

Among the large number of noninvasive stress testing modalities are currently available for CAD, the exercise ECG is still used as a standard diagnostic and prognostic test as it is the least expensive provocative test and less time consuming to do and produce a report. Exercise treadmill test remains a leading test for diagnosing coronary artery disease (CAD) in patients with chest pain and at intermediate risk for CAD.<sup>2</sup> In 2012 a study done on Mongolian ethnicity by Mao et al. have shown majority of male patients could be detected to have CAD by ETT, the accuracy rate was 70.2% while putting the Coronary Angiogram (CAG) as gold standard, which was much higher than that (50.0%) of the female patients ( $p < 0.05$ ). In this study ST changes alone was used to demonstrate ETT positivity.<sup>3</sup> But the sensitivity and specificity of ETT varies considerably. Meta-analysis conducted by Gianrossi et al. (1989) shows there is a wide variability in sensitivity and specificity of ETT [sensitivity  $68 \pm 16\%$  (range 23–100%); specificity  $77 \pm 17\%$  (range: 17–100%)]<sup>4</sup> so is true for accuracy of ST segment response alone to diagnose CAD.

Subsequently Fearon WF et al revealed sensitivity and specificity of ETT is higher when treadmill scores are applied in comparison to ST response alone. They used a consensus score and found predictive accuracy of the consensus score and Duke Treadmill Score (DTS) 80 (74–86)% and 71 (65–77)% ( $p < 0.0001$ ), respectively.<sup>5</sup> Also previously Shaw et al showed DTS which is a treadmill score to predict CAD has better predictability than the ST response alone.<sup>6</sup> Another treadmill score namely, Simple Treadmill Score (STS) has increased accuracy of treadmill test in male and female population separately, which is also more than another treadmill score DTS in some studies (Raxwal et al. 2001 & Morise et al. 2002).<sup>7,8</sup> Cleveland Clinic Score is a prognostic score that was developed by Lauer et al. in 2007 to predict the survivability of patients presenting with stable chest pain is devised to in our study to its predictability to diagnose CAD.<sup>9</sup>

In 2014 Taimur, Khan and Islam evaluated ETT (Treadmill) Positive Patients in a Tertiary Care Hospital of Bangladesh by doing angiogram subsequently. They found the overall positive predictive value of ETT is 77.9%, and for male patient PPV is 86.25% and for female patient it is 50%.<sup>10</sup> Earlier in 2004 Debnath et al. conducted a study to predict the coronary arterial disease by exercise treadmill scoring system (Simple Treadmill Score) and to see the correlation

of angiographic extent of coronary artery disease by high treadmill score in Bangladesh. They concluded, “Approximately 70% of the significant stenosis was predicted as having high probability of 30.8% as intermediate probability and none as low probability with exercise test scores. Multi-vessel coronary artery disease were predicted by high probability exercise test score 82.8%.”<sup>11</sup>

Henceforth, we need a more clear insight into the accuracy of ST segment response and different treadmill scores, namely Duke Treadmill Score, Simple Treadmill Score and Cleveland Clinic Score, so that we can draw conclusion about the need of treadmill scores along with ST segment response to increase the predictability of ETT and thereby utilize this test as a success to diagnose CAD.

### Research Question

How do different treadmill scores vary in comparison to ST segment response alone to predict probability of Coronary Artery Disease?

### Objectives

To estimate and compare accuracy of ST segment response, DTS, Simple Treadmill Score and Cleveland Clinic Score to predict CAD.

### Materials and Methods:

A cross-sectional study was done among patients whose age was between 30–69 years presented with stable chest pain at a Medical University and had undergone ETT according to Bruce protocol. Duration of interval between ETT and CAG was arbitrarily held 6 months.<sup>5,12</sup> After all available previous medical documents were checked meticulously, detailed and thorough clinical assessment was done and recorded. Patients with previous history of myocardial infarction (MI), previous revascularization, already a diagnosed case of CAD were excluded from the study to prevent the falsely elevated accuracy of ETT. Patient with baseline abnormalities that may obscure electrocardiographic changes during exercise e.g., Left bundle branch block or Right bundle branch block, Left ventricular hypertrophy with repolarization abnormality, Digitalis therapy, Ventricular paced rhythm, Wolf-Perkinson-White syndrome, ST abnormality associated with supraventricular tachycardia or atrial fibrillation were excluded. Proper informed written consent was taken from the patient.

ST-segment deviation was measured at the J junction visually. ST slope was measured over the following 80 ms and will be classified as horizontal, down sloping and up

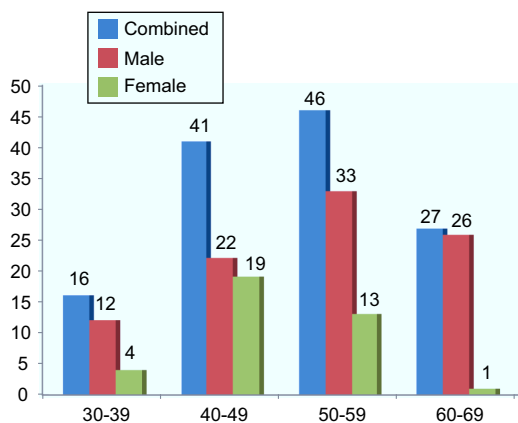
sloping. Slope was coded as 1 horizontal, down sloping, or upsloping ST depression and 0 for normal slope (up sloping <2 mm or ST-segment depression of <0.5 mm). The ST response was considered which has the most horizontal, down sloping or up sloping ST-segment depression in any lead, except aVR, during exercise or recovery. An abnormal response was defined as ≥1 mm of horizontal or downsloping or ≥2 mm up sloping ST-segment depression.<sup>13</sup> The exercise tests were analyzed, and reported per standard protocol and manual calculation.

Coronary artery stenosis was visually estimated in two orthogonal views by interventional cardiologist expressed as percent lumen diameter stenosis. Patients with a 70% narrowing in one or more of the following is considered to have significant angiographic coronary artery disease: the left anterior descending (LAD), left circumflex (LCX), right coronary arteries (RCA) or their major branches, or a 50% narrowing in the left main coronary artery (LMCA).<sup>14</sup>

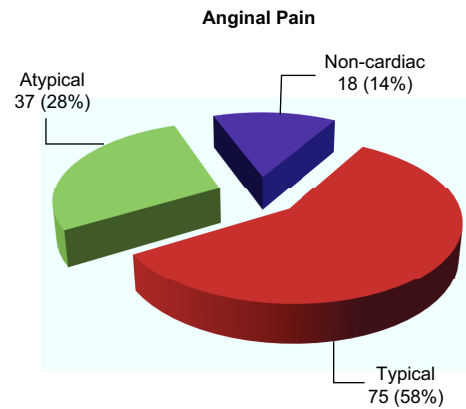
The predictive accuracies of the ST segment response, DTS, Simple Treadmill Score and Cleveland Clinic Score to stratify patients into high or low likelihood for CAD were calculated using the formula “Accuracy = TP +TN / Total Sample” and compared. Statistical analysis was performed with the SPSS version 21 and Medcal statistical software.

**Result:**

Among total sample (n=130) mean age was 50 ± 9 years, whereas mean age among female population (47 ± 7 years) is slightly lower than male population (51 ± 9 years). Near about half of the total sample fell in 5<sup>th</sup> decade according to age group. On the contrary, more than half of females were in 4<sup>th</sup> decade of their age. There was only one elderly female (>60 years) came for ETT compared to 26 male [Fig I]. 75 (57.7%) of total sample presented with typical angina [Fig II], rest of them has atypical and non-cardiac chest pain.



**Fig.-1:** Number of sample according to age group.



**Fig.-2:** Character of Anginal Pain among total sample.

Sensitivity & specificity of ST segment response to diagnose CAD in combined sample revealed high sensitivity (86.9%) & low specificity (34.7%). Almost similar sensitivity and specificity (88.5% & 34.2%, respectively) found in male sample. In both of the above cases chi-square test was significant. Sensitivity and specificity of ST segment response were 78.5% & 34.7%, respectively in female sample which was not statistically significant. (Table I). When calculated from true negative and true positive values, over all accuracy of ETT comes 68.4%.

When calculated by similar manners DTS, STS and CCS had 83.3%, 83.9% and 77.2% accuracy, respectively). Chi-square test shows this result is highly significant (p value 0.000) (Table II). This is worth mentioning from the table II we can see maximum of the patients having low probability in DTS, STS and CCS had no coronary artery disease. At the same time most of the individuals having high probability score had significant (≥70% stenosis) coronary artery disease.

**Table-I**  
Accuracy of ETT ST segment response to diagnose CAD.

Gender	Sensitivity	Specificity	P value	Accuracy = TP +TN / Total Sample
Combined	86.9%	34.7%	0.004	(73+16/ 130)
Male	88.5%	34.2%	0.015	=68.4%
Female	78.5%	34.7%	0.389	

ETT- Exercise Treadmill Test; CAD- Coronary Artery Disease.

**Table-II**  
*Likelihood of CAD among different ETT scores.*

ETT scores	Risk/Probability	CAD		P value	Accuracy (TP+TN/ Total Cases) taking Low and High Probability
		Absent	Present		
DTS	Low	1	0	0.000	83.3%
	Intermediate	35	35		
	High	10	49		
STS	Low	17	3	0.000	83.9%
	Intermediate	19	30		
	High	10	51		
CCS	Low	28	14	0.000	77.2%
	Intermediate	12	30		
	High	6	40		

CAD- Coronary Artery Disease; CCS- Cleveland Clinic Score; DTS- Duke Treadmill Test; ETT- Exercise Treadmill Test; STS- Simple Treadmill Test.

### Discussion:

Exercise Treadmill Test is an important diagnostic and prognostic indicator test for evaluation of chest pain among patients who come with stable features. At the same time it is used for prognostic evaluation of chest pain after unstable medical condition e.g. Non-ST acute coronary syndrome (NSTEMI) and ST elevated MI (STEMI). For decades it has been providing valuable information regarding diagnosis of ischemic heart disease. Though ETT is not a gold standard test to diagnose coronary artery disease, its implication in clinical medicine makes it a near-routine investigation. By exercise test we can diagnose CAD as well as can get idea of patient's functional capacity. Its low cost and non-invasive nature makes it a recommended test in patients with intermediate and high pretest probability.<sup>12</sup>

During our cross-sectional study we have sampled one hundred thirty patients attending at a University Hospital in Bangladesh for evaluation of chest pain where all of them had their ETT done recent days or within 6 months by Bruce protocol.

Among 130 individuals male to female ratio was 2.5: 1. Average age of female patients fell in 4<sup>th</sup> decade (mean age 47±7 years), where age of male sample on average was 51±9 years. The mean age of combined sample population was 50±9 years, which differs significantly from the population who undergo ETT in North America (mean age 59.1±0.3).<sup>5</sup>

A study, conducted by Taimur et al (2004) at a tertiary care hospital in Bangladesh, showed mean age of total and male sample (53.46 ± 8 & 53.63 ± 8.36 years, respectively) which is comparable to our study.<sup>10</sup> But mean age of female

sample was 52 ± 7 years which is a bit higher than our female sample. However this low age among female in our study and their positive menstrual history would have changed the coronary angiogram findings.<sup>15</sup>

According to Islam & Majumder (2013) the mean age of people diagnosed as having ischemic heart disease (IHD) in Bangladesh is lower than other developed country as it is true in other South Asian countries.<sup>16</sup> In 2017 Banerjee et al. showed mean age of people with ischemic heart disease in rural community is 46 ± 16 years (Banerjee et al. 2017).<sup>17</sup>

Maximum of the patients in our study presented with typical angina (57.7%) though Zaman and colleagues (2008) found atypical chest pain is more common among female and South Asian patients in comparison to white patients.<sup>18</sup> Again atypical symptom was not predominantly present in our female study population. Typical, atypical & non-cardiac chest pain were equally distributed among female sample. But as our female sample was small (37 women) this finding may not be significant.

Male patients with typical anginal pain was more common (67% presented with typical angina) which is more than both white and South Asian male (51.5% & 40.7%, respectively). Zaman et al. found this finding among South Asian and white people with recent onset chest pain at 6 chest pain clinics in the United Kingdom.<sup>18</sup>

Our study shows more than two third (75%) of male patients who presented with chest pain had significant (≥70% stenosis) coronary artery disease. On the contrary only 37% of female had significant lesion in coronary angiogram. Thus in comparison to female, male patients



presenting with chest pain has high likelihood of coronary artery disease ( $p < 0.001$ ). This finding is consistent with other studies. As Banerjee et al. discussed in their 2017 study prevalence of CAD in male patients is higher than female (6% and 3.5%, respectively).<sup>17</sup>

As general convention sensitivity & specificity of ETT is lower among female patients which was explained by Kohli & Gulati.<sup>15</sup> Probably, the female patients, who presented with chest pain and underwent ETT, had younger age (mean  $47 \pm 7$ ) in our study, due to this reason significant coronary artery lesions were found less among female sample.

We have found that ST segment response to determine sensitivity & specificity of ETT to diagnose CAD revealed high sensitivity (86.9%) & low specificity (34.7%). But this finding may be due to workup bias as most of the patients (103 total) came with positive stress test, while only 27 patients out of 130 individuals had negative/ equivocal findings.

In the year 1989 Gianrossi et al. underwent a meta-analysis to find out diagnostic accuracy of ETT which showed a wide variability in sensitivity [  $68 \pm 16\%$  (rang 23-100%)] & specificity [  $71 \pm 17\%$  (range 17-100%)] when conducted without abolishing workup bias.<sup>4</sup> Kwok et al., in 1999, showed another Meta-analysis of ETT in women, where sensitivity (61%) & specificity (71%) are comparable to male population.<sup>19</sup> We have found sensitivity of ETT in male & female 88.5% Vs 78.5% respectively. Sensitivity of ETT in female population would have more towards male sample's sensitivity in our population, if more aged females were selected by pretest probability for coronary angiogram. According to the equation "Accuracy =  $\frac{TP + TN}{\text{Total sample}}$ ", we could calculate the accuracy of ETT by ST segment response alone and for combined sample this accuracy was 68.4%.

We have analyzed the accuracy of treadmill scores such as DTS, STS and Cleveland Clinic Score (CCS) in a similar fashion. It was found DTS, STS & CCS have 83.3%, 83.9% & 77.2% accuracy when it was calculated from low and high probability scores and CAG findings as shown in table II. Fearon et al. found DTS had 71% predictive accuracy when calculated similarly. So DTS may have higher predictability in our Bangladeshi population.<sup>5</sup> Debnath et al. (2011) also found similar accuracy in our population.<sup>11</sup>

On the contrary if we use the another equation "Accuracy = (sensitivity) x prevalence + (Specificity) (1- prevalence)" in our male population where average CAD prevalence is 6% accuracy of STS among male will be  $[88 \times 0.06 + 96 \times (1 - 0.06)] \times 95\%$ .

In our study accuracy of STS is 83% which is less than what Raxwal et al. predicted. Interestingly this sensitivity & specificity of STS by Raxwal et al. were calculated only for men.<sup>7</sup> We calculated the STS accuracy in combined (both male and female) population.

In 2002 Morise et al. developed a separate STS for women which had increasing predictability as the score goes up.<sup>8</sup> They even showed 100% accurate predictability of CAD when STS for women score is  $>70$ . Debnath et al. (2011) found 70% of high probability in STS patients had significant CAD. They concluded STS has more predictive accuracy than DTS.<sup>11</sup>

In our study more people were in intermediate probability DTS than STS. That means we may need another tool when DTS of a patient falls in intermediate risk/probability. STS has superiority over DTS in this regard though we have found similar accuracy taking only low and high probability population/ sample.

CCS has been less accurate (77%) than DTS and STS when we calculated it from low and high probability score; though its accuracy is more than ST segment response. We have arbitrarily used 80 as a cut off between low & intermediate, and 100 as a cut off between intermediate & high probability. This prognostic score need to be validated further by other study to confirm its diagnostic accuracy.

In summary, we have found ST segment response alone to label a patient having provokable ischemia is less accurate than other treadmill scores and we may utilize this exercise treadmill test in such matter with more predictability if we use or add one of the treadmill scores to during exercise test.

### Conclusion:

Exercise Treadmill Test (ETT) is a well- accepted non-invasive tool for prediction of coronary artery disease especially among patients with stable chest pain. It can provide useful information to the clinicians if the test is adequate. Using scoring system in ETT interpretation along with ST segment response increases the predictive accuracy of coronary artery disease. On the other hand using only ST segment depression to identify myocardial ischemia is visibly less accurate than Duke Treadmill Score, Simple Treadmill Score or Cleveland Clinic Score.

### Recommendation:

All patients should be categorized according to pretest probability before ETT as it may change the sensitivity and specificity of this test.

**Conflict of Interest:** There is no conflict of interest needs to be disclosed.

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