

SIGNIFICANCE OF CHEST PAIN WITHOUT ST CHANGES DURING EXERCISE TREADMILL TESTING

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Background: Exercise treadmill test is interpreted as positive or negative for ischemia in the presence or absence of ST depression respectively. This study was conducted to evaluate the diagnostic value of chest pain without ST depression during exercise treadmill test. **Methods:** A total of 180 patients who had abnormal exercise treadmill test result and subsequently underwent coronary angiography were studied. Patients were categorized as having ST depression and angina (group A), only ST depression (group B) and only angina (group C). Coronary angiograms of all patients were assessed and compared. **Results:** Out of 180 patients [159 (88.3%) men and 21 (11.7%) women], 84 patients were in Group A, 64 in Group B and 32 in Group C. Characteristics like age, sex distribution and risk factors were similar in three groups. Significant coronary artery disease was seen in 77 (91.7%), 40 (62.5%) and in 25 (78.1%) patients in groups A, B and C respectively ($p=0.02$). Triple vessel disease was seen in 21 (25%), 11 (17.2%) and 5 (15.6%) patients in groups A, B and C respectively. Significant disease of left anterior descending artery was seen in 61 (72.6%), 26 (40.6%) and 23 (71.9%) in groups A, B and C respectively ($p=0.001$). **Conclusion:** Occurrence of both ST depression and angina during exercise treadmill test has strong association with angiographic coronary artery disease whereas occurrence of either of the two has similar association with angiographic coronary artery disease with a trend towards more disease in the latter.

Keywords: Exercise treadmill test, Angina, Coronary angiography, Coronary artery disease

INTRODUCTION

Non invasive diagnostic tests are an important link between detection and appropriate management of coronary artery disease.¹ Among these, exercise treadmill testing (ETT) is a widely available and relatively cheaper test² and hence used as a gateway to other diagnostic modalities like nuclear imaging, echocardiography, or coronary angiography³. The 2002 guidelines from American college of Cardiology/American Heart Association state exercise tolerance test a useful initial diagnostic test in patients with an intermediate (25%–75%) pretest probability of coronary artery disease.^{4,5} The concept of exercise induced ECG changes (ST response) is about a century old.⁶ While interpreting exercise tolerance test, ST response is still the main focus of interest: ST segment depression (STD) ≥ 1 mm signifying a positive test result. Using this criterion there is a wide variability of diagnostic accuracy of exercise treadmill test in various studies. A meta-analysis of 147 consecutive reports involving 24,045 patients who underwent exercise treadmill test and coronary angiography revealed a mean sensitivity of 68% (23–100 \pm 17) and a mean specificity of 77% (17–100 \pm 17).⁷ Hence the criterion of ST depression is not robust and its absence does not imply absence of significant coronary artery disease. Other parameters need to be considered while interpreting an exercise treadmill test result. These include chest pain, workload, haemodynamic response and

arrhythmias. Out of these parameters, chest pain consistent with angina is particularly important.⁷ Predictive value of chest pain associated with STD is well studied and well established. There is little data on the significance of chest pain without STD during exercise treadmill test. We conducted this study to assess the diagnostic value of typical anginal pain without STD by correlating exercise treadmill test results with coronary angiography results.

MATERIAL AND METHODS

This cross sectional comparative study was conducted at Punjab Institute of Cardiology, Lahore from November 1, 2005 to December 31, 2006. Non-probability purposive technique was employed for sampling. All patients who developed STD with or without angina and those who developed angina without STD were offered coronary angiography. Patients who subsequently underwent coronary angiography were included in study population. All patients with borderline positive (0.5–0.9 mm STD), sub-maximal negative (no STD and target heart rate achieved between 70 and 85%) and inconclusive (no STD and target heart rate achieved below 70%) ETT results were excluded. Patients with known coronary artery disease (prior myocardial infarction, coronary intervention or coronary artery bypass grafting) were also excluded. Exercise treadmill test was performed according to standard Bruce Protocol. Drugs with negative chronotropic effect like beta blockers and

calcium channel blockers were stopped 24 hours before the test. Exercise ECG tracings were visually assessed for significant STD (≥ 1.0 mm depression measured 0.08 seconds after J point). If such ST change was found in three consecutive beats in any lead other than aVR during exercise or recovery phase, the result was labelled as positive for ischemia. In addition, presence or absence of angina during exercise treadmill test was specifically noted. The patients were categorized into three groups: Group-A= patients having both STD and angina, Group-B= patients having STD without angina, Group-C= patients having angina without STD. Coronary angiograms of these patients were visually assessed for severe ($\geq 75\%$) stenosis in all vessels with reference diameter of at least 01 mm. Less than 75% non-flow limiting narrowing or minor luminal irregularities were considered non-significant for the purpose of statistical analysis. Angiographic results were categorised with respect to number of vessels having severe stenosis as single vessel disease (1-VD), two vessel disease (2-VD), three vessel disease (3-VD), left main stem (LMS) disease, LMS + single vessel disease, LMS + two vessel disease and LMS + three vessel disease. Involvement of individual vessels was also recorded as the most proximal segment having significant disease. Coronary angiographic data of patients in three groups were compared. Baseline personal and clinical data like age, sex, risk factors for coronary artery disease were also recorded for statistical analysis.

The data was entered and analysed using SPSS-10.0. Mean \pm SD is given for quantitative variables. Frequencies and percentages are given for qualitative variables. Two independent sample *t*-test was applied to observe group mean differences. Pearson Chi Square test was applied to observe associations between qualitative variables. A *p*-value ≤ 0.05 was considered statistically significant.

RESULTS

Exercise treadmill test and coronary angiographic data were obtained for 180 patients [159 (88.3%) men and 21 (11.7%) women]. Out of these, 84 (46.7%) patients had both STD and angina (Group A), 64 (35.5%) patients had STD without angina (Group B) and 32 (17.8%) patients had definite angina without STD during exercise (Group C). Baseline characteristics like age, sex distribution and risk factor profile were similar in three groups (Table-1). Mean age of study population was 50.11 \pm 9 years. Mean ages of patients with STD and angina, STD only and angina only were 49.54 \pm 9.6, 50.7 \pm 8.7 and 50.37 \pm 8.2 respectively. Coronary angiographic data revealed significant coronary artery disease in 77 patients (91.7%) in group-A, 40 patients (62.5%) in group-B and 25 patients (78.1%) in group-C. Triple vessel disease was

seen in 21 (25%), 11 (17.2%) and 5 (15.6%) patients in groups-A, B and C respectively. Left main stem disease was detected in 4 (4.8%) and 1 (3.1%) patients in group-A and group-C respectively (Table-2). On the basis of most proximal segment involvement, disease of individual vessels is presented in Table-3. Significant disease of LAD was seen in 61 (72.6%) patients in group-A, 26 (40.6%) in group-B and 23 (71.9%) in group-C. Ostial/proximal LAD disease was found maximally in group-A, i.e., 42% versus 10.9% in group-B and 18.8% in group-C. Mid/distal LAD and branch vessel disease was more frequent in group-C. Left circumflex artery disease was detected in 39 (46.4%) patients in group-A, 21 (32.8%) patients in group-B and 12 (37.5%) patients in group-C. Ostial/proximal left circumflex artery disease was almost similar in three groups whereas group A patients were more likely to have disease in OMI. Group-C patients were more likely to have disease in all segments as compared to group-B. Right coronary artery was significantly diseased in 46 (54.8%) patients in group-A, 21 (32.8%) in group-B and 9 (28.1%) in group-C. In the study population, 29 (16%) patients had trifurcating LMS and ramus intermedius was diseased similarly in three groups. One patient from group B had myocardial bridging of mid LAD with no other flow limiting lesion.

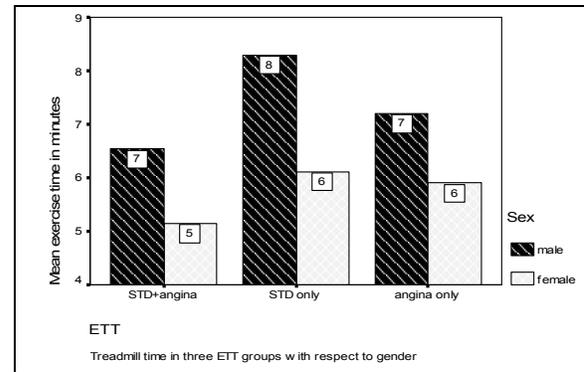


Figure-1: Treadmill time in three groups on the basis of gender

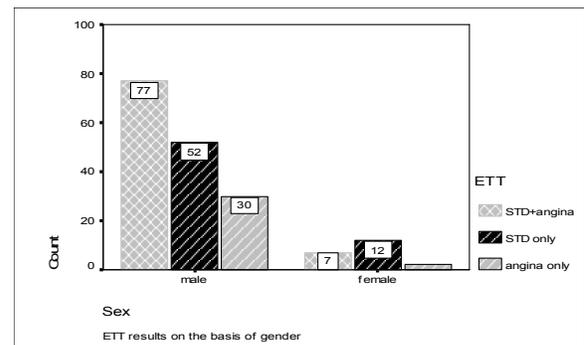


Figure-2: Pattern of ETT results in males and females

Table-1: Baseline Characteristics of Patients

Parameters	Group-A (n=84)	Group-B (n=64)	Group-C (n=32)	p value
AGE (Years)±SD	49.54± 9.6	50.7±8.7	50.37±8.2	0.72
Median	49.5	50	49	
Gender n (%)				
Male	77 (91.7)	52 (81.3)	30 (93.8)	0.08
Female	7 (8.3)	12 (18.8)	2 (6.37)	
RISK FACTORS n (%)				
Smoking	24 (28.6)	14 (21.9)	12 (37.5)	0.27
Diabetes Mellitus	13 (15.5)	17 (26.6)	6 (18.8)	0.24
Hypertension	32 (38.1)	21 (33.3)	7 (21.9)	0.25
Family History	29 (34.5)	22 (34.4)	10 (31.3)	0.94
Hyperlipidemia	6 (7.1)	3 (4.7)	0	0.29
FUNCTIONAL CAPACITY n (%)				
Good (Treadmill time ≥10 min.)	11 (13.1)	18 (28.1)	5 (15.6)	0.047
Moderate (Treadmill time 6–9 min.)	40 (47.6)	31 (48.4)	20 (62.5)	
Poor (Treadmill time <6 min.)	33 (39.3)	15 (23.4)	7 (21.9)	
TREADMILL TIME (minutes): Mean±SD	6.42±2.5	7.89±2.47	7.12±2.1	0.002

Group-A= Patients having both STD and angina, Group-B=Patients having STD without angina , Group-C=Patients having angina without STD.

Table-2: Angiographic findings (number of diseased vessels) of patients.

No of vessels		Group A n=84	Group B n=64	Group C n=32	p-value
Significant CAD n (%)	Totals	77 (91.7)	40 (62.5)	25 (78.1)	0.02
	1VD	18 (21.4)	13 (20.3)	9 (28.1)	
	2VD	29 (34.5)	12 (18.8)	8 (25)	
	3VD	21 (25)	11 (17.2)	5 (15.6)	
	LMS	4 (4.8)	0	1 (3.1)	

Group A=Patients having both STD and angina, Group B=Patients having STD without angina, Group C=Patients having angina without STD, CAD-coronary artery disease, 1VD- single vessel disease, 2VD- two vessel disease, 3VD- three vessel disease, LMS- left main stem.

Table-3: Significantly diseased most proximal segment of individual vessels in three groups.

Diseased vessel	Diseased segment	Group A n=84	Group B n=64	Group C n=32	P Value
Left anterior descending artery	Total	61(72.6)	26(40.6)	23(71.9)	0.001
	Ostial/prox.	35(41.7)	7(10.9)	6(18.8)	
	Mid	20(23.8)	14(21.9)	12(37.5)	
	Distal	1(1.2)	1(1.6)	1(3.1)	
	D1	4(4.8)	4(6.3)	3(9.4)	
	D2	1(1.2)	0	0	
left circumflex artery	Total	39(46.4)	21(32.8)	12(37.5)	0.15
	Ostial/prox.	10(11.9)	6(9.4)	4(12.5)	
	Mid	15(17.9)	5(7.8)	6(18.8)	
	Distal	1(1.2)	0	1(3.1)	
	OM 1	10(11.9)	3(4.7)	1(3.1)	
	OM 2	1(1.2)	6(9.4)	0	
RI n(%) n =29	Total	2/8(25)	2/10(20)	2/11(18.2)	0.64
	Ostial/prox	2(25)	1(10)	2(18.2)	
	Mid /Distal	0	1(10)	0	
Right coronary artery	Total	46(54.8)	21(32.8)	9(28.1)	0.32
	Ostial/prox.	16(19)	9(14.1)	5(15.6)	
	Mid	18(21.4)	6(9.4)	3(9.4)	
	Distal	4(4.8)	2(3.1)	0	
	PDA	5(6)	2(3.1)	1(3.1)	
	PLV	2(2.4)	2(3.1)	0	

Group-A=Patients having both STD and angina, Group-B=Patients having STD without angina, Group-C=Patients having angina without STD, LAD- left anterior descending artery, LCx- left circumflex artery, RI- intermediate artery, RCA- right coronary artery, ostial/ prox.- Ostial and proximal segment, D1- 1st diagonal branches, D2- 2nd diagonal branch, OM1- 1st obtuse marginal branch, OM2- 2nd obtuse marginal branch, AV Circ.- atrioventricular circumflex branch, PDA- posterior descending artery, PLV- posterolateral ventricular branch.

DISCUSSION

This single centre observational study demonstrates that patients who develop both STD and angina during exercise treadmill test are most likely to have

significant obstructive coronary artery disease whereas patients who develop only STD or only angina during exercise treadmill test have similar likelihood for coronary artery disease. Significant

coronary artery disease was found with decreasing frequency in groups A, C, and B in that order proving that group-C (angina only) is worse than group-B (STD only). Left anterior descending artery disease was seen more frequently in group A and C as compared with group-B (72.6% and 71.9% versus 40.6%, $p=0.001$). The same is true for ostial and proximal LAD disease. This shows that absence of angina during exercise treadmill test makes LAD disease less likely, or LAD disease is more likely to induce angina on treadmill.

Exercise treadmill test was more frequently 'true positive' in patients having chest pain during the test in a previous study.⁸ In fact stress induced chest pain may be the only indication of presence of obstructive coronary artery disease in some patients.⁹ The diagnostic value of stress induced chest discomfort is also evident from Duke Treadmill Score of which it is an important component; the other two components being exercise time and ST deviation.⁹ Out of these three parameters, exercise angina is the most important one for predicting severity of coronary artery disease according to some investigators. A study of 114 patients aiming to see the potential of Duke Treadmill Score in prioritising patients for coronary angiography revealed that there were no significant differences among medium risk patients regarding the severity of coronary artery disease in exercise time or ST deviation. The presence of limiting exercise angina, however, was significantly more related with severity of coronary artery disease in this group of patients.¹⁰ An important observation was that none of the patients in group B had left main stem disease as compared to one such patient in group C. This again suggests that only angina is a stronger predictor of coronary artery disease than only STD.

In the current study, treadmill time was minimum in group A patients and maximum in group B patients (6.42 ± 2.5 Vs 7.89 ± 2.47 , p -value 0.002) (Figure-1). Moreover patients with exercise time ≥ 10 minutes were maximum in group-B whereas patients with exercise time 6–9 minutes or < 6 minutes were maximum in groups-C and A respectively. Thus our 'angina only' group had lesser exercise time as compared to 'STD' only group. Chest pain and reduced exercise capacity on treadmill have been shown to predict poor prognosis in terms of increase myocardial infarction, unstable angina, coronary revascularization and all cause mortality.¹¹ This is consistent with observation in a previous study, though with non significant ' p '.⁸

Women are underrepresented in our study and this is due to many possible reasons. There is a general trend in society for not treating and investigating the female gender as often as male¹² and

even after abnormal exercise treadmill test result, the trend is unfavourable for women to undergo coronary angiography¹³. The common perception that exercise treadmill test has poor predictive value for coronary artery disease in women is another reason for bias referral and small number of women.^{14,15} We noted that female patients were more likely to have isolated STD; 12 (57.1%) women in group-B versus 7 (33.3%) and 2 (9.5%) in groups-A and C respectively, though p is not significant (0.085) (Figure-2). Women are known to have false positive exercise stress test results more often.⁸ Furthermore, lack of chest pain during exercise treadmill test has been shown to have a higher negative predictive value especially in younger women.¹⁵ Stress induced non ischemic STD in female patients is partially explained by digitalis like effects of estrogens¹⁶, inappropriate catecholamine release during exercise, a high prevalence of mitral valve prolapse and underlying repolarisation abnormalities, a lower prevalence of obstructive multivessel disease and a different chest wall anatomy^{14,17}. This has led to 'stress echocardiography' being preferred as the initial diagnostic test in women by many cardiologists.¹⁸ However, a careful and thorough evaluation of stress induced symptoms is particularly helpful in detection of ischemia in women and can improve the accuracy of exercise treadmill testing.^{14,19} Patients with hypertension and diabetes mellitus are also more likely to have false positive exercise treadmill test.²⁰ In our study, diabetes mellitus was more frequent in group B, though statistically not significant. Sharieff and Zaman²¹ reported that most ischemic patients were asymptomatic during exercise treadmill test which is contrary to the impression generated by the present study. This contradiction is explained by the fact that the referred study did not include angiographic data and patients were supposed to have ischemic heart disease in presence of abnormal exercise stress test results. This, however, is consistent with the larger size of group B than group C in our study. Small size of group C is a limitation of the present study and is mainly due to smaller number of patients having isolated angina and less likelihood of these patients for undergoing coronary angiography as there is a misconception in medical profession that STD is essential for a positive test being referred for coronary angiography.

There is conflicting data regarding the prognostic significance of an abnormal exercise treadmill test result with or without angina. In the CASS data bank, patients with silent or symptomatic exercise-induced myocardial ischemia were stratified by coronary anatomy and left ventricular function and 7-year survival was found to be similar, the worst

survival being in patients with the most extensive coronary artery disease.⁹ A recently published population based study of middle aged Finnish men, without overt coronary artery disease, revealed that asymptomatic STD during exercise treadmill test was associated with increased risk of sudden cardiac death; hazard ratio 2.1.²² The other view is that the evidence base for an exaggerated concern with silent ischemia is scant and patients with silent ischemia (painless STD) usually have milder forms of coronary disease and a better prognosis.²³ This diversity of opinion is most likely a feature of patient selection in different studies.

It is well established that standard 12 lead electrocardiogram has limited sensitivity in diagnosis of acute myocardial infarction. Partially this is due to some anatomical segments of myocardium not being represented by electrical activity recorded from precordial area. It is possible that some of our 'angina only' patients are with ischemia in LCx territory or right ventricle. We found that LCx disease occurred with marginally higher frequency in group C as compared to group B. Left circumflex disease, in particular, is known to be associated with false negative exercise treadmill test.²⁴ Another possibility is that some of our group C patients exhibited the rare phenomenon of ST normalisation whereby ischemic STD and ST elevation cancel each other.³ Moreover, some of our group B patients might have micro vascular ischemia which is a well known cause of exercise induced STD in patients with angina and normal coronaries.²⁵

There is lack of consensus over categorisation of luminal stenoses in defining significant coronary angiographic disease. Some investigators^{8,26} have used 50% luminal stenosis as the cut point while others differ. To solve this issue, Lipinski *et al*²⁷ analysed exercise treadmill test and angiographic data of 1276 consecutive patients to calculate the number of patients that would be considered to have coronary artery disease at different cut points between 40–100% for angiographic luminal stenosis. They concluded that 75% or greater coronary luminal stenosis was the most appropriate for defining significant angiographic disease when evaluating diagnostic tests of ischemia. We also used 75% or greater luminal stenosis as the cut point for defining significant angiographic disease.

CONCLUSION

It can be concluded that occurrence of both STD and angina during exercise stress test has strong association with angiographic coronary artery disease and occurrence of either STD alone or angina alone has similar association with angiographic coronary

artery disease with a trend towards more disease in the latter. Hence, due importance should be given to angina without STD during exercise treadmill test for deciding further management strategy.

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testing and the risk of sudden cardiac death in middle-aged

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