



CLINICAL AND ANGIOGRAPHIC CORRELATION OF 'RECOVERY ONLY' VS 'DURING STRESS' ST SEGMENT DEPRESSION IN TREDMILL TEST.

Cardiology

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ABSTRACT

Background: Treadmill test is the most widely used test for diagnosis of coronary artery disease (CAD). Exercise-induced ST segment depression is a reliable ECG finding for the diagnosis of obstructive CAD.² However, 12–16% of patient with suspected or documented CAD have ST segment depression only during recovery phase of exercise test.^{6,7} Although the diagnostic and prognostic power of exercise induced ST segment depression has been well characterized, the significance of ST segment depression limited to the recovery phase of an exercise stress test is poorly understood.^{8–10} In the present study, we aim to assess the diagnostic value of recovery-only ST segment depression in exercise stress testing by comparing the clinical and angiographic profiles of patients with 'recovery only' vs. 'during exercise' ST segment depression on exercise stress testing.

Methods and Result: The study was done in the Department of cardiology, R.N.T. Medical college and M.B. Hospital, Udaipur. A total of 240 patients, 208 TMT stress positive and 32 TMT recovery positive, (mean age 55.12 ± 9.16 years) willing to undergo coronary angiography were included during in this study. There was significant difference in TMT stress positive and recovery positive patients in having TVD and or LMCA disease ($p=0.034$). Patients with TMT recovery positive are more likely have TVD and or LMCA disease. No such difference is observed among patients having SVD, DVD or isolated LMCA disease.

Conclusion: We found the similar diagnostic value for both 'during exercise' and 'recovery only' ST segment depressions and even more severe CAD in those having recovery positive TMT as compared to stress positive TMT. So the 'recovery only' ST segment depressions may be one of the high risk feature on TMT for significant coronary disease and patients should be evaluated accordingly.

KEYWORDS

TMT, Recovery positive, Stress positive, CAD.

INTRODUCTION

The diagnostic rate of coronary artery disease (CAD) has been dramatically increasing with the development of interventional technique, which makes coronary angiography (CAG) the “gold standard” tool for CAD diagnosis.¹ However, limited by its invasive property exercise treadmill test is still used as an economic and simple method to screen and assist in diagnosis of patients with known or suspected CAD.¹

Exercise stress testing is the most widely used test for diagnosis of coronary artery disease (CAD). Exercise-induced ST segment depression is a reliable ECG finding for the diagnosis of obstructive CAD.² It also indicates a worse prognosis in patients with documented CAD.^{3–5} The sensitivity and specificity of exercise stress test for detection of angiographic CAD were reported to be 68% and 77%, respectively in a meta-analysis.² However, 12–16% of patient with suspected or documented CAD have ST segment depression only during recovery phase of exercise test.^{6,7} Although the diagnostic and prognostic power of exercise induced ST segment depression has been well characterized, the significance of ST segment depression limited to the recovery phase of an exercise stress test is poorly understood.^{8–10} Previous studies have given conflicting results with some studies reporting similar diagnostic value for both 'during exercise' and 'recovery only' ST segment depression^{6,11} whereas some reporting limited diagnostic value for recovery only ST segment depression.¹² In the present study, we aim to assess the diagnostic value of recovery-only ST segment depression in exercise stress testing by comparing the clinical and angiographic profiles of patients with 'recovery only' vs. 'during exercise' ST segment depression on exercise stress testing.

Methods

The study was done in the Department of cardiology, R.N.T. Medical college and M.B. Hospital, Udaipur in year 2019.

Inclusion And Exclusion Criteria

Inclusion Criteria

All patients who are TMT positive and willing to undergo coronary

angiography. All patients undergone Treadmill test according to modified bruce protocol. The following results will be interpreted as positive, (based on ACC/AHA 2002 guidelines).¹³

During Exercise

- ST segment depression: ECG portion of the exercise test will be considered abnormal (ie, “positive” for ischemia) when there is ≥ 1 mm horizontal or downsloping ST segment depression in one or more leads that persists at 80 milliseconds after the J point especially in Leads V4, V5, and V6 or V5 alone.
- ST segment elevation : ≥ 1.0 mm ST segment elevation in leads without pre-existing Q waves
- ST segment elevation in aVR
- Exertional hypotension: Fall in Systolic Blood Pressure from pre-exercise value as exercise intensity increases
- Exercise capacity: Inability to achieve 3 MET workload
- Exercise-induced angina, particularly that which is exercise limiting or occurs at a low workload
- Heart rate response to exercise or chronotropic incompetence (failure to achieve 85 percent of the age-predicted maximum heart rate in the absence of medications known to slow or blunt the heart rate response to exercise (ie, beta blockers and non-dihydropyridine calcium channel blockers)

During Recovery

- Arrhythmias: Frequent ventricular ectopy (defined as ≥ 7 VPBs per minute, ventricular bigeminy or trigeminy, or more marked ventricular arrhythmia)
- ECG changes ≥ 1 mm ST segment depression
- Heart Rate Recovery (HRR): Defined as difference in heart rate at peak exercise and at 1 minute after cessation of exercise. A HRR of 12 beats/min or less during an upright cool down period will be considered as positive test result.

Exclusion Criteria

Patients not willing to undergo coronary angiography.

Study Assessments

All of patients with stress positive and recovery positive TMT went through a detail interview regarding personal details like name, age, gender, profession along with an appropriate medical history of chest pain. History of Coronary artery disease risk factor: Hypertension, Dyslipidemia, Cigarette Smoking, Family history of CAD, diabetes and obesity.

Ascertainment Of Coronary Artery Disease

All patients with test positive results underwent coronary angiography in Cardiology Department, R.N.T. Medical college and M.B. Hospital, Udaipur. Vascular access for coronary angiography was done either by femoral or radial artery approach. Interpretation of coronary angiogram for CAD and coronary lesion quantification was done in at least two orthogonal views.

The criterion for Significant Coronary artery disease (CAD) was defined as >50% stenosis of the LMCA, >70% stenosis in a major coronary vessel {Left Anterior Descending (LAD), Left Circumflex (LCX) or Right Coronary Artery (RCA)} in coronary angiography. Patients with significant coronary lesions were further classified depending on the number of major coronary vessel lesion as having single vessel disease (SVD), Double Vessel Disease (DVD) or Triple Vessel Disease (TVD).

RESULTS

A total of 240 patients, 208 TMT stress positive and 32 TMT recovery positive, (mean age 55.12 ± 9.16 years) were included during in this study. Among which males were 141 and females were 99. Mean age of TMT stress positive patients was 55.25 ± 9.36 and that of TMT recovery positive was 54.28 ± 7.76 . There was no age or sex difference in TMT stress positive and recovery positive patients.

Table 1 : Distribution Of CAD Risk Factors In TMT Stress Positive And Recovery Positive Patients.

CAD risk factors		TMT Stress Positive (n=208)		TMT Recovery Positive (n=32)		P Value
Sex	Male	122	58.65%	19	59.38%	0.938
	Female	86	41.35%	13	40.62%	
Age		55.25 ± 9.36		54.28 ± 7.76		0.578
HTN		95	45.67%	11	34.38%	0.230
DM		101	48.56%	10	31.25%	0.067
Dyslipidemia		49	23.56%	05	15.63%	0.317
Family History		13	6.25%	03	9.38%	0.509
Obesity		44	21.15%	03	9.38%	0.118
Smoking		41	19.71%	08	25%	0.489
HTN- Hypertension; DM- Diabetes Mellitus; TMT- Treadmill Test; * Fisher Exact Test.						

There was no significant difference in CAD risk factors between TMT stress positive and recovery positive patients. (Table 1)

Table 2 : Distribution Of CAD In Study Population According To CAD Risk Factors.

CAD risk factors	Significant CAD (n= 141)		No or Minor CAD (n= 99)		P Value
HTN	86	61%	20	20.20%	0.001
DM	95	67.38%	16	16.16%	0.001
Dyslipidemia	51	36.17%	03	3.03%	0.001
Family History	16	11.34%	0	0.00%	0.001*
Obesity	42	29.79%	05	5.05%	0.001
Smoking	40	28.37%	09	9.09%	0.001
HTN- Hypertension; DM- Diabetes Mellitus; TMT- Treadmill Test, * Fisher exact test.					

Among all the patients who have significant CAD (n=141), 86 were hypertensive (61%); 95 patients were Diabetic (67.38%); 51 patients with dyslipidemia (36.17%); 16 patients with family history of heart disease (11.34%); 42 patients were obese (29.79%); 40 patients were smoker (28.37%). Among all the patients who have insignificant CAD (n=99), 20 were hypertensive (20.20%); 16 patients were Diabetic (16.16%); 3 patients with dyslipidemia (3.03%); no patients with family history of heart disease; 5 patients were obese (5.05%); 9 patients were smoker (9.09%). (Table 2)

There was a significant difference in CAD risk factors in patients with CAD than patients having minor disease. Patients with significant

CAD were more hypertensive ($P<0.001$), diabetic ($P<0.001$), dyslipidemic ($P<0.001$), smokers ($P<0.001$), obese ($P<0.001$) and have family history of CAD than patients having insignificant CAD.

Coronary angiography of all the patients revealed normal coronaries or minor disease in 85 TMT stress positive patients (40.87%), and 14 TMT recovery positive patients (43.75%). Significant lesions were found in 123 TMT stress positive (59.13%) and 18 TMT recovery positive patients (56.25%).

In TMT stress positive patients who have significant CAD, LAD was involved in 40.87% (n=85), RCA was involved in 30.77% (n=64), LCX was involved in 25.48% (n=53) and LMCA was involved in 4.8% (n=10) of the cases.

In TMT recovery positive patients who have significant CAD, LAD was involved in 46.88% (n=15), RCA was involved in 40.63% (n=14), LCX was involved in 28.13% (n=11) and LMCA was involved in 3.13% (n=1) of the cases.

Table 3 : Distribution Of Vessels Involved In TMT Stress Positive And Recovery Positive Patients.

Vessels involved (Significant Lesion)	TMT Stress Positive (n=208)		TMT Recovery Positive (n=32)		P Value
Significant CAD	123	59.13%	18	56.25%	0.757
Non Significant CAD	85	40.87%	14	43.75%	
LAD	85	40.87%	15	46.88%	0.520
RCA	64	30.77%	14	40.63%	0.144
LCX	53	25.48%	11	28.13%	0.289
LMCA	10	4.8%	1	3.13%	0.671
None	85	40.87%	14	43.75%	0.757
SVD	70	33.65%	6	21.88%	0.091
DVD	18	8.65%	2	9.38%	0.646
TVD and/ or LMCA	33	15.87%	10	25%	0.034
Isolated LMCA	2	0.96%	0	0	0.751*
TMT-Treadmill Test; LAD- Left Anterior Descending Artery; RCA- Right Coronary Artery; LCX- Left Circumflex Coronary Artery; LMCA- Left Main Coronary Artery; SVD- Single Vessel Disease; DVD- Double Vessel Disease; TVD- Triple Vessel Disease, * Fisher exact test.					

Among TMT stress positive patients 33.65% (n=70) had single vessel disease (SVD), 8.65% (n=18) had double vessel disease (DVD), 15.87% (n=33) had triple vessel disease (TVD) and or LMCA disease; 0.96% (n=2) patients had isolated LMCA disease. While among TMT recovery positive patients 21.88% (n=6) had single vessel disease (SVD), 9.38% (n=3) had double vessel disease (DVD), 25% (n=10) had triple vessel disease (TVD) and or LMCA disease; none had isolated LMCA disease. There was significant difference in TMT stress positive and recovery positive patients in having TVD and or LMCA disease ($p=0.034$). Patients with TMT recovery positive are more likely have TVD and or LMCA disease. No such difference is observed among patients having SVD, DVD or isolated LMCA disease (Table 3).

65 TMT stress positive patients and 9 TMT recovery positive patients had atypical chest pain (ACP), out of which 12 TMT stress positive patients and 3 TMT recovery positive patients had significant CAD and 53 TMT stress positive patients and 6 TMT recovery positive patients had insignificant CAD. There was no significant difference between these two groups. ($p=0.298$)

76 TMT stress positive patients and 20 TMT recovery positive patients had angina on exertion class I (AOE I), out of which 52 TMT stress positive patients and 12 TMT recovery positive patients had significant CAD and 24 TMT stress positive patients and 8 TMT recovery positive patients had insignificant CAD. There was no significant difference between these two groups. ($p=0.477$)

Table 4 : Symptoms Distribution In TMT Stress Positive And Recovery Positive Patients

Symptoms	CAD	TMT Stress Positive	TMT Recovery Positive	P value
ACP	Significant CAD	12	3	0.298
	Non Significant CAD	53	6	
AOE I	Significant CAD	52	12	0.477

	Non Significant CAD	24	8	
AOE II	Significant CAD	59	3	0.525
	Non Significant CAD	8	0	
ACP- Atypical chest pain, AOE I- Angina on Exertion Class I (NYHA), AOE II- Angina on Exertion Class II (NYHA).				

67 TMT stress positive patients and 3 TMT recovery positive patients had angina on exertion class II (AOE II), out of which 59 TMT stress positive patients and 3 TMT recovery positive patients had significant CAD and 8 TMT stress positive patients and none of the TMT recovery positive patients had insignificant CAD. There was no significant difference between these two groups. ($p=0.525$)

DISCUSSION:

Graded exercise tread mill test is widely used clinically to assess the ability of an individual to safely tolerate increased physical activity while ECG, hemodynamic, and symptomatic responses are monitored for the development of myocardial ischemia, electrical instability, or other exertion-related abnormalities. Also exercise ECG remains an inexpensive test that has been well validated in the general population, and it can be used as the first diagnostic test for patients with an intermediate risk of having CAD.

Accurate screening and diagnosis of IHD is one of the most important mechanisms of timely intervention and prevention of mortality. TMT and/or myocardial perfusion imaging (MPI) scan are used in many centers for screening to be followed up with CAG, which is used as a gold standard for the diagnosis of CAD. Now with the availability of improved equipment and radiotracers, the present-day role of these noninvasive investigations needs to be restudied.

TMT is the most widely used cardiac stress test. This is described as poor man's angiogram. In a person at high risk for coronary heart disease (e.g., advanced age, multiple coronary risk factors), an abnormal TMT is highly predictive of the presence of coronary heart disease.

TMT data is not only helpful for the diagnosis of CAD but can also be utilized for prognostication. Functional capacity, exercise-induced ST segment depression, ST elevation, duration of ST segment recovery in post exercise period, chronotropic incompetence, heart rate recovery response and number of other variables can be used to determine prognosis.¹³ It is important to identify patients with high risk features, who further needs work-up and aggressive treatment.

Although the diagnostic and prognostic power of exercise induced ST segment depression has been well characterized, the significance of ST segment depression limited to the recovery phase of an exercise stress test is poorly understood.⁷⁻⁹ Previous studies have given conflicting results with some studies reporting similar diagnostic value for both 'during exercise' and 'recovery only' ST segment depression^{5,10} whereas some reporting limited diagnostic value for recovery only ST segment depression.¹²

In our study, we compared the clinical and angiographic profiles of 208 TMT stress positive and 32 TMT recovery positive patients (mean age 55.12 ± 9.16 years).

The importance of ST segment depression limited only to post exercise recovery phase is being supported by a number of studies. Lanza and colleagues had shown that the diagnostic and prognostic value of ST segment depression limited to the recovery phase of an exercise test is largely similar to that of ST segment depression induced during exercise ($p=0.72$).⁶ It has also been pointed out that the ST-depression is a sign of acute subendocardial ischemia and of extensive and severe CAD, which is significant when the TMT effort phase is over, but it increases even more during the first minutes of the recovery phase.¹⁴

Although what causes the ischemic ST depression which occurs only during the TMT recovery phase have not been defined yet, Dimsdale et al¹⁵ consider that during the post-effort phase some patients maintain high levels of plasma catecholamines, which increase the myocardial demand of oxygen because they increase the myocardial contractility and the risk of acute ischemia, since it produces an imbalance between supply and demand in the coronary arteries with significant obstruction.

In our study there was no difference in CAD risk factors between TMT stress positive and TMT recovery positive patients.

Patients having significant CAD in any group have more CAD risk factors like HTN, DM, Dyslipidemia, Family History, Obesity, smoking than patients having no or minor CAD.

There was also no significant difference of significant CAD in TMT stress positive and TMT recovery positive group. This finding is consistent with that by Lanza and colleagues¹⁰, who also showed that the diagnostic and prognostic value of ST segment depression limited to the recovery phase of an exercise test is largely similar to that of ST segment depression induced during exercise.

Tomasz M rywik et al¹⁶ analysed TMT of 825 healthy volunteers, divided them in to 3 groups. Group 0 had no ischemic st-segment changes during or after treadmill exercise while group 1 had st changes during exercise and 63 (group 2) had changes limited to recovery. Groups 1 and 2 were similar in age, sex, smoking status, hypertension prevalence, fasting plasma glucose, and serum cholesterol. However, both groups were older and had higher cholesterol and prevalence of hypertension than group 0. Treadmill exercise duration, peak oxygen consumption, and maximal heart rate were similar between groups 1 and 2 but were lower than in group 0 (each $P<0.05$). During a mean follow-up time of 9 years, 55 subjects developed coronary events (angina pectoris, myocardial infarction, or coronary death): 21 of 611 (3.4%) in group 0, 22 of 151 (14.6%) in group 1, and 12 of 63 (19%) in group 2 ($P<0.001$). By survival analysis, the risk of coronary events was similar in groups 1 and 2 which were significantly higher than in group 0 ($P<0.0001$).

In our study, we analysed the distribution of vessels involved in TMT stress positive and recovery positive patients, a significant difference was observed in patients having TVD and or LMCA disease. TMT recovery positive patients were more likely to have TVD and/ or LMCA disease as compared to TMT stress positive patients ($p=0.034$). Similar observation was made by Bruce lachterman et al¹⁷, who studied a group of 2044 people who underwent routine clinical exercise testing. Of the 168 patients who had abnormal ST-segment responses, 26 had such responses only during recovery. The positive predictive value of this pattern for significant angiographic disease (84%) was not statistically different from the predictive value of ST depression occurring during exercise (87%). Inclusion of ST depression during recovery significantly increased the sensitivity of the exercise test from 50% to 59% ($P = 0.01$) without a change in predictive value. In addition, ST-segment depression occurring during recovery is usually associated with more-severe angiographic coronary artery disease.

Norma crudo et al¹⁸ analysed Clinical and exercise stress test data from 147 patients with positive stress test. All patients had significant ST-segment depression and were divided into three groups: Group I, 94 patients with ST-segment depression during exercise; Group II, 29 patients with ST-segment depression only during the recovery phase; and Group III, 24 patients with borderline ST-segment depression during exercise which became significant during the recovery phase. The results of the exercise stress test were correlated with the coronary angiography findings in each group. A diagnosis of significant CAD was made in 78 patients in Group I (82.9%), in 22 in Group II (75.8%) and in 21 in Group III (87.5%) ($p = 0.52$). Patients in Group III were older, with high prevalence of dyslipidemia, history of previous infarction and three-vessel and/or left main coronary artery disease. Group II presented the higher number of asymptomatic patients with one-vessel disease and high prevalence of CAD. There were no statistical differences in the percentage of patients with significant CAD among the groups. Patients in Group III had high prevalence of significant and severe CAD. A proper evaluation of ST-segment depression occurring or becoming significant during the recovery phase provided additional clinical information to the results of the exercise stress test.

The probable causes of the ischemic ST depression which occurs only during the TMT recovery phase may be,

During the post-effort phase some patients maintain high levels of plasma catecholamines, which increase the myocardial demand of oxygen because they increase the myocardial contractility and the risk of acute ischemia, since it produces an imbalance between supply and demand in the coronary arteries with significant obstruction.

The increased venous return in the supine position raises LVEDP and may precipitate subendocardial ischemia in the coronary arteries with significant obstruction not seen when upright on the treadmill.

However we did not find any significant difference in both groups in patients having SVD or DVD or in patients with isolated LMCA lesion.

We did not also find any significant difference in symptoms (ACP, AOE I, AOE II) in both groups.

CONCLUSION

In conclusion, we found the similar diagnostic value for both 'during exercise' and 'recovery only' ST segment depressions and even more severe CAD in those having recovery positive TMT as compared to stress positive TMT. So the 'recovery only' ST segment depressions may be one of the high risk feature on TMT for significant coronary disease and patients should be evaluated accordingly.

Limitations

The number of patients was small, which is the main limitation of this study. To confirm these findings a study with larger sample size is required. The impact of this disease on morbidity and mortality in asymptomatic or mildly symptomatic patients requires long term follow up.

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