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Original Article

Significance of 'recovery ST-segment depression' in exercise stress test

Rockey Katheria, MD, DM, Subramanyam K. Setty MD,DM, B.S. Arun, MD, DM, DNB *, Prabhavathi Bhat MD,DM, DNB, H.V. Jagadeesh, MD,DM, C.N. Manjunath, MD,DM

Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, India

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ABSTRACT

Objective: To study the significance of ST-segment depression during 'recovery' compared to that 'during stress' and 'both the phases' in exercise stress test.
Methods: Patients with positive exercise stress test who underwent coronary angiography (CAG) from 1st January 2017 to 31st December 2018 were studied. Patients were divided into 3 groups- Group A with ST-depression restricted to recovery phase, group B with ST-depression restricted to stress phase and group C with ST-depression seen both during exercise and recovery. All patients underwent CAG. Sensitivity, specificity, and predictive values of each of these groups in diagnosis of significant coronary artery disease (CAD) were analysed and compared.
Results: Total 300 patients were studied. Mean age of the study population was 48.77 ± 7.94 years. 78.3% of patients with positive exercise stress test had significant CAD. 96% of patients in group A had significant CAD, which was higher than in group B (88.9%) & group C (70.1%). The specificity, positive predictive value and negative predictive value of ST-segment depression in group A (96.92%, 96% and 25.2% respectively) were higher than that of ST-depression in group B (89.23%, 88.89% and 24.47% respectively) and group C (13.85%, 70.05% and 7.96% respectively). Sensitivity and accuracy of ST-depression in group A were lower (20.43% and 37% respectively), compared to other 2 groups.
Conclusion: Patient with ST-depression restricted to recovery phase had highest specificity, positive predictive value, and negative predictive value. However, accuracy was highest in group with both stress phase and exercise ST-segment depression.

1. Introduction

Exercise stress testing is widely used for diagnosis of coronary artery disease (CAD). Exercise-induced ST-segment depression is a reliable electrocardiographic (ECG) finding for diagnosis of CAD.[1] 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.[1] However, 12–16% of patient with suspected CAD have ST-segment depression only during recovery phase of exercise test.[2,3]

Although the diagnostic and prognostic power of exercise induced ST-segment depression has been well characterized, the significance of ST-segment depression limited to recovery phase of stress test is poorly understood.[4–6] Previous studies have given conflicting results with some reporting similar diagnostic value for both ' exercise' and 'recovery only' ST segment depression,[7,8] whereas some reporting limited diagnostic value for recovery only ST depression.[9] In our study, we aim to assess the diagnostic value of recovery only ST-segment depression by comparing the clinical and angiographic profiles of patients with 'recovery only' vs. 'during exercise' ST-segment depression.

2. Materials and methods

It was a cross–sectional observational study conducted at Sri Jayadeva Institute of Cardiovascular Sciences & Research from 1st January 2017 to 31st December 2018. The Institutional Ethics Committee approval was obtained. Informed written consent was taken from all of them.

Inclusion Criteria.

* Corresponding author. Assistant Professor of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bannergatta Road, Jayanagar 9th Bangalore, Bangalore, India.
E-mail addresses: rockeykatheria@gmail.com (R. Katheria), arunbscardiology2017@gmail.com (B.S. Arun).

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- Patients more than 18 years of age with positive treadmill test who underwent coronary angiogram (CAG) within 3 months.

Exclusion Criteria:

- History of recent myocardial infarction (within 1 month),
- Atrial fibrillation or other arrhythmias,
- Baseline ST segment depression >1 mm,
- Left bundle branch block, paced rhythm,
- Clinical evidence of non-coronary heart disease including valvular heart disease and hypertrophic cardiomyopathy,
- ECG evidence of left ventricular hypertrophy,
- Exercise-induced STelevation in leads with no pre-existing Q waves.

Methods: Exercise stress test was done using a treadmill by standard Bruce protocol. Electrocardiograms (ECG) were recorded at the end of each stage of stress, and at 1, 3, and 5 min of recovery.

Patients were divided into 3 groups:

Group A: Patients with ST-depression only during recovery phase.

Group B: Patients with ST-depression only during stress phase.

Group C: Patients with ST-depression both during stress & recovery phase.

Exercise stress test was analyzed for maximum ST-segment depression, duration of exercise, angina, and Duke's treadmill score.

Exercise stress test was considered positive when there was $\geq$1 mm horizontal or down-sloping ST-segment depression at 80 ms after the J point (ST_{80}) in three consecutive beats. ST depression at 60 ms after the J point (ST_{60}) was used as reference point at heart rates higher than 130 beats per min.

All patients underwent CAG within 3 months of exercise stress test. Significant CAD was diagnosed if there was more than 50% stenosis in one or more epicardial arteries.

Statistical analysis: Descriptive and inferential statistical analysis were done. Results on continuous measurements were presented on Mean ± SD and results on categorical measurements were presented in number (percentage). Significance was assessed at 5% level of significance. Chi-square/Fisher Exact test was used to find the significance of study parameters on categorical scale between the groups.

3. Results

Overall, 300 patients with age ranging from 29 to 74 years were studied. Maximum number of patients were in age group between 41 and 50 years, constituting 55%. Mean age was 48.77 ± 7.94 years. 251 patients (83.7%) were male and 49 patients (16.3%) were female. Maximum number of patients were in Group C (183 patients, 61%), followed by group B (67 patients, 22.3%) & least in group A (50 patients, 16.7%).

Table 1 shows comparison of baseline characteristics between the 3 groups. Past history of ischemic heart disease (IHD), coronary artery bypass grafting (CABG) and diabetes mellitus (DM) were more common in group B, compared to other 2 groups.

Overall, 78.3% of the patients with positive exercise stress test had significant lesion in CAG. Details of CAG findings in each of the 3 groups are given in Table 2. In group A, 96% of the patients had significant CAD. In Group B and C, 88.9% and 70.1% had significant CAD respectively.

The validity of each of the 3 groups are shown in Table 3. Specificity (98.92%), positive predictive value (96%), negative predictive value (25.2%) and positive likelihood ratio (6.64) were highest with Group A. Sensitivity (55.74%) and negative likelihood ratio (3.3) were highest in group C. Overall accuracy was highest with group C 46.67%).

Duke's threadmil score in each of the 3 groups is shown in Table 4. On univariate analysis and multivariate analysis, DM and hypertension were significantly more common in significant CAD group, compared to insignificant CAD group as shown in Table 5 and Table 6. There was significant association between high Duke's score and significant CAD (Table 5).

Analysis of the pattern of ST-depression in ECG, showed that group with downsloping ST-depression had 87.8% significant lesion, whereas horizontal ST-depression group had 70.6% significant lesion, which was statistically significant. ($p<0.001$)

4. Discussion

Many studies have demonstrated the clinical importance of exercise stress test for diagnosis, prognosis, risk stratification, and treatment of patients with suspected or documented CAD.[10–12] Many scores have been proposed to improve the accuracy of the exercise stress test. Mark and colleagues derived a prognostic score based on an index of angina, exercise time, and the change in STdepression from rest to maximal exercise.[13] Simoons proposed a nomogram for STdepression during exercise regressed on heart rate.[14] Kligfield et al have proposed an ST-heart rate slope or index that considers ST shift relative to changes in heart rate during exercise as a means of diagnosing CAD.[15] Rautaharju et al[16] used the ST-integral to analyze the data from the Multiple Risk Factor Intervention Trial, and Detrano et al[17] compared careful visual readings with computerized readings of the exercise ECG. None of these investigators or scores considered ST changes that occurred during recovery. It has also been found that the ST-segment depression is a sign of acute subendocardial ischemia and signify extensive and severe CAD, which is significant when it is present at stress phase of exercise stress test. However, if ST-depression increases further more during the recovery phase of stress test, its significance increases.[18] Significance and mechanism of ischemic ST-segment depression restricted to recovery phase of the exercise stress test have not been defined yet. Dimsdale et al[19] concluded that during the post-effort phase some patients maintain high plasma level of 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 demand and supply in the coronary arteries with significant obstruction.

In a study by Tomasz et al, among 825 participants, 611 (74.1%) had no ischemic ST-segment changes during or after treadmill exercise, while 151 (18.3%) had ST changes starting during exercise, and 63 (7.6%) had changes limited to recovery.[20]

In our study, downsloping ST-segment depression were more common in group A and group B, 28 patients (56%) and 43 (68.3%) respectively, whereas horizontal ST-segment depression was more common in group C (63.6%). These findings attained statistical significance with p values < 0.001. However a study by Jayaprasad et al, stress group had predominant horizontal depression, compared to recovery group.[21]

When we analysed the relationship of CAG findings with exercise stress test, we found that there was significant correlation between them with 78.3% of the stress test positive patients having significant CAD. It was similar to study by Jayaprasad et al, where they found 87% of patients with positive exercise stress test had significant CAD.[21]

In our study, significant CAD were found in 96% of group A and 88.9% of group B and 70.1% in group C. Specificity, positive predictive value, negative predictive value and positive likelihood ratio

Table 1
Baseline characteristics of the 3 groups.

	Group A ($n = 50$)	Group B ($n = 63$)	Group C ($n = 187$)	Total ($n = 300$)	p value
History of IHD	1 (2%)	10 (15.9%)	14 (7.5%)	25 (8.3%)	0.024*
Past STEMI	1 (2%)	1 (1.6%)	6 (3.2%)	8 (2.7%)	0.748
Past NSTEMI	0 (0%)	3 (4.8%)	4 (2.1%)	7 (2.3%)	0.240
Past PTCA	0 (0%)	3 (4.8%)	5 (2.7%)	8 (2.7%)	0.296
Past CABG	0 (0%)	3 (4.8%)	0 (0%)	3 (1%)	0.003**
DM	21 (42%)	35 (55.6%)	50 (26.7%)	106 (35.3%)	<0.001**
HTN	23 (46%)	29 (46%)	67 (35.8%)	119 (39.7%)	0.281
Smoking	15 (30%)	19 (30.2%)	51 (27.3%)	85 (28.3%)	0.871
Alcohol	10 (20%)	6 (9.5%)	20 (10.7%)	36 (12%)	0.157

IHD: Ischemic Heart Disease, NSTEMI: Non ST segment elevation myocardial infarction.
STEMI: ST-segment elevation myocardial infarction, CABG: Coronary artery bypass graft.
DM: Diabetes Mellitus, HTN: Hypertension.

Table 2
Coronary artery disease in 3 groups.

Impression	Group A ($n = 50$)	Group B ($n = 63$)	Group C ($n = 187$)	Total ($n = 300$)
Insignificant CAD	2 (4%)	7 (11.1%)	56 (29.9%)	65 (21.7%)
Significant CAD	48 (96%)	56 (88.9%)	131 (70.1%)	235 (78.3%)
•SVD	27 (54%)	16 (25.4%)	76 (40.6%)	119 (39.7%)
•DVD	12 (24%)	20 (31.7%)	28 (15%)	60 (20%)
•TVD	5 (10%)	7 (11.1%)	20 (10.7%)	32 (10.7%)

SVD: Single vessel disease, DVD: Double vessel disease, TVD: Triple vessel disease.

Table 3
Validity of group A (Recovery only), group B (Stress only) and group C (Both stress and recovery) ST-depression in diagnosis of significant CAD.

	Group A	Group B	Group C
Sensitivity	20.43%	23.83%	55.74%
Specificity	96.92%	89.23%	13.85%
Positive predictive Value	96%	88.89%	70.05%
Negative Predictive Value	25.2%	24.47%	7.96%
Positive likelihood ratio	6.64	2.21	0.65
Negative likelihood ratio	0.82	0.85	3.3
Accuracy	37%	38%	46.67%

Table 4
Duke's threadmill score in three groups.

DUKES RISK	Group A	Group B	Group C	Total
High risk	2 (4%)	14 (22.2%)	8 (4.3%)	24 (8%)
Intermediate risk	48 (96%)	49 (77.8%)	179 (95.7%)	276 (92%)
Total	50 (100%)	63 (100%)	187 (100%)	300 (100%)

Table 5
Univariate analysis of various factors for significant CAD.

	Significant CAD		p value
	Present ($n = 235$)	Absent ($n = 65$)	
	No. of patients (%)	No. of patients (%)	
Effort angina	233 (99.1%)	62 (95.4%)	0.060
STEMI	7 (3%)	1 (1.5%)	1
NSTEMI	6 (2.6%)	0 (0%)	0.346
DM	99 (42.1%)	7 (10.7%)	<0.001*
HTN	105 (44.7%)	14 (21.5%)	<0.001*
Smoking	72 (30.6%)	13 (20%)	0.119
Alcohol	24 (10.2%)	12 (18.5%)	0.084
High Duke's score	25 (10.6%)	0 (0%)	0.004*

CAD: Coronary artery disease, STEMI: ST-segment elevation myocardial infarction, NSTEMI: Non ST-segment elevation myocardial infarction, DM: Diabetes Mellitus, HTN: Hypertension.

were highest with Group 1. Specificity and negative likelihood ratio were highest in group C. Overall accuracy was highest with group C.

However, when considering the number of coronary vessels with significant obstructive lesion in patients from each group, we observed that Group B patients had the highest prevalence of three-vessel disease, but it was not statistically significant.

In our study, maximum number of patients were in intermediate class according to Duke's treadmill score with 96% in group A, 81% in group B & 95.7% in group C (Table 4), this parameter was not studied in other studies. When we compared the metabolic equivalents (METS) achieved with the CAD, out of 77 patients who could walk 6–8 METS, significant lesion was present in 92.8% and insignificant lesions were in 7.8%, which was statistically significant.($p<0.001$)

On analysing the relationship between Duke's treadmill score and CAD in our study, we found significant association between high risk Duke's score and double vessel disease, triple vessel disease, significant Left main disease.

5. Study limitation

A limitation of our study is that we did not follow up our patients. Thus, prognostic assessment could not be done.

6. Conclusion

This study concludes that there is a strong correlation between positive exercise stress test and CAD. Patient with ST-depression restricted to recovery phase had highest specificity, positive predictive value, negative predictive value and positive likelihood ratio. However, accuracy was highest with both stress phase and exercise ST-segment depression. Based on the pattern of ST depression we found that downsloping ST depression are more specific than horizontal ST depression to identify significant lesion. Our study showed strong correlation between DM, hypertension and high Duke's score significant CAD.

Table 6
Multivariate analysis to determine the risk factors for significant CAD.

	B (OR)	*p* value	Exp(B) Adjusted OR	95% C.I.for EXP(B)	
				Lower	Upper
Effort Angina Present	0.825	0.387	2.282	0.352	14.769
DM	1.933	<0.001*	6.908	2.933	16.275
HTN	1.165	0.001*	3.205	1.617	6.353
Smoking	0.672	0.067	1.959	0.953	4.025
Alcohol	−0.232	0.585	0.793	0.345	1.821

DM: Diabetes Mellitus, HTN: Hypertension, OR: Odd's ratio.

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Declaration of competing interest

All author has none to declare.

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Abbreviations

CAD: : coronary artery disease
IHD: - Ischemic heart disease
ECG: : Electrocardiogram
MET: : Metabolic equivalents
NSTEMI: : Non ST segment elevation myocardial infarction
STEMI: : ST segment elevation myocardial infarction
CABG: : Coronary artery bypass graft
CAG: : coronary angiogram
TVD: : Triple vessel disease
LMCA: : Left main coronary artery
DVD: : Double vessel disease
DM: : Diabetes Mellitus
HTN: : Hypertension