

Clinical Usefulness of ST Depression Limited to Recovery Phase of Treadmill Test

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Abstract

Background: Despite the current availability of diagnostic image tests with excellent diagnostic and prognostic accuracy, Treadmill test (TMT) remains as the procedure most commonly used for the evaluation, diagnosis and risk stratification of patients with coronary artery disease (CAD).

Objectives: To investigate the diagnostic value of ST segment depression limited to the recovery phase of an exercise stress test, as compared with that of ST segment depression (ST-d) appearing during exercise only and with ST depression in both exercise and recovery.

Material and Methods: Clinical data and TMT from 142 patients with positive stress test were analyzed. All patients had significant ST- segment depression and were divided into three groups: Group A, 81 patients with significant ST- depression during exercise; Group B, 33 patients with borderline ST- depression during exercise which became significant during the recovery phase: Group C, 28 patients with ST- d only during the recovery phase. Clinical and angiographic data were compared in each group.

Results: A diagnosis of significant CAD was made in 68 patients in group A (83.9%), in 28 patients in group B (84.8%) and in 22 patients in group C (78.5%) ($p = 0.10$). Patients in group C were older and higher prevalence of single vessel disease ($p=0.04$). There was no statistical significant difference in terms of normal coronaries, significant CAD, double and triple vessel disease ($p > 0.05$).

Conclusion: The diagnostic 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 effort. Patient with recovery only ST segment depression are more likely to have single vessel disease on coronary angiogram compared to exercise phase ST changes.

Key words: Diagnosis, Treadmill test, Evaluation

INTRODUCTION

Exercise induced ST segment depression is considered a valuable ECG finding for the diagnosis of obstructive CAD.^[1,2] It has also been associated with a worse prognosis for patients with a known CAD.^[3] However, while the diagnostic value of ST - d occurring during the active phase of exercise test is well known, only a few studies have evaluated the clinical significance of ST -d appearing

only during the recovery phase of exercise testing.^[4-7] Thus, in this study we aimed at evaluating the diagnostic power of recovery-only ST -d in a sufficiently large group of consecutive patients who were referred for exercise testing because of suspected or known CAD and who underwent coronary angiography within six months of the stress test.

MATERIALS AND METHODS

Study Population

An observational prospective study was conducted with patients over 18 years old who developed significant ST changes on TMT and underwent coronary angiogram subsequently for evaluation of suspected coronary artery disease in the department of cardiology of a tertiary hospital, in the period between November, 2014 and

Access this article online



www.ijss-sn.com

Month of Submission : 07-2018

Month of Peer Review : 08-2018

Month of Acceptance : 09-2018

Month of Publishing : 09-2018

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November, 2016. This study consist of three different group of population, in which group A ($n = 81$), B ($n=33$) and C ($n = 28$) consist of patients who developed significant ST depression prominently in exercise irrespective of ST changes in recovery, ST depression developed in exercise but prominent in recovery and significant ST depression in recovery phase only respectively. Indications for an exercise stress test were diagnostic assessment for suspected angina pectoris, follow up assessment of patients with a known history of CAD (for example, previous angina, myocardial infarction (MI), or coronary revascularisation procedures), and pre-discharge evaluation of patients admitted for unstable angina. Patients were excluded if they presented with one or more of the following features: recent (6 months) acute MI; ECG abnormalities at rest that could have interfered with ST segment analysis, including left ventricular hypertrophy, atrial fibrillation, baseline ST segment depression (0.5 mm), left bundle branch block, and pacemaker rhythm; and clinical evidence of non-coronary heart disease, including valvular heart disease and cardiomyopathy.

For every patient we obtained information about their age, sex, clinical diagnosis, history of diabetes, previous MI or coronary revascularisation procedures, use of anti-ischaemic drugs, and left ventricular ejection fraction (LVEF) measured by two dimensional echocardiography within two months of the exercise test.

Exercise Stress Test

All patients underwent a symptom and sign limited treadmill test according to either a Bruce or modified Bruce protocol. Indications for interruption of the test were crescendo angina, ST segment changes >1.5 mm compared with baseline, clinically significant arrhythmias, hypotension (0.20 mm Hg reduction in systolic blood pressure compared with a previous measurement) or hypertensive (systolic blood pressure ≥ 220 mm Hg or diastolic blood pressure >120 mm Hg) response to exertion, and other potentially serious clinical conditions (such as arrhythmias or dyspnoea). Three ECG leads (II, V2, and V5) were continuously monitored during the test. The recovery phase of exercise always lasted six minutes, but it was prolonged if clinically indicated. ST segment depression was considered to be significant when it was >1 mm at 0.08 seconds from the J point and was either horizontal or down sloping.

The patient clinical characteristics including age, sex, smoking status, diabetes mellitus and hypertension were recorded. All the routine blood investigations, ECG, Echocardiography, TMT followed by coronary angiogram were done. Indication for CAG was either the presence of typical angina and positive TMT in patient groups. Group A, B and C were consist of total 142 patients.

These groups were compared for clinical characteristics and coronary artery distribution. Written consents were taken from all the patients.

HTN was defined as previous use of antihypertensive medications, systolic pressure >140 mm Hg or diastolic pressure >90 mm Hg in at least two separate measurements. Diagnosis of DM was based on previous history of diabetes with or without drug therapies or fasting blood glucose ≥ 126 mg/dL. Hyperlipidaemia was defined as total cholesterol of ≥ 200 mg/dL or current statin therapy. Body mass index (BMI) was calculated as weight kg/height m^2 . A BMI of ≥ 30 kg/ m^2 was defined as obese. Current smokers were defined as those who had smoked for some period during the past year. Echocardiography (VIVID S-5 General Electric Medica System 3.6 MHz) was performed according to the American Society of Echocardiography guidelines, and LVEF was evaluated using the visual assessment.

Coronary Angiography

All patients underwent CAG within six months of the TMT. Coronary stenoses were assessed visually by two experienced angiographers independently. A stenosis $>50\%$ of the lumen diameter in a major epicardial coronary artery was considered to be obstructive.

Statistical Analysis

Continuous variables had a normal distribution, are expressed as mean \pm standard deviation, and were analyzed with the ANOVA test to compare three groups. When differences were found among the groups, post-hoc test was used to determine which groups had the statistically significant difference.

Categorical variables are expressed as frequency and percentage, and they were evaluated with the chi square test, and partitioning chi squares with degrees of freedom. P value < 0.05 was considered significant.

RESULTS

This study included a total of 142 patients. Patients were divided into three groups. Group A (Patients with prominent ST depression in exercise), Group B (ST depression in exercise but prominent in recovery) and Group C (ST depression in recovery only) had 81, 33 and 28 patients respectively. Mean age of group C patients was relatively older as compared to group A and B but not statistically significant different (C: 58.53 ± 8 years; B: 56.18 ± 8 years, and A: 54.6 ± 9 years; p 0.09 NS). Male constituted 75.3 % of overall patients and no differences were observed in the distribution by sex. The demographic characteristics of the groups are compared in Table 1.

Most common presentation in group A was typical angina (58.7%) followed by atypical chest pain (38.7%) and dyspnea (32.0%), In group B the commonest presentations were atypical chest pain (45.7%) then typical angina (33.3%) and dypnea (27.2%). In group C the commonest presenting feature was typical angina (42.8%). On comparing the groups with reference to presence of cardiovascular comorbidities like hypertension, diabetes and smoking no significant statistical difference between the two groups.

12.3% of the cases from group A, 9% group B and 10.7 % of the patients from group C had normal coronaries and showed no statistical differences between the three groups. Non - obstructive CAD was seen in 4.9 %, 7.1% and 3.5 % of cases in group A, B and C respectively with no statistical difference between the groups. There were also no significant statistical difference between the groups on the basis of overall obstructive CAD ($p > 0.05$).

However presence of single vessel disease was significantly more common in Group C than in Group A and B with a p value of 0.04. The results of the angiographic findings and EST between the groups have been shown in Table 2. LAD, LCX and RCA are left anterior descending artery, left circumflex artery and right coronary artery respectively.

Our study shows that patients with ST changes in recovery only are more likely to have single vessel disease (SVD). However, patients with ST changes in recovery only stage were not more likely to have double vessel (DVD) or triple vessel disease(TVD) when compared to those patients with prominent ST depression in exercise or those with ST depression in exercise but prominent in recovery.

DISCUSSION

The diagnostic value of ST segment depression is well studied in many group of patients worldwide.^[8-9] However, the clinical usefulness of ST segment depression limited to recovery phase of exercise stress test is poorly understood. There are no international consensus as to how these findings should be appreciated.

The prevalence of ST segment depression limited to the recovery phase of exercise test ranges widely among the few studies published in the literature. The variability can probably be explained mainly by differences in the characteristics of the study cohorts and methods applied for positivity of ST segment depression.^[4-7] Among positive exercise tests, quite high proportions of recovery-only ST

Table 1: Comparison of demographic characteristics of the groups

Parameters	Group A (n=81)	Group B (n=33)	Group C (n=28)	P value
Age (years)	54.60	56.18	58.53	0.09
Sex (M/F)	62/19	27/6	18/8	0.74
Atypical chest pain (%)	31 (38.7)	15 (45.4)	11 (39.2)	0.54
Angina (%)	42 (51.8)	11 (33.3)	12 (42.8)	0.07
Dyspnea (%)	26 (32.0)	09 (27.2)	11 (39.2)	0.92
Hypertension (%)	68 (83.9)	21 (75.0)	18 (64.2)	0.74
Diabetes mellitus (%)	31 (38.2)	13 (39.3)	14 (50.0)	0.56
Smoking (%)	39 (48.1)	10 (30.3)	09 (32.1)	0.77

Table 2: Showing angiographic and EST characteristics between the groups

Parameters	Group A (n=81) ST-d in exercise	Group B (n=33) ST- d in exercise but prominent in recovery	Group C (n=28) ST-d in recovery only	P value
Normal coronaries	10 (12.3%)	03 (9.1%)	03 (10.7%)	0.57
Non-obstrusive CAD	04 (4.9%)	02 (7.1%)	01 (3.5%)	0.90
Obstructive CAD	68 (83.9%)	28 (84.8%)	22 (78.5%)	0.10
SVD	26 (38.2%)	09 (32.1. %)	12 (54.5%)	0.04
LAD	13 (50.0%)	04 (44.4%)	07 (58.3%)	
LCX	05 (19.2%)	03 (33.3%)	02 (16.6%)	
RCA	08 (30.8%)	02 (22.2%)	03 (25.0%)	
DVD	31 (45.5%)	12 (42.8%)	07 (31.81%)	0.10
LAD+RCA	13	04	03	
LAD+LCX	08	03	02	
RCA+LCX	10	05	03	
TVD	11 (16.1%)	07 (25.0%)	03 (13.6%)	0.10
Left main disease	06	03	02	0.12
>90% stenosis	29	08	09	0.24
Type A lesion	28	11	08	
Type B lesion	23	10	07	
Type C lesion	17	07	07	

segment depression have been reported in two studies of asymptomatic, apparently healthy patients, young male aircrew (36%) in one study (5) and volunteers of both sexes, with a broad age range (29%), in the other (10%). In contrast, in stable patients with a history of MI (>1 year), a lower prevalence of recovery-only ST segment depression were found in two previous studies 6% and 4.6% (4-5) respectively.

In the present study we observed recovery-only ST segment depression in 15.4% of patients with a positive exercise test, a prevalence comparable with that found in two previous studies (15.5% and 16%) of populations of patients similar to ours—that is, with suspected or documented CAD and clinical indications for an exercise test.^[4]

The reasons for the appearance of ST depression in the recovery phase, rather than during exercise, are unclear. However, consistently with all previous studies, it cannot be predicted by the clinical characteristics of patients. The relatively frequent occurrence of recovery-only ST segment depression, however, highlights the importance of having an appropriate recovery phase, which should be prolonged to at least five minutes.

ST segment is part of ECG tracing immediately succeeding QRS complex and its depression is considered significant, if it is depressed more than 1 mm at 0.08 second from J-point and is either downsloping or horizontal.^[1-6] Screening with ECG and ETT could potentially reduce CHD events either by detecting people at high-risk for CHD events who could benefit from more aggressive risk factor modification, or by detecting people with existing severe CAD whose life could be prolonged by coronary artery bypass graft (CABG) surgery or PCI. However, the current evidence is inadequate to determine the extent to which people detected through screening in either situation would benefit from either type of intervention.

Whether ST segment depression in recovery phase alone adds to positive predictive value of ETT was not proved to be true as the data suggest that the diagnostic value of ST segment depression only in recovery phase of exercise stress test is almost similar to ST segment depression occurring during exercise phase of TMT.

Although, it increased the sensitivity but positive predictive value was same. The reason for appearance of ST segment depression in the recovery phase rather than exercise is unclear. So as in previous studies, it could not be predicted clinically. This also highlights that recovery only ST segment depression has frequent occurrence. So if patients develop ST segment depression during recovery phase of ETT, this should also be carefully assessed in patients of suspected

or documented CAD and should be prolonged to at least 5 minutes and more, if needed.

Fewer studies have demonstrated the reliability and clinical importance of the data provided by EST for diagnosis, prognosis, risk stratification, and treatment of patients with suspected or documented CAD.^[2-3] The diagnostic accuracy of CAD and the prognostic value of cardiac sudden death, particularly in hypertensive patients, smokers, and patients with dyslipidemia of significant ST-d that is only present in the recovery phase of EST, have been proved in previous works.^[5-7] It has also been pointed out that the ST-d is a sign of acute subendocardial ischemia and of extensive and severe CAD, which is significant when the EST effort phase is over, but it increases even more during the first minutes of the recovery phase.^[10]

The results of our study confirm the clinical value of the presence of ST-d, which occurs only in the EST recovery phase; these results show the importance of the ST-d diagnosis, which is at equivalent risk of obstructive CAD. Our study shows that patients with ST changes in recovery only are more likely to have single vessel disease. However, patients with ST changes in recovery only were not more likely to have double vessel or triple vessel disease when compared to those patients with prominent ST depression in exercise or those with ST depression in exercise but prominent in recovery. Although what causes the ischemic ST-d which occurs only during the EST recovery phase have not been defined yet, Dimsdale *et al.*^[11] 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.

The correlation between the EST result and the analysis of the coronary angiography showed no statistical differences in the percentage of patients with significant CAD in each group. However, when considering the number of coronary vessels with significant obstructive lesion in patients from each group, we observed that group C patients had the higher prevalence of single vessel disease as well as statistically significant different from compared to group A and B ($p < 0.05$) but similar prevalence of double and triple vessel disease in all three groups and not statistical different among groups ($p = NS$).

The lesion in a coronary vessel was not significant different in all three groups in, which matches the results published by Rashid *et al.*^[12] When comparing our results with those reported in previous works, we observe that the percentage of GA and GC patients with significant CAD was similar

to the percentage referred by Lanza *et al.*^[13], and by Rashid *et al.*^[12] (Group A: 83.9% vs Lanza 85%, and Rashid 93%; Group C: 78.5% vs Lanza 78%, and Rashid 85%).

The consequences of false-positive tests may potentially outweigh the benefits of screening. False positive tests are common among asymptomatic adults, especially women, and may lead to unnecessary diagnostic testing, over treatment, and labeling. Because the sensitivity of these tests is limited, screening could also result in false-negative results. A negative test does not rule out the presence of severe CAD or a future CHD event. Potential harms of screening asymptomatic patients for CHD include unnecessary invasive testing (for example, coronary angiography) and “labeling” of those who have had false-positive test results.

STUDY LIMITATIONS

Major limitation of this study is lack of follow-up in patients to prove the prognostic value of ST-d in the patients from each group. This study was an observational study, although it can measure association, they are not strong enough to prove causality.

CONCLUSIONS

The results of this study show that the presence of significant ST-d in an EST occurring only in the recovery phase, and the borderline ST-d during the exercise phase but then increasing and becoming positive in the recovery phase has a value and clinical importance similar to the significant ST-d present during the active phase of exercise. In our study, patients with ST changes in recovery only are more likely to have single vessel disease. However, patients with ST changes in recovery only were not more likely to have double vessel or triple vessel disease when compared to those patients with prominent ST depression in exercise or those with ST depression in exercise but prominent in recovery.

Thus careful evaluation of ST segment depression occurring only in recovery phase may add significantly to the clinical information derived from the results of TMT.

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How to cite this article: Kavi G, Sharma S, Kapoor M. Clinical Usefulness of ST Depression Limited to Recovery Phase of Treadmill Test. *Int J Sci Stud* 2018;6(6):138-142.

Source of Support: Nil, **Conflict of Interest:** None declared.