Evaluation of TMT Abnormalities in Asymptomatic Persons Using Myocardial Perfusion Study

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Abstract

Exercise ECG (TMT) is one of the very common investigations being used in the periodic medical examination of high risk professionals like airline pilots and executives. We have done a retrospective analysis of 152 asymptomatic persons who reported for myocardial perfusion imaging after being found to have positive TMT in the form of ST-T changes in inferolateral leads. Stress myocardial perfusion scan of all of them were normal. The fact that so many cases of positive TMT based on ST-T changes in inferolateral leads is found to be false positive should make us retrospect on the criteria for deciding positive TMT. The data available with other centers can be examined and a prospective multicentric study can be done to see whether the present criteria for positive TMT need revision.

Introduction

S everal people undergo regular health check up as awareness increases about preventive healthcare as well as part of organizational requirements. Along with detailed clinical examination, these involve investigations like blood counts, metabolic parameters and electrocardiogram (ECG). ECG is established method to identify many cardiac problems like ischemia, arrhythmias, chamber enlargement, electrolyte imbalance etc. It is very simple, easily available, inexpensive and noninvasive. In spite of its multiple applications, the most important use is in identifying ischemic heart disease (IHD) in emergency set up as well as in screening procedures.

As an extension of resting ECG, we use exercise ECG in the form of treadmill test (TMT) in routine screening of high risk professionals like airline pilots, asymptomatic people with other cardiac risk factors, person who are detected to have ECG abnormalities in check ups like the ones before surgical procedures, symptomatic patients with inconclusive resting ECG etc. The sensitivity and specificity of TMT is 68% and 77% respectively.1 That means about one third of those undergoing TMT can expect an abnormal graph coming out without having any actual problem, putting them to further tests to prove or disprove the abnormality noted. Can we reduce this fallacy and avoid putting people through mental tension and unnecessary procedures. Our experience during last few years has shown some useful findings related to the criteria for defining positive TMT.

Criteria for Positive TMT

The Selzer criteria that is used in analyzing TMT divide the results into mildly positive, moderately positive and strongly positive.

Mildly positive: horizontal ST depression of 1 to 1.5 mm and slowly rising junctional depression, which remains depressed 1.5 mm or more than 80 ms after the J point.

Moderately positive: horizontal ST depression of 1.5 to 2.5 mm, slowly rising ST depression which remains depressed more than 2.5 mm 80 ms after the J point and down slopping ST depression with J point depressed 1.2 mm.

Strongly positive: flat ST depression of 2.5 mm or more, slowly rising ST depression at J point of 2 mm or more and horizontal or down slopping ST depression appearing in first stage of the exercise and remaining for more than 8 minutes into recovery.

False Positive TMT

Airline pilots and high risk professionals undergo TMT at different ages according to prevailing regulations. As we know already, almost a third of them get a false positive report and go through further evaluation. From the time a person is told that there is something wrong in his TMT, he/she starts getting sleepless nights. A totally asymptomatic person is thus put into a lot of mental stress till the time he is cleared of the doubt. This apart, all these people are in key appointments in their field of work and have to spend precious time for all these procedures.

In standard textbooks on TMT, there is no definite mention about any difference between various leads in deciding sensitivity. Whether it is lead I, II or any of the chest leads, it is interpreted in the same way. In our experience in last several years of doing stress myocardial perfusion imaging (MPI) in TMT positive asymptomatic persons, we have come across some interesting findings. It might be not only interesting but can be of use in deciding the policies regarding medical examinations.

Myocardial Perfusion Imaging: More commonly known as stress Thallium, this procedure is now an established method for evaluation of myocardial perfusion at stress as well as at rest.13 Most of the nuclear medicine centers are doing Technetium based study rather than Thallium due to several advantages. But the name stress Thallium is still more familiar to doctors and patients. There is single day as well as two day protocols in stress myocardial perfusion imaging (MPI). Most of the centers are doing single day stress-rest protocol as it is convenient to patients. Both protocols are equal in the final outcome of the study. The exact protocol depends on the convenience of the patient as well as physician. We are doing single day stress-rest protocol using 99mTc-Tetrofosmin. If patient is on any medicines which can alter the heart rate response (like beta blockers), it is stopped 48 to 72 hrs in advance. Patient comes for the test after overnight fast or four hours after light meal. This will keep the splanchnic circulation dormant and myocardial and skeletal

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muscle perfusion gets primacy at the time of exercise so that the person can achieve optimum level of exercise. Thus the tracer uptake by cardiomyocytes is made better giving better scans. Diabetic patients should not take their anti-diabetic medicine on the day of test as they are fasting. They should carry the medicines along with them so that they can take it after the stress test along with breakfast. Chest has to be shaved to put the ECG electrodes for the TmT.

Patient is made to do TmT as per Bruce protocol. The end points are achieving target heart rate (THR) which is 220 minus age or at least 85% of the same, achieving double product (the product of peak systolic blood pressure and peak heart rate) of 25000. Anginal symptoms, severe breathlessness, fatigue, arrhythmias appearing after starting exercise or fall in systolic blood pressure during exercise.

At one of these end points, patient is injected with 8 to 10mCi of the tracer and exercise stopped one minute after tracer injection. The stress will be stopped by emergency button in case patient develops any significant symptom or sign warranting the same. Stress perfusion images are acquired with ECG gating at 30 to 45 minutes from the time of injection. The distribution of tracer at the time of injection is proportionate to the perfusion of myocardium at that time as blood is the carrier for the tracer. Since the tracer is taken up and retained by mitochondria in cardiomyocytes, it will show the same distribution pattern at the time of imaging even though imaging is done 30 to 45 minutes after injection. If tracer is reaching all parts of myocardium at peak exercise (Fig. 1), it means there is adequate blood supply to all regions of the heart at the time of high demand due to exercise (there can be different color coding for the tracer distribution). That excludes the doubt of IHD and the TmT, which had shown abnormality, can be considered as false positive. Apart from the perfusion image, patient’s effort tolerance, symptoms, blood pressure response, heart rate response, LV volumes, wall motion, wall thickening and post stress LVEF are all taken into consideration before deciding that the stress study is normal. Taking into account all these factors, an experienced nuclear medicine physician can decide with good level of confidence whether stress image is normal. But some centers prefer to take a rest perfusion image also for comparison even if stress image is normal. This is a good practice as it gives more confidence about the study result. In case there is an area of myocardium where the tracer is not reaching at peak exercise, then the patient is made to take rest for 4 hours and 20 to 24 mCi of the tracer is injected intravenous and rest perfusion images are acquired 45 to 60 minutes after the injection. There can be two possibilities. The perfusion abnormality remains same- fixed perfusion defect (scar tissue meaning that the person had an infarct at some point of time involving the area as seen in Fig. 2) or the perfusion becomes normal at rest- called reversible perfusion defect (meaning that there is viable and salvageable myocardium which becomes ischemic at times of high demand like exercise and has normal blood supply at rest as seen in Fig. 3). Fig. 3 shows reversible perfusion defect in anterior wall and septum. Careful analysis of the Fig. 3 reveal that there is exercise induced dilatation of the left ventricle (LV) and cascading effect in right ventricle (RV). In the stress images, RV wall is more clearly seen and RV cavity is more prominent compared to that in rest perfusion images. This indicates stress induced biventricular dysfunction. In normal myocardial perfusion studies, we don’t see the RV clearly because the RV is very thin compared to LV. In cases of RV hypertension and hypertrophy, we see the RV in myocardial perfusion images. More interestingly, there can be apparent

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**Fig. 1**: Normal myocardial perfusion image. The computer reconstructed axial, vertical and horizontal sections of left ventricle shows normal tracer distribution in all regions of left ventricle.

**Fig. 2**: Fixed perfusion defect in septum. There is perfusion defect in septum during stress as well as rest indicating scar in that region.

**Fig. 3**: Reversible perfusion defect in anterior wall and septum.
normal perfusion in all regions in cases of triple vessel disease due to evenly reduced perfusion in all regions. In such cases, stress induced left ventricular cavity dilatation is a subtle sign indicating presence of triple vessel disease. Fig. 4 is the stress MPI image of a person with hypertrophic cardiomyopathy showing stress induced left ventricular dilatation. We can easily make out that the septum is thicker than the lateral wall in the image clearly giving the diagnosis of hypertrophic cardiomyopathy. In hypertrophic cardiomyopathy, the LV cavity dilatation can be due to triple vessel disease or because of the inability of the normal coronaries to perfuse the thickened myocardium at high levels of intra-myocardial pressure. Fig. 5 shows the MPI of a person with triple vessel disease and showing stress induced LV cavity dilatation and extensive reversible perfusion defect in all regions except septum which has normal perfusion at stress. A person detected to be having ischemic salvageable myocardium should undergo angiography to delineate the lesion and myocardial salvage procedures like angioplasty or bypass surgery.

### Material and Methods

A retrospective analysis of the outcome of stress MPI in asymptomatic persons with positive TmT is done to see the outcome. Inclusion criteria was asymptomatic persons with positive TmT in inferolateral leads. During a period of two years, a total 152 asymptomatic persons were referred for stress myocardial perfusion study as they were detected to have positive TmT in the form of ST-T changes in inferolateral leads. There were 24 females in the group. The age ranged from 26 to 74 for males and 36 to 69 for females. The group included serving military personal undergoing regular medical examination and patients detected to have ECG and TmT abnormalities during medical check up for non-cardiac conditions like pre-anesthesia check up. Nobody had any cardiac symptoms. The age profile of patients is given in Table 1.

All these persons with positive TmT did good exercise for their age and had no symptoms during the exercise. They had normal blood pressure and heart rate response during exercise. At peak exercise, they were injected with 8 to 10 mCi of 99m Tc-Tetrofosmin and stress perfusion images were acquired 30 to 45 minutes after the injection. If stress study shows any obvious or even doubtful perfusion defect, rest perfusion study was done four hours after the stress perfusion study with another injection of 20 to 24 mCi of the tracer at rest and rest perfusion images acquired 45 to 60 minutes after injection.

### Discussion

None of the asymptomatic persons with inferolateral TmT changes had positive MPI study. That means all these TMTs with inferolateral abnormality were false positive. This is an interesting finding and needs further analysis.

In accepted diagnostic criteria for positive TmT, there is no clear mention of differential sensitivity between anterior or inferior leads. ST-T changes in all leads are interpreted with equal importance. But here we find that all 152 asymptomatic cases having inferolateral ischemia changes in TmT are found to be false positive. As per ACC/AHA Practice Guidelines—2002, in patients with a normal resting ECG, exercise induced ST segment depression confined to inferior leads is of little value for identification of coronary artery disease. Our experience shows that exercise ECG abnormalities involving inferior as well as lateral chest leads in asymptomatic persons with no cardiac risk factor has no real significance and should be interpreted as normal variation. But, as per present criteria, all these cases are made to undergo further evaluation in the form of stress myocardial perfusion study and even worse, coronary angiography in many cases. Coronary angiography may show lesions which are of doubtful physiological significance creating further confusion.

All cases in the study group with positive TmT in inferolateral leads were asymptomatic healthy persons with no cardiac risk factors and were found to have positive TmT during medical examination.

### Table 1: Age profile of patients

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Fig. 4: Hypertrophic cardiomyopathy with stress induced LV cavity dilatation.

Fig. 5: Stress induced LV dilatation with reversible perfusion defect in anterior wall, lateral wall, apex and inferior wall in a case of triple vessel disease.
Fig. 6a to 9b: Sample cases of false positive TMT and their normal stress MPI.

Fig. 10a to 11b: Sample cases of positive stress induced ischemia in septum and anterior wall showing TMT changes in inferolateral leads.

examination. The figures 6a to 9b shows peak exercise ECG and MPI in same individuals to illustrate the point as sample cases. The fact that none of them had evidence of IHD as proved by normal stress MPI should make us introspect on the procedure being followed in medical evaluation of airline pilots and similar military and civil personals who have to undergo regular medical evaluation including TMT as part of present policy. The reason for the high rate of false positive TMTs showing changes in inferolateral leads also needs further evaluation. This type of false positive findings are not commonly seen in anterior and anteroseptal leads. Rather than ischemia, it may be the diaphragmatic and chest wall movements which are giving rise to ST-T changes in inferolateral leads in exercise ECG. As all physicians know, resting ECG gives very reliable information in asymptomatic as well as symptomatic persons. Ischemic changes in resting ECG are very reliable. But, the exercise ECG probably clouds the information because of the overlap of cardiac, diaphragmatic and chest wall muscle movement voltages.

Having seen so many such cases with these types of abnormal TMT in asymptomatic persons, I have stopped giving much credence to ST-T changes in inferolateral leads and confidently
make the person do exercise to adequate levels (10 METS or more) and achieve heart rate of 100 % of THR before injecting tracer so that there is no doubt in the mind of the person as well the referring physician about the credibility of the myocardial perfusion scan result and the physical fitness including that of cardiovascular system of the person. I depend on the person’s symptom profile and hemodynamic (systolic blood pressure as well as heart rate) response. If the patient develops any of the cardinal cardiac symptoms, the tracer is injected at that point and exercise is stopped irrespective of heart rate and blood pressure. If the tracer distribution at this point is normal, it means that the patient’s symptom is not due to ischemia. If it shows perfusion abnormalities, it means that the symptom is actually due to ischemia.

It is known that ST-T changes in TMT do not reflect the arterial territory or region of myocardial ischemia. We had several cases with TMT abnormality in inferolateral leads and perfusion defect in anteroseptal region of left ventricle as shown in pictures 10a to lib as examples. In these patients with true ischemia, the TMT is showing changes in inferolateral leads that does not represent the ischemic region. In Fig. 12a, the TMT does not show significant ischemic changes while the person has actually a large area of exercise induced ischemia as shown by the stress MPI (Fig. 12b). These three cases shown in pictures 10 to 12 had reported with cardiac symptoms and had angina during the TMT and are not part of the study group. They are included just to emphasize the point that inferolateral changes in TMT is nonspecific and also that TMT can be misleading in patients with actual stress induced ischemia.

These types of cases have really shaken the credibility of exercise ECG as a tool to assess myocardial ischemia and its role in the battery of investigations in patients with cardiac symptoms as well as the asymptomatic persons who are forced to undergo exercise ECG as per the prevailing regulations. This needs to be analyzed in detail and can be done by a two pronged approach. First, already existing records of airline pilots and other healthy personal who have undergone MPI can be checked to see what were the TMT findings and MPI results. Second, a multicentric prospective study can be done involving all asymptomatic persons who are found to have positive TMT referred for MPI. In the prospective study, to avoid any doubt about the outcome and final interpretation, a rest study also should be done even if stress study is normal. That will add to the credibility of the study and avoid even the remote possibility of missing out a case of triple vessel disease. In such a study, if it is found that all inferolateral TMT abnormalities in asymptomatic end up in normal MPI studies, we can safely consider them as normal variants and stop sending such cases for MPI. That will save a lot of resources, time and effort.

References