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Prternational C	OMPARATIVE STUDY OF TREADMILL STRESS TES CORONARY ANGIOGRAPHY (CAG) IN PATIENTS CORONARY ARTERY DISEAS	T(TMT) WITH INVASIVE S WITH SUSPECTED E
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ABSTRACT Backgr	cound- There are few studies which compared invasive coronary of	angiography (CAG) in patients

Background- There are few studies which compared invasive coronary angiography (CAG) in patients presenting with chest pain (atypical, probably ischemic) in outpatient department with negative or inconclusive treadmill stress test (TMT).

Objective-To assess CAG findings in patient with suspected iscemic chest pain, with negative or inconclusive TMT.

Methods- Patients with chest pain (atypical, probably ischemic) underwent TMT and classified as TMT negative or inconclusive. These patients underwent CAG and findings were analysed.

Results - 50 patients completed the study protocol. Of these 50 patients who underwent TMT, 31 (62%) were TMT negative and 19 (38%) were TMT inconclusive. In TMT negative group CAG showed obstructive lesion in 6(19.4%), and non obstructive lesion in 25(80.6%). In TMT inconclusive group CAG showed obstructive lesion in 11(57.8%), while non obstructive lesion in 8(42.2%).

Conclusion-In patients with atypical chest pain with negative or inconclusive TMT with suspicion of coronary ischemia CAG provides an important diagnostic tool for assessing, especially with TMT inconclusive group.

KEYWORDS : TMT (treadmill stress test), CAG (invasive coronary angiography)

INTRODUCTION

Coronary artery disease (CAD) is leading cause of death worldwide with an enormous burden on health care systems. Annually, more than 10 million stress tests and approximately one million diagnostic cardiac catheterizations are being performed in the United states of america.

In the present health care scenario with urbanized and changes in lifestyle are major cause of increased prevalence of diabetes, obesity, hypertension and hypercholesterolemia. Hence these predisposes to cardiovascular diseases (CVDs) including coronary heart disease and stroke.[1]

The accuracy of the TMT in predicting significant coronary heart disease depends on Bayes' theorem. In asymptomatic patient with predisposing factors for CADs can be diagnosed with an abnormal TMT by > 90% accuracy.[2] Accurate screening and diagnosis of CADs is very important for timely intervention and prevention of mortality. CAG, which is used as a gold standard for the diagnosis of CAD. Even though the TMT is a cost-effective, easily available, and widely applicable approach for early diagnosis of CAD, it has a relatively low sensitivity and specificity.

Specificity of TMT is lowered somewhat by resting ST depression of less than 1 mm, although it is still the first option in evaluation of possible CAD in such patients with an intermediate pre-test probability. Specificity is also lowered by LVH with less than 1 mm of ST depression and use of digoxin with less than 1 mm of ST depression, but the standard exercise test is still a reasonable option in such patients[6]

In contrast, other baseline ECG abnormalities such as preexcitation, ventricular pacing, greater than 1 mm of ST depression at rest, and complete left bundle branch block greatly affect the diagnostic performance of the exercise test. Imaging modalities are preferred in these subsets of patients. Also, TMT has got lower diagnostic accuracy in women.[7] In the elderly, due to the greater prevalence of CAD, it has got a

slightly higher sensitivity than in younger patients with a slightly lower specificity, which may reflect the coexistence of LVH due to valvular disease and hypertension.

Though in a high risk patient abnormal TMT is highly predictive of a coronary heart disease with more than 90% accuracy but a relatively normal or inconclusive TMT may not reflect the absence of significant disease in a person with the same risk factors.

Similarity, in a low-risk patient a normal TMT is very predictive of the absence of significant coronary heart disease with more than 90% accuracy but an abnormal test may reflect a "false-positive TMT".

For low pretest probability of disease, TMT is a good non invasive test to assess functional capacity and functional testing of patients. To avoid risks of invasive procedure of angiography in low to intermediate risk patients there are many non invasive methods for evaluation including the exercise treadmill test(TMT), stress echocardiography, stress myocardial perfusion scintigraphy, pharmacologic nuclear stress testing, electron beam Computed Tomography (EBCT), multi detector CT (MDCT), and stress cardiac magnetic resonance imaging.

Duke treadmill score (DTS) in TMT is done for risk stratification, functional assessment and outcomes after TMT. For anatomical assessment a multi-detector computed tomography technology can help us in assessment of presence, location, severity of coronary artery disease especially in patients with negative or borderline TMT yet clinically symptomatic.

Exercise Treadmill Test being non-invasive, relatively inexpensive and widely used in the clinical setting. Exercise tolerance testing is widely used as a diagnostic test in the initial evaluation of patients with symptoms suggestive of myocardial ischaemia and in persons with previously recognized coronary heart disease.

MATERIALS AND METHODOLOGY

The study was a prospectively planned analysis of 50 patients with atypical chest pain, who presented in the out-patient department of Cardiology.

Patients presenting as chest pain, possibly ischaemic in origin (atypical chest pain) underwent baseline evaluation followed by TMT using standard Bruce protocol. Only patients with negative or inconclusive TMT were enrolled in the study and planned for coronary angiography with consent.

INCLUSION CRITERIA:

- 1. Patients presenting with chest pain, possibly ischaemic in origin (atypical chest pain).
- Patient symptoms not suggestive of acute coronary syndrome.
- 3. Not a known case of CAD.
- 4. No prior acute coronary syndrome, prior PCI or CABG.
- Possibly ischemic pain but TMT negative / inconclusive, not responding to treatment

EXCLUSION CRITERIA:

Exclusion for TMT:

- 1. Patients presenting as classical angina or non cardiac chest pain.
- 2. Baseline ECG abnormalities such as LVH with ST depression of >1 mm, LBBB, pre-excitation, ventricular pacing, > 1mm of ST depression
- 3. Patients not able to perform TMT or are having contraindications for TMT.

BASELINE EVALUATION

- (i) Detailed history and physical examination of all patients who were enrolled in the study.
- (ii) Routine blood investigations e.g. Hb. TLC, DLC, blood urea, serum creatinine, serum Na+ /k+, random blood sugar
- (iii) Treadmill testing using standard Bruce protocol

TREAD MILL TESTING:

The exercise ECG testing facility conformed to the American Heart association (AHA) guidelines 3 for clinical exercise ECG testing laboratories. All the enrolled patients then underwent TMT. TMT was done according to standard Bruce protocol.

On the basis of ECG response to exertion and symptoms, results of TMT were judged as:

- 1. **TMT positive:** >1mm ST depression below baseline or slow upsloping ST depression or ST elevation on exertion.
- TMT inconclusive: patients who failed to achieve 6 METs or who failed to achieve 85% of age-predicted maximum heart rate without ischemic responses in ECG.
- TMT negative: patient who completed their protocol, achieved target heart rate, without symptoms and ECG changes of ischaemia.

ECG changes with rapid upsloping changes or ST depression $< 1\,\rm{mm}\,was$ also considered as negative.

INVASIVE CORONARY ANGIOGRAPHY (CAG):

Selected patients then underwent CAG (Siemens Axiom Artis uniplane coronary angiography machine) using the standard procedure. Multiple views were taken and the cine images were then assessed by the experienced cardiologists using the QCA (Quantitative Coronary Angiography) method. All the lesions were then grouped as follows: plaquing; <50%; 50-70%; and >70% stenosis. We considered lesion with >50% stenosis as obstructive lesion.

STATISTICAL ANALYSIS:

Statistical analysis was performed with the use of SPSS 15.0 software package and Graph Pad InStat online software. A probability value of <0.05 was considered significant for statistical testing.

Comparison of the factors between the groups was done by Chi-square test or Fischer's test. To determine the accuracy of coronary angiography we calculated conventional measures of diagnostic accuracy. The Chi-square test was used to compare proportions and measures of diagnostic accuracy between groups.

RESULTS:

A total of 50 patients completed the study protocol. Mean age of patients was 51.74 ± 7.65 years , 22% were females, 28% were hypertensive and 38% were diabetic. (table 1)

Table 1: Baseline variables

Variables	No. of patients (n=50)
Age (years)	51.74± 7.65
Female sex	11 (22%)
Hypertension	14 (28%)
Diabetes mellitus	19 (38%)

After TMT, patients were classified as having negative or inconclusive TMT. Out of 50 patients, 31(62%) were TMT negative and 19(38%) were TMT inconclusive.

Baseline characteristics were nearly same in both the groups, although there were more co-morbidities in patients with inconclusive TMT with higher prevalence of hypertension and diabetes mellitus. (table 2)

Table	2 :	Baseline	characteristics	of	TMT	negative	and
incond	lus	sive group	s				

Variables	TMT-	TMT-	Total	р
	Negative	inconclusive	(n=50)	value
	(n= 31)	(n= 19)		
Age (years)	51.42 ± 7.38	52.26 ± 8.24	51.74 ± 7.65	0.741
Female sex	6 (19%)	5 (26%)	11 (22%)	0.727
Hypertension	7 (22%)	7 (37%)	14 (28%)	0.339
Diabetes Mellitus	10 (32%)	9 (47%)	19 (38%)	0.372

Patients with inconclusive TMT had poor exercise capacity and achieved less METs, as compared to patients with negative TMT. Both of these variables were statistically significant, with p value < 0.05. (table 3)

Table 3: Comparison of exercise capacity and METs achieved in TMT negative and inconclusive groups

Variables	TMT-	TMT-	Total	р
	Negative (n= 31)	inconclusive $(n = 19)$	(n= 50)	value
Exercise time (minutes)	7:13±1:37	5:24±1:14	6:32±1:43	0.0001
METs	7.86±1.97	6.33 ± 1.67	7.28 ± 1.99	0.007

Patients with TMT negative group has 6(19.4%) patients with obstructive disease on CAG, while with non obstructive disease were 25(80.6%). TMT inconclusive has 11(57.8%) patients with obstructive disease, while 8(42.2%) patients has non obstructive disease.

In CAG with obstructive disease, TMT negative patient were 6(35.3%) while TMT inconclusive were 11(64.7%). Among CAG non obstructive disease, TMT negative group has 25(75.8%) patients while TMT inconclusive patients were 8(24.2%). (Table 4) shows significant obstructive disease in TMT inconclusive subjects with p value 0.0052

Table 4: Comparison of obstructive CAD on CAG with the TMT Results:

Variables	TMT Negative Total-31	TMT Inconclusive Total-19	Total-50
CAG (Obstructive CAD)	6(19.4%)	11(57.8%)	17(34%)
CAG (Non Obstructive CAD)	25(80.6%)	8(42.2%)	33(66%)

(Pvalue-0.0052)

DISCUSSION

Chest pain presenting to the outpatient department is triaged into classical angina, atypical chest pain, or non cardiac chest pain. Patients with atypical chest pain and with intermediate probability of CAD are further investigated with stress studies. TMT is the most commonly used stress study in such cases.

TMT as a tool in diagnosing CAD have a low sensitivity. Exercise testing for the diagnosis of CAD is most commonly expressed by sensitivity and specificity.

A meta-analysis[3] of 58 consecutively published reports involving 11,691 patients without prior myocardial infarction who underwent coronary angiography and exercise testing revealed a wide variability in sensitivity and specificity. Mean sensitivity and specificity were 67% and 72%, respectively. In the three studies, where work-up bias was avoided by having the patients agree to undergo both procedures, the approximate sensitivity and specificity of 1 mm of horizontal or down sloping ST depression for diagnosis of CAD were 50% and 90%, respectively. The authors concluded that the true diagnostic value of the exercise ECG lies in its relatively high specificity.

Gianrossi et;al[4] applied meta-analysis to 147 consecutively published reports comparing exercise-induced ST depression with coronary angiography. These reports involved 24,074 patients who underwent both tests. There was a wide variability in sensitivity and specificity (mean sensitivity, 68%; range, 23-100%; standard deviation (SD), 16%; and mean specificity, 77%; range, 17-100%; SD, 17%). Later on, results of 41, out of 147 studies were re-analysed. These 41 studies excluded patients with prior myocardial infarction (MI). It showed a lower mean sensitivity and specificity of 68% and 74%, respectively.

Kusljiguc et al [5]reported that the sensitivity of TMT is less than optimal, and should be supplemented by other noninvasive techniques (such as myocardial perfusion scintigraphy, radionuclide ventriculography and stress echocardiography) in diagnosis of CAD.

In our study, 50 patients of atypical chest pain underwent TMT, followed by coronary angiography. Mean age of the patients was 51.74 ± 7.65 years and 22% of the patients were females. After TMT, patients were labelled as either with negative or inconclusive test. Out of 50 patients, 31 (62%) were TMT negative and 19 (38%) were TMT inconclusive. Number of patients in the two groups were not equal, as 50 consecutive patients were enrolled in the study. Despite this, baseline characteristics were similar in the two groups in terms of age, sex, and risk factors (hypertension and diabetes mellitus), but there were more percentage of patients with hypertension and diabetes mellitus in TMT inconclusive group.

Patients with inconclusive TMT, as compared to patients with negative TMT, had poor exercise capacity (exercise time: $5:24 \pm 1:14 \text{ v/s} 7:13 \pm 1:37 \text{ minutes}, p = 0.0001$) and achieved less METs ($6.33 \pm 1.67 \text{ v/s} 7.86 \pm 1.97$, p= 0.007). The difference of both these variables in the two groups were statistically significant with p value < 0.05

By using CAG, obstructive CAD observed in both the groups In 6 (19%) patients out of 31 negative TMT were found to have obstructive CAD on CAG while 11 (58%) patients out of 19 TMT inconclusive patients were found to have obstructive CAD on CAG which is statistically significant with p value <0.05. Suggesting that TMT inconclusive have higher chances of obstructive CAD.

As per study of R.Gunasekaran and P.Kannan(8), the relationship of CAG with TMT, there was statistically significant correlation between CAD and TMT, in diabetics and non-diabetics (P = 0.005 highly significant) from the study.

METs in an independent predictor of the exercise of TVD or LMS. Relationship between METS and diabetes mellitus, it was found that METS 7 was 18% in diabetic and 31.5% in nondiabetic. As per Bartel AG et;al, who reported a positive relationship between workload and existence of TVD or LMS in diabetics and non-diabetics. Similarly in our study we found that, there were more comorbidities, including diabetes mellitus and hypertension in TMT inconclusive group. (table 2)

Patient with TMT inconclusive had poor exercise capacity and achieved less METs, as compared to TMT negative group.(table 3)

In our study there is a strong correlation between the TMT negative and inconclusive group with exercise time achieved and METs achieved, which being less METs and small duration of exercise time achieved with TMT inconclusive group. Similarly obstructive disease on CAG was found to be more linked with TMT inconclusive group as compared to TMT negative group. The risk factors like hypertension, diabetis mellitus were found to be more in patients with TMT inconclusive group, suggesting that obstructive CAD is more associated with these risk factors.

CONCLUSION

An important drawback of the present study was the relatively small sample size. TMT is a good test for functional assessment of patient, esp with low pretest probability of disease.Because of the low sensitivity and all other drawbacks of TMT, negative test or inconclusive test should not be considered as normal, should be confirmed by further tests such as repeat TMT, CT coronary angiography, invasive coronory angiography, thallium scan, stress echo test. Thus for patient with low probability of disease and post myocardial infarction TMT can be used as an tool for functional assessment, while invasive coronary angiography (CAG) for anatomical assessment.

ABBREVIATIONS-

TMT- treadmill stress test CAD- coronary artery disease MET- metabolic equivalent of task CAG- coronary angiography CVDs- cardiovascular disease **EBCT**- electron beam computerized tomography MDCT- multidetector computed tomography DTS- duke treadmill score PCI- percutaneous coronary intervention CABG- coronary artery bypass graft LVH- left ventricular hypertrophy AHA- American heart association QCA- quantitative coronary angiography M.I- myocardial infarction TVD- triple vessel disease LMS- left main stenosis

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