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EVALUATION OF USEFULNESS OF TREADMILL TEST IN DETECTION OF SUBCLINICAL OR LATENT MYOCARDIAL ISCHAEMIA IN NON-INSULIN DEPENDENT DIABETES MELLITUS PATIENTS.

General Medicine

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ABSTRACT

Background: The risk of Coronary artery disease (CAD) is 2-3 times higher in diabetics than non-diabetics. Exercise ECG can identify the majority of patients likely to have significant ischemia during their daily activities and remains the most important screening test for significant CAD. This study was designed to evaluate importance of TMT in the early diagnosis of ischemic heart disease or prediction of CAD in asymptomatic NIDDM patients. **Methodology:** The present 2-year prospective study was conducted at Kolhapur, Maharashtra on 100 2 DM patients without clinical evidence of CAD. TMT was done as a routine screening procedure in otherwise 'normal' individuals. The detailed history and investigations were recorded in case proforma. All individuals undergone a routine X-ray chest & 12 lead ECG prior to performing the TMT. **Results:** Mean age of the patients was 45.5 years and majority of the patients belong to age group 51 to 60 years (60%). 62% patients were male and 38% were females. The frequency of TMT positivity increased as the age interval increases. Positive TMT is more associated with anormal ECG than symptomatic. The most common parameter found in our patients is albuminuria (67%), least common is chest pain. Among TMT positive group, most common associated finding is autonomic neuropathy (60.65%) followed by habit history (includes smoking and/or tobacco chewing), and least common is again chest pain or equivalent symptoms. Most patients (58%) were in normal range group, but most TMT positive cases were in overweight group (44.44%). Total 41/100 patients (includes males and females) had abnormal waist circumference, of which 26 patients (63.41%) were TMT positive. More females are having abnormal circumference 29 (76.31%) than males 12 (19.67%). Most patients were having poorly controlled DM (47%). Maximum TMT positive patients were in uncontrolled groups i.e. 43.47% in fair control group and 46.80% in poor control group. **Conclusion:** TMT is a useful and safe procedure in diabetic patients. TMT considerably improves the specificity of diagnosis of IHD in diabetes mellitus. TMT also improves sensitivity of diagnosis of IHD. TMT is useful in the diagnosis of silent ischemia in 56.4 % of patients having IHD confirmed after TMT.

KEYWORDS

Subclinical myocardial ischaemia, Latent myocardial ischaemia, Treadmill test, Non-insulin dependent diabetes mellitus

INTRODUCTION

Diabetes mellitus is the commonest endocrine disease affecting mankind. The incidence of this disease continues to be on the rise all over the world. The risk of Coronary artery disease (CAD) is 2-3 times higher in diabetics than non-diabetics. CAD is the leading cause of death in patients with type 2 diabetes and is often asymptomatic because of silent myocardial ischemia[1]. The prevalence of CAD in our country varies from 25.27/1000 and 64.37/1000 population for rural and urban areas respectively.' Data from Framingham Heart Study demonstrate the increased and poor prognosis of cardiac disease in diabetes. Mortality related to cardiovascular disease is doubled in diabetic men and quadrupled in diabetic women over that in their non diabetic counterparts[2].

CAD can be asymptomatic in diabetes and may present with sudden death, myocardial infarction, arrhythmia, silent myocardial ischemia or heart failure. The association between diabetes and asymptomatic coronary artery disease has been attributed to an autonomic neuropathy[3]. Early detection of asymptomatic CAD in type 2 diabetes may prevent catastrophic cardiac events. However, periodic thorough clinical examination and resting ECG may fail to detect coronary artery disease. Hence sophisticated cardiovascular non-invasive tests should then be proposed for early detection of CAD in these patients. Exercise electrocardiograph can identify the majority of patients likely to have significant ischemia during their daily activities and remains the most important screening test for significant CAD[4]. This study was designed to evaluate importance of TMT in the early diagnosis of ischemic heart disease or prediction of CAD in asymptomatic NIDDM patients.

Objectives:

1. To Study prevalence of silent ischemia in diabetics and usefulness of TMT in diabetic patients in detection of subclinical or latent myocardial ischemia.
2. To evaluate the clinical correlation and correlation of major CAD risk factor with the occurrence of CAD.

MATERIAL AND METHODS:

The present two-year prospective study was conducted at Niramaya hospital, Ichalkaranji, Kolhapur, Maharashtra on 100 patients of type 2 diabetes mellitus in age group of 30-60 year without clinical evidence of coronary artery disease among patients attending to diabetic clinic and medicine OPD, diabetic association centre, diabetic camps from February 2022 to February 2023. Asymptomatic individuals with resting ECG change suggestive of ischemia (e.g. Non-specific ST-T wave changes), Symptomatic Patients who complain of chest pain not classical of angina but have a normal ECG and individuals who have no symptoms and have normal ECG were included. TMT was done as a routine screening procedure in otherwise 'normal' individuals.

Patients with clinical or documented evidence for contraindication of treadmill test and those who cannot perform test, patients with known case of CAD, documented myocardial infarction, unstable angina, LBBB, severe LVH, stenotic valvular heart disease, tachyarrhythmia or bradyarrhythmia, cardiomyopathy and those who had undergone bypass surgery and patients with severe arterial hypertension- SBP >200 and DBP>110 were excluded.

In all the study subjects a detailed history was taken including a history of smoking and alcohol and any other risk factor. A complete physical examination done with detailed cardiovascular assessment and evaluation of peripheral pulses in all cases. All individuals undergone a routine X-ray chest & 12 lead ECG prior to performing the TMT.

Technique Of Treadmill Test

The patient was instructed not to eat or drink caffeinated beverages three hours prior to testing and to wear comfortable shoes. A standard 12 lead electrocardiogram was taken following which a torso ECG was obtained in the supine position and in the sitting or standing position. Blood pressure was recorded and the patient was instructed on how to perform the test. Standard multistage maximal exercise test was done on a computerized treadmill machine using same machine in collaboration with cardiologist. The heart rate, blood pressure and ECG were recorded at the end of each stage of exercise, immediately before and after stopping the exercise and for each minute for at least 8 to 10 minutes in the recovery phase. Exercise test was terminated in all

patients following the achievement of target heart rate or an abnormal ischemic response. Exercise test was also terminated if patient developed dyspnoea, fatigue or chest pain.

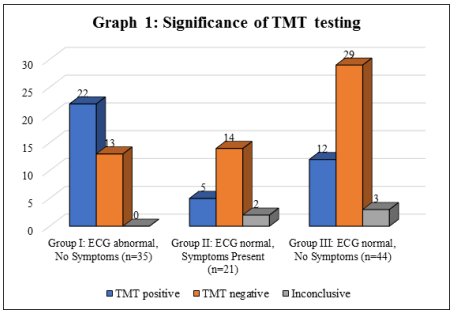
RESULTS:

We studied total 100 cases of type 3 diabetes mellitus without clinical evidence of ischemic heart disease. Mean age of the patients was 45.5 years and majority of the patients belong to age group 51 to 60 years (60%). 62% patients were male and 38% were females.

Table 1: Age And Gender Profile Of The TMT Positive Patients:

Patient Variables		Total No.	TMT positive	TMT negative	Inconclusive
Age (Years)	30 to 40	13 (13%)	4 (10.25%)	8 (14.29%)	1
	41 to 50	27 (27%)	6 (15.38%)	19 (33.93%)	2
	51 to 60	60 (60%)	29 (74.35%)	29 (51.78%)	2
Gender	Male	62 (62%)	22 (56.41%)	37 (66.07%)	3
	Female	38 (38%)	17 (43.59%)	19 (33.93%)	2
Total		100 (100%)	39 (100%)	56 (100%)	5

The frequency of TMT positivity increased as the age interval increases. For age group 51 to 60, it is maximum (74.35%). Although a slightly higher prevalence was seen among females, this failed to reach statistical significance.



Significance Of TMT Testing:

Among abnormal ECG, 22 (62.86%) patients had positive TMT and among symptomatic patients, only 5 (23.81%) had positive TMT, and among asymptomatic patients, 34 (43.03%) had positive TMT. Thus, positive TMT is more associated with anormal ECG than symptomatic (Graph 1).

Table 2: Clinical Characteristics Of TMT Positive Patients:

Groups	TMT positive	TMT negative	t-statistics	P value
Age (Years)	53.2±2.29	50.8±2.08	1.58	0.12
Duration of DM (Years)	6.12±1.65	5.42±1.44	0.63	0.53
Systolic BP (mm of Hg)	132.21±4.27	132.21±3.66	0	1
Diastolic BP (mm of Hg)	79.18±2.91	80.75±2.05	-0.87	0.39
Body Mass Index	24.28±0.91	24.27±1.05	0.02	0.99
Waist Circumference (cm)	**93.21±2.24**	**89.21±1.76**	**2.79**	**0.01**

The age of the patients, duration of diabetes and systolic blood pressure and BMI were higher in the treadmill positive patients but failed to reach statistical significance. Only the waist circumference had a positive correlation with TMT positivity.

Symptomatology Of The Diabetes Patients And TMT Positivity:

The most common parameter found in our patients is albuminuria (67%), least common is chest pain. Among TMT positive group, most common associated finding is autonomic neuropathy (60.65%) followed by habit history (includes smoking and/or tobacco chewing), and least common is again chest pain or equivalent symptoms (Graph 2).

Body Mass Index, Waist Circumference Of The Diabetes Patients And TMT Positivity:

Most patients (58%) were in normal range group, but most TMT positive cases were in overweight group (44.44%). Total 41/100 patients (includes males and females) had abnormal waist circumference, of which 26 patients (63.41%) were TMT positive. More females are having abnormal circumference 29 (76.31%) than males 12 (19.67%) (Table 3).

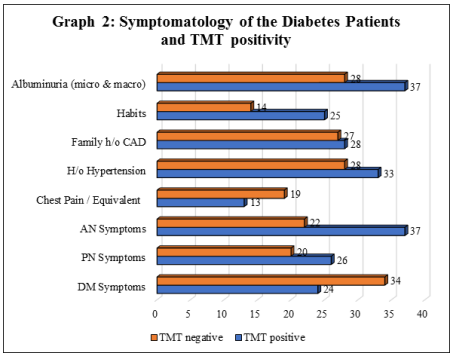


Table 3: Body Mass Index, Waist Circumference Of The Diabetes Patients And TMT Positivity:

Anthropometric Parameters			Total No.	TMT positive	TMT negative	Inconclusive
Body Mass Index	Normal (18.5 to 24.9)		58(58%)	23(39.66%)	35(62.5%)	0
	Overweight (25 to 29.9)		36(36%)	16(44.44%)	16(28.57 %)	4
	Obesity (≥ 30)		6(6%)	0(0.0%)	5(8.93%)	1
Total			100 (%)	39(100%)	56(100%)	5
Waiste Circum-ference	Male	Normal	50(80.65 %)	12(54.55%)	37(100%)	1
		Abnormal(≥102)	12(19.35 %)	10(45.45%)	0(0.0%)	2
		Total	**62(100 %)**	**22(100%)**	**37(100%)**	**3**
	Female	Normal	9(23.68 %)	1(6.25%)	7(36.84%)	1
		Abnormal(≥88)	29(76.32 %)	16(93.75%)	12(63.16 %)	1
		Total	**38(100 %)**	**17(100%)**	**19(100%)**	**2**

Table 4: Glycosylated Haemoglobin And TMT Positivity:

HbA1c (gm%)	Total No.	TMT positive	TMT negative	Inconclusive
Normal (<6.2)	14 (100%)	2 (14.28%)	12 (85.71%)	0
Good Control (6.2 to 6.7)	16 (100%)	5 (31.25%)	8 (50%)	3
Fare Control (6.8 to 7.5)	23 (100%)	10 (43.47%)	11 (47.82%)	2
Poor Control (<7.6)	47 (100%)	22 (46.80%)	25 (53.19%)	0

Most patients were having poorly controlled DM (47%). Maximum TMT positive patients were in uncontrolled groups i.e. 43.47% in fair control group and 46.80% in poor control group.

DISCUSSION:

Coronary atherosclerosis occurs more commonly in diabetics compared to non-diabetic individuals. patients with diabetics may have advance IHD, but remain asymptomatic. treadmill testing is a useful procedure to diagnose silent ischemia, especially in diabetics. The present study was aimed at the early diagnosis asymptomatic coronary artery disease in diabetes mellitus patient by simple, sensitive and safe non-invasive test.

Clinical Characteristics Of TMT Positive Group:

The age of patients and duration of diabetics is slightly higher in TMT positive patients, but statistically no significant difference is found in our study but a study of **G. Premalatha et al**[5] had reported a positive association of age and duration of diabetes with that of TMT positivity . Similarly, **Gupta et al**[6] and other study by **Athuwalia V et al**[7] also reported the same. A study of **Sargin H et al**[8]**,** including 500 patients with type 2 diabetes mellitus with normal resulting ECG reported that, the abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$).

Our study reported statistically no significant difference in average blood pressure in TMT positive and TMT negative group. On the contrary, epidemiology evidence shows a continuous and graded relationship between increasing blood pressure and increasing risk of cardiovascular events[9]. The **UKPDS** has identified hyperglycemia,

hyperlipidemia, hypertension, and smoking as the most important factors for CVD risk in people with diabetes[10].

The present study found that 53.06% (26/49) with peripheral neuropathy and CAD by tread mill test, while only 25.49%(13/51) without peripheral neuropathy had positive TMT. Thus, in our study diabetes with peripheral neuropathy had a greater incidence of asymptomatic coronary artery disease than those without it (53.06% vs 25.49%). In study of **Athuwalia V et al [7],** 61.5% subject with peripheral neuropathy had silent myocardial ischemia. These finding are consistent with **Marin Huerta E et al[11].**

In our study, 60.65 of subjects (37/61) with autonomic neuropathy had asymptomatic coronary artery disease while only 5.12% of subjects (2/39) without autonomic neuropathy had asymptomatic coronary artery disease. Thus, we found that, diabetes with autonomic neuropathy had higher incidence of associated asymptomatic coronary artery disease than those without it (60.65% vs 5.12%). **Murray DP et al[12],** reported silent myocardial ischemia much more common with autonomic neuropathy (92% vs 39%). **Gupta SB et al[6],** found 38.3% to have silent myocardial ischemia with greater prevalence in those with autonomic neuropathy (59%) than those without it (20%). **Langer A et al[13] and Quek DK et al[14]** also supports this finding.

In our study 63/100 patients had history of hypertension and of those i.e. 33.63 (52.38) had positive TMT. Likewise, 59 patients had family history of CAD, of which 28 (47.45) were TMT positive. This suggests hypertension and family history of CAD increases the like hood of TMT positivity in diabetics patients. **Sang Yoo study group[15],** showed that family history of CAD (odd ratio [OR]=9.41; 95% confidence interval [CI], 1.60-55.49) is independent CAD risk factor in asymptomatic patients. The habit mainly cigarette smoking and tobacco chewing are also important risk factor for CVD in diabetics.

In our study history of smoking and /or tobacco chewing was strongly associated with asymptomatic coronary artery disease in diabetics. In the Nurse Health study , cigarette smoking markedly augmented the risk of CAD across those of smoking were 1.21 for current smoker. Results were also similar in the **UKPDS**. Thus, smoking cessation can have a important effect on CAD risk reduction among diabetes patients[10].

Present study observed the close association of diabetic neuropathy and CAD ,as evident by albuminuria (micro and macro albuminuria). 55.22% patients of albuminuria had TMT positive. The strong **UKPDS** also found micro albuminuria associated with abnormal electrocardiogram in type 2 diabetics. The Steno Diabetes centre group clearly demonstrated that renal disease statistically accounted for much, but not all, of the excess cardiovascular risk in diabetics[10].

In present study, average BMI in TMT positive group 24.28±0.91 vs 24.27±1.05 in TMT negative group. Total 41/100 patients having abnormal waist circumference, of these 26 patients (63.41%) had CAD. This indicate abdominal obesity is associated with more TMT positivity in diabetics patients. These results are consistent with the **NCEP-ATP III report[16], Framingham cohort[17] INTERHEART study[18].** Many other studies also demonstrated that each component of metabolic syndrome increases risk for developing of CVD by as much as fourfold[19,20].

Our study also found that abnormal waist circumference, which is an important component of the most recent and frequently applied diagnostic criteria for the metabolic syndrome is more common in females (76.31%) than males (19.67%). This result is comparable with data from **NHANES III[21],** the age-adjusted prevalence of the metabolic syndrome in is 34% for men and 35% for women.

Our study revealed degree of glycemia is associated with occurrence of CAD. Maximum TMT positive patients were in uncontrolled groups i.e. 43.47% in fair control group and 46.80% in poor control group. The **European Prospective Investigation (EPIC-Norfolk)** study supports our finding[22]. **Wild SH et al[23]** had shown an association between levels of glycemia and macrovascular events like CAD. The **ACCORD Trial[24]** concluded that average A1C is strongly associated with macrovascular complication and death in diabetics. Their results are also similar with epidemiologic analyses from **UKPDS study[25].**

CONCLUSION:

We conclude that TMT is a useful and safe procedure in diabetic patients. TMT considerably improves the specificity of diagnosis of IHD in diabetes mellitus. On routine screening for IHD, TMT can be diagnostic in 27.27% of individuals with diabetes. Thus, TMT also improves sensitivity of diagnosis of IHD. TMT is useful in the diagnosis of silent ischemia in 56.4 % of patients having IHD confirmed after TMT. Abnormal ECG is not always CAD, it can over diagnose IHD in 37.14 % cases. Normal ECG does not exclude CAD, it can miss 26.15% cases. So, TMT is useful in such situations.

Waist circumference, which is an important component of the metabolic syndrome, increases the CVD risk. The autonomic neuropathy is most closely related to TMT positivity. The increased frequency of silent ischemia in diabetics may be due to the associated cardiac autonomic neuropathy. Other symptoms like peripheral neuropathy, nephropathy, history of hypertension, family history of CAD and habits is also associated with occurrence of CAD. Degree of glycemia is also closely associated with CAD in diabetes.

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