International Journal of Advances in Medicine
Nagrani S et al. Int J Adv Med. 2021 Apr;8(4):557-562
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20211055

Original Research Article

Study of exercise treadmill test in type 2 diabetes mellitus patients

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Received: 11 February 2021
Accepted: 16 March 2021

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ABSTRACT

Background: The aim of this study was to assess the prevalence and clinical predictors of silent myocardial ischemia in patients with type 2 diabetes mellitus, and the early diagnosis of coronary artery disease.
Methods: A cross sectional prospective study was conducted including all confirmed diabetic patients in the age group between 40-60 in Bharati medical college hospital Pune in western Maharashtra. A detailed clinical examination and history was taken and relevant laboratory investigations, Electrocardiogram and Treadmill Stress test was done using Bruce protocol. The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. All analysis was carried out by using SPSS software version 21.
Results: Male preponderance was seen in the study with 64% of the study subjects. The mean age of the study subjects was 50.67±5.51 years. A $p<0.001$ was obtained showing positive correlation between BMI and TMT positivity. TMT positivity steadily increased with the duration of diabetes mellitus. Obtained $p<0.001$. The correlation between dyslipidemia and TMT positivity was significant, with a $p=0.007$. Correlation of Fasting as well as Post-prandial blood glucose levels with TMT positivity proved to be statistically significant, with a $p<0.001$.
Conclusions: Exercise Treadmill test in diabetic patients has a significant role in screening diabetic individuals for coronary ischemia. The results obtained clearly indicate that an exercise treadmill test may be proposed as the first test for screening for coronary ischemia in diabetic population as it is safer, cheaper and non-invasive.

Keywords: Diabetes Mellitus, Treadmill test, Coronary heart disease, Blood sugar, Bruce protocol

INTRODUCTION

Thirty million people suffer from diabetes in India according to the study of diabetic society of India. Type 2 diabetes is the most prevalent form of diabetes. There has been a global epidemic of type 2 diabetes mellitus more so in the developing world.[1,2]

Myocardial involvement in diabetes may occur relatively earlier impairing early diastolic relaxation. The greatest cause of mortality in type 2 diabetes is coronary artery disease and its sequelae.[3] The Framingham study has shown that cardiovascular mortality is twice in diabetic men and four times in diabetic women as compared to non-diabetic counterparts. Exercise is a common physiological stress used to elicit cardiovascular abnormalities not present at rest and to determine adequacy of cardiac function. It has emerged as the most practical and non-invasive means of discovering latent ischemic heart disease. The diagnostic value of the stress test is maximum when applied to a population in which the diagnosis is most uncertain.

Even when there is no history of chest pain, there exists a strong possibility of significant narrowing in the coronary tree in patients with appropriate risk factors, especially diabetes mellitus.

An attempt will be made through this study to detect early disease and offer treatment modalities to asymptomatic patients having diabetes mellitus.

The aim of this study was to assess the prevalence and clinical predictors of silent myocardial ischemia in patients with type 2 diabetes mellitus, and the early diagnosis of coronary artery disease.

METHODS

A hospital based cross-sectional prospective study was undertaken at Bharati medical college hospital Pune in western Maharashtra for a period of two years between June 2016 and June 2018.

All the patients in the study were diagnosed cases of diabetes mellitus, either taking oral hypoglycemic agents or Insulin for diabetes control.

100 diabetic patients, either presenting to the medicine OPD or admitted to the wards were included in the study by using simple random method, after ethical clearance from review board and informed consent taken from the patients. A detailed clinical history was taken in all the patients, with emphasis on cardiac symptoms, duration of diabetes mellitus as well as personal habits like smoking and alcohol abuse.

Laboratory investigations especially blood glucose fasting and post-prandial, a complete blood count, glycated hemoglobin (HBA1C) levels were performed for all the patients. A baseline electrocardiogram was done for all the patients. Exercise treadmill test was performed for each patient in the cardiac cath lab of the hospital. Investigations were done.

Statistical analysis

The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The t-test was used for analyzing quantitative data, or else non-parametric data was analyzed by Mann Whitney test. All analysis was carried out by using SPSS software version 21.

RESULTS

The mean age of the study subjects was 50.67±5.51 years. Maximum number of cases were in the age group of 56-60 years of age. Six of the cases were of 40 years of age. Male preponderance was seen in the present study with 64% of the subjects being males. 47 of the total 100 cases were in overweight category with a BMI ranging between 25-29.9 kg/m^2. 24 of the cases were in the obese category with a BMI of >30 kg/m^2. 31 of total cases were in healthy weight category with their BMI being between 18.5-24.9 kg/m^2. More than half of the total cases had a duration of diabetes less than or equal to 5 years. 41 out of the total 100 cases had duration ranging between 06 to 10 years (Figure 1).

05 of the total cases had a duration >10 years.41 out of the total 100 cases were smokers. 59 denied being addicted to smoking (Table 1).

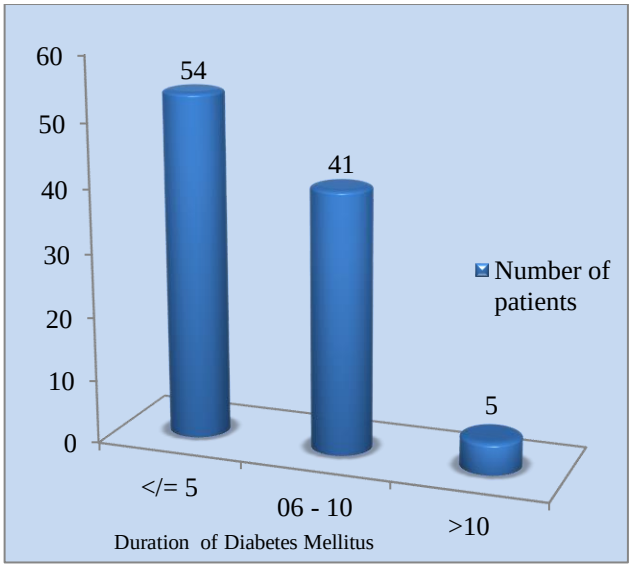

Figure 1: Distribution of cases based on duration of diabetes mellitus.

Dyslipidemia was found in 29% of the patients.26% of the total cases were alcoholic. 74 patients denied being alcoholic. 24% of the total number of cases were hypertensive (Table 2).

Table 1: Distribution of cases based on smoking

Smoker	TMT		Total
	Positive	Negative	
Yes	22	19	41
No	10	49	59
Total	32	68	100
P value<0.001			

Table 2: Distribution of cases based on dyslipdemia.

Dyslipidemia	TMT		Total
	Positive	Negative	
Yes	15	14	29
No	17	54	71
Total	32	68	100
P value=0.007			

TMT positivity steadily increased from the age group of 46-50 years. Out of the total 32 cases with positive TMT, 15 were in the age group of 56-60 years. A p=0.010 was obtained, showing positive correlation between age and TMT, and hence proving that TMT positivity increases with age.

18 of the 64 male cases were TMT positive (~28%). 14 of the 36 female cases were TMT positive (~39%). Thus, TMT positivity was found to be more among the female cases than males.

Out of the 47 cases in the BMI category of 25.0-29.9, 19 had a positive TMT (~40%). 9 out of 11 cases in the BMI

category of 30.0-34.9, had a positive TMT (~82%). A p-value of <0.001 was obtained showing positive correlation between BMI and TMT positivity, showing that TMT positivity is higher in patients with higher BMI More than 50% of the patients with a duration of DM between 06-10 years, had a positive TMT. 100% of the patients with a BMI>10 had a positive TMT. Obtained p<0.001 is suggestive of a highly significant correlation between duration of DM and TMT positivity.

A positive correlation with a highly significant p=<0.001 was obtained between smoking and TMT positivity. More than 50% of the 41 TMT positive cases were smokers. Only 10 of the TMT positive cases were non-smokers.

11 out of the total 26 alcoholics were TMT positive, while the rest 15 had a negative TMT. A p=0.190 showed that the correlation is not significant. However, it is not very high to state that the correlation is insignificant.

The correlation between dyslipidemia and TMT positivity was significant, with a p-value of 0.007. More than 50% of the patients with dyslipidemia had a positive exercise treadmill test. Only 17 out of 54 (~31%) of the patients not having dyslipidemia, were positive for TMT.

Hypertension is not a proven risk factor for TMT positivity in type 2 diabetes mellitus patients. In the present study, correlation between hypertension and a positive TMT was not statistically significant, with a p=0.733.

A significant correlation between age of the study subjects, duration of diabetes, BMI of the patients and a positive TMT result was obtained. The mean age of subjects with a positive TMT was 53.25±6.6 years, whereas it was 49.46±6.12 years in the ones who had a negative TMT. Similarly, the duration of diabetes and BMI of the study subjects was significantly higher in patients with a positive TMT, than in those with a negative TMT result (Table 3).

Also, the fasting and post-prandial blood sugar levels in patients with a positive TMT were higher than in those with a negative TMT. A highly significant correlation was obtained between blood sugar levels and TMT positivity. A similarly significant correlation was obtained between the glycated hemoglobin levels and a TMT positive result.

There was no significant correlation between the blood pressures of the patients and TMT positivity. Insignificant p values of 0.82 and 0.320 were obtained for correlation between TMT positivity and systolic and diastolic blood pressures, respectively.

A positive correlation was obtained between BMI, smoking, dyslipidemia and TMT positivity, with p<0.001, <0.001 and 0.007 respectively. Correlation between alcohol abuse, hypertension and TMT positivity was not significant with p=0.190 and 0.733, respectively (Table 4).

Table 3: Comparison of diabetic subjects with positive and negative TMT results.

Parameter	TMT positive		TMT negative		P value	Inference
	Mean	S.D.	Mean	S.D.		
AGE (years)	53.25	6.66	49.46	6.12	0.009	Highly Significant
Duration of DM (years)	8.09	3.16	4.47	1.71	<0.001	Highly Significant
BMI (kg/m^2)	28.35	3.08	25.29	2.28	<0.001	Highly Significant
Systolic BP (mmHg)	120.00	8.8	119.6	9.04	0.82	Not Significant
Diastolic BP (mmHg)	75.63	5.04	76.76	5.84	0.320	Not Significant
FBS (mg/dl)	191.56	38.32	162.26	34.94	<0.001	Highly Significant
PPBS (mg/dl)	282.91	52.41	229.66	51.43	<0.001	Highly Significant
HBA1C (%)	7.963	1.77	7.12	1.02	0.017	Highly Significant

Table 4: Risk factor association.

Parameter	TMT		P value	Inference
	Positive	Negative		
BMI				Highly
25-29.9	19	28	<0.001	Significant
≥30	09	02		
Smoking	22	19	<0.001	Highly Significant
Alcohol	11	15	0.190	Not Significant
Dyslipidemia	15	14	0.007	Highly Significant
Hypertension	7	17	0.733	Not Significant

DISCUSSION

The incidence of coronary artery disease has been on the rise in the last few years. Hence there is a need for not just treating the disease on time, but also predicting the disease early and thus reducing the morbidity and mortality by starting treatment in the initial stages of the disease.

One approach towards the prevention and reduction of coronary artery disease related complications is the early detection of the subclinical disease, as well as a careful subsequent supervision and follow-up.

The present study was undertaken to review the diagnostic and prognostic value of the exercise treadmill test in screening diabetic individuals for coronary ischemia.

In our study in relation to the total number of patients (100), for the study of exercise treadmill test, there was a low representation of females (36%) and predominance of males (64%).

Bellet et al in their studies found a representation of 66% males, respectively, in their study.[4]

Abenavoli et al in their study had also found a higher incidence of male predominance. A total of six patients were 40 years of age. The maximum number of patients were in the age group of 55-60 years, a total of 28.[5] In our study, we found that the prevalence of inducible ischemia increased in the age group of 56-60 years. Premlatha et al also found the frequency of TMT positivity to be increasing for every age interval.[6] Sharda et al also had similar findings. They found the prevalence of inducible ischemia to be maximum in the age group of 51-60 years of age, steadily increasing for every age interval.[7]

In the present study, with an increasing BMI, the percentage of patients with a positive TMT result increased. Only 1 out of 11 patients (~9%) with a BMI<18.5 had a positive TMT. 9.6% (03 out of 31) patients with a BMI between 18.5-24.9 had a positive TMT. The percentage increased to 40% in patients with a BMI ranging between 25.0 to 29.9, with 19 out of 47 patients having a positive TMT result. 81% of the patients with a BMI ≥30, had a positive TMT. A p<0.001 was obtained showing a positive correlation between BMI and TMT positivity.

A study done by Sharda et al also demonstrated a positive correlation between BMI and TMT positivity, with an obtained p=0.0077.[7]

In the current study, the average duration of type 2 diabetes in all TMT positive cases was 8.09±3.16 years, whereas in TMT negative cases it was 4.47±1.71 years.

In our study, TMT positivity was 50% in cases with a duration of DM between 06-10 years, whereas it was 100% in patients with a duration of DM>10 years.

A study by Sharda et al concluded that the greater is the duration of type 2 DM, greater are the chances of TMT positivity, hence, myocardial ischemia.[7]

Kim et al also recommend screening for type 2 DM in the elderly patients, with a duration of diabetes ≥ 10 years.[8]

Smoking is a proven risk factor for coronary artery disease in type 2 diabetes mellitus patients. In the present study, 41 out of 100 cases were smokers, of whom 22 had a positive TMT. Only 10 of the 59 non-smoker cases were TMT positive. A p<0.001 was obtained, showing a highly significant correlation between smoking and TMT positivity.

Sharda et al demonstrated a highly significant correlation between smoking and TMT positivity, with a p=0.00000062.[7]

A study by Premlatha et al also had a greater number of smokers in the TMT positive group, but it failed to reach statistical significance.[6] Sarkar et al also smoking as a significant risk factor for diabetics to have a positive TMT.[9]

In the current study, 11 out of the 26 alcoholics had a positive TMT, whereas only 21 out of the 74 non-alcoholics had a positive TMT.

The percentage of alcoholics with a positive TMT is higher, but the correlation between alcoholism and TMT positivity failed to reach a statistical significance, with a p value of 0.190. This shows that though the correlation is not statistically significant, there still is a clinical inclination of alcoholic diabetic patients having a positive TMT.

Lavekar et al also did not demonstrate a statistically significant correlation between alcoholism and TMT positivity in their study (p=0.280).[10]

Sharda et al demonstrated a statistically significant correlation between alcohol and TMT positivity (p=0.0004). 78.5% of their alcoholic study subjects were in the TMT positive group, as compared to 27.8% in the TMT negative group.[7]

In the present study, 15 out of the total 29 patients with dyslipidemia had a positive TMT. Only 17 out of the 71 patients who were not dyslipidemic, had a positive TMT.

An obtained p=0.007, showed that the correlation between dyslipidemia and TMT positivity is statistically very significant.

Sharda et al also demonstrated a significant correlation between smoking and TMT positivity. The obtained p-value in their study was 0.0274.[7]
Lavekar et al also found dyslipidemia to be significantly associated with TMT positivity (p=0.004).[10]

However, Sarkar et al in their study obtained a p=0.2085, concluding the correlation between to be insignificant.[9]

In the present study, only 7 out of the total 32 TMT positive patients were hypertensive. A p=0.733 was obtained, the correlation was insignificant.

Bellet et al and Becci et al demonstrated a higher incidence of positive TMT in hypertensive diabetic subjects, but was statistically insignificant.[3,4]

Sharda et al found the correlation between hypertension and TMT positivity to be significant. Hypertension was present in 75% and 44.6% patients, with positive and negative TMT results, respectively. P value obtained was 0.0105.

In the present study, the mean FBS (mg/dl) was 191.56±38.32, in the TMT positive group. In the TMT negative group, the mean FBS (mg/dl) was 162.26±34.94. PPBS (mg/dl) was 282.91±52.41 and 229.66±51.43 in TMT positive and TMT negative groups respectively. A p value<0.001 was obtained ascertaining the fact that fasting and post-prandial blood sugar levels are significantly associated with TMT positivity.

Sharda et al found the correlation between fasting, post-prandial blood sugar levels and TMT positivity to be statistically insignificant, with p=0.4946 and 0.1848 respectively.

HBA1C levels in the TMT positive group were 7.963±1.77%, whereas in the TMT negative group these were 7.12±1.02%. The p-value obtained was 0.017, which showed a highly significant correlation between HBA1C levels and TMT positivity in our study.

Sarkar et al also obtained a p<0.0001 showing the correlation between HBA1C levels and TMT positivity to be highly significant.

In the present study, resting ECG showed significant ST-T changes or T wave inversion in 21 patients out of the 100 patients.

Gamini et al in their study observed that 18% of their patients with ECG changes were not having typical anginal pain.[11] Kennel et al observed in their study that 23% of ECG documented myocardial infarctions were asymptomatic.[12] Giri et al in their studies observed a prevalence of silent ischemia in 10-20% of their patients.[13]

Positive cardiac stress test is seen in all the 21 patients with resting ECG changes (100%). While another 11 patients (34%), who had a normal ECG and underwent cardiac stress test were found to be positive for stress induced ischemia. Thus, in the present study, cardiac stress test was positive in 32% patients, while 68% of the patients had a negative cardiac stress test.

Gupta et al in their study found 38.3% of the patients to have a positive cardiac stress test.[14] Fuster et al., in their study found that 30% of his patients had a positive cardiac stress test.[15] In the present study, out of the total 32 patients with positive cardiac stress tests, males are 28% and females are 39%. Dave et al in their study found 45% positivity of cardiac stress test in male patients and 25% in females.[16] Bouchard et al failed to detect a higher prevalence of positive stress test in diabetic patients.[17]

Limitations

Our study had several limitations.as a retrospective design it is prone to selection bias. The data on family history of premature CAD, autonomic neuropthy and retinopathy was not available for all the cases. The small number of study subjects could be a limitation in itself.

CONCLUSION

Exercise Treadmill test in diabetic patients has a significant role in screening diabetic individuals for coronary ischemia. Prevalence of coronary ischemia in diabetic patients is 32%. Increasing age in diabetic patients is an indicator for increased risk of developing coronary ischemia.

Duration of diabetic state also has a highly significant correlation with coronary inducible ischemia on TMT.

A significant correlation also exists between risk factors of coronary artery disease like smoking and dyslipidemia and evidence of ischemia on TMT in diabetic patients.

Thus, an exercise treadmill test may be a safer, cheaper, reliable and easily available non-invasive screening tool for earlier detection and thus prevention of coronary artery disease in diabetic patients. The results obtained clearly indicate that an exercise treadmill test may be proposed as the first test for screening for coronary ischemia in diabetic population.

Coronary angiography remains the gold standard for identifying obstructive lesions, though it is never used as an initial screening test.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Nagrani S, Patil P, Barsode SS, Momale N, Mehta P. Study of exercise treadmill test in type 2 diabetes mellitus patients. Int J Adv Med 2021;8:557-62.