Treadmill(Cardiac Stress) Test in the Diagnosis of Ischaemic Heart Disease in NIDDM Patients: Usefulness and Safety

G. Premalatha, M.K. Anirudhan, V. Mohan, N.G. Sastry

It is well known that patients with non-insulin dependent diabetes mellitus (NIDDM) have a higher prevalence of ischaemic heart disease than the general population [1]. Moreover quite often diabetic patients do not exhibit the classic symptoms of angina because of the presence of neuropathy involving the thoracic nerve fibres and this is referred to as 'silent ischaemia' [2]. Cardiac stress testing or Treadmill testing (TMT) is a useful and relatively a safe and non invasive test for diagnosis of subclinical or latent ischaemia [3]. However there are few large-scale studies on TMT in Indian diabetic patients.

A preliminary survey done among cardiologists at Madras prior to the commencement of this study showed that there was considerable difference of opinion regarding the usefulness/safety of doing a TMT in diabetic patients. While some cardiologists felt that a TMT should be done on a routine basis in all diabetics, others felt that a TMT was contraindicated in diabetics, because of silent ischaemia and higher frequency of arrythmias. Given the high prevalence of both NIDDM [4, 5] and IHD [6] among Indian and the younger age of onset of diabetes [7], we thought it fit to take up a study to assess the value of doing a TMT in Indian diabetics.

We basically set out to answer four questions:

1) Is TMT useful in diabetic patients?

2) Is TMT safe in diabetics?

3) At what age should TMT be done in Indian diabetics?

4) What are the clinical and biochemical correlates of TMT positive diabetics?

MATERIALS and METHODS

The study group comprised of 599 NIDDM patients attending the M.V. Diabetes Specialties Centre, Madras. There were 414 males and 185 females.

The mode of selection was as follows:-

Group I (n =167): Asymptomatic individuals with resting ECG changes suggestive of ischaemia (eg. T-wave changes).

Group II (n=168): This group consisted of patients who complained of chest paid but had a normal ECG.

Group III (n=264): Comprised of individuals who had no symptoms and who had a normal ECG, i.e. the TMT was done as a routine screening procedure in otherwise 'normal' individuals.

In all study subjects a detailed history was taken including a history of smoking and alcohol abuse. A complete physical examination was done with a detailed cardiovascular assessment and evaluation of peripheral pulses in all cases. The blood pressure was recorded in both supine and standing postures. The laboratory investigations included fasting and post-prandial plasma glucose estimations, serum creatinine, blood urea and a complete lipid profile using Boehringer Mannheim kits on Corning Express Auto Analyser. Glycosylated haemoglobin (HbA$_1$C) was done by HPLC using the Variant Machine (Bio Rad, USA). All individuals underwent a routine X-ray chest and a computerized 12 lead ECG prior to performing the TMT.

Exclusion criteria included individuals with documented myocardial infarction, unstable angina, left bundle branch block or severe left ventricular hypertrophy, those who had undergone bypass surgery and patients with severe osteoarthritis or other disabilities.

Treadmill Test Procedure

The TMT was done using a computerized machine with built-in protocols. The tests were done by a medical officer who had already performed over 500 TMT's earlier using the same machine in collaboration with a cardiologist. Graded metabolic workloads [8] were administered for fixed intervals. Continiuous ECG recordings were made throughout the test. Blood pressure was recorded at the end of each stage. Bruce protocol was used in 96% of cases while 4% of patients underwent a modified Bruce protocol. The test was terminated either when the target heart rate (THR) was achieved or if symptoms/signs of ischaemia or arrythmias were noticed.

The interpretation of TMT was done using standard criteria [9] using the degree of ST depression, heart rate achieved, blood pressure changes and occurrence of arrythmias.

Statistical Analysis

All values are expressed as mean ± SD. Statistical analysis was done using SPSS package on an IBM compatible computer. Student's t-test was used to compare differences between means. P < 0.05 was considered statistically significant.

RESULTS

1) Is TMT Useful for Diabetics?

Table 1 shows the results of the TMT testing in the three study groups. It can be seen that only 44 of the 167 patients in group I who had an abnormal resting ECG had evidence of IHD on TMT. Thus had we used only ECG criteria, IHD would have been overdiagnosed in 72.4% of patients in this group. Alternatively, had we ignored the ECG findings, we would have missed the diagnosis in 26.4% of patients.

Table 1
Significance of TMT Testing

	TMT Positive n (%)	TMT Negative n (%)	Inadequate Tests n (%)
Specificity of TMT: Group I: ECG abnormal (n=167) No symptoms	44(26.4)	121(72.4)	2 (1.2)
Group II: ECG normal (n=168) Symptoms present	65(38.7)	98(58.3)	5(3.0)
Sensitivity of TMT: Group III : ECG normal (n=264) No symptoms	30(11.4)	227(85.9)	7(2.7)

In group II among those who complained of chest pain, the diagnosis of IHD was confirmed after TMT in 38.7% of patients. If chest pain alone was used to diagnose IHD, 58.3% of those without IHD would have been wrongly treated.

Thus a TMT considerably improves the specificity of diagnosis of IHD.

It is of even greater interest that tin group III, i.e. individuals who were totally asymptomatic and had normal ECG's, the TMT was positive in 11.4% of patients. Thus the TMT considerably improves the sensitivity of diagnosis of IHD as in these patients, the diagnosis would have been totally missed but for the TMT testing.

Silent Ischaemia

Table 2 shows the prevalence of 'silent ischaemia' in this study. Silent ischaemia was defined as a definitely positive stress test in the absence of any symptoms such as angina or breathlessness (angina equivalent). It can be seen that 59.1% of group I patients, 33.8 % of group II patients and 56.6% of group III TMT positive patients remained totally asymptomatic despite a positive TMT (silent ischaemia). This shows that silent ischaemia is indeed a feature of NIDDM patients, once again demonstrating the usefulness of TMT.

Tabel 2
Silent Ischaemia

	TMT Positive	Symptoms During Test	Asymptomatic During Test
Group I: (n=167) Abnormal ECG No Symptoms	44	18(40.9%)	26(59.1%)
Group II: (n=168) Normal ECG Chest pain	65	40(66.2%)	22 (33.8%)
Group III: (n=264) Normal ECG No symptoms	30	13(43.7%)	17(56.6%)

2) Is Cardiac Stress Test Safe for Diabetics?

Out of the 599 patients studied, only 18 (3.0%) developed complications requiring premature termination of the test. Table 3 shows the break-up of these complications. None of the arrhythmias were serious enough to warrant any anti-arrythmic therapy. There were also a small group of patients who developed severe angina and/or dyspnoea but all cases obtained relief with sublingual nitrates. There was no instance of TMT induced myocardial infarction or death in our study.

Table 3
Complications of TMT
(n = 599)

Arrythmias (Total)	=	18 (3.0%)
Break-up:		
Ventricular Ectopics	=	14
Atrial Ectopics	=	1
Bigeminy	=	1
Left Bundle Branch Block	=	2

3) Age and Sex Profile of Treadmill Positive Group

Table 4 shows the age distribution of treadmill test positive diabetics. There were no positive TMTs in the age group of < 30 years although the number of patients studied was quite small. However in the 31-40 age group, 11.3 % were positive for ischaemia. The frequency of TMT positivity increased for every age interval thereafter until by the age group of 60 years or above when the figure rose to 48.4%.

Table 4
Age Profile of TMT Positive Patients

Age Group (Years)	Total No.	TMT Positive
< 30	5	0 (0%)
31 – 40	70	8 (11.3%)
41 – 50	224	28 (12.5%)
51 – 60	205	57 (27.8%)
> 60	95	46 (48.4%)
Total	599	139

Table 5 shows the sex distribution of the TMT positive diabetics. Although a slightly higher prevalence was seen among males, this failed to reach statistical significance. This shows that IHD is as common in female as in male diabetic patients.

Table 5

Sex Distribution of TMT Positive Patients

Group	Number		TMT Positive	
	Male	Female	Male No.(%)	Female No.(%)
Group I (n=167) Asymptomatic clinically Resting ECG changes Positive	112	55	34 (30.4)	10 (18.2)
Group II (n=168) Symptomatic clinically Normal Resting ECG	102	66	45 (44.1)	20 (30.3)
Group III (n=264) Asymptomatic clinically Normal Resting ECG	200	64	22 (11.0)	8 (12.6)
Totals (n=599)	414	185	101 (24.4)	38 (20.8)

4) Clinical and Biochemical Characteristics of TMT Positive Group

Table 6 summarizes the clinical characteristics of the treadmill positive group. The age of the patient, duration of diabetes and systolic blood pressure had a positive association with TMT positivity. Diastolic blood pressure and cigarette smoking were also higher in the treadmill positive group but they failed to reach statistical significance.

Table 7 shows the biochemical characteristics of the TMT positive patients. Only the fasting plasma glucose was significantly higher among the TMT positive group. The post-prandial plasma glucose, total cholesterol, triglycerides, HDL cholesterol, urea, creatinine and glycosylated haemoglobin levels were

not significantly different between the TMT positive and negative groups.

Table 6
Clinical characteristics of TMT Positive Patients

Variable	TMT Positive (n=139)	TMT Negative (n=446)
Age (years)	55.5* ± 8.2	49.3 ± 8.9
Duration of DM (years)	12.2* ± 8.2	7.5 ± 6.3
BP – Systolic (mm/Hg)	139* ± 16.9	131 ± 15.1
BP – Diastolic (mm/Hg)	85 ± 10.1	84 ± 7.4
Body Mass Index (kg/m2)	25.4 ± 3.5	26.0 ± 4.4
No. of Cigarettes (mean)	14 ± 13	16 ± 15

* Statistically significant (P ≤ .05)

Table 7
Biochemical Characteristics of TMT Positive Patients

Variable	TMT Positive (n=139)	TMT Negative (n=446)
Plasma Glucose Fasting (mg%) Post-prandial (mg%)	189* ± 71 286 ± 82	173 ± 64.2 274 ± 81.0
Serum Cholesterol (mg%)	217 ± 38	212 ± 45.1
Serum Triglycerides (mg%)	217 ± 162	214 ± 174
HDL Cholesterol (mg%)	44 ± 8	42 ± 13
Blood Urea (mg%)	27* ± 7	26 ± 6
Serum Creatinine (mg%)	0.82 ± .18	0.81 ± 16
HbA$_1$C (%)	9.3 ± 2.2	8.9 ± 2.1

* Statistically significant (P ≤ .05)

Discussion

Coronary atherosclerosis occurs more commonly in diabetics compared to non-diabetic individuals. Patients with diabetes may have advance IHD, but

remain asymptomatic. Treadmill testing is a useful procedure to diagnose silent ischaemia, especially in diabetics. In our study 65 out of 139 TMT positive cases (46.8%) had silent ischaemia. These results are similar to those of Gupta et al [10] who reported a 38.3% prevalence of silent ischaemia in a group of diabetic patients who underwent treadmill testing.

Treadmill test is a relatively safe procedure in diabetics provided a careful selection of cases is done. Only 3% of our patients had complications which required premature termination of the test. Gupta et al [11] in a series of 1015 successive TMT procedures also concluded that TMT is a safe procedure with no mortality. However in a large meta-analysis of 1,70,000 treadmill tests performed at different medical centers, a mortality rate of 3.3 to 10 per 1,00,000 tests has been reported [12].

As expected, the age of the patients and duration of diabetes had positive association with TMT positively in our study. Similar results were obtained by Gupta and Gupta [13]. Our study also confirms the well known fact that hyperglycaemia and hypercholesterolaemia are associated with TMT positively. These results are similar to those of Kumar et al [14].

In summary, we conclude that TMT is a useful and safe procedure in diabetic patients. We suggest that all diabetics after the age of thirty years should be subjected to a treadmill test. Even if negative, the TMT should be repeated once in two or three years. Depending on the degree of severity of the IHD on TMT testing further, cardiac work-up including coronary angiography can be considered wherever necessary.

REFERENCES

1. Kannel WB, McGee DL. Diabetes and cardiovascular disease: The Framingham Study. J Am Med Assoc 1979; 241 : 2035-8.

2. Nesto RW. Phillips RT, Asymptomatic myocardial ischaemia in diabetic patients. Am J Med 1986; 80 : 40-6.

3. Froelicher VF, Thomas P. Pillow C. An epidemiologic study of asymptomatic men screened with exercise testing for latent coronary artery disease. Am J Cardiol 1974; 34 : 770-6.

4. Mather HM, Keen H. The Southall diabetes survery: prevalence of known diabetics in Asians and Europeans. Br Med J 1985; 291 : 1081-4.

5. Ramachandran A, Jali MV, Mohan V, Snehalatha C. High prevalence of diabetes in an urban population in South India. Br Med J 1988; 297 : 587-90.

6. Mckeigue PM, Marmot MG, Court YDS, Cotttier DE, Rahman S, Riemersman RA. Diabetes, hyperinsulinaemia and coronary risk factors in Bangladesh in East London. Br Heart J 1988; 60:390-6

7. Mohan V, Ramachandran A, Snehalatha C, Mohan R, Bharani G, Viswanathan M. High prevalence of maturity onset of diabetes of the young (MODY) among Indians. Diabetes Care 1985; 8 : 371-4.

8. Bruce RA. Exercise testing of patient with coronary heart disease: principles and normal standards for evaluation. Ann Clin Res 1971; 3 : 323-32.

9. Irving JB, Bruce R. Exertional hypotension and post exertional ventricular fibrillation. Am J Cardiol 1977; 39 : 849-51.

10. Gupta SB, Pandit RB, Munsi SC. Treadmill Test – A screening method for detection of latent coronary artery disease in diabetics. J Asso Phys India 1986; 34 : 489-90.

11. Gupta R, Sharma DK , Gupta KD. Prospective study of complications during treadmill exercise ECG test in 1015 procedures. J Asso Phys India 1988; 36 : 551-2.

12. Rochmis P. Blackburn H. A survery of procedures, safety and litigation experience in approximately 1,70,000 tests. J Am Med Asso 1971; 217 : 1061-6.

13. Gupta R, Gupta S. Assessment of asymptomatic coronary artery disease in diabetes mellitus. J Asso Phys India 1986; 34 : 783-4.

14. Kumar A, Aneja VK, Hasan M, Chandra M. Sub-clinical cardiovascular involvement in asymptomatic males with hypercholesterolemia and diabetes mellitus. J. Asso Phys India 1987; 35 : 488-9.