Clinical study of risk stratification of coronary artery disease in high-risk patients by Treadmill stress test

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Abstract
Background: Stress testing is a simple, reliable and excellent non-invasive method for diagnosing coronary artery disease in asymptomatic patient and predicting future coronary events, particularly in patient with coronary risk factors. Present study was aimed to study risk stratification of coronary artery disease in high-risk patients by Treadmill stress test. **Material and Methods:** Present study was single-center, Cross sectional, observational study, conducted in patients of 30-70 years of age with, asymptomatic with increased risk of developing ischemic heart disease (hypertension, Diabetes Mellitus, smoking, hyperlipidemia, obesity, Type A personality and sedentary lifestyle). Treadmill was performed according to 'Bruce' protocol. **Results:** Among 200 patients, 138 (69%) were male and 62 (31%) were females. Out of 138 Male patients 39 (79.5%) showed positive treadmill test and of 62 female patient 10(20.4%) showed positive treadmill test. Out of 49 positive treadmill tests, 27 patients (55.1%) were above the age group 50 years and 22 were below 50 years. Majority patients having diabetes mellitus as a sole risk factor (38.7%) showed positive treadmill test results followed by hypertensive patients (33.3%). In between hypertension and diabetes, as per chi square test p value was 0.8414 (>0.05) which was not significant. 17 (8.5%) patients had Exercise induced Hypotension during test. 17 (8.5 %) had noted Chronotropic incompetence. 168 (84%) case were had MHR achieved in stage III, 29 (14.5%) were achieved MHR in stage II and remaining 3 (1.5%) were had achieved MHR in stage I (high risk to develop coronary artery disease). Common reasons to terminate tread mill exercise test were chest pain (27.5 %) followed by dyspnea (24 %), dizziness (15.5 %) & fatigue (14.5 %). Most of patients achieved MET SCORE > 7 (70.5%) & 27 (13.5%) were achieved MET SCORE between 6.1 to 7. **Conclusion:** Treadmill stress test is the only noninvasive, reliable and cost-effective tool for diagnosis and better prognosis of coronary artery disease.
Keywords: Treadmill stress test, coronary artery disease, MET score, stress test.

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Introduction

Ischemic heart disease (IHD) is the leading cause of death and disability in industrialized countries. In India also there is increasing trends of death and disability due to IHD. Risk factors of interest for ischemic heart disease may be hypertension, diabetes mellitus, smoking, Hyperlipidemia, obesity, and physical inactivity.[1] Hypertension, a key risk factor for cardiovascular disease morbidity and mortality, is a highly prevalent condition in the adult population of our country.[2,3,4]

Exercise testing historically has been considered a useful modality for diagnosing coronary heart disease (CHD). However, false positive tests are common in asymptomatic adults, especially among women, and there is no evidence currently to recommend exercise electrocardiography as a routine screening test. Thus, conventional guidelines recommend against the use of exercise testing for risk assessment in asymptomatic subjects with a, 10% pre-test likelihood of underlying CHD.[5]

Stress testing is a simple, reliable and excellent non-invasive method for diagnosing coronary artery disease in asymptomatic patient and predicting future coronary events, particularly in patient with coronary risk factors. Cardiovascular exercise stress testing in conjunction with ECG has been established as one of the focal points in the diagnosis and prognosis of cardiovascular disease, specifically coronary artery disease (CAD).[6,7] Findings from the Henry Ford Exercise Testing (FIT) Project appear to indicate a graded, inverse relationship between Cardio respiratory fitness and incident atrial fibrillation, particularly for obese patients.[7] Present study was aimed to study risk stratification of coronary artery disease in high risk patients by Treadmill stress test

Material And Methods

Present study was single-center, Cross sectional, observational study, conducted in department of XXX, at XXX medical college & hospital, XXX, India. Study duration was of 2 years (November 2015 October 2017). Study approval was obtained from institutional ethical committee.

Inclusion criteria

- Patients of 30-70 years of age with, asymptomatic with increased risk of developing ischemic heart disease (hypertension, Diabetes Mellitus, smoking, hyperlipidemia, obesity, Type A personality and sedentary lifestyle), willing to participate in present study

Exclusion criteria

- Patients who had already undergone the TMT stress test were excluded from the study.
- Patients with history of MI, Percutaneous transluminal coronary angioplasty, Coronary artery bypass graft, arrhythmia, valvular heart diseases, co-morbid condition, chronic conditions like cirrhosis, Cerebrovascular stroke, Osteoarthritis, chronic renal disease

Study was explained to patients in local language & written consent was taken for participation & study. Every patient was evaluated with detailed history and physical examination pertaining to coronary artery disease risk factors. They were subjected to investigations like complete hemogram, urine analysis, liver function test, kidney function test, BSL, fundus examination, 12 lead ECG. Twelve hours fasting blood sample was collected from everyone, to perform biochemical analysis and levels of fasting blood glucose and lipid profile were determined. Instructions were given to patients regarding overnight fasting, discontinuation of smoking and drugs one day before the test.

Treadmill was performed according to 'Bruce' protocol. 12 lead ECG was taken just prior to test, pulse and blood pressure were recorded in supine and standing position. Height and weight were also recorded. The entire procedure was explained to the patient in detailed

and for anxious patients a brief demonstration of the procedure was given. All patients were subjected to perform treadmill test on SCHILLER CS 200 Treadmill machine. Blood pressure was recorded in each stage of TMT and compared to baseline blood pressure .Heart rate and ECG were recorded in monitor itself. Patients were instructed to report immediately when they experience unusual or significant symptoms (e.g., chest pain, dizziness etc.) during exercise. In addition, the patients were also assured that they may request termination of exercise prematurely, whenever necessary.

Results in the form of total exercise time, maximum heart rate, percentage of maximum heart rate achieved, work done in METS, reasons for the termination of the test, exercise tolerance, arrhythmias, hemodynamic response and chronotropic response were noted. In all patients who were subjected to treadmill stress test, procedure was uneventful.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

RESULTS

Among 200 patients, 138 (69%) were male and 62 (31%) were females. Out of 138 Male patients 39 (79.5%) showed positive treadmill test and of 62 female patient 10(20.4%) showed positive treadmill test. Male had higher risk to develop coronary artery disease than females, but difference was statistically non-significant. (p- 0.1624)

Table No.1: Gender distribution with Positive TMT Test

Sex	No. of patients	Percentage (%)	No. Of patients with +ve TMT test	Percentage (%)	P value
Male	138	69%	39	79.5%	0.1624
Female	62	31%	10	20.4%	

In present study, majority patients were from age group 50 years and above (61%). Out of 49 positive treadmill tests, 27 patients (55.1%) were above the age group 50 years and 22 were below 50 years. Majority patient with positive treadmill stress test were from 60- 69 years age group (38.5 %). As per Fisher exact test (p value -0.0346) difference was statistically significant.

Table no.2: Age-wise distribution of results of treadmill stress test.

Age (Yrs)	Positive	Percentage	Negative	Total
30-39	2	8.3 %	22	24
40-49	9	16.6 %	45	54
50-59	16	24.6 %	49	65
60-69	22	38.5%	35	57
Total	49	24.5 %	151	200

Majority patients having diabetes mellitus as a sole risk factor (38.7%) showed positive treadmill test results followed by hypertensive patients (33.3%). In between hypertension and diabetes, as per chi square test p value was 0.8414 (>0.05) which was not significant.

Table no 3: Risk factor-wise distribution of treadmill test

Risk Factor	+ VE TMT (Percentage)	- VE TMT	TOTAL
Hypertension	15(33.3%)	30	45

Diabetes mellitus	19(38.7%)	30	49
Smoking	11(26.1%)	31	42
Hyperlipidemia	9(26.4%)	25	34
Obesity	7(28.0%)	18	25
Physical Inactivity	5(25%)	15	20
Family H/O IHD	6(28.5%)	15	21
Type A personality	3(13. %)	10	13
Multiple Risk Factor	26(53. %)	23	49

Among 200 patients, patients with diabetes had maximum number of cases with positive TMT. Of 49 cases with Diabetes as risk factor 19 (38.7%) were positive test. Overall, those patients who had multiple risk factors were associated with positive TMT test. Of 49, 26 (53. %) cases were positive Test. As per chi square test p value was 0.0279 (>0.05) which was statistically significant.

Table no.4: Risk Factor wise Distributions of Treadmill Test

Risk Factors		Positive	Percentage	Negative	Total
Hypertension	Isolated	7	21.2%	26	33
	>1 Risk factor	8	66.6%	4	12
Diabetes mellitus	Isolated	9	45%	11	20
	>1 Risk factor	10	62.5%	6	16
Smoking	Isolated	1	4.1%	23	24
	>1 Risk factor	10	55.5%	8	18
Hyperlipidemia	Isolated	4	18.1%	18	22
	>1 Risk factor	5	41.6%	7	12
Obesity	Isolated	-	-	11	11
	>1 Risk factor	7	50%	7	14
Physical Inactivity	Isolated	1	8.3%	11	12
	>1 Risk factor	4	50%	4	8
Family H/O IHD	Isolated	-	-	8	8
	>1 Risk factor	6	46.1%	7	13
Type A personality	Isolated	-	-	4	4
	>1 Risk factor	3	33.3%	6	9

17 (8.5%) patients had Exercise induced Hypotension during test, of 49 TMT positive patients 11 (22.4%) were had exercise hypotension and remaining 6(3.9%) of 151 patient had TMT negative. Among those who were had exercise hypotension's 12 were male and 5 were female.

Table no.5: Exercise induced hypotension

	Frequency	Percentage
Male	12	70.5 %
Female	5	29.4 %

In our study out of 200 patients subjected to TMT, 17 (8.5 %) had noted Chronotropic incompetence. Of which 13 (76.4%) were male and 4 (23.5%) were female. Among 17 patients, 8 (47%) patient were TMT Positive whereas 9 (52.9 %) were TMT Negative.

Table no.5: Frequency distributions of positive and negative TMT test.

	Frequency	Percentage
Male	13(17)	76.4 %

Female	4(17)	6.4 %
TMT Positive	8(17)	47%
TMT Negative	9(17)	52.9 %

Maximum Heart rate achieved during exercise was noted according to stage of TMT, 168 (84%) case were had MHR achieved in stage III, 29 (14.5%) were achieved MHR in stage II and remaining 3 (1.5%) were had achieved MHR in stage I (high risk to develop coronary artery disease). As per chi square test p value was 0.0001 (>0.05) which was statistically extremely significant.

Table no.6: Maximum Heart rate (MHR) achieved according to stages of TMT

Stages of TMT	Frequency	Percentage	P value
Stage I	3	1.5 %	0.0001
Stage II	29	14.5 %	
Stage III	168	84 %	

Common reasons to terminate tread mill exercise test were chest pain (27.5 %) followed by dyspnea (24 %), dizziness (15.5 %) & fatigue (14.5 %).

Table no.7: Reason to terminate test

Symptoms	NO. of patient	Percentage (%)
chest pain	55	27.5%
Dyspnea	48	24%
Dizziness	31	15.5%
Fatigue	29	14.5%
Syncope	20	10%
Palpitations	17	8.5%

Most of patients achieved MET SCORE > 7 (70.5%) & 27 (13.5%) were achieved MET SCORE between 6.1 to 7, 19(9.5%) Cases were achieved MET SCORE between 5 -6, about 7 (3.5%) cases were achieved Those patient achieved score less than 7 with Positive treadmill test have high Risk to develop coronary artery disease. Among positive treadmill test Patient (49) most of patient 21(42.8%) was achieved MET SCORE between 6-7 but those patient who were achieved MET SCORE 3-4 have high risk to develop coronary artery disease in future. As per chi square test p value was 0.0001 which was (>0.05) extremely statistically significant.

Table no. 8: MET SCORE

MET SCORE	NO. of patient	Percentage (%)
3-4	6	3%
4.1-5	7	3.5%
5.1-6	19	9.5%
6.1-7	27	13.5%
>7	141	70.5%

Discussion

A risk factor is a feature of individual or population that is present early in life and is associated with increased risk of developing disease in future Exercise testing is a cardiovascular stress test that uses treadmill bicycle exercise with electrocardiography (ECG) and blood pressure monitoring.[6] The limited sensitivity and specificity of standard

exercise ECG testing for detection of coronary artery disease have stimulated increased use and development of noninvasive stress imaging technologies.[8]

Silent coronary artery disease is an important cause of premature death. Sudden death is the first and only manifestation of disease in 18% of patients with coronary artery disease. The resting state frequently does not provide a complete evaluation so the introduction of a stressful condition (like treadmill test) may be necessary to detect underlying or latent ischemia.[9]

Smoking, hypertension, diabetes mellitus, obesity and hyperlipidemia are the main risk factors for IHD. A unique human habit of smoking has been identified as a major IHD risk factor with several possible mechanisms as carbon monoxide induced atherogenesis, nicotine stimulation of adrenergic drive raising both blood pressure and myocardial oxygen demand fall in protective high-density lipoprotein.[10] In diabetes abnormalities relating to platelet function, coagulation, fibrinolysis and endothelial function have been described. Elevated blood sugar levels in diabetes induce vascular damage and promote atherosclerosis which favors intraluminal thrombus formation.[11]

Obesity especially abdominal obesity is associated with atherogenic lipid profile with increased LDL-C, VLDL and triglyceride and decreased HDL-C.[12] Hypertension accelerates atherosclerotic process especially if hyperlipidemia is present. Increased blood pressure causes injury to endothelium which favors atherosclerosis and thrombus formation. Thus, all the above-mentioned risk factors directly or indirectly leads to atherosclerosis which further leads to increased peripheral resistance and hypertension. Thus, increased workload of myocardium leads to concentric left ventricular hypertrophy and this increased muscle mass leads increased oxygen requirement.

Agrawal et al.,[13] found abnormal ECG findings only during exercise in 4 subjects and both during and after exercise in 7 subjects. Thus, they noted positive stress test in 22% cases.

Nagamaniet et al.,[14] noted positive test in 18% cases. Frans J. H. Wackers et al.,[14] studied 1123 asymptomatic subjects with type II diabetes mellitus of age group 50-75 yrs with no known or suspected IHD. The subjects undergone either stress testing and clinical follow up or follow up only. They observed that total 113 patients (22%) were having silent ischemia including 83 with regional myocardial perfusion abnormalities. They have also concluded that strong predictors for abnormal stress test were abnormal valsalva (Odds ratio 5.6), male sex (2.5) and diabetes duration (5.2).

Mahmoud Abd El Wahab.,[15] stated that prevalence of IHD increase with advancing age. At any even age prevalence of IHD in men was higher than that in women. Diabetes is a strong risk factor for IHD. Hypertension substantially increases the risk of both micro-vascular and macro- vascular complications of diabetes.10 mm of Hg decrease in mean systolic blood pressure was associated with reduction in risk of 12% for any complication related to diabetes, 15% related to death and 11% for myocardial infarction.

In the present study, 200 asymptomatic patients with important risk factors for coronary artery disease were subjected to treadmill stress test. In the present study, 24.5% patients showed positive treadmill stress test which is nearly like that of Agrawal et al.,[13] and FransJ. H. Wackers et al.,[15] (22%). In the present study, maximum patients of age group 60-69 yrs have shown positive treadmill stress test. Also, there was increasing trend of positive test with age which was like that of Mahmoud Abd El Wahab et al.,[16] study. In the present study, maximum patients of Diabetes mellitus (38.7%) had positive treadmill stress test followed by hypertensive patients (33.3%). Also, there was positive treadmill test in more no. of patients having multiple risk factors as comparable to that of only one risk factor.

Treadmill testing represents invaluable, non-invasive method for diagnosing myocardial ischemia early in asymptomatic patients with important risk factors for coronary artery

disease like diabetes, hypertension, dyslipidemia, obesity and smoking so that patients can be detected at an early stage and can be properly treated and protected from the hazards of overt ischemic heart disease.

Limitations of present study were, we have not compared the results with that of the gold standard method which in this case is angiography. In the rural set-up in-spite of lack of resources the study has been conducted. From this, diabetes mellitus is the most important risk factor for IHD followed by hypertension. Still further study is necessary in this context for evaluating the treadmill stress testing along with comparison with more advanced and definitive tests.

Conclusion

Treadmill stress test is the only noninvasive, reliable and cost-effective tool for diagnosis and better prognosis of coronary artery disease. It also helps in educating patients to alter their lifestyle and to correct the modifiable coronary risk factors. Most patients with modifiable risk factors are unaware of their condition and coronary artery disease can be reduced efficiently if these patients are made aware of the risk and proper action is taken to control the risk factors.

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