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ORIGINAL RESEARCH ARTICLE

CORONARY ANGIOGRAPHY FINDING OF EXERCISE TREAD MILL TEST POSITIVE PATIENTS IN A TERTIARY CARE CENTER

Amit Shrestha [1]*, Sanjeev Thapa [1], Shilendra Shakya [1], Ravi Shahi[1]

[1] Department of Cardiology, Manmohan Cardio Vascular Thoracic and Transplant Centre (MCVTC), Institute of Medicine, TUTH,Nepal

***Correspondence to:** *Dr. Amit Shrestha, Department of Cardiology, Manmohan Cardio Vascular Thoracic and Transplant Centre (MCVTC), Institute of Medicine, TUTH, Nepal. Email: amitshrestha32@hotmail.com*

ABSTRACT

Background: The diagnosis rate of coronary artery disease (CAD) has been dramatically increased with the development of interventional technique. Coronary angiography (CAG) is the "gold standard" tool for CAD diagnosis. Due to its invasive property, CAG has been limited. Treadmill test (TMT) is still broadly used as an economic and simple method to screen and assist the diagnosis of CAD. However, correct interpretation of such data is essential in determining diagnostic and treatment strategies. **Methods:** All the patients attending outpatient department of Manmohan Cardiothoracic Vascular and Transplant Center (MCVTC) and having positive findings in tread mill stress test (TMT) using Bruce protocol underwent selective coronary angiography (CAG), in MCVTC Cath Lab using standard technique and were analyzed in multiple views with significant coronary stenosis defined as of ≥70 % lesion, 50-60% as borderline and 20-30% as minor coronary artery disease. **Results:** A total of 303 patients (mean age 52.8 ±9.7 yrs) were included during a study period of approximately 1½ yrs (Oct 2015 to Dec 2016), among whom male were of average 53.6 ±10.5 yrs and female were of 51.7±8.6 yrs. Risk factor estimation among patients showed that 49.3 % were hypertensive, 29.9% were overweight, 15.2% were diabetic and 5.7% were smoker. Coronary angiography of patients revealed normal coronaries in 114(54.0%), borderline lesion in 29(13.7%) and significant lesion in 68 (32.2%). Among those with diagnosed coronary artery disease (CAD), 48(22.7%) had single vessel disease, 29(13.7%) had double vessel disease and 14(6.6%) had triple vessel disease. The sub group analysis based on of risk factor and coronary artery disease showed coronary artery diseases was highest among diabetics (57.7%) followed by smokers (55%) compared. The risk of Coronary artery disease found to be significantly higher among patient with ≥2 CAD risk factor. Males with stress test positive had significantly higher chances of having CAD than females (53% vs 35% respectively). **Conclusion:** Coronary artery disease (CAD) among patients with TMT positive status is higher in patients with diabetics and smokers, especially those with two or more CAD risk factors. Results of this study showed that the pretest probability of treadmill stress-test is higher in males with two or more CAD risk factor especially diabetes and smoking compared to the female counterparts with similar factors ,so should be supplemented by other non-invasive techniques(such as stress echocardiography, myocardial perfusion imaging) for further confirmation of diagnosis. (such as stress echocardiography, myocardial perfusion imaging) for further confirmation of diagnosis.

Key words: *Coronary angiography (CAG), Coronary artery disease (CAD), Tread mill stress test (TMT).*

INTRODUCTION

The diagnosis rate of coronary artery disease (CAD) has been dramatically increasing with the development of interventional technique, which makes coronary angiography (CAG) the "gold standard" tool for CAD diagnosis.[1] However, the use of selective CAG has is limited due to its invasive property that is why treadmill exercise test (TET) is still broadly used as an economic and simple method to screen and assist in diagnosis ,risk assessment and prognostication of patients with known or suspected coronary heart disease (CHD). The exercise electrocardiogram (ECG) is also helpful in assessing exercise capacity (i.e., functional capacity) which increases its prognostic value and has been the strongest predictor of

mortality and cardiovascular events, particularly in older adults.[2] The pathophysiology behind exercise ECG indirectly detecting myocardial ischemia is the physiologic consequence of a mismatch between myocardial oxygen delivery (coronary blood flow) and myocardial oxygen demand (myocardial work) during exercise.

Evaluation of ECG changes, specifically ST segment depression during or after exercise, has been the traditional criterion for evaluating the exercise tolerance test. However, problems with false positive and negative tests, especially in patients with atypical or no angina pectoris,[3] have stimulated efforts to examine other aspects of the exercise response besides the presence or absence of exercise-induced ST segment depression in order to increase the diagnostic utility of the test[4]. These include poor exercise capacity[5], exercise-induced angina[6], particularly that which is exercise-limiting or occurs at a low workload, abnormally low peak systolic blood pressure (<130 mmHg) or a fall in systolic blood pressure below baseline during exercise[7] and chronotropic incompetence.[8] However, correct interpretation of such data is essential in determining diagnostic and treatment strategies of coronary artery disease.

In this study attempts will be made to interpret the various parameters determining the detection of coronary artery disease in exercise tread mill test positive patients.

METHODS

Study Design

This was a quantitative cross sectional study done on patients of with positive tread mill test that underwent coronary angiographic procedure in department of cardiology, Manmohan Cardiothoracic Vascular and Transplant Center, Institute of medicine, Maharajgunj, Kathmandu

Study Assessments

All the patients with stress test positive went through a detail interview regarding personal details like name, age, gender, profession along with an appropriate medical history which include: history of chest pain classified as below based on the Coronary Artery Surgery Study (CASS) Definite or classic angina ,Nonanginal or non-ischemic chest pain and Probable or atypical angina ; History of Coronary artery disease risk factor: Hypertension, Dyslipidemia, Cigarette Smoking ,Family history of coronary artery disease, diabetes and life style. Each patient had his/her height and weight measured for calculation of BMI.

Ascertainment of Coronary artery disease

All patients with exercise tread mill test positive will undergo coronary angiographic evaluation in Manmohan Cardiothoracic Vascular and Transplant Center CATH Lab by DM cardiology resident or cardiology faculty. Vascular access for coronary angiography was done either by femoral or radial artery approach. Interpretation coronary angiogram for coronary artery disease: Coronary Lesion quantification was done in at least two orthogonal views.

The criterion for Significant Coronary artery disease (CAD)was defined as >50% stenosis of the left main stem, >70% stenosis in a major coronary vessel {Left Anterior Descending (LAD), Left Circumflex (LCX)or Right Coronary Artery(RCA)} in coronary angiography ; Borderline significant as 50-70% Stenosis and minor or insignificant coronary artery disease as <50% stenosis. Patients with significant coronary lesions were further classified depending on the number of major coronary vessel lesion as having single vessel disease (SVD), Double Vessel Disease (DVD) or Triple Vessel Disease (TVD).

Statistical Analysis

We estimated that a sample size of 132 patients would be required to obtain a two-sided 95% confidence interval for an estimated population of approximately 200 patients undergoing coronary angiography after stress test.

The prevalence of coronary artery disease and the associated 95% confidence interval were calculated for the entire group of patients and for relevant subgroups. To compare the baseline characteristics between patients with and those without coronary artery disease, we used the chi-square test for categorical variables and Student's t-test for continuous variables. Odds ratios with 95% confidence intervals were calculated with the use of logistic regression. The 95% confidence intervals

and P values were calculated according to the normal approximation of the binomial distribution. No adjustments were made for multiple testing. All calculations were performed with the use of SPSS software, version 18.0 (SPSS).

RESULTS

Patient Characteristics

A total of 303 patients (mean age 52.8 ±9.7 yrs) were included during a study period of approximately 1 and ½ yrs (Oct 2015 to Dec 2016) among whom male were of average 53.6 ±10.5 yrs and female were of 51.7±8.6 yrs. The baseline clinical characteristics of the patients were as provided in table 1.

Overall the patients were matched for age and CAD risk factors in both gender groups. Although female patients who underwent exercise test for chest pain as a complaint was significantly higher than males {male 39.27% (n-119) vs 60.72% (n-184)}. Risk factor estimation among patients showed that 47.85 % (n-145) were hypertensive, 29.57 % (n-63) were overweight, 12.67% (n-27), 10.56 % (n-32) were diabetics, 5.94 % (n-18) were smoker with patients having at least one risk factor being 65.96%(n-188) and those with two or more risk factor being 34.03% (n-97).

Subgroup analysis of baseline characteristics based on gender distribution revealed that most of risk factors were matched except smoking which significantly higher in female than male (66.66% vs33.33% respectively) and that female higher BMI(>28.0kg/m2) than male (66.66% vs33.33% respectively).

Table 1: Baseline clinical characteristics of the patients

Characteristics	Overall Patients (N-303)
Age	
Average age of Patients(yrs)	52.8 ±9.7 yrs
Male Patients	53.6 ±10.5 yrs
Female patients	51.7±8.6 yrs
Gender Distribution	
Male (%)	39.27%(n-119)
Female (%)	60.72%(n-184)
Risk Factor for CAD distribution	
Hypertensive	47.85%(n-145)
Male	52.9%(n-63)
Female	44.6%(n-82)
Diabetes	10.56 % (n-32)
Male	59.37 %(n-19)
Female	40.62 %(n-13)
Smoker	5.94% (n-18)
Male	33.33% (n-6)
Female	66.66% (n-12)
Body Mass Index(BMI)	
Normal BMI (18.5 -22.9 kg/m^2)	63.36%(n-192)
Male	35.41%(n-68)
Female	64.58%(n-124)
Overweight (BMI-23.0-27.5 kg/m^2)	29.57%(n-63)
Male	66.66%(n-42)
Female	58.33% (n-21)
Obese (BMI-≥27.5kg/m^2)	12.67%(n-27)
Male	33.33%(n-9)
Female	66.66%(n-18)
≥2 CAD risk factors	31.35 %(n-95)
At least 1 CAD risk Factor	67.65%(n-205)

Coronary angiography of all the patients revealed normal coronaries in 54.0% (n- 114), minor coronary artery disease in 13.7% (n-29) and significant lesion in 32.2% (n-68) (Fig1.)

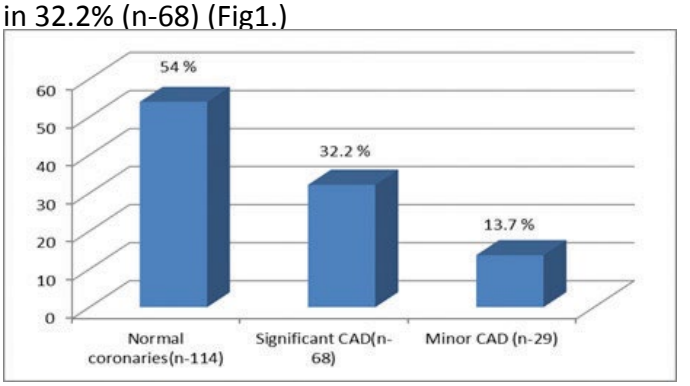

Fig 1. Percentage based on coronary angiographic finding

Among those with diagnosed coronary artery disease (CAD) 22.7 %(n-48) had single vessel disease (SVD), 13.7 %(n-29) had double vessel disease (DVD), 6.6 %(n-14) had triple vessel disease (TVD)

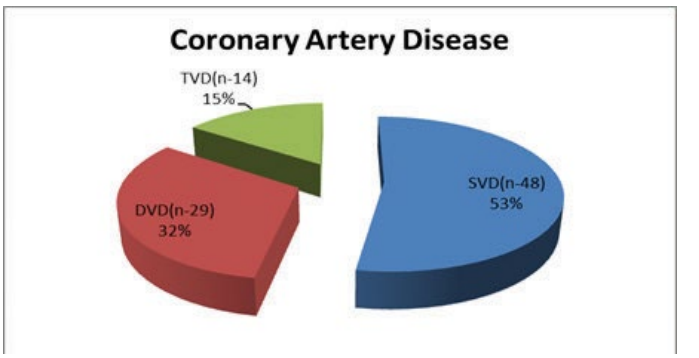

Fig 2. Distribution of coronary artery disease

The sub group analysis based on of risk factor and coronary artery disease showed coronary artery diseases was highest among diabetics (57.7%, Odds ratio 1.72 (95 % CI:0.92 to3.20) ,p value-0.08) followed by smokers (55%,Odds ratio 1.52 (95 % CI:0.59 to3.93), p value -0.38) compared with all the patient groups though not statistically significant.

Table 2: Subgroup analysis between risk factor and Coronary artery disease(CAD)

CAD Risk Factors	CAG finding			Odds Ratio (95% CI)	P Value
	Normal Coronaries (n-173)	Minor CAD (n-41)	Significant CAD (n-89)		
HTN	45.66% (n-79)	51.21 % (n-21)	50.56% (n-45)	1.00 (95% CI:0.68 to 1.48)	0.97
DM	10.98% (n-19)	19.51% (n-8)	20.22% (n-18)	1.72 (95 % CI:0.92 to3.20)	0.08
Smoker	4.6% (n-8)	12.19% (n-5)	5.61% (n-5)	1.5259 (95 % CI:0.59 to3.93)	0.38
BMI					
Normal	65.31% (n-113)	73.17% (n-30)	55.05% (n-49)	0.75 (95 % CI:0.52 to 1.08)	0.13
Overweight	26% (n-45)	26.82% (n-11)	31.46% (n-28)	1.05 (95 % CI:0.65 to 1.68)	0.83
Obese	8.6% (n-15)	0	13.48% (n-12)	1.01 (95 % CI:0.46 to 2.21)	0.97

Further analysis of patients comparing the risk of having coronary artery disease two or more CAD risk factors to at least one CAD risk factor showed significantly higher chance among patient with ≥2 CAD risk

factor (OR: 8.10,95 % CI:4.96 to 13.24 ,P < 0.0001).

Gender distribution of coronary artery disease showed that males with stress test positive had significantly higher chances of having CAD than females (53% vs 35% respectively) with odds ratio(OR) : 2.08, 95 % CI: 1.30 to 3.32 ,p value-0.002).

DISCUSSION

Graded exercise tests are widely used clinically to assess the ability of an individual to safely tolerate increased physical activity while ECG, hemodynamic, and symptomatic responses are monitored for the development of myocardial ischemia, electrical instability, or other exertion-related abnormalities. The exercise ECG remains an inexpensive test that has been well validated in the general population, and it can be used as the first diagnostic test for patients with an intermediate risk of having CAD.

Given the differences in presentation of CAD within the diabetic population and particularly the higher incidence of silent myocardial ischemia, exercise ECG testing has been used to assess asymptomatic diabetic patients for CAD. Koistinen et al [9] studied 136 asymptomatic diabetic patients who underwent exercise ECG testing and thallium imaging, with subsequent cardiac catheterization if noninvasive testing was positive. Exercise ECG testing was abnormal in 14% of these asymptomatic patients, with a positive predictive value of 94%. This result is higher than previous studies and may reflect the relatively older, male, and poorly controlled diabetic cohort (mean HgA1c 11.3%) with a higher incidence of CAD. Similar to the study sub group analysis based on of risk factor and coronary artery disease showed that coronary artery diseases was highest among diabetics (57.7%, Odds ratio 1.72 (95 % CI:0.92 to3.20) ,p value-0.08) though not satistically significant which probably could be due to small sample size of the study group.

Bacci et al [10] evaluated 206 consecutive higher-risk, asymptomatic, T2DM patients with peripheral arterial disease (PAD) and at least 2 cardiovascular risk factors (CRFs); 19% had an abnormal test. Coronary angiography was performed in 71 patients (27 with a positive test and 44 randomly selected patients with a negative test). Of these, 29% had significant CAD. The positive predictive accuracy of the exercise ECG was 79%. During the study comparing the risk of having coronary artery disease two or more CAD risk factors to at least one CAD risk factor showed significantly higher chance among patient with ≥2 CAD risk factor (OR: 8.10,95 % CI:4.96 to 13.24 ,P < 0.0001) which is comparable .

Nayak K C et al [11]performed treadmill exercise test has been performed in 50 chronic smokers and 50 non-smokers (93 males and 7 females) who were not having any clinical or electrocardiographic manifestation of ischemic heart disease. The test was positive in 18% chronic smokers and 4% in non-smokers, the chances of positivity of stress test was 4-5 times greater in chronic smokers than in non-smokers. The duration of smoking and number of/cigarettes/bidis smoked per day was directly proportional to the incidence of a positive stress test. There was no significant difference in the incidence of a positive exercise test amongst purely cigarette smokers (17.64%), purely bidi smoker, (16.16%), and in both bidi and cigarette smokers (20%). In study too smokers had higher chance of having CAD (55%, Odds ratio 1.52 (95 % CI: 0.59 to3.93), p value -0.38) compared with other patient groups though not statistically significant.

Risk stratification of asymptomatic patients, amending the correct paradigm for the diagnosis may be warranted. Similar to men, only symptomatic women with intermediate to high pre-test probability of CHD should undergo noninvasive testing. Unlike symptomatic men, symptomatic women may have more non-obstructive disease in addition to single vessel disease than age-matched men, which can decrease the diagnostic accuracy and result in a higher false positive rate .Miller TD et al [12] directly compared the sensitivity and specificity of treadmill testing in 3,213 women vs. 5,458 men using myocardial perfusion as the reference standard. Although more women (14%) than men (10%) had a false positive ECG (p<0.001), the false-negative rate was considerably lower in women (17% vs. 32%, p <0.001) (45). Compared with men, women had lower test sensitivity (30% vs. 42%, p <0.001) and positive predictive value (34% vs. 70%, p <0.001) but higher specificity (82% vs. 78%, p = 0.002), negative predictive value (78% vs. 52%, p <0.001), and accuracy (69% vs. 58%, p <0.001). In the smaller subset of patients referred for coronary angiography

(205 women, 838 men), the false-positive rate was again higher in women (13% vs. 7%, p = 0.003), but neither specificity (69% vs. 74%, p = NS) nor accuracy (60% vs. 66%, p = NS) was different between the sexes. Gender distribution of coronary artery disease in this study showed that males with stress test positive had significantly higher chances of having CAD than females (53% vs 35% respectively) with odds ratio(OR) : 2.08, 95 % CI: 1.30 to 3.32 ,p value-0.002).

In this study exercise test has proved to be important to detect early coronary artery disease in patient with stable ischemic heart disease but significantly more those of male gender , diabetics & smoker or combination of 2 or more CAD risk factors compared to those of female in whom chances of having a false positive test positive is much higher.

CONCLUSION

Coronary artery disease (CAD) among patients with TMT positive status is higher in patients with diabetics and smokers, especially those with two or more CAD risk factors. Along with significantly greater gender distribution among males than females even with age group matched.

Results of this study shows that the pretest probability of treadmill stress-test is higher in males with two or more CAD risk factor especially diabetes and smoking compared to the female counterparts with similar factors ,so should be supplemented by other non-invasive techniques(such as stress echocardiography, myocardial perfusion imaging) for further confirmation of diagnosis.

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