

# To study Incidence of Coronary Artery Disease in Asymptomatic Chronic Smokers by Using Exercise Stress Test

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## Abstract

**Introduction:** Identification of coronary artery disease (CAD) in asymptomatic individuals is helpful in preventing future coronary events. The electrocardiographic exercise test is an easy, non-invasive, and reliable method for the diagnosis of latent CAD.

**Purpose:** The purpose of the study was to study the incidence of CAD in asymptomatic chronic smokers using exercise stress test, relationship between CAD risk and duration of smoking and to study the effect of smoking as an independent risk factor for CAD.

**Materials and Methods:** This study was conducted on 82 asymptomatic chronic smokers (duration of smoking at least 10 years and number of bidis/cigarettes >5 per day). Persons having history of angina pectoris, history of myocardial infarction, family history of IHD, significant abnormalities in the resting electrocardiogram, history of diabetes mellitus, history of hypertension, hypercholesterolemia, and severe non-cardiac disease were excluded from the study. Smoking history was taken with reference to years of smoking, type of smoking, and number of bidis/cigarettes per day. Study patient underwent exercise stress test as per modified Bruce protocol and other relevant blood investigations.

**Results:** In non-smoker group, only 7.3% subjects observed with positive treadmill test (TMT) but in bidi and cigarette smoker group positive TMT was observed in 33.3% and 39.1%, respectively. Inadequate exercise was noted in about 40% in smokers group while negative TMT was noticed in 20% in this group. The positive finding of TMT was strongly associated with smokers group ( $P < 0.0001$ ). The study revealed that about 80% of non-smokers achieved the target heart rate while only 24.39% of smokers could achieve that and this is statistically highly significant ( $P < 0.00001$ ). Non-smoker group has good exercise effort tolerance with an average of  $10.74 \pm 4.18$  METS while smokers reported to have intermediate exercise effort tolerance with an average of  $7.79 \pm 4.55$  METS. Among the chronic smokers and non-smokers, no subject developed any arrhythmias or cardiac decompensation during or after TMT. The mean pack-year (1 pack of bidi/cigarette = 10 bidis/cigarettes) of negative and positive cases was  $24.12 \pm 20.55$  and  $64.61 \pm 15.45$  ( $P < 0.001$ ) and it was statistically significant.

**Conclusion:** This study concluded that chronic heavy smoking is an independent major risk factor for CAD and is about 5 times more frequently associated with the positive TMT and incidence of positive TMT is directly proportional to years of smoking ( $P < 0.001$ ). Exercise electrocardiography is an important non-invasive tool for detection of latent CAD.

**Key words:** Coronary artery disease, Treadmill test, Target heart rate

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## INTRODUCTION

Coronary artery disease (CAD) is common heart disease in the developing as well as developed countries and accounts for large number of sudden cardiac death. It is the major cause of morbidity and mortality in the western world. patients of acute myocardial infarction or sudden cardiac

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death may not have any related clinical manifestations before their illness. Reports indicate that many apparently healthy persons have silent C.A.D.<sup>[1]</sup>

Smoking constitutes one of the definite and foremost preventable risk factors for the development of CAD.<sup>[2]</sup> It has been found that in men who smoke >20 cigarettes per day, the risk of myocardial infarction was about 3 times higher than those who do not smoke. Sudden cardiac deaths are much more frequently associated with heavy smokers than in non-smokers. In women smoking >35 cigarettes per day, the incidence of myocardial infarction was estimated 20 folds higher than those who had never smoked.

Therefore, identification and quantification of such asymptomatic individual with this risk factor can be much helpful in preventing future coronary events. The electrocardiographic exercise test is an easily applicably non-invasive and reliable method for the diagnosis of latent CAD.<sup>[3]</sup>

Stress testing was started in 1928 by Feil and Seigal,<sup>[4]</sup> to assess the latent CAD modern stress was started in 1956 by Bruce. The basic aim of exercise test is to increase the oxygen demand of myocardium so as to unmask relatively reduced coronary blood flow. Treadmill exercise test is now an established non-invasive diagnostic, prognostic and evaluative technique in Cardiovascular Medicine. Although various other techniques are also available, for the developing countries such as India testing are economical and convenient methods to identify “at-risk” population.

This study was, thus, carried out to assess the relationship between asymptomatic chronic smokers and treadmill exercise test response as an indicator of latent CAD.

## MATERIALS AND METHODS

This study was conducted on 82 asymptomatic males 28–60 years of age (mean 46 years) at the Department of Medicine, Netaji Subhash Chandra Bose Medical College Hospital, Jabalpur (M.P.), from June 2017 to May 2018. The study group consisted of 41 chronic smokers (having no other major risk factor for CAD) and 41 non-smokers (without any major risk factor for CAD). The smokers smoked Either bidis or cigarettes. The length of bidi or cigarette, whether filtered or non-filtered was not taken into consideration.

### Criteria for Chronic Smoker (Arbitrary)

1. Duration of smoking: At least 10 years
2. Number of bidis/cigarettes: >5 per day.

Following persons were not included in the study:

1. Those having history of anginal chest pain
2. History of acute coronary syndrome

3. Family history of CAD
4. Abnormal resting electrocardiogram (ECG)
5. History of diabetes mellitus
6. History of hypertension
7. Hypercholesterolemia
8. Severe comorbid condition.

A detailed clinical history was taken from each individual. Family history of CAD, occupational history, and other risk factors for CAD were enquired. Smoking history was taken with reference to years of smoking, type of smoking, and number of bidis/cigarettes used per day.

A thorough physical examination was done with special reference to cardiovascular system. Any evidence of cardiac enlargement or failure such as S3-S4 and lungs for basal crackles was observed.

### Criteria for Positive Treadmill Test (TMT)

(Based on Goldschlager and Seizers classification sept.1976)<sup>[5]</sup>

Type Ia positive response: 1 mm or more of J-point depression with downsloping ST segment.

Type Ib positive response: 1 mm or more of 1-point depression with flat/horizontal St segment.

Type II positive response: 1.5 mm or more slowly upsloping ST-segment depression at 80 ms after i-point.

(Slow upsloping: ST slope <1.25mV/s)

Next, they are subjected to the following investigations:

1. Blood sugar
2. Fasting lipid profile
3. Renal function test: Blood urea and serum creatinine
4. Resting ECG.

The following instructions were given to each individual:

1. To have a light dinner on the night before the test and a light breakfast at least 4 h before the test.
2. To shave anterior chest wall and abdominal wall to facilitate proper placement of electrodes.
3. To bring at least one attendant with him.

**Table 1: TMT result**

TMT result	Groups		
	Non-smokers	Bidi's	Cigarettes
Positive	3 (7.3)	6 (33.3)	9 (39.1)
Inadequate	5 (12.2)	7 (38.9)	9 (39.1)
Negative	33 (80.5)	5 (27.8)	5 (21.7)
Total	41	18	23

TMT: Treadmill test

**Table 2: Distribution of pack-years and positive TMT**

Pack-years	Bidi Smokers			Cigarette smokers		
	Negative	Inad	Positive	Negative	Inad	Post.
5–40	3	1	0	4	4	0
41–80	2	3	3	1	4	8
81–20	0	2	3	0	1	1
<120	0	1	0	0	0	0
Total	5	7	6	5	9	9
Mean±SD	37.40±25.16	71.80±35.66	78.34±11.86	24.12±20.55	40.79±19.63	64.64±15.45

SD: Standard deviation, TMT: Treadmill test

**Table 3: Workload attained during treadmill test**

METS	Groups		
	Non-smokers	Bidi's	Cigarettes
<4	1 (2.4)	3 (16.7)	3 (13.0)
4–7	6 (14.6)	6 (33.3)	2 (8.7)
7–10	13 (31.7)	4 (22.2)	12 (52.2)
10–13	9 (22.0)	2 (11.1)	3 (13.0)
13+	12 (29.3)	3 (16.7)	3 (13.0)
Total	41 (100.0)	18 (100.0)	23 (100.0)
Mean±SD	10.74±4.18	7.79±4.55	7.82±4.51

SD: Standard deviation

- To abstain from smoking at least 2 h before the test.
- To wear comfortable clothes and foot wears to facilitate proper test.

### Procedure

Height and weight of all individuals were recorded. The skin over the anterior chest wall at the site of application of the electrodes was cleaned with spirit and abraded until it becomes hyperemic, and the patient was asked to lie down, and the resting blood pressure was recorded followed by a pre-test 12 lead ECG was recorded. Now the patient was asked to stand up, and again the blood pressure and ECG changes were recorded. Now the patient was advised to hyperventilate for 30 s. After 30 s of hyperventilation blood pressure and ECG changes if any were recorded.

After demonstration and explanation regarding the procedure, the patient was subjected to exercise stress test according to Bruce protocol.

The blood pressure was recorded every 3 min. Test continued till patient reached target heart rate (THR= 220- age in years) or terminated prematurely due to some other reasons.

After completion of the test, the patient was asked to lie down on bed and was re-examined for signs of cardiac decompensation, i.e., S3, S4, or basal crypts. Blood pressure was recorded at 2 min interval from onset of recovery and then at least every 3 min. ECG monitoring was done until ECG changes return to normal or for at least 4 min in recovery phase.

## RESULTS

This study was conducted in 82 asymptomatic males 28–30 years (mean 46.44 ± 9.43). The study groups consisted of 41 chronic smokers, of which 23 smoked cigarettes and 18 smoked bidis and 41 non-smokers. Each individual performed symptoms limited treadmill exercise following Bruce protocol on a case 12 system “UNI-EM TREADMILL SYSTEM” until the termination criteria were achieved.

In our study we found in non-smoker group, 7.3% subjects observed with positive TMT. In bidi and cigarette smoker group positive TMT was observed in 33.3% and 39.1%, respectively. Inadequate exercise was noted in 38.9% and 39.1%, respectively, for bidi and cigarette group while both of these groups showed negative TMT by 27.8% and 21.7%, respectively. The positive finding of TMT was observed strongly associated with smoker group (either bidi or cigarette) ( $P < 0.0001$ ).

It is also obvious in this study that total 33 of 41 (80.5%) non-smokers achieved the THR while only 24.39% of smokers 5 bidi and 5 cigarette smokers could achieve that. It is statistically very highly significant ( $P < 0.00001$ ).

The ST criteria (with positive TMT) were met with 3 non-smokers (7.3%) while it was met in 15 smokers with 6 (33.3) of bidi smokers and 9 (39.1%) of cigarette smokers. It was also statistically highly significant ( $P < 0.001$ ).

Majority of cases in non-smoker group (51.3%) achieved >10 METS with an average of 10.74 ± 4.18 METS. While the bidi smokers reported 16.3% cases with <4 METS, 71.8% of the bidi smokers could achieve only up to 10 METS with an average of 7.79 ± 4.55 METS. A similar observation was noted among the cigarette smokers with the mean of 7.82 ± 4.51. The control group showed significantly higher amount of workload as compared with overall case group ( $P < 0.05$ ). The cigarette and bidi smokers were almost comparable and showed equal amount of workload, i.e., METS ( $P > 0.05$ ) but definitely significantly different with the non-smokers ( $P < 0.05$ ).

Among the chronic smokers and non-smokers, no subject developed any arrhythmias during or after TMT, and none of the persons among both the groups developed any signs of cardiac decompensation during or just after exercise.

This study describes the correlation between number of bidi's and cigarettes smoking in terms of pack-years of smoking in relation with the TMT findings (1 pack of bidi/cigarette = 10 bidis/cigarettes). In bidi smokers, the negative TMT was confined to 5–80 pack-years, while the cases found positive on TMT showed the observation of 41–120 pack-years with the mean of  $37.40 \pm 25.16$  and  $78.34 \pm 11.86$  pack-years, respectively. The positive cases showed a significantly higher amount of bidi smoking compared to non-smokers. In cigarette smoker group, the negative TMT cases were primarily concentrated in 40–120 pack-years. The mean pack-year of negative and positive cases was  $24.12 \pm 20.55$  and  $64.61 \pm 15.45$  ( $P < 0.001$ ). It is statistically significant [Tables 1-3].

## DISCUSSION

Coronary heart disease is the chief single cause of death in developed as well as developing countries. 40% or more of patients of acute myocardial infarction or sudden death due to CAD have no previous clinical manifestations.<sup>[1]</sup> This occurs as the results of advanced coronary atherosclerosis which has evolved slowly over many years without notable clinical manifestations.

In light of these considerations, a simple objective means of detecting latent coronary heart disease is of the utmost importance. A considerable number of such coronary prone subjects can be identified by exercise testing. The predictive value, i.e. probability of developing coronary heart disease in patients with an abnormal test in three careful follow-up studied in healthy men of a wide age group ranged from 13.6 to 23.0%.<sup>[6]</sup>

Exercise electrocardiography is one of the most important and valuable non-invasive diagnostic tests for patients suspected or known to be having cardiovascular disease, particular CAD.

Doan *et al.*<sup>[7]</sup> claimed that maximum exercise (treadmill) increase the sensitivity of the electrocardiographic exercise test nine folds in comparison to the double two-step test.

The positive ischemic ST-segment changes, produced by treadmill exercise test, are more sensitive and specific (75–90%) as compared to Master's two-step test (50%). It is because of this reason we preferred to do treadmill exercise test rather than Master's two-step in the present study.

In the asymptomatic population where the incidence of CAD is expected to be low, the chance of a positive results being false positive is obviously higher than in a population with typical anginal discomfort due to CAD. In this asymptomatic population<sup>[6]</sup> found 44% and Borer *et al.* (1975) found 37% of positive test to be true positive tests.

A positive exercise results indicates that the likelihood of CAD is 98% in patients with typical angina, 88% in patient with atypical pain, 44% in patients with non-anginal chest pain, and only 33% in asymptomatic persons (Braunwald 1989).

Many retrospective studies have been conducted to determine the association between smoking and coronary heart disease, but few studies have been conducted in asymptomatic healthy persons to find out the incidence of latent heart disease among those having risk factors. The number of risk factors is protean, but we have restricted to only one, i.e. chronic-smoking (>5 cigarettes per day for at least 10 years) in this study.

We studied 82 asymptomatic subjects, 41 were non-smokers without any clinical or electrocardiographic features suggestive of CAD and chronic smokers, of which 18 were smoking bidis, and 23 were smoking cigarettes. All cases were males. In the present study, among 41 chronic smokers, total 15 (36.58%) had positive TMT whereas only 3 (7.3%) persons in the non-smokers group had positive test. Among the smokers total 6 of 18 (33.33%) had positive results whereas in cigarette smoker Group 9 of 23 (39.1%) had positive TMT. The incidence of positive TMT was >5 times in chronic smokers than in non-smokers. The difference between these groups is statistically significant ( $P < 0.05$ ). There was no significant difference found among bidi and cigarette smokers. Our observations are quite consistent with those of Nayak *et al.* (1989) 136 where they found incidence by 4.3 times more in chronic smokers. They found no significant difference between bidi and cigarette smokers.

In a study by Pais *et al.* (2001) found that smoking 10 or more bidis or cigarettes per day carries an independent four-fold increase risk of AMI. Odds ratio for cigarette was 3.58 ( $P < 0.08$ ) and bidis was 4.36 ( $P < 0.001$ ). The results are very close to our observations. They studied the incidence among the AMI cases, but we studied it in asymptomatic patients.

Other published reports, however, were not quite comparable with the present study as they were either on unselected healthy persons or with multiple risk factors.

Bellet and Roan<sup>[3]</sup> found 2.7% positive exercise tests in normal persons without any risk factors while in our study it is 7.1%; however, his study group was large. Of 710 persons 19 were having positive test. Cumming *et al.* (1981) used maximum exercise as bicycle ergometer in asymptomatic men found 12% positive exercise tests.

Agarwal *et al.*<sup>[1]</sup> studied 50 middle-aged subjects with important coronary risk factors and yielded 22% positive tests.

Jayant *et al.* (1983) in the case–control study in India shown that cigarette smokers are more than twice as likely to develop coronary heart disease and 3 times more likely to develop myocardial infarction than non-smokers.

In our study, the incidence of positive stress testing in chronic smokers shows an increasing trend with the rise in age, i.e., 12.19% in age group below 50 years while 24.39% in subject >50 years. Statistically, it is just significant ( $P < 0.1$ ).

Bellet and Roan<sup>[3]</sup> screened 1390 subjects for latent CAD using treadmill exercise test. The results were as follows:

Age group	Positive TMT (%)
20–29 years (253)	8 (3.2)
30–39 years (563)	31 (5.5)
40–54 years (574)	101 (17.6)

In the present study, the incidence of positive test in chronic smokers is directly proportional to the total amount of smoking, i.e., duration and number of cigarettes smoked represented as pack-years. Prevalence positive TMT was 66.6% in those who had >40.30 pack-years cigarette smoking compared to only 1% in those who had for 5–40 pack-years and the difference is statistically highly significant. These observations are consistent with those of Kannel (1976, 1981) 87 and Nayak *et al.* (1989) 136. In their study out 10 cases of heavy smokers (>20 cigarettes per day), 5 were having positive tests.

The interpretation of a positive exercise test is beset with many difficulties, particular when performed in asymptomatic persons.

Bellet and Roan<sup>[3]</sup> found 2.7% positive stress tests in normal healthy persons. A positive test may be due to various reasons:

- Unmasking of latent CAD
- False positivity
- A direct consequence of heavy smoking.

It has been reported in literature (Chung *et al.* 1979) that exercise test may be positive if one smoked shortly before performing a stress test, which might suggest that it may be a pharmacologic action since no details are available.

## CONCLUSION

Chronic heavy smoking is about 5 times more frequently associated with the positive TMT as compared to no smoking and incidence of positive TMT is directly proportional to years of smoking ( $P < 0.001$ ). There is no significant difference between bidi and cigarette smoking and a positive TMT result ( $P > 0.05$ ), but chronic smoking (either bidis or cigarettes) serves as an independent major risk factor for CAD.

Exercise electrocardiography is an important non-invasive test for detection of latent CAD. Hence, this study goes a long way in providing a useful non-invasive method to detect high-risk cases among chronic bidi and cigarette smokers and this is useful from both preventive and curative aspects.

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