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Correlation of Clinical Characteristics and Risk Factors of Treadmill Exercise Test in Patient with Myocardial Bridge in Population From Northwest India

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ABSTRACT

AIM: The main objective is to investigate the value of the treadmill exercise test (TET) in relation to myocardial bridge through various clinical characteristic and risk factor for guiding the clinical therapy of myocardial bridging (MB) patients.

METHOD: This was cross-sectional, single centre, observational prospective study conducted from January 2022 to June 2023. Total coronary angiography was performed on 4,321 cases of angina pectoris and suspected myocardial infarction at our hospital, 104 cases were confirmed as myocardial bridges, and exercise stress test was performed on 44 cases among them was investigated and evaluated the relationship between the TET results and the patients clinical characteristics, including sex, age, bridge length, reference diameter in systole and diastole and the degree of systolic stenosis.

RESULTS: No Statistical differences were found between baseline clinical characteristic (age, sex, clinical features, ECG findings) between the Nobel I with less than 50% of systolic stenosis and the Nobel II with more than 50% of systolic stenosis. Quantitative coronary data in study population mean ref. vessel diameter was 2.41±0.33 mm, and the diastolic vessel diameter was 2.16±0.44 mm, 85% of the ref. vessel diameter, and the systolic vessel diameter was 1.16±0.43 mm, 46% of the ref. vessel diameter. The average systolic stenosis rate was 45±18% on average. The average myocardial bridge length was 11.86 ±4.92 mm, which did not match the degree of systolic compression. 44 patients performed the Treadmill exercise test in which 34 cases (77%) positive and 10 cases (23%) negative. No relationships were found between the quantitative coronary data, bridge length, lesion location, bridge compression, and Treadmill exercise test results and between the positive and negative groups.

CONCLUSION: Our study found that patients with MB had high positive rate of treadmill exercise test. it is judged that various mechanisms other than simple mechanical compression may be involved as the cause of myocardial ischemic symptoms. The treadmill exercise test can improve our understandingofthecharacteristicsofbloodsupplytothemyocardium,clarify whether MB can cause myocardial ischemia and help develop appropriate treatment strategies for MB patients

Keywords: Treadmill Exercise Test, Myocardial Bridge, Coronary Angiography

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Introduction

Myocardial bridging (MB) is anatomically defined by the intra myocardial course of portions o the coronary arteries, mainly the mid portion of the left anterior descending (LAD)coronary artery.[1]Theusual anatomical position of the coronary arteries is between the pericardium and epicardium. Myocardial bridge was first describe by Reyman in the year 1732, as an incidental autopsy finding in which a part of an epicardial coronary artery gets "tunneled" either partially or completely within the myocardial fibers and takes an intramuscular course for a different length[2.]

The prevalence rate of myocardial bridge is unknown, and rate of detection varies with the imaging modality of choice. The reported prevalence of myocardial bridge is between 2 and 6% by coronary angiography and 19 and 22% by coronary computed tomography angiography.[3,4] The current gold standard in identification of myocardial bridge are autopsy studies, with a prevalence approaching 33 to 42%.[3,5,6] Around 67 to 98% of Myocardial bridges were found in the LAD, mostly in the proximal and mid LAD segments. Left circumflex and RCA are infrequently involved.[7]

Various factors have been linked to the significant variation in prevalence of myocardial bridge across imaging modalities; these include the varying length and depth of myocardial tissue encompassing the tunneled vessel,the axial placement of the coronary artery in relation to the myocardial fibers, the presence of a fixed stenosis proximal to the myocardial bridge, the presence of connective or adipose tissue opposing the tunneled segment, intrinsic tone of vessel wall of the coronary artery, low blood pressure, vasopressor use at the time of imaging, and intra observer variability.[8]

Previous studies had shown that myocardial bridge is a relatively benign disorder. However, recent studies suggest that Myocardial bridge may cause cardiac adverse events, including myocardial angina, myocardial infarction,and even cardiac sudden death.[9-15]Therefore,itis critical for clinical therapy to obtain an early diagnosis and evaluation of Myocardial bridge. Coronary angiography and coronary computed tomography have great diagnostic value to identify MB. However, X-ray exposure is inevitable in these two examinations. Conversely, it is difficult to conclude if myocardial bridge is responsible for ischemia in these two examinations. The treadmill exercise test is applied to diagnose myocardium ischemia, but few studies have been conducted to analyse correlation between Myocardial bridge and treadmill exercise test.

Therefore, this study (1) tried to understand the clinical variability of patients withmyocardial bridge, (2) the significance of exercise stress test and myocardial muscle through coronary angiography in patient with myocardial ischemia clinically complaining of symptoms of myocardial ischemia.

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Subjects and Methods

Subjects

This was cross-sectional, single centre, observational prospective study conducted from January 2022 to June 2023. Total coronary angiography was performed on 4,321 cases of angina pectoris and suspected myocardial infarction at our hospital, 104 cases wereconfirmed as myocardial bridges, and exercise stress test was performed on 44 cases among them was investigated.

Inclusion criteria was patients who were more than 18 years with symptoms of angina or shortness of breath and have undergone a non-invasive stress test; and found to have normal coronaries or an otherwise insignificant disease but with MB as the only finding were includedinthestudy.Exclusioncriteria-Patientswithcomorbiditylikedecompensatedheart failure, , severe aortic stenosis, severe bronchial asthma, advanced degree of heart block, chronic obstructive pulmonary disease, patients with significant coronary artery disease, , physical disability that precludes safe and adequate testing were excluded from the study.

Method

Clinical feature and baseline ECG

Stable angina pectoris is 1. Substernal 2. induced by exercise 3. relieved at rest for 2-15 minutes 4. pain radiating to the lower jaw, neck, back and left arm. When 1,2,3 criteria or when all four criteria are satisfied called as stable angina. When only two criterion is satisfied then described as an atypical angina.

Treadmill exercise test (TET)

The Bruce protocol was used for the TET. Blood pressure and ECG were recorded both in standingandhorizontalposition.Testresultswererecordedevery3minduringthetest,atthe peak, and every 2 min after the test. The usual criterion applied is 1 mm or greater or 0.1 mV or more of horizontal or down sloping ST-segment depression in 3 consecutive beats in ecg. the point of ST- segment measurement is 60 to 80 milliseconds after the J point compared to PQ segment or a rise of more than 0.1 mV in the ST-T segment, or occurrence of significant ventricular arrhythmia.

Coronary angiography

Coronary angiogram was performed using 5F diagnostic catheter and traditional 6 to 8 views were taken for left coronary system analysis. Patients fitting the inclusion criteria were selected. QCA analysis was conducted coronary angiographic image acquired at a rate of fifteenframes/second,utilizingspecializedQCAsoftwarepackages.Theanalysisfocusedon selecting angiographic views that exhibited minimal foreshortening and provided the most accurate representation of the stenotic coronary segments. Measurements taken by QCA was Reference vessel diameter, Diastolic Lumen Diameter, Systolic lumen diameter and Area stenosis rate.

(1) Systolic stenosis rate (%) = 100- (diameter at systole phase / diameter at diastolic phasediameter×100)

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(2) The morphological classification was measured on the tangential view and classified as concentric when the difference was less than 50%, and eccentric when the difference was more than 50% classified as eccentric.

(3) Provocation test is performed when dysplastic angina is clinically suspected in the clinical history.

Patients were classified into Nobel I (systolic stenosis rate <50%) and Nobel II (systolic stenosis rate >50%) according to the degree of systolic stenosis rate. Laboratory and cardiovascular data were comparatively analysed.

Statistical analysis

Statistical analysis was performed using SPSS 29.0 statistical program (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation and compared with Student's t-test. Categorical variables were expressed as counts and percentages then compared using a Chi-square test. $P < 0.05$ was considered statistically significant.

Results

The frequency of Myocardial bridge in coronary angiography was 2.4%, which was 104 out of 4321 patients. The age distribution ranged from 34 to 81 years (average 54.4 ± 10 years), and there were 56 (54%) and 48 (46%) male and female patients, respectively.

Table1.Clinicalcharacteristicofstudypopulation

Variable	**Number (%)**	**Nobel I Number**	**NobelII Number**	**p***
Number(M/F)	104(56/48)	68(26/36)	36(24/12)	<0.05
Age(year)	54.4 ± 10	56 ± 10	53 ± 10	<0.05
Clinicaldiagnosis				
Stableangina	66(63)	40	26	<0.05
Atypicalchestpain	30(29)	26	4	<0.05
Vasospasticangina	4(4)	1	3	<0.05
AcuteMI	4(4)	2	2	<0.05
ECG				
Normal	64(62)	44	20	<0.05
ST-Tchanges	34(34)	22	12	<0.05
AMI	4(4)	2	2	<0.05

Valuearemean±SD

*：comparingvaluesintheNobelI(<50%systolicstenosis)andNobelII(>50%systolicstenosis) M : male, F : female,AMI：acute myocardial infarction,ECG ：electrocardiography

Clinical features were stable angina in 66 patients (63%), atypical chest pain in 30 patients (29%),andvasospasticanginain4patients(4%),acutemyocardialinfractionin4(4%).

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Electrocardiogram was normal in 64 patients (62%), and ST and T changes were in 34(34%) patients, acute myocardial infraction in 4(4%). (**Table 1)**

Coronary angiography findings of myocardial bridge

The distribution of location was intermediate in 70 patients (67%), intermediate to distal in 6 (6%), and distal in 28 (27%). The morphological classification was concentric in 58 patients (56%) and eccentric in 46 patients (44%). The average total reference vessel diameter of the patient was 2.41±0.33 mm, and the vessel diameter during the diastolic phase of the lesion was 2.16±0.44 mm, which was 85% of the reference vessel diameter, and the systolic vessel diameter was1.16±0.43 mm, which was 46% of the reference vessel diameter. The mean systolic stenosis rate was 45±18% %. The average pericardial bridge length was 11.86±4.92 mm, which did not match the degree of systolic stenosis. (Table2 and Table 3 and Fig 1)

Table2:AngiographicFeaturesof Myocardial bridges

	Number	**%**
Location		
LADmid	70	67%
LADmid-distal	6	6%
LADdistal	28	27%
Morphology		
Concentric	58	56%
Eccentric	46	44%

LADMID：left anteriordescendingartery

Table3Angiographicvariables ofmyocardial bridges

	Diameter	**Stenosis rate***
Referencediameter(mm)	2.41±0.33	
Diastolicdiameter(mm)	2.16±0.44	85%
Systolicdiameter(mm)	1.16±0.43	46%
Lengthofsegment(mm)	11.86±4.92	

Valuearemean±SD

*：Stenosis rate is percentage of each diameter per reference diameter

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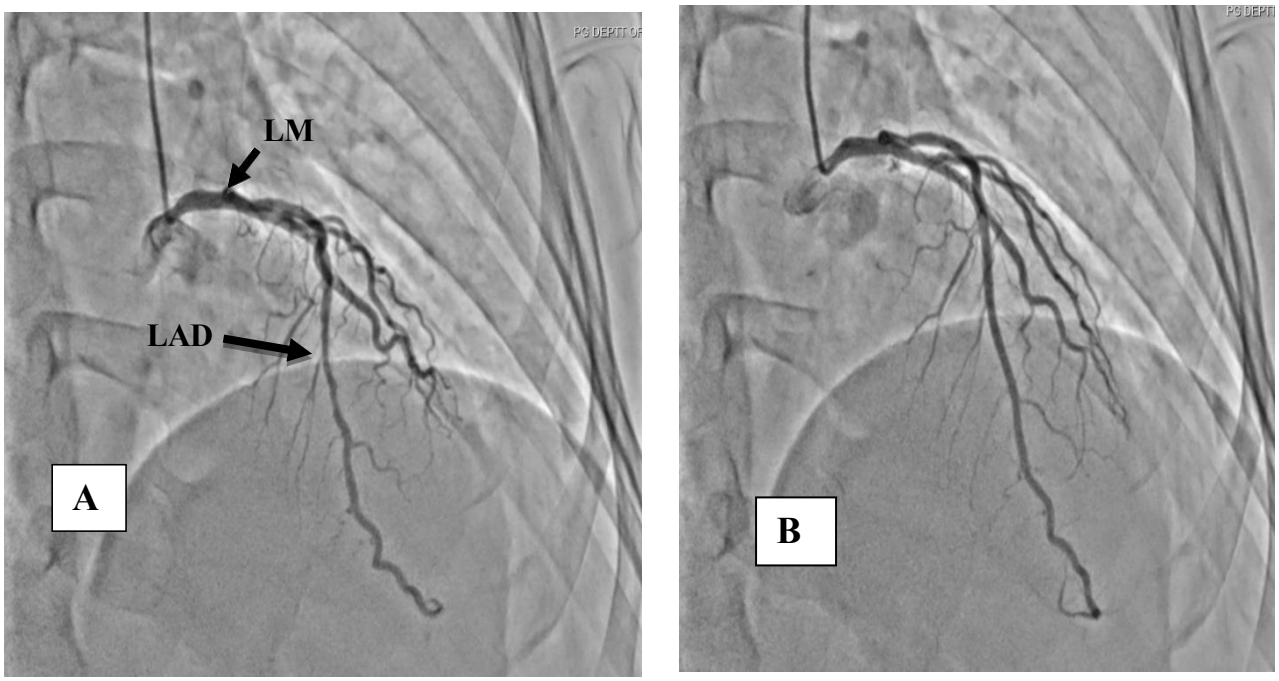

Fig. 1. A case of stable angina due to severe myocardial bridge(a male patient aged 57 years). Left coronary angiogram is shown in systolic phase (A) and diastolic phase (B). There is marked systolic narrowing of the mid left anterior descending artery (arrow) consistent with severe myocardial bridging that developed leading to anginal pain.

Treadmill test in study population with Myocardial bridge

44 patients of 104 myocardial bridge patients performed a treadmill exercise test. 34 patients (77%) were positive, and most of them showed positive findings in 3rd and 4th stage of treadmilltest,andtheheartrateincreasewasapprox200%.Therewere10patients(23%) who were treadmill test negative, and test wasterminatedwithoutECGchangesin3rdand4th stage of treadmill test. and at this time, the heart rate increase was approx 200%. There were not statistically significant differences in clinical variables, quantitative coronary artery variables (QCA), and lesion location between the positive treadmill test and negative treadmill test groups.(**Table 4 and Table 5)**

Table 4 TMT observation

	TMTpositive	**TMTnegative**
Stage	34(77%)	10(23%)
II	4	0
III	10	5
IV	20	5
RestHR(beats/min)	79.3	76.2
MaxHR (beats/min)	161.4	158.2

Among104myocardialbridgecases,44caseswerecompletedtreadmilltest TMT：

treadmill test

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Table5correlation ofTMTpositive and TMT negative

Variable	TMTpositive	TMTnegative	p*
Number(%)	34(77)	10(23)	
Age(year)	53.4 ± 9.10	47.1 ± 9.10	<0.05
Clinicaldiagnosis			
Stableangina	20	5	<0.05
Atypicalchestpain	14	3	<0.05
Variantangina	0	2	<0.05
QCA data			
Referencediameter(mm)	2.420 ± 0.220	2.730 ± 0.350	<0.05
Diastolicdiameter(mm)	2.150 ± 0.360	2.25± 0.590	<0.05
Systolicdiameter(mm)	1.270 ± 0.390	1.080 ± 0.260	<0.05
Lengthofsegment(mm)	11.160 ± 4.900	9.970 ± 5.450	<0.05
Systoliccompression(%)	41.40 ± 16.00	52.50 ± 12.00	<0.05
Location			
LADMID	22	7	<0.05
LADMID-DIS	2	1	<0.05
LADDISTAL	10	2	<0.05

Comparison between Nobel I (systolic stenosis<50%)and Nobel II(systolic stenosis >50%)

Out of 104 patient with myocardial bridge 68 had systolic stenosis rate < 50% (36.20 ± 10.10%) and 36 had systolic compression of > 50% (64.10 ±14.50). There were no statistical differences in clinical features and electrocardiograms between the 2 groups. The length of coronary arterystenosiswas12.460±3.860mminNobeland,12.160±4.750mminNobel II. There is no correlation with the degree systolic stenosis in Nobel I and in Nobel II. TMT was positive in 26 (87%) of 30 people in Nobel I showed positive findings in the treadmill exercise test whereas in Nobel II 6 out of 14(43%) showed a positive result. **Table 6**

Table 6 correlation of Nobel I and Nobel II

Nobel	Mean stenosis(%)	Mean length(nm)	TMT Positive	TMT Negative
Nobel I (1-49%)	36.2 ± 10.1	12.46 ± 3.86	26	4
Nobel II (50-100%)	64.1 ± 14.5	12.16 ± 4.75	6	8
Total	51.0 ±17.9	11.89 ± 4.89	32	12

Valueare mean±SD

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Discussion

Previous studies intimated that MB is considered a benign condition. The myocardial blood flow occurs mainly in the diastolic period; compression by MB happens in the systolic period. Therefore, the effect on diastolic blood flow is minimal. However, previous studies suggest myocardial bridge compression on the coronary artery lasted until the early or even middle diastolic phase, leading to decline in distal blood supply reserve and the occurrence of myocardial is chemia, specially when the heart rate is increased. In addition, the contractile pressure of the myocardial bridge sometimes causes coronary artery spasm.[16] In this way, myocardial bridge may cause adverse cardiac events, including cardiac angina, myocardial infarction, even sudden cardiac death. In this study the frequency of myocardial bridge in coronary angiography was 104 out of 4317 patients. It shows a frequency of 2.4% (Table 1). In addition, usually myocardial stenosis occurs mostly around the LAD branch [17-19] of the coronary artery branch. It is known to be mostly present in the region of junction of proximal and middle LAD. [19-21]. In this study, all cases showed a myocardial bridge in the LAD , with 70 cases (68%) located in the mid LAD. (Table 2 and 3).

Myocardial bridges can present with other heart diseases more common in patients with hypertrophic cardiomyopathy than secondary myocardiopathy. [22,23]

In this study, 34 out of 44 patients (77%) who underwent the Treadmill exercise test showed positive results. During test heart rate (HR) increase was approx 200%,and the max HR was about 161.4 beats per minute on average. However, in the group with a negative Treadmill exercise test, the HR increase was also approx 200%, and the max HR was 158.2beats/minute on average, which was not statistically significant compared to the positive group (Table 4). Analysis of the clinical dataand cardiovascular data of these two groups,the age of the positive TMT test group was more(53.4 years, 47.1 years), and the degree of systolic stenosis was rather less evere at 41% than that of the negative TMT test group,52%. The average length of myocardial bridge lesions was 11.160 ± 4.90 mm in the positive TMT group, bigger than the average of 9.970 ± 5.450 mm in the negative TMT group, but it was not statistically significant. While analyzing the treadmill test results according to the location of the myocardial bridge, no statistical difference was found between the two groups (Table 5). It is not known which parameters are involved in the positive findings of the TMT test because they are not listed, it is known that increased HR is an important contributing factor to the positive findings of the treadmill exercise test in patients with myocardial infarction. However, it is known that the large complex hemodynamic factors in the coronary arteries act rather than by this single factor.[24]

The symptoms of myocardial bridge are very different. Most cases are without any symptoms, and in some patient, coronary angiography is performed for typical chest pain and atypical chest pain that occurs during stress. All patients in this study population had symptoms, and stable anginal pain accounted for a large % (63%). In particular, there was 40 cases who presented with stable anginal pain and 26 cases who presented with atypical chest pain in Nobel I, where as 26 patients in Nobel II presented with stable anginapectoris ,suggesting that the clinical features was variable depending on the degree of stenosis (Table 1).

Myocardial bridges can be diagnosed by conventional coronary angiography, and treadmill stress testing cannot localize the ischemic area of heart and has a high false-positive rate. In

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the treadmill stress test of 30 people in Nobel I, 26 people (87%) showed positive TMT test, whereas in the Nobel II, 6 out of 14 (43%) showed positive TMT test (Table 6). The Thallium^{201} perfusion scan is mostly useful for localizing cardiac ischemia. It is already known fact that chances of recurrent cardiac arrest is high in cases with a positive TMT test, perfusion failure on a thallium^{201} perfusion scan of heart, or severe stenosis of the LAD.[24] Myocardial bridges can be differentiated from fixed coronary artery stenotic lesions by contraction of the compression area during systole and return of the narrowed area during relaxation. The myocardial bridge can be seen better with IVUS.

Myocardial bridges show various clinical features, including stable coronary angina or atypical anginal chest pain, vasospastic angina, and MI. There were more positive findings in patients who underwent TMT (77%) with myocardial bridge. Although there were more patient than in the Nobel I, no significant finding was found that the degree of systolic stricture was consistent with the findings of the Treadmill exercise test (Table 6)

Treatment of angina pectoris by myocardial bridge can be divided into drug treatment, such as beta-blockers and CCBs, and non-drug treatment, such as stent placement and cardiac surgery. Beta-blockers and CCBs lowers heart rate, decrease myocardial contractility, and lowers consumption myocardial O_2.Use of nitrate containing drugs requires caution because nitrate containing drugs reduce the intrinsic tone of the coronary artery, and leading to exacerbation of contractility by reactive sympathetic nerve stimulation which may exacerbate symptoms.[25,26]In the analysis of drugs treatment in this study population, aspirin was given in 86 patients, and beta-blockers and CCBs were given in 42 and 56 patients, respectively.

Surgical treatment can be considered in high-risk patients who show symptoms of persistent or recurrent myocardial ischemia without drug response. As a surgical treatment, the coronary artery can be completely exposed by dissection of the myocardium carefully. There patient also get significant clinical improvement in patients with severe myocardial bridges with coronary artery disease by coronary artery bypass surgery or a combination of resection and bypass surgery. [26-30]

In this study, 68 out of 104 patients were followed up and observed outpatient, and up to now, pharmacotherapy has been administered out of which 58 cases did not complain of recurrent symptoms. The prognosis of myocardial bridges is excellent regardless of the degree of systolic stenosis, although there is a risk of severe arrhythmias and sudden death.

Conclusion

Our study found that patients with MB had high positive rate of treadmill exercise test. We can say that various other factors than simple mechanical compression may be involved as the cause of myocardial ischemic symptoms. The treadmill exercise test can improve our understanding of the characteristics of blood supply to the myocardium, clarify whether myocardial bridge can cause myocardial ischemia and help develop appropriate treatment strategies for patient with myocardial bridge.

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