Angiographically evident atherosclerotic stenosis associated with myocardial bridging and risk factors for the artery stenosis located proximally to myocardial bridging

Heng Hong, Ming-Sheng Wang, Qun Liu, Jing-Cheng Shi[1], Hai-Ming Ren, Zhi-Min Xu[2]

Department of Cardiology, Shijingshan Teaching Hospital of Capital Medical University, Beijing Shijingshan Hospital; Beijing-*China*
[1]Department of Epidemiology and Health Statistics, School of Public Health, Central South University; Changsha-*China*
[2]Department of Cardiology, Fu Wai Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences; Beijing-*China*

Abstract

Objective: The purpose of this study was to determine the prevalence of coronary angiographically evident atherosclerotic stenosis associated with myocardial bridging (MB) and to explore related risk factors of coronary artery stenosis located proximally to MB.
Methods: Overall, 603 patients with MB-mural coronary arteries (MB-MCAs) diagnosed by angiography initially were enrolled in this observational study during May 2004 to May 2009. One-way ANOVA, t-test, Pearson correlation test and stepwise multiple regression analysis were performed to explore related risk factors.
Results: Totally 644 MB-MCAs were examined. Prevalence of lesions located distally to MBs was significantly lower than those proximally to MBs [36 (5.9%) vs. 382 (62.4%), p<0.001]. Diastolic vessel diameters in MB segments were significantly smaller than reference segments p<0.001. Ulcer-like lesion was found in MB-MCA in 1 patient. Multivariate analysis suggested that vascular bifurcation lesions, the degree of narrowing and the number of diseased coronary vessels of non-MB-MCA arteries, age, low-density lipoprotein cholesterol (LDL-C)/high density lipoprotein cholesterol (HDL-C), male, course of diabetes, and systolic narrow rate (SNR) of MB-MCAs were positively related with the narrow degree of the first coronary artery stenosis (FCAS) located proximally to MBs (all p<0.05). Vascular bifurcation lesions, the degree of narrowing and the number of diseased coronary vessels of non-MB-MCA arteries, age, LDL-C/HDL-C, male, diabetes and dyslipidemia were positively related with the narrow degree of the most severe coronary artery stenosis(MSCAS) located proximally to MB (all p<0.05).
Conclusion: The intramural and distal portions of a bridged artery are not the forbidden zone of artery atherosclerosis formation. SNR of MB-MCA may be one of the important decision factors to coronary artery stenosis located proximally to MB.
(Anadolu Kardiyol Derg 2014; 14: 40-7)
Key words: myocardial bridging, atherosclerosis, coronary angiography, regression analysis

Introduction

Myocardial bridging (MB) is a congenital coronary abnormality where a segment of an epicardial coronary artery or its major branch, which is defined as mural coronary artery (MCA), descends into the myocardium for a variable distance.

MB was initially recognized at autopsy by Reyman in 1737 and the radiological appearance of systolic narrowing was first described angiographically by Portmann and Iwig in 1960 (1, 2). Traditionally, MB is considered as a benign condition. However, MB has been known as one of myocardial ischemia causes (3-13). The following complications have been reported as acute coronary syndrome (4-8), cardiac arrhythmia (9, 10), stunning and sudden death (11, 13). It widely accepts that the intramural and distal portions of a bridged artery usually remain free from atherosclerotic disease, which may be explained by protective effects of MB and atherosclerosis may be more frequent in segments proximal to the bridging (14-20). These changes in atherosclerotic distribution have been recognized in autopsy, pathology and clinical imaging studies (14-20).

However, whether MB or systolic narrow rate (SNR) of MB-MCA is one of independent risk factors of coronary athero-

Address for Correspondence: Dr. Heng Hong, Department of Cardiology, Shijingshan teaching hospital of Capital Medical University, Beijing Shijingshan Hospital, Beijing, No. 24, Shijingshan Road, Beijing, 100043, *China* Phone: +86 10 88689099 E-mail: hongheng74@126.com
Accepted Date: 04.06.2013 **Available Online Date:** 09.12.2013

doi:10.5152/akd.2013.4702

sclerosis formation proximal to the bridging is still a controversial issue (14, 17, 21, 22). The larger sample study about related risk factors of coronary artery stenosis located proximally to myocardial bridging has not been approached so far. Hence, further related investigation is necessary.

The purpose of this study was to determine the prevalence of coronary angiographically evident atherosclerotic stenosis associated with myocardial bridging (MB) and to explore related risk factors of coronary artery stenosis located proximally to MB.

Methods

Study design

This was a retrospective observational study.

Study population

The data collection protocol was approved by the Ethics Committee of our hospital. Continuous 603 patients with MB-MCAs diagnosed by angiography initially were enrolled in our hospital from May 2004 to May 2009. This population consists of 14.1% of the patients who underwent coronary angiography of our institution in the same period. Angiographic and clinic data were collected according to uniform protocol. The information of patients' demographic and clinical examination was obtained by using standard questionnaires.

Research indicators

Atherosclerosis risk factors [age, male, hypertension, dyslipidemia, diabetes mellitus, smoke, related family history, admission blood lipids, body mass index (BMI) and so on] and coronary arteriography results [diastolic vessel diameter (DVD) of MCA, adjacent lumen diameter (LD), SNR of MCA, the most severe narrow rate and the numbers of diseased coronary vessels (diameter ≥2 mm) of non-MB-MCA arteries, the narrow degrees of the first coronary artery stenosis (FCAS) and the most severe coronary artery stenosis (MSCAS) located proximally to MB, and these lesions whether located in vascular bifurcation, the length of MCA and so on] were included.

The FCAS located proximally to MB was defined as the stenosis of nearest artery segment proximal to MB. The MSCAS located proximally to MB was defined as the most severe degree of narrowing of several lesions proximal to MB.

Smoking index was calculated as [course of smoking x (Smoking count per day)]. Hypertension grading diagnosis following the Chinese related guideline (23), which includes normal or high normal, grade 1, grade 2 and grade 3. Dyslipidemia was defined in light of the Chinese guideline on prevention and treatment of adult dyslipidemia (24). Diabetes mellitus was defined in light of the standard from the Chinese Diabetes Association (CDA), the same standard as the American Diabetes Association (ADA) (25). The definition of related family history in light of related references (23, 24). BMI was defined as body weight (kg)/height (m^2). Diseased coronary vessels were defined as the coronary arteries included any fixed narrowing of the LD, which could be detected by coronary arteriography. The numbers of diseased coronary vessels (diameter ≥2 mm) of non-MB-MCA arteries were calculated in those narrow rates which were more than or equal to 50%.

Coronary angiography

Coronary angiographies were performed via radial arteries (in 597 patients) or femoral arteries (in 6 patients) using standard Judkins' technique in standard projections. 200 µg nitroglycerin and 3 mg diltiazem were used for preventing vasospasm via artery sheath catheter before operation in transradial artery angiographies. Our radiographic equipment was the GE Medical Systems (Advantx Lcv+, GE, France).

Every coronary artery segment was carefully observed in the whole cardiac cycle. The presence of MB at angiography was defined as no less than 30% reduction in the diameter of the coronary artery at systole, which returns to complete or partial recovery at diastole, in two different projections at least. A validated quantitative coronary angiographic system (GE Medical System, France) using guiding catheters was used to measure of within-MCA diameter, reference LDs of coronary artery proximal and distal to MB, length of MCA and so on. The diastolic reduction of within-MCA diameter was estimated after a detailed frame-by-frame study of the diagnostic coronary angiogram. Angiographically determined percent narrowing of the MB-MCA was calculated as [(end-diastolic diameter-end-systolic diameter)/end-diastolic diameter] ×100. The narrowing degrees of diseased coronary vessels were calculated as [(reference LD - narrowing luminal diameter)/reference LD] ×100. All angiography data were assessed in the fashion of average by two senior cardiologists.

Statistical analyses

Statistical analyses were performed using SPSS version 18.0 for Windows (SPSS Inc, Chicago, IL, USA). Quantitative data and qualitative data are expressed as mean±standard deviation (SD) and percentage value, respectively. Adequacy of continuous variables to normal distribution was tested using Kolmogorov-Smirnov test. DVDs of MCAs were compared with adjacent LDs by paired-samples t-test. Chi-square test was used to determine relationships between non-continuous variables. Univariate analysis was used to reveal the relationship between all possible factors and the narrow degree of the FCAS or MSCAS located proximally to MB. Quantitative data in approximately normal distribution were compared between two groups with independent-samples t test. Quantitative data in approximately normal distribution in graded multiple groups were compared using one-way ANOVA. Pearson correlation test was used to assess correlation between two continuous variables. For reducing the mistaken deletion of significant variables and minimizing the probability of making error type 2, all independent variables with $p<0.15$ in univariate analysis were admitted into stepwise multiple regression analysis. The dependent variable was the narrow degree of the FCAS or MSCAS located proximally to MB in multivariate analysis. Condition index was calculated in stepwise multiple regression analysis. If condition index was less than 30, independent variables in the regression equation could be considered as having little possibility of collinearity. A p value <0.05 was considered statistical significant.

Results

Patient characteristics and angiographic results

Clinical and laboratory patient characteristics are illustrated in Table 1.

General angiographic results of patients are presented in Table 2. Totally 644 MB-MCAs in 603 patients were examined. These MB-MCAs were spread in 612 coronary arteries. The most frequently involved segment in this study population was the middle of left anterior descending artery (LAD). Varying narrow degrees of diseased coronary vessels (diameter ≥2 mm) of non-MB-MCA arteries existed in 423 patients (70.1%). Diseased coronary vessels, narrowing rates of which were more than 50%, existed in 224 patients (37.1%). The average maximum narrow degree of diseased coronary vessels of non-MB-MCA arteries was 53.7±29.9%.

DVDs in MB segments were significantly smaller than in proximal reference segments (p<0.001) and in distal reference segments adjacent MB-MCAs (p=0.001). The MCAs diastolic narrow rates ≥30% of were found in 8 patients and ulcer-like lesion was found in MCA in 1 patient (Fig.1).

Overall, 48.7% (186 lesions) of the FCAS and 52.6% (201 lesions) of the MSCAS were located in vascular bifurcation. Prevalence of lesions located distally to MB were significantly lower than those proximally to MB [36 (5.9%) vs. 382 (62.4%) ; p<0.001].

Correlation analysis results

Univariate analysis results are presented in Tables 3 and 4. All independent variables with p<0.15 in univariate analysis are demonstrated.

These patients with the characteristics, such as male, former smoking, dyslipidemia history, diabetes history, higher hypertension grading or vascular bifurcation lesions, had more severe narrowing degree of the FCAS located proximally to MB(all p<0.05).

There was a significant relation between the narrowing degree of the FCAS located proximally to MB and age (r=0.316, p<0.001), smoking index (r=0.157, p<0.001), course of diabetes (r=0.156, p<0.001), course of hypertension (r=0.114, p=0.008), HDL-C (r=-0.193, p<0.001), LDL-C (r=0.089, p=0.029), LDL-C/HDL-C (r=0.232, p<0.001) , SNR of MB-MCAs (r=0.117, p=0.006), the most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries (r=0.534, p<0.001) ,the numbers of diseased coronary vessels of non-MB-MCA arteries (r=0.474, p<0.001). There was a significant relation between the narrowing degree of the MSCAS located proximally to MB and age (r=0.335, p<0.001), smoking index (r=0.163, p<0.001), course of diabetes (r=0.150, p<0.001), course of hypertension (r=0.127, p=0.002), HDL-C (r=-0.206, p<0.001), LDL-C/HDL-C (r=0.212, p<0.001), SNR of MB-MCAs (r=0.114, p=0.007), the most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries (r=0.577, p<0.001), the numbers of diseased coronary vessels of non-MB-MCA arteries (r=0.520, p<0.001).

Multiple regression analysis results

Multivariate analysis results are showed in Table 5. All independent variables with p<0.05 in the final stepwise multiple regression equation are demonstrated.

In ultimate equation of the stepwise multiple regression analysis, vascular bifurcation lesions, the degree of narrowing and the numbers of diseased coronary vessels of non-MB-MCA arteries, age, LDL-C/HDL-C, male, course of diabetes, and SNR of MB-MCAs independently associated with the narrowing degree of the FCAS located proximally to MB (all p<0.05). Vascular bifurcation lesions, the degree of narrowing and the numbers of diseased coronary vessels of non-MB-MCA arteries, age, LDL-C/HDL-C, male, diabetes history, and dyslipidemia history independently associated with the narrowing degree of the MSCAS located proximally to MB (all p<0.05).

Table 1. Baseline characteristics of study population

Variables	n=603
Age, years	57.1±10.9
Gender, male, n (%)	379 (63.1)
BMI, kg/m^2	25.4±3.3
The patients with typical angina, n (%)	247 (40.1)
TC, mmol/L	4.5±1.0
LDL-C, mmol/L	2.4±0.6
HDL-C, mmol/L	1.2±0.3
TG, mmol/L	1.9±1.6
Former smokers, n (%)	275 (45.6)
Current smokers, n (%)	214 (35.5)
Long-term drinkers, n (%)	68 (11.3)
Dyslipidemia, n (%)	223 (37.0)
History of hypertension, n (%)	314 (52.1)
History of diabetes mellitus, n (%)	119 (19.7)
Old myocardial infarction, n (%)	12 (2.0)
Family history of coronary heart disease, n (%)	56 (9.3)
Family history of hypertension, n (%)	87 (14.4)
Family history of diabetes mellitus, n (%)	19 (3.2)

Data are presented as mean±SD and as numbers (percentage)
BMI - body mass index; HDL-C - high density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; TC - serum total cholesterol; TG - triglyceride

Table 2. Angiographic results

Distribution of diseased coronary vessels in patients	n=603
Patients with no stenosis, n (%)	134 (22.2)
Patients with less than 50% stenosis, n (%)	167 (27.7)
Patients with SVL, n (%)	131 (21.7)
Patients with DVL, n (%)	88 (14.6)
Patients with TVL, n (%)	71 (11.8)
Patients with LM and SVL, n (%)	1 (0.2)
Patients with LM and DVL, n (%)	3 (0.5)
Patients with LM and TVL, n (%)	8 (1.3)
MB segment distribution in patients	
Patients with single MB segment, n (%)	562 (93.2)
Patients with double MB segments in same coronary artery, n (%)	32 (5.3)
Patients with double MB segments in different coronary arteries, n (%)	9 (1.5)
Prevalence of MB according to segment involvement	n=644
LAD system, n (%)	634 (98.4)
LAD proximal	5 (0.8)
Proximal-middle	17 (2.6)
Middle	474 (73.6)
Middle-distal	115 (17.9)
Distal	16 (2.5)
Diagonal branches	2 (0.3)
Septal branch	5 (0.8)
LCX system, n (%)	6 (0.9)
LCX proximal	3 (0.4)
Distal	2 (0.3)
Obtuse marginal branch	1 (0.2)
RCA system, n (%)	4 (0.6)
LCX proximal	1 (0.2)
Posterior branch of left ventricle	1 (0.2)
Posterior descending branch	2 (0.3)
Characteristics of MB-MCAs	
The average length of MB-MCAs, mm	16.03±9.62
The SNR of MB-MCAs, %	61.3±15.3
The LD of proximal reference segments adjacent MB-MCAs, mm	2.64±0.44
The LD of distal reference segments, mm	2.32±0.41
The DVD of MB-MCAs, mm	2.29±0.39
Angiographically evident atherosclerotic stenosis associated with myocardial bridging	Coronary arteries (n=612) including MB-MCAs
Lesions located proximally to MB, n (%)	382 (62.4)
The ANR of the FCAS located proximally to MB, %	42.2±23.6
The ANR of the MSCAS located proximally to MB, %	46.9±24.5
Lesions located distally to MB, n (%)	36 (5.9)
The ANR of lesions located distally to MB, %	43.6±19.2

Data are presented as mean±SD and as numbers (percentage)
ANR - average narrow rate; DVD - diastolic vessel diameter; DVL - double vessel lesion; FCAS - first coronary artery stenosis; LAD - left anterior descending artery; LCX - left circumflex coronary artery; LD - lumen diameter; LM - left main stem; MB - myocardial bridging; MB-MCAs - myocardial bridging-mural coronary arteries; MSCAS - most severe coronary artery stenosis; RCA - right coronary artery; SNR - systolic narrow rate; SVL - single vessel lesion; TVL - triple vessel lesion

Discussion

Our study results indicated that artery atherosclerosis could form in the intramural and distal portions of a bridged artery. SNR of MB-MCA was found to be independently associated with the narrowing degree of the FCAS located proximally to MB.

The angiographic prevalence of MB has previously been reported with a frequency of between 0.5% and 33% (14, 15, 26). In present study, the incidence was shown as 14.1%, which was similar to the prevalence of 16.1% in a large Chinese cohort undergoing coronary angiography (26). A variety of factors, such as the length and thickness of MB, anatomic relationship of MB and MCA, percentage of connective tissue and fat tissue around MCA, the using of vessel dilator, the angle of view and the experience of the viewers, may contribute to the discrepancy of the prevalence of MB from study to study (14, 27-29). In this study, we paid much attention to detect MB-MCAs while performing angiography. Before entering into catheter room, 84.2% patients had utilized nitrates: 200 µg nitroglycerine had been used via artery sheath catheter for up to 99% patients to prevent vasospasm before transradial artery angiography. All of these would contribute to achieve a higher MB-MCAs detection rate in present study. However, selective intracoronary administration of vasodilating drugs was not used, which could assure comparability of measurement of MB-MCAs SNRs on some level.

In present study, the most frequently involved MB segment was the middle LAD and the number of male with MB was higher, which were consistent with previous researches (14, 16, 19, 26). DVDs in MB segments were significantly smaller than in proximal reference segments, and even, smaller than in distal reference segments. This phenomenon is considered as resulting from the limit of MB to the diastolic dimensions of the external elastic membrane and lumen of MCA (29). The higher proportion of lesions located proximally and obvious lower proportion of lesions located distally to MB was found in present study, which were consistent with previous studies (14, 15, 19, 30). At present the exact mechanism of MCA and distal segment of the bridged artery usually free from atherosclerosis remains unclear. The mechanisms may include decreased blood flow and volume, increased endothelial shear stress and reduced bioavailability of nitric oxide and endothelin-1 (15, 31). Although the protective effect of MB exists, the diastolic narrow rates ≥30% of MCAs in 8 patients, ulcer-like lesion in MCA in 1 patient and 36 lesions located distally to MBs were detected. These suggested that the protective effect of MB might be malfunction in a few of patients, the cause of which deserves further investigation.

For a long time, MB has been considered benign based on angiographic findings, and patients with MB in the LAD are given a good long-term prognosis (32). However, more and more researches suggested that MB might be one of causes of myocardial ischemia (3-13, 33). Two distinct mechanisms of MB causing myocardial ischemia have been reported so far (16). One is direct MB compression of MCA at cardiac systole,

Table 3. Comparison of the narrowing degree of coronary artery stenosis located proximally to MB indifferent groups

	Variables	Stenosis degree (%)	**P*
Comparison of the narrowing degree of the FCAS located proximally to MB	Male		
	Yes	31.6±29.3	<0.001
	No	19.5±22.7	
	Former smoking		
	Yes	30.5±28.9	0.001
	No	23.1±25.9	
	Current smoking		
	Yes	29.5±29.5	0.053
	No	24.8±26.3	
	Dyslipidemia history		
	Yes	31.7±28.2	<0.001
	No	23.4±26.8	
	Diabetes history		
	Yes	36.0±29.2	<0.001
	No	24.1 ±26.7	
	Hypertension grading		
	normal or high normal	23.9±28.0	0.035
	grade 1	24.9±25.4	
	grade 2	26.6±27.8	
	grade 3	31.5±27.1	
	Hypertension family history		
	Yes	27.3±27.4	0.067
	No	21.5±28.1	
	The lesions located in vascular bifurcation		
	Yes	43.2±24.4	<0.001
	No	19.1±25.6	
Comparison of the narrowing degree of the MSCAS located **proximally to MB**	Male		
	Yes	33.9±31.3	<0.001
	No	22.0±25.6	
	Former smoking		
	Yes	34.5±31.1	<0.001
	No	25.4±27.9	
	Current smoking		
	Yes	33.3±31.9	0.025
	No	27.4±28.3	
	Dyslipidemia history		
	Yes	35.5±30.4	<0.001
	No	26.0±28.9	
	Diabetes history		
	Yes	40.2±31.1	<0.001
	No	26.6 ±29.0	
	Hypertension grading		
	normal or high normal	25.7±29.9	0.01
	grade 1	28.2±27.6	
	grade 2	31.7±31.5	
	grade 3	34.5±29.0	
	Hypertension family history		
	Yes	30.4±29.6	0.064
	No	24.0±30.4	
	Diabetes family history		
	Yes	29.9±30.0	0.078
	No	17.7±21.8	
	The lesions located in vascular bifurcation		
	Yes	47.6±24.9	<0.001
	No	20.5 ±27.8	

Data are presented as mean±SD
*independent-samples t test and one-way ANOVA test
FCAS - first coronary artery stenosis; MB - myocardial bridging; MB-MCAs - myocardial bridging-mural coronary arteries; MSCAS - most severe coronary artery stenosis

continue upper of other colum ➡

continued for left colum

resulting in delayed arterial relaxation at diastole, reduced blood flow reserve, and thus leading to myocardial ischemia. The other is the stenosis of the coronary artery proximal to MB due to the enhancement of coronary atherosclerosis.

There was not enough data to support that MB or SNR of MB-MCA is an independent factor of atherosclerosis formation proximal to MB (14, 17, 21, 22). The autopsy study of Ishikawa et al. (17) suggested that anatomic properties of MB enhance the development of atherosclerosis in the LAD proximal to MB. However, Poullis et al. (21) disagreed the standpoint and claimed that MB is likely to be protective factor, and not as a risk factor as describing by Ishikawa et al. (17). The 64-slice computed tomography coronary angiography study of Bayrak et al. (22) suggested that there may be no relationship between MB and proximal atherosclerosis. At present, large sample study (>500 cases) about whether SNR of MB-MCA is one of independent risk factors of coronary atherosclerosis formation proximal to the bridging is still empty. Previous related studies had shortcomings of design and small sample (29, 34). Multivariate analysis of common evaluation of the role of SNR of MB-MCA with traditional risk factors and related susceptible factors to coronary atherosclerosis was little reported.

The LAD segment proximal to MB is vulnerable to atherosclerosis. However most of MB-MCAs locate in middle LAD. In fact, the formation of stenosis located proximally to MB is influenced by multiple factors and univariate analysis is different to confirm the true relationship of the SNR of MB-MCA locate in middle LAD and the narrowing degree of proximal LAD stenosis.

Table 4. Correlation of the degree of coronary artery stenosis located proximally to MB with clinical variables

	Variables	*r	*P
Correlation between related variables and the narrowing degree of the FCAS located proximally to MB	Age	0.316	<0.001
	Smoking index	0.157	<0.001
	Course of diabetes	0.156	<0.001
	Course of hypertension	0.114	0.008
	HDL-C	-0.193	<0.001
	LDL-C	0.089	0.029
	LDL-C/HDL-C	0.232	<0.001
	SNR of MB-MCAs	0.117	0.006
	LD of proximal reference segments adjacent MB-MCAs	-0.073	0.099
	The most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries	0.534	<0.001
	The numbers of diseased coronary vessels of non-MB-MCA arteries	0.474	<0.001
Correlation between related variables and the narrowing degree of the MSCAS located **proximally to MB**	Age	0.335	<0.001
	Smoking index	0.163	<0.001
	Course of diabetes	0.150	<0.001
	Course of hypertension	0.127	0.002
	HDL-C	-0.206	<0.001
	LDL-C	0.062	0.105
	LDL-C/HDL-C	0.212	<0.001
	SNR of MB-MCAs	0.114	0.007
	LD of proximal reference segments adjacent MB-MCAs	-0.087	0.074
	The most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries	0.577	<0.001
	The numbers of diseased coronary vessels of non-MB-MCA arteries	0.520	<0.001

*Pearson correlation tests
FCAS - first coronary artery stenosis; HDL-C - high density lipoprotein cholesterol; MB - myocardial bridging; MB-MCAs - myocardial bridging-mural coronary arteries; MSCAS - most severe coronary artery stenosis; LDL-C - low-density lipoprotein cholesterol; LD - lumen diameter; SNR - systolic narrow rate

Vascular bifurcation is predilection site of atherosclerosis as well. But common evaluation of the effect of SNR of MB-MCA and vascular bifurcation to coronary atherosclerosis was not reported in previous studies. In some cases, systolic narrowing degree of MB-MCA of LAD amounted to 90%, but the segment proximal to MB-MCA had no obvious lesion, by contrast, obvious stenosis located in the other arteries (Left circumflex or right coronary artery). This phenomenon could be found in angiography. Therefore, evaluation of the role of stenosis of non-MB-MCA arteries contributing to lesion located in the segment proximal to MB is helpful to reveal the effect of patients' own atherosclerosis susceptibility. Finally, vascular bifurcation lesions, the degree of narrowing and the numbers of diseased coronary vessels of non-MB-MCA arteries, age, LDL-C/HDL-C, male, course of diabetes, and SNR of MB-MCAs were positively related with the narrowing degree of the FCAS located proximally to MB (all $p<0.05$). Although statistical significance was found in SNR of MB-MCA, the standardized coefficients was minimum in these variables. It probably meant that SNR of MB-MCA was one of independent factors of atherosclerosis formation proximal to MB, but with a small effect as comparing to other factors in ultimate equation.

The investigation of Duygu et al. (30) suggested that older age, multiple risk factors and more importantly the ratio of systolic compression of MB-MCA might be related to atherosclerosis. The autopsy study of Ishikawa et al. (17) suggested that patients with myocardial infarction had an increased muscle thickness and muscle bridge index (multiplication of MB thickness by MB length) compared than patients without myocardial infarction with MBs. In present clinical study, correlation of the ratio of systolic compression of MB-MCA and the FCAS located proximally to MB was proved in multivariate analysis mode. But the reason of that remains unclear (15). Endothelial injury of the segment proximal to MB can be caused by localized arterial hypertension and turbulent or even retrograde blood flow up toward the coronary ostium at cardiac systole (16, 19). The intima of the segment proximal to MB is subject to lower shear stress, which may contribute to the increase of vasoactive substances, such as endothelial nitric oxide synthase, endothelin-1, and angiotensin-converting enzyme, and further formation of atherosclerotic plaques (14, 16, 19). Pathological studies have revealed that the shape of the endothelial cells are flat and polygonal with defected surface likely to be exfoliated in the segment proximal to MB and the segment is susceptible to atherosclerosis (16, 19). Thickness of MB is obviously related with compression degree of MCA (16, 19, 20) and longer bridges is associated with more severe systolic compression (29), too. So, higher systolic compression of MB-MCA might induce more endothelial injury and severe atherosclerosis in the segment proximal to MB. But the length of MCA may not be always equal to that of MB (35). The relation between the length of MCA and the coronary artery stenosis located proximally to MB had not been demonstrated in present study. In addition, correlation of the SNR of MB-MCA and the most severe coronary artery stenosis located proximally to MB was not found in multivariate analysis mode, which might mean the other some factors, rather than SNR of MB-MCA, play a greater role in atherosclerosis formation proximal to MB.

Table 5. Mutliple regression analysis results

	Variables	* Unstandardized Coefficients (95% CI)	*Standardized coefficient (β)	*P
+Related analysis with the narrowing degree of the FCAS located proximally to MB	Vascular bifurcation lesions	18.61 (14.94-22.27)	0.312	Pp<0.001
	The most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries	0.20 (0.1-0.31)	0.258	Pp<0.001
	Age	0.36 (0.19-0.53)	0.144	Pp<0.001
	LDL-C/HDL-C	4.14 (1.88-6.40)	0.113	Pp<0.001
	Male	5.39 (1.76-9.03)	0.095	p0.004
	Course of diabetes	0.76 (0.27-1.28)	0.087	p0.005
	SNR of MB-MCAs	0.12 (0.01-0.23)	0.067	p0.032
	The numbers of diseased coronary vessels of non-MB-MCA arteries	4.89 (0.35-9.44)	0.135	p0.035
#Related analysis with the narrowing degree of the MSCAS located proximally to MB	The lesions located in vascular bifurcation	18.97 (15.17-22.78)	0.301	p<0.001
	The most severe narrow rate of diseased coronary vessels of non-MB-MCA arteries	0.20 (0.09-0.31)	0.237	p<0.001
	Age	0.47 (0.29-0.64)	0.171	p<0.001
	LDL-C/HDL-C	2.96 (0.49-5. 43)	0.075	p0.019
	Male	6.61 (2.84-10.39)	0.108	p0.001
	Diabetes history	5.88 (1.43-10.32)	0.079	p=p0.010
	The numbers of diseased coronary vessels of non-MB-MCA arteries	6.77 (2.01-11.53)	0.173	p0.005
	Dyslipidemia history	3.93 (0.10-7.77)	0.064	p0.045

CI - confidence interval; FCAS - first coronary artery stenosis; HDL-C - high density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; MB - myocardial bridging; MB-MCAs - myocardial bridging-mural coronary arteries; MSCAS - most severe coronary artery stenosis; SNR - systolic narrow rate
+Maximum condition index =23.6 #Maximum condition index =28.7
*stepwise multiple regression analysis

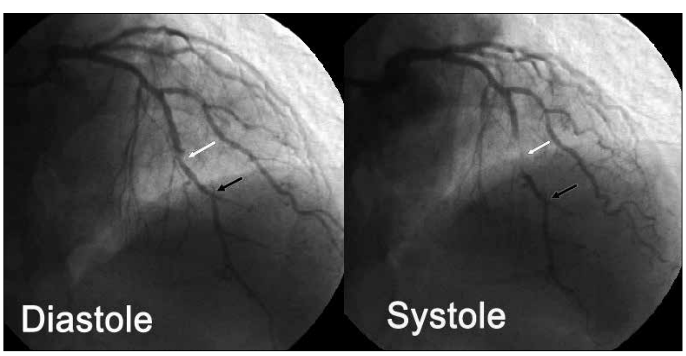

Figure 1. Ulcer-like lesion (white arrow) was found in diastolic lumen, which was combined with diastolic narrow. Approximate 100% compression (white arrow) of the LAD was found during cardiac systolic phase. 60% focal stenosis (black arrow) existed in the artery segment located distally to MB

We considered that the narrowing degree of coronary artery stenosis located proximally to MB and SNR of MB-MCA were continuous variables, for reserving their information at the extreme, grouping or grading method was not adopted and so multivariate logistic regression analysis was also not used. For preventing collinearity problem of independent variables, we examined condition index.

Study limitations

Coronary artery angiography may underestimate the occurrence and narrowing degree of coronary artery atherosclerosis located proximally to MB. When positive remodeling occurs, coronary artery atherosclerosis stenosis could not be detected by angiography. However, routine intravascular ultrasound examinations in large sample of consecutive MB-MCA patients are difficult. At present, coronary artery angiography, as the extensive used method of coronary heart disease inspection, may be more important than intravascular study to seek out the "clinical significance" of angiographically evident atherosclerotic disease associated with MB (34). This study is actually a retrospective observational study, so cause-and-effect linkage between independent and dependent variable is only a kind of speculation. Nevertheless prospective cohort study method, routine examination for MB and coronary artery lesions in young people and follow-up are very difficult.

Conclusion

In summary, the intramural and distal portions of a bridged artery are not the forbidden zone of artery atherosclerosis formation. SNR of MB-MCA may be one of the important decision factors to coronary artery stenosis located proximally to MB. Whereas some traditional coronary heart disease (CHD) risk factors and the patient's own susceptibility of CHD are likely to play more important roles.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept - H.H.; Design - H.H., J.C.S.; Supervision - M.S.W., H.H.; Resources - M.S.W., Z.M.X.; Materials - M.S.W., Q.L.; Data collection&/or processing - H.H., H.M.R.; Analysis &/or interpretation - H.H., J.C.S.; Literature search - Q.L., H.M.R.; Writing - H.H., H.M.R.; Critical review - Q.L., J.C.S.; Other - H.H.

References

1. Reyman H.Diss. de vasis cordis propriis. Bibl Anat 1737; 2: 359-79.
2. Portmann WC, Iwig J. Die intramurale koronarie im angiogramm. Fortschr Rontgenstr 1960; 92: 129-32. [CrossRef]
3. Xiang DC, Gong ZH, He JX, Ruan YJ, Xie ZH. Characteristics of stress tests and symptoms in patients with myocardial bridge and coronary artery spasm. Coron Artery Dis 2009; 20: 27-31. [CrossRef]
4. Ciampricotti R, El Gamal M. Vasospastic coronary occlusion associated with a myocardial bridge. Cathet Cardiovasc Diagn 1988; 14: 118-20. [CrossRef]
5. Zhang F, Ge JB, Qian JY, Dong LL, Lu Y. Variant angina associated with isolated myocardial bridging: evaluation using intravascular ultrasound and quantitative coronary angiography. Chin Med J 2007; 120: 171-3.
6. Arjomand H, AlSalman J, Azain J, Amin D. Myocardial bridging of left circumflex coronary artery associated with acute myocardial infarction. J Invasive Cardiol 2000; 12: 431-4.
7. Gowda RM, Khan IA, Ansari AW, Cohen RA. Acute ST segment elevation myocardial infarction from myocardial bridging of left anterior descending coronary artery. Int J Cardiol 2003; 90: 117-8. [CrossRef]
8. Kurt IH. A case of muscular bridge resulting in myocardial infarction following heavy effort: a case report. Cases J 2009; 2: 135. [CrossRef]
9. Feld H, Guadanino V, Hollander G, Greengart A, Lichstein E, Shani J. Exercise-induced ventricular tachycardia in association with a myocardial bridge. Chest 1991; 99: 1295-6. [CrossRef]
10. den Dulk K, Brugada P, Braat S, Heddle B, Wellens HJ. Myocardial bridging as a cause of paroxysmal atrioventricular block. J Am Coll Cardiol 1983; 1: 965-9. [CrossRef]
11. Marchionni N, Chechi T, Falai M, Margheri M, Fumagalli S. Myocardial stunning associated with a myocardial bridge. Int J Cardiol 2002; 82: 65-7. [CrossRef]
12. Fabre A, Sheppard MN. Sudden adult death syndrome and other non-ischemic causes of sudden cardiac death. Heart 2006; 92: 316-20. [CrossRef]
13. Cutler D, Wallace JM. Myocardial bridging in a young patient with sudden death. Clin Cardiol 1997; 20: 581-3. [CrossRef]
14. Li JJ. Is myocardial bridging a bridge connecting to cardiovascular events? Chin Med J 2010; 123: 964-8.
15. Loukas M, Von Kriegenbergh K, Gilkes M, Tubbs RS, Walker C, Malaiyandi D, et al. Myocardial bridges: A review. Clin Anat 2011; 24: 675-83. [CrossRef]
16. Ishikawa Y, Kawawa Y, Kohda E, Shimada K, Ishii T. Significance of the anatomical properties of a myocardial bridge in coronary heart disease. Circ J 2011; 75: 1559-66. [CrossRef]
17. Ishikawa Y, Akasaka Y, Suzuki K, Fujiwara M, Ogawa T, Yamazaki K, et al. Anatomic properties of myocardial bridge predisposing to myocardial infarction. Circulation 2009; 120: 376-83. [CrossRef]
18. Ishii T, Asuwa N, Masuda S, Ishikawa Y, Kiguchi H, Shimada K. Atherosclerosis suppression in the left anterior descending coronary artery by presence of myocardial bridge: an ultrastructural study. Mod Pathol 1991; 4: 424-31.
19. Nakanishi R, Rajani R, Ishikawa Y, Ishii T, Berman DS. Myocardial bridging on coronary CTA: an innocent bystander or a culprit in myocardial infarction? J Cardiovasc Comput Tomogr 2012; 6: 3-13. [CrossRef]
20. Takamura K, Fujimoto S, Nanjo S, Nakanishi R, Hisatake S, Namiki A, et al. Anatomical characteristics of myocardial bridge in patients with myocardial infarction by multi-detector computed tomography. Circ J 2011; 75: 642-8. [CrossRef]
21. Poullis M. Letter by Poullis Regarding Article, "Anatomic Properties of Myocardial Bridge Predisposing to Myocardial Infarction". Circulation 2010; 121: e263. [CrossRef]
22. Bayrak F, Değertekin M, Eroğlu E, Güneysu T, Sevinç D, Gemici G, et al. Evaluation of myocardial bridges with 64-slice computed tomography coronary angiography. Acta Cardiol 2009; 64: 341-6. [CrossRef]
23. Liu LS; Writing Group of 2010 Chinese Guidelines for the Management of Hypertension. 2010 Chinese guidelines for the management of hypertension. Zhonghua Xin Xue Guan Bing Za Zhi 2011; 39: 579-615.
24. Hu DY, Ding RJ. Guidelines for management of adult dyslipidemia in China. Zhonghua Nei Ke Za Zhi 2008; 47: 723-4.
25. American Diabetes Association. Diagnosis and classification of diabetes mellitus 2007; 30: 42-7.
26. Qian JY, Zhang F, Dong M, Ma JY, Ge L, Liu XB, et al. Prevalence and characteristics of myocardial bridging in coronary angiogram-data from consecutive 5525 patients. Chin Med J 2009; 122: 632-5.
27. Jeong YH, Kang MK, Park SR, Kang YR, Choi HC, Hwang SJ, et al. A head-to-head comparison between 64-slice multidetector computed tomographic and conventional coronary angiographies in measurement of myocardial bridge. Int J Cardiol 2010; 143: 243-8. [CrossRef]
28. Fazlıoğulları Z, Karabulut AK, Kayrak M, Uysal II, Ünver Doğan N, Altunkeser BB. Investigation and review of myocardial bridges in adult cadaver hearts and angiographs. Surg Radiol Anat 2010; 32: 437-45. [CrossRef]
29. Tsujita K, Maehara A, Mintz GS, Doi H, Kubo T, Castellanos C, et al. Comparison of angiographic and intravascular ultrasonic detection of myocardial bridging of the left anterior descending coronary artery. Am J Cardiol 2008; 102: 1608-13. [CrossRef]
30. Duygu H, Zoghi M, Nalbantgil S, Kırılmaz B, Türk U, Özerkan F, et al. Myocardial bridge: a bridge to atherosclerosis. Anadolu Kardiyol Derg 2007; 7: 12-6.
31. Hostiuc S, Curca GC, Dermengiu D, Dermengiu S, Hostiuc M, Rusu MC. Morphological changes associated with hemodynamically significant myocardial bridges in sudden cardiac death. Thorac Cardiovasc Surg 2011; 59: 393-8. [CrossRef]
32. Juilliere Y, Berder V, Suty-Selton C, Buffet P, Danchin N, Cherrier F. Isolated myocardial bridges with angiographic milking of the left anterior descending coronary artery: a long-term follow-up study. Am Heart J 1995; 129: 663-5. [CrossRef]
33. Kim SS, Jeong MH, Kim HK, Kim MC, Cho KH, Lee MG, et al. Long-term clinical course of patients with isolated myocardial bridge. Circ J 2010; 74: 538-43. [CrossRef]
34. Ökmen AS. Myocardial bridge and atherosclerosis. Anadolu Kardiyol Derg 2007; 7: 17-8.
35. Ertaş G, Ural E, Kılıç T. A very rare image in cardiology: posterolateral artery myocardial bridge. Neth Heart J 2009; 17: 442-3. [CrossRef]