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Myocardial bridge characteristics and coronary atherosclerotic markers

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SOUHRN

Kontext: Klinický význam svalového můstku (myocardial bridge, MB) pro celý systém věnčitých tepen a koronární aterosklerózu je stále předmětem diskuse. Cílem této studie bylo zjistit možnou spojitost mezi charakteristikami MB (délka, hloubka, přítomnost a místo proximální stenózy) a markery koronární aterosklerózy (kalcifikace koronárních tepen [coronary artery calcification, CAC], pláty, stenózy a objem perikardiálního tuku [pericardial fat volume, PFV]).
Pacienti a metody: Z celkového počtu 225 po sobě následujících pacientů s podezřením na ischemickou chorobu srdeční, u nichž byla provedena multidetektorová (64-slice) CT koronarografie (multi-detector CT, MDCT), bylo do studie zařazeno 41 pacientů s MB.
Výsledky: Přítomnost MB byla nejčastěji zaznamenána v ramus interventricular anterior (RIA) (92,5 %). Délka MB nebyla statisticky významně spojena s hodnotami CAC, PFV, koronárními pláty ani závažností stenózy. Hloubka MB vykazovala významnou spojitost s hodnotami CAC (r = 0,4; $p < 0,00$), přítomností koronárních plátů ($p < 0,00$) a s výjimkou proximální stenózy i se stenózou koronárních tepen ($p = 0,03$). Nebyla nalezena významná spojitost mezi hloubkou MB a PFV (r = 0,1; $p = 0,4$). Přítomnost proximální stenózy v MB vykazovala významnou souvislost s celkovou hodnotou CAC ($p < 0,00$), přítomností koronárního plátu ($p < 0,00$) a stenózou koronárních tepen na jiných místech ($p < 0,00$) bez významné spojitosti s hodnotou PFV ($p = 0,4$). Spojitost mezi hloubkou MB a koronární stenózou i plátem a přítomností proximální stenózy v MB a hodnotou CAC i plátem přetrvávala i po adjustaci na klasické faktory kardiovaskulárního rizika.
Závěr: Hloubka MB a přítomnost proximální stenózy byly významně spojeny s přítomností koronárních plátů a stenóz. Stanovení přesného vlivu MB na celý systém koronárních tepen si vyžádá další studie s kontrolními skupinami.

ABSTRACT

Background: The clinical significance of myocardial bridge (MB) on the whole coronary system and coronary atherosclerosis is still a matter of debate. This study aimed to investigate the possible association between MB characteristics (length, depth, proximal stenosis presence and site) with coronary atherosclerotic markers (coronary artery calcification [CAC], plaque, stenosis and pericardial fat volume [PFV]).
Patients and methods: From a total of 225 consecutive patients with suspected coronary artery disease who underwent 64-slice multi-detector CT (MDCT) angiography examination, 41 patients with MB were enrolled in the study.
Results: MB occurred most commonly in the left anterior descending artery (92.5%). The MB length showed no significant association with CAC, PFV, coronary plaque and stenosis severity. The MB depth showed a significant association with CAC (r = 0.4, $p < 0.00$), coronary plaque presence ($p < 0.00$) and coronary stenosis ($p = 0.03$), apart from proximal stenosis presence. There was no significant association between MB depth with PFV (r = 0.1, $p = 0.4$). MB proximal stenosis presence showed a significant association with total CAC ($p < 0.00$), coronary plaque presence ($p < 0.00$) and coronary stenosis presence at other sites ($p < 0.00$) while showed no significant association with PFV ($p = 0.4$). After adjustment for conventional cardiac risk factors, MB depth association with coronary stenosis and plaque and the association of MB proximal stenosis presence with CAC and plaque persisted.
Conclusion: MB depth and proximal stenosis presence were significantly associated with coronary plaque and stenosis presence. Follow up studies with control group is required to highlight the exact role of MB on whole coronary system.

Keywords:
Coronary calcification
Myocardial bridge
Pericardial fat
Plaque
Markers

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Introduction

Myocardial bridge (MB) is an anatomical variant of coronary artery course in which a segment of the artery is enclosed by band of myocardial muscle fibers most commonly in the left anterior descending artery (LADA) and rarely in the left circumflex artery (LCx) and right coronary artery (RCA).[1,2]

In the literature, the prevalence of MB varies between 5% to 86% depending on the type of study and modality used (postmortem examination versus coronary CT versus intracoronary US versus conventional angiography) to assess MB presence. As such, autopsy series have estimated a high prevalence of MB as approximately 80% while coronary angiographic studies have shown a less prevalence of MB as approximately 5%.[1,2]

Although MB is considered a benign coronary variation and carried a favorable long term prognosis, MB presence can be associated with development of atherosclerosis proximal to a bridged artery, angina, acute myocardial infarction, arrhythmia and sudden cardiac death. As such, whether MB is simply a benign phenomenon or a double-edged sword with detrimental effect on the whole coronary system is still controversial and debated issue in the clinical practice.[3,4]

MB anatomical characteristics such as the presence of proximal stenosis, site, length, and depth are assumed to define the hemodynamic consequences for the coronary system and assess the impact of MB in coronary atherosclerosis process.[4]

Recently, multi-detector CT (MDCT) is a non-invasive and novel 3D modality with advantages of increased detection rate of MB and a better assessment of its anatomical characteristics due its high spatial and temporal resolution.[4–6]

Additionally, MDCT permits assessment of coronary atherosclerotic markers (stenosis, calcification, plaque) and cardiac fat deposition which has been proposed as an emerging marker of increased risk of coronary atherosclerosis.[5]

The main aim of this study was to investigate the possible relationships between MB characteristics (coronary stenosis proximal to MB, depth, length and site) with coronary atherosclerotic markers (coronary calcium score [CAC], plaque and pericardial fat volume [PFV]).

Patients and methods

This cross-sectional study was carried out at the Cardiology Center at Al-Sader Teaching hospital between January 2016 and July 2018.

Two hundred and twenty five consecutive Iraqi patients with suspected coronary artery disease who underwent 64-slice MDCT angiography examination were recruited. Of these, 41 patients with MB were enrolled in the study.

Using standard physician-based questionnaires, a history of conventional cardiac risk factors for coronary artery disease was obtained from each patient at the time of coronary MDCT angiography examination including a positive family history of premature coronary artery disease (occurring before the age of 55 years in men and before 65 years in women), current smoking history (more than 10 cigarettes per day in the last year), a history of hypertension or use of anti-hypertension medications, hyperlipidemia (defined as levels of total cholesterol ≥ 200 mg/dL or triglyceride ≥ 150 mg/dL) or use of lipid-lowering drugs ,a history of diabetes mellitus or use of insulin or diabetes lowering drugs and measurement of body weight and height to calculate body mass index (BMI).[7]

Informed consent was obtained from all patients enrolled in the study. The study was approved by our medicine college board.

MDCT scan protocol

CT coronary angiography was performed with a 64-slice scanner (Aquilon 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan). Any adipose tissue located within the pericardial sac was considered to denote pericardial fat; this was measured three-dimensionally with a contrast-enhanced phase. Coronary plaque was defined as a structure of > 1 mm within and/or adjacent to vessel lumen. The MDCT data analyses including coronary calcium score and PFV measurement were assessed as per our previous study.[7]

Severity of coronary artery stenosis was visually graded as no CAD (coronary artery disease) (normally appearing lumen or less than 50% reduction in lumen diameter), or CAD with a mean lumen diameter reduction of ≥ 50% in a single vessel by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections. The presence of coronary artery stenosis at proximal part of MB was not included in the assessment of coronary artery stenosis severity

MB length depth and proximal stenosis

The length of the MB was defined as the distance of the bridged artery from the entrance to the exit beneath the myocardial band. The depth of the MB was defined as the thickness of the deepest part from the surface of the overlying myocardial fibers to the bridged segment, on the cross-sectional images.[6]

The presence of MB proximal stenosis was defined as luminal diameter stenosis ≥ 50% of proximal part of bridged segment. The MB proximal stenosis presence was excluded from total coronary artery stenosis of all coronary arteries in the statistical analysis.

The analysis of MDCT images were performed by two independent radiologists with more than 5 years' experience in coronary MDCT angiography data interpretation.

Statistical analysis

Data were presented as median values and inter-quartile range (IQR) or mean ± standard deviation or as numbers with percentages, as appropriate. The association between coronary plaque with MB characteristics was examined using analysis of unpaired t test or chi square as appropriate. The associations between CAC and PFV with MB characteristics were examined using Spearman's rank correlation for nonparametric data or Non Parametric test (Mann–Whitney U test) as appropriate. The multiple regression analysis was used to analyze the association of

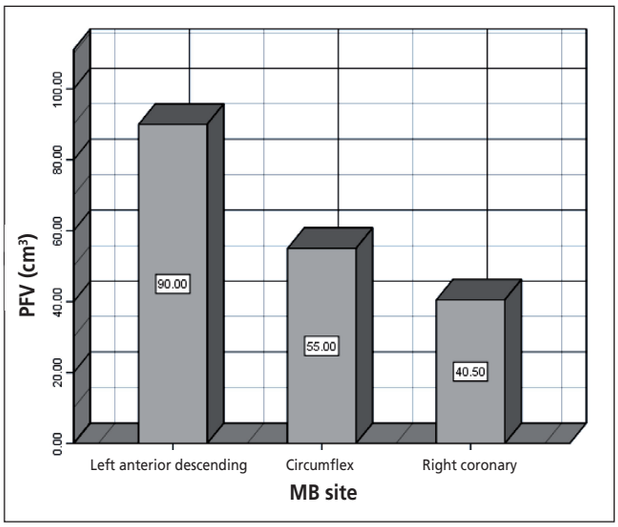

Fig. 1 – Association of MB site with PFV.

Table 1 – Patients' characteristics

Parameters	Mean ± SD or n (%) or median (IQR)
Age	56 ± 10
Male	56%
Hypertension	54%
Diabetes mellitus	20%
Hyperlipidemia	36%
Family history	10%
Smoking	27%
BMI	29 ± 5
MB characteristics	
Length (mm)	21 ± 9
Depth (mm)	3.5 ± 1.7
Proximal stenosis presence	39%
LADA MB	93.5%
RCA MB	5%
LCx MB	2.5%
Coronary atherosclerosis markers	
Plaque presence	49%
PFV (cm^3)	88 (62–111)
CAC	0 (0–54)

Table 2 – Association of MB characteristics with CAC and PFV

MB characteristics	PFV r	*p*	CAC r	*p*
Length	0.0	0.9	0.0	0.9
Depth	0.1	0.4	0.4	0.006
Proximal stenosis	0.0	0.4	0.4	0.002
Site	0.3	0.03	0.1	0.5

CAC, PFV, stenosis severity and coronary plaque with MB characteristics after adjustment for age, sex, hypertension, smoking, diabetes mellitus, hyperlipidemia, BMI and family history of premature coronary disease. A *p*-value of less than 0.05 was considered statistically significant. SPSS ver. 23.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis

Results

The prevalence of MB was 18% in our study. MB occurs most commonly in the LADA (92.5%) and less commonly in the RCA (5%) and LCx (2.5%). The median (IQR) of PFV and CAC were 88 (62–111) cm^3 and 0 (0–54), respectively. Patients' characteristics are shown in Table 1.

MB length and coronary atherosclerotic markers: the MB length was 21 ± 9 mm (ranged from 8.5 to 45 mm). The MB length showed no significant association with CAC, PFV, coronary plaque and stenosis severity as in Tables 2 and 3.

MB depth and coronary atherosclerotic markers: The MB depth mean was 3.5 mm (ranged from 1.5 to 9 mm). The MB depth showed a significant association with CAC ($r = 0.4$, $p < 0.00$), coronary plaque presence ($p < 0.00$) and coronary stenosis ($p = 0.03$). There was no significant association between MB depth with PFV ($r = 0.1$, $p = 0.4$) as in Tables 2 and 3.

MB proximal stenosis and site association with coronary atherosclerotic markers: MB proximal stenosis presence showed a significant association with CAC ($p < 0.00$), coronary plaque presence ($p < 0.00$) and coronary stenosis presence at other sites ($p < 0.00$) while it showed no significant association with PFV ($p = 0.4$). MB at LADA showed a significant association with higher values of PFV in comparison with MB at RCA ($p = 0.03$) as in Table 2 and Figure 1.

MB site showed no significant association with CAC, plaque and coronary artery stenosis presence as in Tabls 2 and 3.

Multivariable logistic regression: After adjustment for conventional coronary risk factors, MB depth association with coronary stenosis and plaque persisted while MB depth association with CAC not persisted. The association of MB proximal stenosis presence with CAC and plaque, but not with stenosis severity presence at other sites, persisted after adjustment for coronary risk factors (Table 4).

Discussion

MDCT can provide a valuable assessment of MB anatomical properties and accurate visualization of the coronary arteries lumen and wall, pericardium and myocardium, and the relationship between these structures with MB anatomical properties.[2]

Recently, coronary CT-based prevalence of MB has been reported to be between 3.5 and 30.5%.[8]

The mid segment of LADA was the most common site for MB followed by the other coronary arteries. According to a review of 256 reported symptomatic MB cases registered in PubMed (1968–2008), MB was most fre-

Table 3 – Association of MB characteristics with coronary stenosis severity and plaque presence

MB indices	Coronary stenosis None	≥ 50%	*p*	Plaque presence No plaque	Plaque	*p*
Length	21 ± 10	21 ± 8	0.9	20 ± 10	22 ± 8	0.6
Depth	3 ± 1.1	4.4 ± 2	0.03	2.8 ± 1	4.2 ± 2	0.008
Site (LADA)	92%	93%	0.9	90%	95%	0.5
Proximal stenosis	19%	60%	0.008	5%	70%	< 0.00

Table 4 – Regression analysis

Variables	PFV β	*p*	CAC β	*p*	Plaque β	*p*	CAD β	*p*
MB length	0.4	0.5	0.1	0.4	6.0	0.9	0.9	0.1
MB depth	0.2	0.2	0.0	0.9	0.4	0.04	4	0.04
MB site	0.2	0.1	0.2	0.1	8.1	0.9	2	0.5
MB proximal stenosis	0.0	0.7	0.4	0.01	3.7	0.03	2	0.2
Age	0.2	0.06	0.1	0.8	0.1	0.8	1	0.4
Male	0.2	0.09	0.2	0.2	0.7	0.9	0.1	0.1
Hypertension	0.3	0.03	0.1	0.4	0.1	0.7	5	0.3
Diabetes mellitus	0.1	0.3	0.1	0.4	0.2	0.9	2	0.5
BMI	0.6	0.00	0.0	0.6	0.0	0.3	1	0.7
Family history	0.1	0.8	0.0	0.8	0.3	0.9	0.2	0.9
Smoking	0.1	0.4	0.0	0.9	4.1	0.03	0.0	0.09
Hyperlipidemia	0.3	0.01	0.0	0.8	0.1	0.7	0.8	0.8

quently seen in the LADA (92%) and rarely found in the RCA (5%) and LCx (2%).[9]

The findings of this study showed a significant association between MB proximal stenosis presence and depth with coronary atherosclerotic markers particularly coronary stenosis severity and coronary plaque and this association persisted after adjustment for conventional coronary risk factors while MB length showed no significant association with coronary atherosclerotic markers.

Several studies reported that preferential development of atherosclerosis just proximal to bridged segment while the bridged segment itself was free from atherosclerosis.[10–12]

The reasons for confinement of atherosclerosis at proximal part of MB while sparing the bridged segment were due to hemodynamic disturbances and significant pressure gradients between the bridged segment and the proximal coronary segment leading to chronic coronary pressure overload with significant endothelial changes.[11]

Moreover, the absence of exposure to pericoronary adipose tissue at MB site and increased lymph drainage of the vessel wall, protecting against lipid accumulation within the bridged segment.[8,11]

Elmali et al. found that a significant association was observed between the MB depth and systolic narrowing, while there was no significant association between the MB length and systolic narrowing and MB depth was related to patient symptoms of chest pain whereby increased MB depth, but not MB length, causing further diminishing in the diastolic filling of coronary artery especially during physical exertion.[8]

On the same line, Ishikawa et al. found that MB length tended to be longer in patients with MB and myocardial infarction than in patients with MB and without myocardial infarction while the depth of the MB and the MB muscle index (MB depth times MB length) were significantly greater in patients with MB and myocardial infarction than in patients without myocardial infarction suggesting that MB muscle index, rather than MB length per se, may increase the risk of coronary ischemia.[13]

Moreover, Wang et al. found that MB depth is positively associated with stenosis in non-bridged arteries. The most likely explanation for their finding was that deep MB has hemodynamic significance causing a disturbed flow in the other coronary arteries leading to atherosclerotic changes.[14]

In our study, there was no significant association between PFV with MB length, depth and proximal stenosis presence and higher PFV was observed in patients with LADA MB.

Pericardial fatty tissue, owing to its anatomic proximity to the coronary vessels and myocardium, is associated with endothelial dysfunction and the increased risk of coronary atherosclerosis via local secretion of numerous pro-inflammatory hormones and cytokines.[7]

In this study, we measured total volume of fat present in the pericardial space surrounding the heart, rather than perivascular fat or fat at the MB site per se, and this

may not give the true interaction or relationship between cardiac fat and MB characteristics.

Saidi et al. reported that there was prominent perivascular space under the MB characterized by preponderance of fatty tissue that may limit the compressive forces on the bridged segment during systole.[15]

On the other hand, Verhagen et al. found that the association between MB and total calcium score was influenced by the amount of perivascular fatty tissue adjacent to the coronary artery segment suggested that the absence of atherosclerosis and plaque formation in the bridged segment of coronary vessel is highlighted by a lack of exposure to perivascular adipose tissue at that site that protect the MB wall against different types of adipokines and cytokines secreted by cardiac fatty tissue and thus inhibit atherosclerosis at MB site.[12]

However, total absence of cardiac fat such as in congenital lipodystrophy does not inhibit coronary atherosclerosis development and progression.[16]

Nevertheless, the relationships of cardiac fatty tissue with MB is complex and not fully clear in the literature that may reflect the possible role of other factors influencing interaction between pericardial fat with MB characteristics.

There are potential limitations in this study. First, this cross sectional study was a single-center study consisted of patients with suspected coronary artery disease, without control population that did not allow determination of a causal relationship between coronary atherosclerotic markers and MB indices. Second, the functional significance of the MB and relationship between myocardial bridge and symptoms or compare with control group were not assessed in our study as the primary focus was the assessment the associations between coronary atherosclerosis markers with MB characteristics.

Conclusion, MB depth and proximal stenosis presence were significantly associated with coronary plaque and stenosis presence. There was a significant change in the PFV according to the MB site. Further large scale and follow up studies are required to clarify the exact relationship between MB and coronary atherosclerosis and whether MB has protective, in reaction to risk factors of atherosclerosis, or detrimental role in the atherosclerosis process and progression.

Conflict of interest

The authors declare that they have no conflict of interest.

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