Myocardial Bridge as a Structure of “Double-Edged Sword” for the Coronary Artery

Toshiharu Ishii, MD,1 Yukio Ishikawa, MD,2 and Yoshikiyo Akasaka, MD3

Myocardial bridge (MB) is a chance anatomical structure, comprised of the myocardial tissue, with which the coronary artery running in epicardial adipose tissue is partly covered. It is predominantly present in the left anterior descending artery (LAD) and recognizable through imaging techniques as changes in blood flow within the LAD that arises from MB contraction at cardiac systole. Such changes in blood flow influence the pathophysiology of coronary circulation and atherosclerosis development, thus generating controversy as to whether MB predisposes individual to myocardial infarction (MI). However, recent histomorphometric studies have shown that the individual anatomic properties of MB, such as location, length and thickness, consistently play a critical role in the occurrence of MI. This review article comprehensively addresses the pathophysiological mechanisms of MI occurrence together with the benign suppressive effect of coronary atherosclerosis by MB.

Keywords: myocardial bridge, coronary artery, myocardial infarction, atherosclerosis, pathology

Introduction

Myocardial bridge (MB) is a chance anatomic structure, under which the coronary artery running in epicardial adipose tissue is partly covered with myocardial tissue. It is the most frequent in the left anterior descending coronary artery (LAD) than in any other coronary artery regardless of age and sex in any ethnic group.

Since the dawn of angiography, MB has been indirectly identified as a milking or squeezing effect arising from changes in the blood flow.1) At cardiac systole, myocardial tissue comprising MB contracts and directly presses the coronary artery beneath it. Hemodynamic force driven by MB contraction influences blood flow within the coronary artery, in which blood can be retrograde towards the coronary ostium and accelerated towards the cardiac apex. Hemodynamic force is modulated by MB contraction, but such force may vary according to the anatomic features of individual MB, such as location, length and thickness.

Hemodynamics within the coronary artery may pathophysiologically affect coronary circulation and natural history of coronary atherosclerosis. Whether or not MB predisposes individual to myocardial ischemic condition has long been controversial, and perhaps this is because objective identification of MB using early imaging devices has been difficult. In fact, angiographic follow-up has indicated that the prognosis of patients with hypertrophic cardiomyopathy having MB in the LAD is benign2) and an autopsy study that ignored the anatomic properties of MB found that MB does not significantly affect the occurrence of coronary heart disease.3) However, a recent study found that myotomy and concomitant
myocardial unroofing improved the prognosis of patients with hypertrophic myocardial infarction having MB determined by multi-detector computed tomography (MDCT) compared with myotomy alone (100% vs. 67%). This difference paradoxically indicates that the burden imposed by MB evidently causes problems for the coronary circulation. In addition, over 200 symptomatic patients with coronary artery diseases having MB have been so far described. Furthermore, cardiac sudden death from acute circulatory deterioration during vigorous exertion imposed by various sports has been sporadically, but consistently uncovered in youth with an MB, but without atherosclerosis of the LAD. Thus, whether or not MB comprises an anatomical risk factor for myocardial ischemia requires reappraisal.

**Frequency of MB**

The frequency of histopathologically defined MBs remains much higher than that determined even by recent imaging techniques, depending on the nature of direct macro- and/or microscopic observations. After the first autopsy documentation of MB by Craniancu in 1922, a myocardial covering over the coronary artery was initially classified into two modes by Polacek in 1961 as a muscular bridge, in which the artery submerges during its course, and a muscular loop, in which the artery is attached to the atrial myocardium during its course in the atrioventricular groove (Fig. 1). The relative frequencies of MB existing exclusively in the LAD, in a muscular loop in the left circumflex artery and in the right coronary artery are 70%, 40% and 36%, respectively. However, both modes have since been collectively termed MB.

**Coronary artery imaging in clinical practice**

Existence of MB is still defined by coronary angiography as a “milking effect” and a “step down-step up” appearance during cardiac systole. The reported frequency of MB in the LAD determined by coronary angiography is 0.4%–5.4%. However, that the frequency of MB detection by angiography increases from 1.7% to 9.7% when the same images are reviewed specifically to detect MBs is noteworthy. Although coronary angiography can demonstrate coronary circulation within the LAD, it should be applied together with MDCT to gain actual images of the heart and the LAD when MB is a specific concern. With recent advances in imaging techniques such as MDCT and intravascular ultrasound (IVUS), cardiologists have gradually been aware of MB in clinical practice through direct image capture. The frequency of MB in the LAD of patients with coronary heart disease assessed by MDCT in Turkey, Japan and Israel are 3.5%, 15.8% and 26%, respectively (Fig. 2), but remains lower than that found at autopsy. However, the frequency of MB thick determined by MDCT in Japan approximates that of a similar thickness determined by autopsy in Japan, which is 15.8% vs. 13.3%. Detecting MB with MDCT is thus an efficient way to objectively demonstrate MB in vivo. Furthermore, the recent development of 64-row MDCT has increased the frequency of MB detection to 32% in the US and 58% in Korea. Ongoing improvements in MDCT resolution may further increase the frequency of detecting MB.

**Direct histopathological observation**

Direct histopathological observation of MB at autopsy remains the most effective way to establish a standard for identification and quantification of MB structure, and this is fundamental to the relevance of MB. Myocardial bridge is almost exclusively found in the LAD, and rarely in the right coronary artery. The reported frequency MB in the LAD ranges from 22.2% to 60% in Western countries.
Several direct histopathological results have long supported these findings (Fig. 3).7,21,23,32,33) Hemodynamic changes across the entrance to MB have been variously focused as the mechanism of atherosclerosis suppression. Such changes may generate high shear stress in the LAD intima beneath MB because blood flow velocity in the LAD increases under these conditions at both systole and diastole,34) and systolic compression of MB is followed by delayed MB relaxation during diastole.35) These results agree with those determined by a scanning electron microscopy on endothelial cells lining the human LAD. That study found that these cells are polygonal and flat in the LAD intima proximal to the MB entrance, but they then become spindle and engorged and align in the direction of blood flow beneath MB (Fig. 4).32) These findings indicate that the LAD intima beneath MB is pressured by high shear stress, which results in atherosclerosis suppression through reduced substance permeability by such shear stress across the LAD intima.36)

Effects of MBs on the Coronary Artery

Histopathological findings have shown that the development of coronary atherosclerosis is remarkably suppressed in LAD segment covered by MB since the first description by Geiringer in 1951.21) In addition, almost all investigators who have identified MB by angiography or MDCT also agree with this phenomenon. However, the question of whether or not MB provokes myocardial infarction under certain circumstances remains unanswered. Despite several clinical reports of benign outcomes for patients with angina and MB in the LAD, >200 patients with symptomatic MB have been actually described.5)

Atherosclerosis suppression in the LAD beneath MB

Clinical coronary angiography, IVUS and MDCT have shown the absence of atherosclerotic changes in the LAD intima beneath MB, whereas atherosclerotic changes are always found in the LAD segment proximal to an MB entrance in the various extent.14,15,17,18,31) Several direct histopathological results have long supported these findings (Fig. 3).7,21,23,32,33)

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Despite consistent atherosclerosis suppression beneath MB, hemodynamics differs in the LAD segment proximal to the entrance of MB. Assessment by IVUS has shown that blood pressure is higher in the LAD segment proximal to MB than in the aorta, which might locally enhance the development of atherosclerosis.35) The cross-sectioned cut-surface of atherosclerotic lesions proximal to MB is usually eccentric (Fig. 5),14,23,33) indicating that this segment...
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Among them, 172 (79.6%) had coronary heart diseases including angina, myocardial ischemia, myocardial infarction (MI), and sudden cardiac death (Table 1). We assigned all of these patients to one group without considerable coronary atherosclerosis that develops around middle age and another with coronary atherosclerosis that is probably exacerbated by MB mainly in older persons.

1) Coronary heart diseases without atherosclerosis and with MB

Myocardial bridge was mostly found in the LAD and its branches among patients with symptomatic MB,\(^5\) which was consistent with the results obtained from routine autopsy series\(^3,7,21–23\) that revealed MB usually in the middle LAD. However, significant atherosclerotic lesions other than MB were undetectable in the coronary intima of 183 (84.5%) of the patients.\(^5\) In addition, that the average age of symptomatic MB onset was younger (48.2 ± 16.7 y) than that encountered in clinical practice in US (65.8 and 70.4 y for males and females, respectively)\(^39\) was rather conspicuous. However, this obvious difference might have originated from natural selection mechanisms under which only patients with a distinct effect of MB contraction leading to myocardial ischemia, but who were free from coronary atherosclerosis, have been investigated. In routine clinical practice especially for elderly patients, as it is often difficult to differentiate myocardial ischemia provoked by MB contraction from ongoing coronary atherosclerosis, experienced cardiologists might have considered the relationship between MB and coronary ischemia too complicated, and thus did not report such patients.

Nevertheless, MB should be considered as a cause of sudden cardiac death. Among 16 sudden cardiac deaths caused by non-atherosclerotic coronary diseases in individuals aged under 35 years, MB was discovered in the LAD of 6 (37.5%) of them.\(^40\) Notably, sports medicine has recognized MB as a leading cause of sudden death among young basketball, football and soccer players.\(^41,42\) This indicates that MB that vigorously compresses the LAD during cardiac systole due to physical exertion might cause life threatening events even among superficially “healthy” individuals without coronary atherosclerosis. When the blood pressure of such individuals with MB is high at baseline, physical exertion would further increase blood pressure because blood pressure at systole is ruled by turbulent, complex blood flow. Apart from these, a study of the canine coronary artery found that the incorporation of\(^35\) S into glycosaminoglycans increases proximal to MB.\(^37\) In addition, ferritin permeability across the endothelium increases only at the proximal segment to the entrance of a myocardial covering in the left coronary artery of cholesterol-fed rabbit, in which the beginning part of the left coronary artery shortly runs within the epicardial adipose tissue and then is always covered by myocardial tissue analogous to human MB (Fig. 6).\(^38\) Furthermore, in the rabbits, the endothelial cell shapes by scanning electron microscopy exhibited similar changes to those of human LAD across MB. These findings indicate that the LAD intima proximal to the entrance of the human MB or rabbit myocardial covering is susceptible to atherosclerosis due to increased permeability through high shear stress across the endothelium, when either MB or myocardial covering is present in the LAD.

Effect of MB on the occurrence of myocardial ischemia

We reviewed 216 patients in the previously reported literatures of symptomatic MB published in English registered in the PubMed from 1968 to 2008.\(^5\) Among
Fig. 5 Cross-section of the left anterior descending coronary artery (LAD) proximal to myocardial bridge (MB) and beneath MB in the normal and infarcted heart. Eccentric intimal thickening of the LAD is abruptly suppressed beneath MB surrounded by myocardial tissue.

Fig. 6 In cholesterol-fed rabbit, changes of endothelial cell shape are basically similar to those of human coronary artery across myocardial covering. Macrophages attached in more numbers at 20 weeks than 2 weeks. Epi-LC: epicardial left coronary artery; Myo-LC: myocardial left coronary artery.
physiologically higher in the segment proximal to the MB than the aorta.\textsuperscript{33)}

Myocardial ischemia or infarction can occur in individuals who are free of atherosclerosis but have MB in the LAD also via coronary artery spasm at the bridged LAD segment.\textsuperscript{43)} Acetylcholine administration just proximal to MB can provoke up to 90\% stenosis of the LAD lumen.\textsuperscript{44)} In addition, either acetylcholine administration or physical exertion more frequently provokes such spasm at MB site compared with those who do not have MB.\textsuperscript{45)} Immunohistochemistry has demonstrated an abrupt decrease in the expression of endothelin-1, e-nitric oxide synthase and angiotensin converting enzyme in the endothelium lining the LAD intima beneath MB (Fig. 7).\textsuperscript{46)} Furthermore, in the cases of coronary spasm with MB, serum level of endothelin-1 increases, and that of nitric oxide decreases, compared with that without MB.\textsuperscript{45)} Sudden coronary stenosis arising from coronary artery spasm might be a potential risk for myocardial ischemia in the LAD with MB. In addition, a recent extensive study using combinations of various imaging techniques has also suggested a close association between MB and apical myocardial ballooning (Takotsubo) syndrome.\textsuperscript{47)}

2) Occurrence of MI through changes of coronary atherosclerosis caused by MB

\begin{table}
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\begin{tabular}{|l|c|}
\hline
**Table 1** & Reported symptomatic MB cases registered in PubMed (1968–2008) \\
\hline
Age & 48.2 ± 16.7 y.o. \\
Gender (M/F) & 155/61 (71.8\%/28.2\%) \\
Clinical diagnosis & Ischemic heart disease 172 (79.6\%) \\
& Arhythmia 6 (2.8\%) \\
& H C M 20 (9.3\%) \\
& Cardiac sudden death 5 (2.3\%) \\
Intimal lesion & None 183 (84.5\%) \\
& LAD 200 (92.6\%) middle 147 (68.1\%) \\
& RCA 11 (5.1\%) \\
& LCX 5 (2.3\%) \\
\hline
\end{tabular}
\end{table}

We histomorphometrically studied 200 autopsied normal hearts with MB in the LAD and 100 normal hearts without MB, all of which were free of cardiovascular diseases, to determine basic associations between MB and the both topographic and quantitative atherosclerotic changes in the LAD.\textsuperscript{33)} We assessed cross-sections of the LAD at 5 mm intervals together with the surrounding MB for the entire length of the LAD, the extent of intimal thickening in each LAD segment, and measured the anatomical properties of MB, such as the location within the LAD, length and thickness.\textsuperscript{33)} Atherosclerosis was distinctly suppressed in the LAD intima beneath MB irrespective of MB anatomic properties. In addition, the anatomic integrally influence blood flow to compress the LAD wall.

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properties of MB are critical for regulating atherosclerosis development not only in the LAD intima beneath MB, but also in the LAD intima proximal to MB. Furthermore, MB thickness and length significantly correlated and longer MB tend to be more proximally located in the LAD. The extent of intimal thickening beneath MB is lower in patients with thick or long, than with thinner or shorter MB.33 Thus, the development of coronary atherosclerosis is naturally modulated by the anatomic properties of MB in the LAD of the normal heart.

b. Underlying changes in atherosclerosis caused by MB in MI heart.

The anatomic properties of MB change the extent and distribution of atherosclerosis in the LAD, which raises the question of whether they ultimately cause MI. Addressing this issue will require thorough and objective comparisons of MI by MB status in the LAD to understand actual association between MB and MI. Histomorphometric methods will still function as an accurate assessment tool for a given proposition.

A comparative autopsy study of 150 consecutive patients of MI regardless of MB has shown that despite an equally prevalent burden of hyperlipidemia and hypertension in groups with and without MB, the mean age at onset of MI was significantly younger among those with MB, than without MB (acute and old MI: 66.3 vs. 74.5 and 73.5 vs. 79.1 y, respectively). The anatomic properties of MB in the 67 infarcted hearts having MB and 100 age-matched non-infarcted normal hearts having MB, which were randomly selected. The both length and thickness of MB is longer and thicker in the infarcted heart than non-infarcted heart. The myocardial muscle volume comprising MB is distinctly large in the infarcted heart. MB: myocardial bridge; MI: myocardial infarction; AMI: acute myocardial infarction; OMI: old myocardial infarction.

Table 2  Profiles of 150 patients of myocardial infarction by MB status

<table>
<thead>
<tr>
<th>MB status</th>
<th>Number of cases</th>
<th>MI by acute/old</th>
<th>Onset age of AMI</th>
<th>OMI</th>
<th>acute-on-old</th>
<th>Gender (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB (+)</td>
<td>67 (45%)</td>
<td>23/44</td>
<td>66.3 ± 14.1 y.o.</td>
<td>73.5 ± 10.8</td>
<td>88.0 ± 16.1</td>
<td>54/13</td>
</tr>
<tr>
<td>MB (-)</td>
<td>83 (55%)</td>
<td>28/55</td>
<td>74.5 ± 11.0 y.o.</td>
<td>79.1 ± 8.4</td>
<td>71.4 ± 11.1</td>
<td>61/22</td>
</tr>
</tbody>
</table>

Table 3  Anatomic properties of MB in MI hearts

<table>
<thead>
<tr>
<th></th>
<th>MI cases (n = 67)</th>
<th>Non-MI cases (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70.0 ± 13.2 y.o.</td>
<td>70.0 ± 12.5 y.o.</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>54/13</td>
<td>81/19</td>
</tr>
<tr>
<td>MB entrance from left coronary ostium (cm)</td>
<td>4.80 ± 1.17</td>
<td>4.57 ± 1.25</td>
</tr>
<tr>
<td>MB length (mm)</td>
<td>19.0 ± 12.9</td>
<td>15.2 ± 9.7</td>
</tr>
<tr>
<td>MB thickness (mm)</td>
<td>0.81 ± 0.44</td>
<td>0.62 ± 0.45</td>
</tr>
<tr>
<td>MB length × thickness (MB muscle vol.)</td>
<td>98.2</td>
<td>74.5</td>
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</table>

Fig. 8  Schematic drawing on the difference in the atherosclerotic lesion proximal to myocardial bridge (MB). In the myocardial infarction patient (lower half of the figure), atherosclerotic intimal lesions are extensive 2 cm proximal to MB and plaque fissure preferentially occurs at this site, when compared with those in left anterior descending coronary artery (LAD) of the patient free from myocardial infarction (MI) (upper half of the figure).
The location of MB within the LAD also influences the extent and distribution of LAD atherosclerosis. In fact, ignoring MB, although the most stenotic LAD lesion for anterior wall MI appears within 2–3 cm of the origin of the LAD or at sites 3–4 cm from the left coronary ostium, another study found that the most stenotic lesion in the LAD of MI heart with MB located 2.0 cm from the left coronary ostium, being more proximally situated than in the MI heart without MB (Fig. 8). The presence of MB with a greater MM index further contributes to a shift of a severe intimal lesion upwards towards the left coronary ostium. Thus, an increase in the MM index functions in aggregation of advanced atherosclerotic lesions at specific site within the LAD. Microscopic structural changes underlying such topographic shift of atherosclerosis in the LAD include the tendency for unstable plaque-related lesions to be located proximally in MI with MB, and they are frequently 2.0 cm or more proximal to the entrances of MB in MI. Among them, the frequency of the most advanced lesion of plaque fissure/rupture in the proximal LAD is significantly higher in MI cases than without MB (Table 4). The direct or indirect effect of MB in Western populations might overlap ongoing coronary atherosclerosis caused by hypercholesterolemia, generating complex situations to consider the culpability of MB for MI.

Myocardial bridge located within the LAD is unequivocally associated with the occurrence of MI under certain conditions. Another histomorphometric comparison of 100 consecutive MI hearts either with or without MB and 200 normal hearts with MB, found significantly thicker MB in hearts with MI than in normal hearts with MB. In addition, when the mass volume of the myocardium comprising MB, which is assessed as a multiplication of MB thickness and length, the mass volume index of the myocardium (MM index) is also greater in the MI than in the normal heart with MB (Table 3). The location of the entrance of MB in heart with MI closely correlates with the location of the segment that exhibits the greatest intimal thickening, which is included in the MM index. These results indicate that such a large dimension of the MB mass volume generates greater hemodynamic force during contraction, and thus might lead to the occurrence of MI through lasting modulation on the natural history of coronary atherosclerosis in the LAD.

Table 4  Distribution ratio of unstable plaque-related lesions in the proximal LAD with AHA classification in acute MI by MB

<table>
<thead>
<tr>
<th>AMI (+) MB (-)</th>
<th>AMI (+) MB (+)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>(n = 19, 190 sections)</td>
<td>(n = 13, 113 sections)</td>
<td></td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td>80% (0–100)</td>
<td>44% (0–100)</td>
</tr>
<tr>
<td><strong>Foam cell aggregation at shoulder portion</strong></td>
<td>40% (0–100)</td>
<td>44% (0–100)</td>
</tr>
<tr>
<td><strong>Intra-plaque hemorrhage</strong></td>
<td>10% (0–80)</td>
<td>16% (0–64)</td>
</tr>
<tr>
<td><strong>Plaque fissure</strong></td>
<td>0% (0–4)</td>
<td>5% (0–25)</td>
</tr>
<tr>
<td><strong>Thrombus</strong></td>
<td>10% (0–90)</td>
<td>19% (0–56)</td>
</tr>
</tbody>
</table>

Frequency of unstable plaque-related lesion by the AHA histopathologic classification. Plaque fissure preferentially occurs in the infarction patient having MB. On the contrary, calcification tends to occur in the infarction patient having no MB. It might have resulted from aging effect in the latter patient who is older than those having MB. LAD: left anterior descending coronary artery; AHA: American Heart Association; MI: myocardial infarction; MB: myocardial bridge; AMI: acute myocardial infarction.
than the LAD that can be the culprit of serious malady promoted by its externally-existing anatomical structure such as MB.

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Disclosure Statement

None to declare.

References