Background: Recent development of multi-detector computed tomography (MDCT) has made the detection of myocardial bridge (MB) easier on the left anterior descending coronary artery (LAD). The LAD segment proximal to the MB is well known to be susceptible to atherosclerosis. Anatomical characteristics of MB on LAD in patients with myocardial infarction (MI) were examined by MDCT.

Methods and Results: Subjects were 43 MI patients who had MB in the LAD and comprised 2 groups: 14 with culprit lesions in the LAD proximal to MB (culprit group) and 29 without culprit lesions in the LAD (non-culprit group). MB length, MB thickness, and the distance from the orifice of left main trunk (LMT) to MB entrance were compared. Age and coronary risk factors showed no significant difference between the 2 groups. MB length (P=0.011), MB thickness (P=0.035), and index of the length multiplied by thickness of MB (P=0.031) were significantly greater in the culprit group. The distance from the orifice of the LMT to MB entrance was significantly shorter in the culprit group (P=0.006).

Conclusions: Anatomical properties of MB, such as length and thickness of MB as well as MB location, are associated with the formation of culprit lesions of LAD proximal to MB in MI. (Circ J 2011; 75: 642–648)

Key Words: Multi-detector computed tomography; Myocardial bridge; Myocardial infarction

Coronary artery, after bifurcating from the aorta, generally courses within adipose tissue beneath the epicardium. However, a segment of coronary artery is sometimes partly covered by myocardial tissue in the original course. This situation is recognized as a myocardial bridge (MB), which is most often detected in the left anterior descending coronary artery (LAD). MB does not have a hereditary background and is an anatomical subtype of congenital and accidental occurrence. Its frequency has been reported to be 22.9–88.0% by autopsy and 0.4–5.4% by coronary angiography, revealing quite a discrepancy between them. A reason for this discrepancy is thought to be as follows. In coronary angiography, the presence of MB is diagnosed based on the findings of local stenosis, which is identified only at the systolic phase as milking effect as well as step-down and step-up phenomenon. Therefore, when MB-caused pressure gradient in the coronary artery is mild, the above angiographic findings due to the MB compression may be vague. It has long been considered that MB is mostly asymptomatic, and the cases of patients with MB have relatively favorable long-term outcome. However, MB is associated with ischemic heart diseases, arrhythmia, and sudden cardiac death. The clinical significance of MB has thus been still controversial. It has generally been accepted that, while atherosclerosis development is suppressed in the segment of coronary artery beneath MB, atherosclerotic lesions develop in the segment proximal to MB. A recent autopsy study demonstrated that anatomical properties of MB muscle were closely associated with a shift of coronary intimal lesion more proximally, an effect that may increase the risk of myocardial infarction (MI). In clinical case reports, the positive association of MB with MI occurrence has also been repeatedly described but there have been no investigations to our knowledge on the relationship between plaque formation in the LAD segments proximal to MB and the anatomical characteristics of MB.

In recent years, the advance of multi-detector computed tomography (MDCT) technique has enabled us to easily and...
noninvasively detect the presence and anatomical localization of coronary arteries, leading to recent studies on MB detection using MDCT. In these reports, the frequency of MB detected by MDCT is distinctly higher than those by coronary angiography. In the present study, we analyzed the anatomical characteristics of MB in the LAD, such as the length, thickness, and location of MB entrance, in patients with MI by MDCT images, and further tried to elucidate a cut-off value of anatomical properties of MB causing the formation of culprit lesions at the LAD segment proximal to MB.

Methods

Study Population
A total of 228 patients consecutively underwent MDCT within 2 weeks after the occurrence of acute MI (AMI) during the period from April 2004 to December 2008 at the Department of Cardiovascular Medicine, Toho University Omori Medical Center. All patients underwent coronary angiography at admission, and the culprit lesions causing AMI were confirmed. The culprit lesion was angiographically defined as a totally or subtotally occlusive lesion causing AMI. In all patients, percutaneous coronary intervention (PCI), such as stent placement, was carried out to treat the culprit lesions. The presence of MI was confirmed by electrocardiogram at admission and further confirmed by elevation of serum creatine phosphokinase and troponin I. The quality of the culprit lesions were not determined by MDCT images in all patients because MDCT was performed after PCI.

Of the 228 patients, 43 cases had an MB in the main running course of LAD confirmed by MDCT, which consisted of 14 cases with AMI at the cardiac area supplied by the LAD and 29 cases with AMI at the area supplied by the left circumflex artery or the right coronary artery. The 14 cases had the culprit lesions at the LAD segment proximal to MB (culprit group), and the 29 cases had the culprit lesions in coronary arteries other than LAD (non-culprit group). In addition, in this study 47 cases with AMI at the area supplied by the LAD with no MB were also used as control group (non-MB group) (Figure 1).

Definition of Risk Factors
Hypertension was defined as systemic blood pressure $\geq 140/90$ mmHg or the use of antihypertensive treatment. Diabetes mellitus was defined as fasting blood sugar $\geq 126$ mg/dl, postprandial blood sugar $\geq 200$ mg/dl, hemoglobin A1c $\geq 6.5\%$ or the use of treatment. Hyperlipidemia was defined as total cholesterol $\geq 220$ mg/dl, low-density lipoprotein cholesterol $\geq 140$ mg/dl, fasting triglycerides $\geq 150$ mg/dl or the use of lipid-lowering treatment. Smokers were defined as someone who smoked every day at the time of diagnosis of AMI.

MDCT Protocol
A 16-row MDCT scanner (Aquilion 16, Toshiba, Tokyo, Japan) was used for coronary examination, and the coronary imaging sequence was obtained at collimation 16$\times$0.5 mm, helical pitch 2.8–4.8, rotation time 500 ms, tube current 300 mA and voltage 120 KV during a single-breath hold. The contrast medium was injected according to the bi-phasic contrast material injection protocol using real prep: 70 ml of Iopamidol 370 was injected at 3.0 ml/s followed by 20 ml at 2.0 ml/s and finishing with 30 ml of physiological saline at 2.0 ml/s. Imaging processes were as follows: patients received $\beta$-blockers as premedication to maintain heart rates at $>70$ beats/min. After monitors were attached, subjects went through 2 breath-holding exercises and received a single spray of myocol as well as an oxygen mask. When the position was determined, imaging was started.
Image Reconstruction
The initial retrospective ECG-gated reconstruction was generated with the reconstruction window starting at the end-diastolic phase; that is, 75% of the R-peak to R-peak interval. When the data were insufficient due to motion artifacts, additional reconstruction data were obtained in increments and decrements of 10%. MDCT images were evaluated by axial image, volume rendering (3D) image, curved multiplanar reconstruction (MPR) image and oblique MPR image.

Measurement and Evaluation of MB
MB was defined as the existence of tissues exhibiting soft tissue density covering a part of the LAD, which had the same contrast enhancement as myocardial tissue, by an observation of the MPR image. The length of MB was defined as the distance of the covering myocardial tissue from the entrance to the exit of the tunneled artery, which was measured in both MPR and axial images. The thickness of MB was defined as the thickness of the deepest part from the surface of the covering myocardial tissue to the tunneled artery, which was also measured in an axial image. MB location was defined as the distance from the orifice of the left main trunk (LMT) to MB entrance in the MPR image. The length and thickness of the MB as well as MB location were expressed in millimeters (Figure 2).

Definition of CT Plaque Characteristics
Degree of Stenosis
Visual assessment of the stenotic lesion was undertaken based on the AHA classification. The percentage ratio of the stenotic lumen to the original vessel diameter of the lesion analogized by a presumed-to-be-healthy site distal and proximal to the stenosis was obtained and the degree of stenosis was expressed by subtracting this from 100. From the end-diastolic still images taken from multiple projections, measurements were taken at the angle showing the greatest degree of stenosis to classify the lesion into 6 stages: 25% for stenosis of 0–25%, 50% for 26–50%, 75% for 51–75%, 90% for 76–90%, 99% for 91–99%, and 100% for total occlusions. Lesions with stenosis of ≥75% were defined as significant stenotic lesions.

Plaque Consistency
Multiple region-of-interest (ROI) in each plaque and lumen were determined on the basis of the cross-sectional image, and the density of the ROI was measured (expressed by Hounfield units (HU)). Low attenuation plaque was defined as a CT value <50HU.

Calcification
Plaque calcification was classified as spotty, moderate and large. Spotty calcification was defined as <3 mm in size on curved multiplanar reformation images and occupied only one side on cross-sectional images. Moderate calcification was defined as calcification larger than spotty and to a plaque circumference of ≤180°. Severe calcification was defined as calcification larger than spotty and to a plaque circumference of >180°.

Statistical Analyses
Statistical analyses were performed using SPSS 11.0 for Windows (SPSS Japan Inc, Tokyo, Japan). Mean data were expressed as the median (minimum–maximum) or the mean± standard deviation. One-way ANOVA with Scheffe’s F test and χ2 test (for non-parametrically distributed values) were used for multiple comparisons of clinical characteristics among the 3 groups. Mann-Whitney’s U test was employed for comparisons of MB parameters between the groups because these MB parameters did not abnormally distribute statistically. Correlation between the length and thickness of MB or the MB length and MB location was determined by Pearson’s correlation coefficient method. The optimum cut-off value for prediction of the occurrence of the culprit lesion in the LAD segment proximal to MB was calculated using receiver operating characteristic (ROC) curve and area under curve (AUC). Values at P<0.05 were considered statistically significant in all instances.

Results
Comparison of Clinical Characteristics in All Groups
Among the culprit, non-culprit, and non-MB groups, there were no significant differences in age, gender, and the prevalence of coronary risk factors (hypertension, diabetes mellitus, hyperlipidemia and smoking) (Table 1).
Anatomical Characteristics of MB in MI by MDCT

Table 1. Comparison of Clinical Characteristics Between All Groups

<table>
<thead>
<tr>
<th></th>
<th>Culprit (n=14)</th>
<th>Non-culprit (n=29)</th>
<th>Non-culprit (n=29)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.2±9.5</td>
<td>63.4±8.0</td>
<td>62.3±10.0</td>
<td>0.227</td>
</tr>
<tr>
<td>M/F</td>
<td>13/1</td>
<td>28/1</td>
<td>37/10</td>
<td>0.065</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>57.1</td>
<td>48.3</td>
<td>46.8</td>
<td>0.792</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>14.3</td>
<td>31.0</td>
<td>51.1</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Table 2. Comparison of MB Characteristics Between the Culprit Group and Non-Culprit Group

<table>
<thead>
<tr>
<th></th>
<th>Culprit (n=14)</th>
<th>Non-culprit (n=29)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MB length (mm)</td>
<td>23.7 (12.4–54.7)</td>
<td>16.3 (2.42–36.1)</td>
<td>0.011</td>
</tr>
<tr>
<td>MB thickness (mm)</td>
<td>1.92 (0.74–9.69)</td>
<td>1.45 (0.37–4.60)</td>
<td>0.034</td>
</tr>
<tr>
<td>Product of length and thickness of MB</td>
<td>43.9 (11.3–288.8)</td>
<td>25.0 (2.70–157.3)</td>
<td>0.017</td>
</tr>
<tr>
<td>Distance from LMT to MB (mm)</td>
<td>45.7 (34.8–70.1)</td>
<td>56.1 (37.9–90.2)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

MB, myocardial bridge; LMT, left coronary main trunk.

Figure 3. Correlation of myocardial bridge (MB) length with MB thickness and the distance from the orifice of the left coronary artery to MB entrance. (A) Significant correlation between the MB length and MB thickness (P=0.0069) by Pearson’s correlation coefficient method. (B) MB length is inversely correlated with the distance from the orifice of the left coronary artery to MB entrance (P=0.0022).
Comparison of Anatomical Properties of MB Between the Culprit and Non-Culprit Groups

The length, thickness, and the product of length multiplied by thickness of MB (MB product) were significantly greater in the culprit group than in the non-culprit group (24.5±10.4 mm vs. 17.1±7.5 mm, P=0.011 for MB length; 2.81±2.26 mm vs. 1.75±0.96 mm, P=0.035 for MB thickness; and 70.5±71.0 mm vs. 34.6±35.5 mm, P=0.031 for MB product). MB location was significantly shorter in the culprit group than in the non-culprit group (46.3±9.0 mm vs. 57.9±13.7 mm, P=0.006) (Table 2).

Relationship Between the Length and Thickness of MB

In MB patients, there was a significantly positive correlation between the length and thickness of MB (r=0.403, P=0.0069). The MB length negatively correlated with MB location (r= -0.450, P=0.0022) (Figure 3).

Estimation of Cut-Off Values of the Length and Thickness of MB

In patients with MI, the optimum cut-off value for prediction for the occurrence of culprit lesion in the LAD segment proximal to MB was calculated by obtaining ROC curves of the length, thickness and MB product. The AUCs of the length, thickness and MB product were 0.743, 0.703, and 0.739, respectively. Based on the ROC curve of the MB length, which had the greatest area under curve, the optimum cut-off value was established to predict that the segment proximal to MB was the responsible lesion of myocardial infarction (arrow). (Figure 4).

Plaque Characteristics of Proximal to MB and Prevalence of Milking Effect in the Non-Culprit Group

We examined plaque characteristics of proximal to MB and prevalence of milking effect in the non-culprit group.

Discussion

The present study demonstrated that, in patients with culprit lesions in the LAD segment proximal to MB, the length and thickness of MB were significantly greater, and the distance from the orifice of the left coronary artery to the entrance of MB was significantly shorter than those in patients with no culprit lesion in the LAD segment proximal to MB. These results obtained from analyses of MDCT suggest that the anatomical properties of MB, such as the length, thickness, and location, were associated with the development of intimal lesions causing MI in the LAD segment proximal to MB.

In the present study, of 228 patients showing distinct culprit lesions causing MI in a coronary artery, MB in the LAD was detected in 43 cases (18.9%) by MDCT. This frequency of MB detection is similar to those shown in previous studies examining patients with coronary heart diseases including angina and MI. However, the MB frequency (18.9%) obtained from MI patients in the present study was lower than those found in autopsy studies of MI cases (46%) and non-MI cases (45%) in Japan. This discrepancy on MB frequency in MI patients between MDCT and autopsy studies is simply due to the detection method because the results of the previous autopsy studies included thin and/or short MBs observed by microscopy. Nevertheless, the resolution power of a 16-row MDCT is almost the same as that by autopsy for relatively thick and/or long MB. Therefore, MDCT is clinically useful for detecting MB in patients with coronary heart diseases.

In the present study, the thickness and length of MB in patients with culprit lesions in LAD were significantly larger than those in patients without MI in the cardiac area supplied by blood from the LAD. The presence of MB is considered to regulate the distribution of atherosclerotic lesions within the affected LAD. In the intima of LAD with MB, while atherosclerosis evolution is markedly suppressed in the coronary artery segment beneath MB and atherosclerosis develops only in the segments proximal to MB. Such susceptibility to atherosclerosis in the LAD intima proximal to MB originates from the retrograde blood flow toward proximal LAD by MB compression force at cardiac systole because this abnormal blood flow causes the increases in local wall tension and stretch in LAD segments, which induces functional damage of the endothelial cells. Histopathological studies have also demonstrated that the LAD intima proximal to MB is influenced by low shear stress resulting in an increase of endothelial permeability, and that the expression of vasoactive agents, such as endothelial nitric oxide synthase, endothelin-1, and angiotensin-converting enzyme, are higher in the LAD endothelium proximal to MB than those in the LAD endothelium beneath the MB. In fact, plaques were present in approximately 55% of cases even in the non-culprit group in which the proximal MB was not the culprit, and the plaque CT value was low in approximately...
80% of cases, which shows the characteristic of unstable plaques not accompanied by severe calcification on CT. In addition, the difference of the extent of intimal lesion between the LAD intima proximal to MB and the LAD intima beneath MB is influenced by anatomical properties of MB such as MB thickness and length. Previous studies confirm that the culprit lesions observed in the LAD proximal to MB in the culprit group were also influenced by strong retrograde blood flow produced by the strong compression by MB having thicker and/or longer structures.

Regarding the contractile force of the MB muscle, a recent autopsy study emphasizes that MB muscle index, such as the value of MB thickness multiplied by MB length, has a significant relationship to the formation of severe intimal lesions at the settled site of the proximal LAD intima because the magnitude of the contractile force of MB is considered to be dependent on the muscle volume composing MB. In contrast, the statistical analyses from the present study suggest that the greatest value of AUC predisposed to the formation of culprit lesions in the LAD segment proximal to MB was obtained from the ROC curve of the MB length. In the culprit group of the present study, the characteristics and location of intimal lesions in the LAD segment proximal to MB could not be observed due to stent replacement at the segment before MDCT examination. In general, the analyses of MDCT images gives us useful information on plaque structures, such as soft plaque, fibrous plaque, and calcification. Considering the data obtained from MDCT examination, when a progressive or unstable plaque is observed by MDCT in the LAD segment proximal to a long and thick MB, more aggressive therapy may be required for a prevention of MI occurrence.

Study Limitations
The difference in the MB length between the MI and non-MI groups was not significant in an autopsy study, which suggests that the small number of patients in the present study was a cause for this discrepancy. Other causes could be differences in the MB measurement method between autopsy and MDCT and the subjects (non-MI group in the autopsy study vs. non-culprit group in which the proximal MB was not the culprit lesion in the present study). However, significant differences in the MB thickness and product of the MB thickness multiplied by length, and a slight difference in the length were also observed in the autopsy study. Another study reported that a long MB is an independent predictor of long-term cardiac events. Based on these results, the mechanism described in the Discussion does not contradict the findings of the present study. The culprit lesions were observed using CAG and intravascular ultrasound as much as possible in the culprit group, but it is possible that the actual plaque property before the onset of MI or the positional relationship between the culprit lesion and MB was not observed as accurately as those in the autopsy study because MDCT was acquired after stenting in all cases.

Conclusion
The present study first demonstrated that the anatomical properties of MB are associated with the formation of culprit lesions at the LAD segment proximal to MB through analyses of MDCT. This significant association is also supported not only by an autopsy study, but also by the fact that the incidence of MI was significantly higher in patients with MB with severe stenosis at systole. Thus, further therapeutic strategy may be necessary for patients with long and/or thick MB. In addition, a long-term follow-up study of patients with MB on LAD will elucidate the accurate cut-off values of MB length and thickness predisposing to MI.

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