Prevalence and Clinical Significance of Papillary Muscle Infarction Detected by Late Gadolinium-Enhanced Magnetic Resonance Imaging in Patients With ST-Segment Elevation Myocardial Infarction

Takashi Tanimoto, MD; Toshio Imanishi, MD, PhD; Hironori Kitabata, MD; Nobuo Nakamura, MD; Keizo Kimura, MD, PhD; Takashi Yamano, MD; Kohei Ishibashi, MD; Kenichi Komukai, MD; Yasushi Ino, MD; Shigeho Takarada, MD, PhD; Takashi Kubo, MD, PhD; Kumiko Hirata, MD, PhD; Masato Mizukoshi, MD, PhD; Atsushi Tanaka, MD, PhD; Takashi Akasaka, MD, PhD

Background—The frequency of papillary muscle infarction (PapMI) without rupture has not been fully investigated in vivo. Furthermore, the relationship between papillary muscle dysfunction and mitral regurgitation (MR) has been controversial in patients with ST-segment elevation myocardial infarction. Therefore, the aim of this study was to assess the frequency and clinical characteristics of PapMI without rupture using late gadolinium-enhanced magnetic resonance imaging (MRI) in patients with ST-segment elevation myocardial infarction.

Methods and Results—One hundred eighteen ST-segment elevation myocardial infarction patients with primary percutaneous coronary intervention underwent cardiac MRI twice 9±4 days and 8±1 months (n=104) after myocardial infarction. MR was categorized by echocardiography. Of these patients, 40% were found to have late gadolinium enhancement of papillary muscle, in which the posterior papillary muscle was involved more frequently than the anterior papillary muscle (77% versus 26%; P<0.001). PapMI was encountered more frequently in patients with left circumflex and right coronary artery lesions compared with left anterior descending artery lesion (78%, 48%, and 13%; P<0.001). By multiple logistic regression analysis, only coaptation height was identified as an independent predictor of the presence of MR. The second cardiac magnetic resonance imaging showed that the infarct size had a positive correlation with left ventricular end-diastolic volume (r=0.41, P<0.001) and that PapMI was not associated with left ventricular remodeling (P=0.31). Deterioration of MR was not observed in patients with PapMI.

Conclusions—PapMI is more frequent than previously thought yet appears to have significant clinical latency. The size of the myocardial infarction, but not the presence of PapMI, seems to affect left ventricular remodeling, and PapMI is not obligatorily associated with MR. (Circulation. 2010;122:2281-2287.)

Key Words: myocardial infarction ■ magnetic resonance imaging ■ mitral regurgitation ■ papillary muscles

Clinical Perspective on p 2287

Although the frequency of papillary muscle rupture after ST-segment elevation MI (STEMI) has been reported by previous studies in both the nonreperfusion and reperfusion era, the frequency and clinical features of papillary muscle infarction (PapMI) have not been investigated in patients with reperfused STEMI because papillary muscle necrosis is difficult to visualize premortem. Noninvasive investigation by late gadolinium-enhanced magnetic resonance imaging (LGE-MRI) can detect myocardial necrosis as a hyperenhanced area noninvasively and is currently recognized as the gold standard for identification of myocardial necrosis and myocardial viability compared with other imaging modalities. Although necrosis of the papillary muscle is also visualized by LGE-MRI after MI, the relationship between the infarct-related artery and PapMI has not been fully investigated yet.

Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.

Received January 6, 2010; accepted September 20, 2010.
From the Department of Cardiovascular Medicine, Wakayama Medical University, Wakayama, Japan.
Correspondence to Takashi Akasaka, MD, Department of Cardiovascular Medicine, Wakayama Medical University, 811-1, Kimiidera, Wakayama, 641-8509, Japan. E-mail akasat@wakayama-med.ac.jp
© 2010 American Heart Association, Inc.
Circulation is available at http://circ.ahajournals.org

DOI: 10.1161/CIRCULATIONAHA.109.935338
The mitral papillary muscle is an important component of the mitral valve complex, and papillary muscle dysfunction had been implicated in the pathogenesis of ischemic mitral regurgitation (MR). In contrast, some experimental and clinical studies demonstrated that isolated papillary muscle dysfunction failed to cause MR\(^9,10\). Therefore, the role of papillary muscle dysfunction in ischemic MR remains unclear.

The aim of the present study was to evaluate the frequency of PapMI without rupture in various culprit vessels and to investigate the relationship between PapMI and the presence of ischemic MR in patients with STEMI using LGE-MRI.

**Methods**

**Study Population**

The present study population was drawn from 132 consecutive patients with STEMI who were admitted to Wakayama Medical University Hospital between July 2006 and March 2008. The diagnosis of STEMI was established by the presence of typical chest pain lasting \(>30\) minutes, sustained \(>1.0\)-mm ST-segment elevation in at least 2 contiguous leads on ECG, and cardiac enzyme elevation. All patients underwent emergency coronary angiogram and coronary intervention. No patients received thrombolytic therapy. After thrombectomy by the catheter (Export, Medtronic Japan, Tokyo, Japan), balloon angioplasty was performed, followed by deployment of bare metal stents. Patients with prior MI (n=2), renal insufficiency (n=3), organic mitral valve disease (n=1), atrial fibrillation (n=2), claustrophobia (n=1), and hemodynamic unstable condition (n=2) were excluded. One patient presented acute MR resulting from rupture of the anterior papillary muscle and underwent emergency mitral valve replacement with a mechanical valve. Two patients who underwent emergency surgery for left ventricular (LV) free wall rupture were also excluded from the study. Thus, the final study population was a consecutive 118 patients.

Blood samples were obtained on admission and serially every 3 hours for the first 24 hours after primary percutaneous coronary intervention, and peak values of creatinine phosphokinase and MB fraction were determined. MRI was performed 9±4 days after the onset of STEMI in all patients. Echocardiography was also performed to assess MR within 2 days of MRI and read independently. In 104 of 118 patients (88.1%), follow-up MRI and echocardiography were performed 8±1 months after the event. All patients gave their written informed consent. The study was carried out in accordance with the Declaration of Helsinki.

**Angiographic Analysis**

In all patients, coronary angiography was performed with a SF Judkins-type catheter via the femoral approach. The culprit lesion was identified on the findings of coronary angiography, ECG, and transthoracic echocardiography. Perfusion was evaluated according to the Thrombolysis in Myocardial Infarction criteria.\(^11\) Segments of coronary arteries were numbered from 1 to 15 according to the guidelines of the American Heart Association.\(^12\) Coronary angiograms were reviewed separately by 2 independent observers blinded to the MRI findings.

**MRI Protocol**

All cardiac MRI procedures were performed with a 1.5-T clinical scanner (Intera Achieva, Philips Medical Systems, Best, the Netherlands) equipped with a 5-element cardiac phased-array coil for signal reception, as previously described.\(^13,14\) First, breath-hold cine steady-state free precession images with a time resolution of 35 ms were acquired. Next, a breath-hold 3-dimensional turbo gradient echo with inversion recovery was used to obtain the late enhanced images. Contiguous short-axis slices and representative long-axis slices of the LV were obtained 10 minutes after intravenous injection of 0.1 mmol/kg Gd-DTPA (Magnevist, Schering AG, Berlin, Germany). Scan parameters were as follows: repetition time, 4.1 milliseconds; echo time, 1.25 milliseconds; flip angle, 15°; field of view, 350×350 mm; partial echo; matrix, 224×256; and spatial resolution, 1.56×2.24×10 mm\(^3\) reconstructed to 0.68×0.68×5 mm\(^3\). All images were acquired during breath-hold at end expiration. The inversion time was optimized (200 to 300 milliseconds) to null the normal myocardium. There were no complications related to the MRI procedures, and all patients tolerated the procedure well.

**MRI Analysis**

All MRI analyses were performed by the consensus of the 2 blinded observers (H.K. and N.N.) on an offline workstation (View Forum, Philips Medical Systems). The LV volume and ejection fraction (LVEF) were calculated by tracing the end-diastolic and end-systolic LV slice contours and using the modified Simpson rule method. End-diastolic and end-systolic volumes were defined as the largest and the smallest LV cavity, respectively. Displacement of mitral coaptation toward the LV apex (coaptation height) was measured as the distance between the leaflet coaptation and the mitral annular plane in the 4-chamber view at midsystole. To assess the LV shape, the sphericity index was calculated by the LV diameter-to-length ratio measured in the 2-chamber view at end diastole. Mitral annular diameter was measured in the 2-chamber view at end systole.

LGE of the left ventricle was documented in all patients. After the total volume of enhanced tissue was determined, infarct size was expressed as percentage of LV volume as follows: volume of enhanced tissue×100/total volume of LV myocardium (in percent). Microvascular obstruction was defined as hypodense regions within the hyperenhanced infarcted area and was included in the calculation of the total infarct size. A total of 20 short-axis images with 5-mm thickness after reconstruction were obtained to cover the whole LV. LGE of papillary muscles was evaluated by LGE-MRI images from 2 different views (short-axis and 2-chamber views). The signal intensity of both anterior and posterior papillary muscles was measured and compared with that of remote noninfarcted LV myocardium. Papillary muscles with signal intensity 2 SD above the mean signal obtained in the remote noninfarcted myocardium, in at least 3 consecutive slices in the short-axis and corresponding 2-chamber views, were considered necrosis in a binary fashion. Representative 3-dimensional LGE images obtained by LGE-MRI in patients with and without PapMI are shown in Figure 1.

**Echocardiography and Data Analysis**

Transthoracic Doppler echocardiography was performed with a commercially available ultrasound machine. The presence and grade of MR were screened by color-flow imaging with the MR jet area-to-left atrium area ratio. In patients with more than trace regurgitation, the regurgitant orifice area was calculated by the proximal isovelocity surface area method, and the degree of MR was graded as mild (regurgitant orifice area <0.2 cm\(^2\)), moderate (regurgitant orifice area, 0.2 to 0.4 cm\(^2\)), or severe (regurgitant orifice area >0.4 cm\(^2\)).\(^16\) The direction of the MR jet was defined by the initial direction of the jet; eccentric jets were in close contact with a mitral leaflet behind the regurgitant orifice, whereas central jets were initially directed into the central of the left atrium.\(^17\)

**Statistical Analysis**

Continuous variables are expressed as mean±SD. They were compared with the use of an unpaired Student t test. Categorical variables were compared by the \(\chi^2\) test or Fisher exact test as appropriate. Comparisons of continuous variables among 3 groups were performed with 1-way ANOVA analysis. The Spearman rank correlation test was used to analyze the correlation between the change in MR grade and LV end-diastolic volume. Multiple logistic regression analysis was performed to determine independent predictors of MR. Univariate variables with values of \(P<0.10\) were included in the multiple variable analysis. SPSS version 11.0 (SPSS Inc, Chicago, III) was used for all statistical analyses. A value of \(P<0.05\) was considered statistically significant.
Results

Patient Characteristics

The clinical characteristics of the 118 patients (87 men; mean age, 64±12 years) are summarized in Table 1. LGE of mitral papillary muscles was detected in 47 of 118 STEMI patients (40%). The mean time to reperfusion was 5.2±3.5 hours. The mean peak creatine phosphokinase level was 2717±2004 IU/L. The infarct-related artery was the LAD in 45 patients (38%), RCA in 50 patients (42%), and LCx in 23 patients (20%). There were no significant differences in the Thrombolysis in Myocardial Infarction flow grade and Rentrop score before intervention between the 2 groups.

Table 1. Patient Characteristics and Angiographic Data

<table>
<thead>
<tr>
<th>PapMI</th>
<th>Yes (n=47)</th>
<th>No (n=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64±13</td>
<td>65±12</td>
<td>0.67</td>
</tr>
<tr>
<td>Male/female, n</td>
<td>39/8</td>
<td>48/23</td>
<td>0.09</td>
</tr>
<tr>
<td>Coronary risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>30 (64)</td>
<td>40 (57)</td>
<td>0.45</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (40)</td>
<td>25 (36)</td>
<td>0.70</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>24 (51)</td>
<td>32 (46)</td>
<td>0.57</td>
</tr>
<tr>
<td>Current smokers</td>
<td>27 (57)</td>
<td>28 (40)</td>
<td>0.06</td>
</tr>
<tr>
<td>Family history of ischemic heart disease</td>
<td>13 (28)</td>
<td>12 (17)</td>
<td>0.18</td>
</tr>
<tr>
<td>Time to reperfusion, h</td>
<td>5.3±3.5</td>
<td>5.0±3.6</td>
<td>0.66</td>
</tr>
<tr>
<td>Maximum total CK, IU/L</td>
<td>2878±2043</td>
<td>2610±1986</td>
<td>0.48</td>
</tr>
<tr>
<td>Maximum CK-MB fraction, IU/L</td>
<td>245±193</td>
<td>229±191</td>
<td>0.68</td>
</tr>
<tr>
<td>Infarct-related artery, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>6 (13)</td>
<td>39 (55)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LCx</td>
<td>17 (36)</td>
<td>6 (8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RCA</td>
<td>24 (51)</td>
<td>26 (37)</td>
<td>0.12</td>
</tr>
<tr>
<td>TIMI flow grade before PCI, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>32 (68)</td>
<td>45 (65)</td>
<td>0.30</td>
</tr>
<tr>
<td>1</td>
<td>10 (21)</td>
<td>10 (14)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (9)</td>
<td>12 (17)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (2)</td>
<td>4 (6)</td>
<td></td>
</tr>
<tr>
<td>TIMI flow grade after PCI, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.73</td>
</tr>
<tr>
<td>1</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6 (13)</td>
<td>6 (15)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>41 (87)</td>
<td>65 (85)</td>
<td></td>
</tr>
<tr>
<td>Rentrop classification, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>26 (55)</td>
<td>43 (61)</td>
<td>0.87</td>
</tr>
<tr>
<td>1</td>
<td>13 (28)</td>
<td>16 (23)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5 (10)</td>
<td>9 (13)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3 (7)</td>
<td>3 (4)</td>
<td></td>
</tr>
</tbody>
</table>

CK indicates creatine phosphokinase; TIMI, Thrombolysis in Myocardial Infarction; and PCI, percutaneous coronary intervention. Data presented are mean±SD when appropriate.

PapMI and Culprit Vessel

In 47 patients with PapMI, the posterior papillary muscle was involved more frequently than the anterior papillary muscle: 36 posterior versus 12 anterior papillary muscles (77% versus 26%; P<0.001). Only 1 patient, who had a proximal LCx lesion, showed delayed enhancement in both anterior and posterior papillary muscles. Figure 2 shows the prevalence of PapMI in each culprit vessel. PapMI was observed more frequently in patients with LCx lesions (74%) and RCA lesions (48%) compared with LAD lesions (13%) (P<0.001).

Table 2 demonstrates the incidence of PapMI in each culprit site. Among patients with an RCA lesion, the incidence of PapMI was 47% in patients with a culprit site at the RCA proximal to the crux, 100% at the segment 4 atrioventricular branch lesion, and 0% at the segment 4 posterior papillary muscles was detected in 47 of 118 STEMI patients (40%). The mean time to reperfusion was 5.2±3.5 hours. The mean peak creatine phosphokinase level was 2717±2004 IU/L. The infarct-related artery was the LAD in 45 patients (38%), RCA in 50 patients (42%), and LCx in 23 patients (20%). There were no significant differences in the Thrombolysis in Myocardial Infarction flow grade and Rentrop score before intervention between the 2 groups.

Table 2. Incidence of PapMI in each culprit site

<table>
<thead>
<tr>
<th>Culprit Site</th>
<th>PapMI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>RCA proximal to the crux</td>
<td>47</td>
<td>100%</td>
</tr>
<tr>
<td>Segment 4 atrioventricular branch lesion</td>
<td>47</td>
<td>100%</td>
</tr>
<tr>
<td>Segment 4 posterior</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 1. Representative LGE-MRI images in various locations of MI. Late enhancement images from patients with STEMI involving an RCA lesion (A, B), LAD lesion (C), and LCx lesion (D). Both papillary muscles are not enhanced in A. Contrast enhancements of the posterior papillary muscle (B), anterior papillary muscle (C), and both papillary muscles (D) are clearly detected (arrow, posterior PapMI; arrowhead, anterior PapMI). Note that B and C show nontransmural MI. Top, short-axis view; bottom, vertical long-axis view.

Figure 2. Prevalence of PapMI in each culprit vessel. LGE of papillary muscle was detected in 40% of all patients with STEMI. The posterior papillary muscle was involved more frequently than the anterior papillary muscle. PapMI was observed more frequently in patients with LCx and RCA lesions than in those with LAD lesions.
Total 118 12 (10) 36 (31)

LCX (n=23)

11 8 3 (38) 3 (38)*
12 2 2 (100) 0
13 10 0 8 (80)
14 2 0 1 (50)
15 1 0 1 (100)
Total 118 12 (10) 36 (31)

Abbreviations as in Table 3.

Table 3. MRI and Echocardiographic Data (n=117)

<table>
<thead>
<tr>
<th>Anterior PapMI</th>
<th>Posterior PapMI</th>
<th>No PapMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior (n=10)</td>
<td>Posterior (n=36)</td>
<td>No (n=71)</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>120±39.7</td>
<td>122±28.7</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>63.4±38.2</td>
<td>64.2±21.1</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>50.6±13.5</td>
<td>48.4±7.6</td>
</tr>
<tr>
<td>Infarct size, %</td>
<td>17.3±7.7</td>
<td>17.9±10.3</td>
</tr>
<tr>
<td>MVO, n (%)</td>
<td>2 (20)</td>
<td>12 (33)</td>
</tr>
<tr>
<td>Sphericity index</td>
<td>0.52±0.07</td>
<td>0.60±0.06</td>
</tr>
<tr>
<td>Mitral annular diameter, mm</td>
<td>33.7±3.7</td>
<td>35.0±2.7</td>
</tr>
<tr>
<td>Coaptation height, mm</td>
<td>3.9±1.6</td>
<td>6.0±2.9</td>
</tr>
<tr>
<td>LA diameter, cm</td>
<td>33.7±3.7</td>
<td>31.7±6.6</td>
</tr>
<tr>
<td>Mitral regurgitation, n (%)</td>
<td>None or trace 8 (80) 23 (64) 53 (75)</td>
<td>Mild 2 (20) 8 (22) 17 (24)</td>
</tr>
</tbody>
</table>

LVEDV indicates LV end-diastolic volume; LVESV, LV end-systolic volume; MVO, microvascular obstruction; and LA, left atrium. Data presented are mean±SD when appropriate. One patient with both PapMIs was excluded from this table.

height than those without MR (Table 5). Multiple logistic regression analysis, however, determined that the coaptation height was the only independent predictor of the presence of MR (per 1.0-mm increase; odds ratio, 1.98; 95% confidence interval, 1.46 to 2.68). In all patients, infarct size was significantly associated with the severity of MR (P=0.02), but the presence and laterality of PapMI were not (P=0.12).

In nonanterior MI patients, both end-diastolic volume and infarct size (P<0.01 and P=0.02, respectively), but not the

Table 4. MRI and Echocardiographic Data (Nonanterior Infarction)

<table>
<thead>
<tr>
<th>PapMI (+)</th>
<th>PapMI (−)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior MI (n=73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>123±31</td>
<td>112±29</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>65±24</td>
<td>52±21</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>49±9</td>
<td>55±9</td>
</tr>
<tr>
<td>Infarct size, %</td>
<td>18±10</td>
<td>10±6</td>
</tr>
<tr>
<td>MVO, n (%)</td>
<td>12 (29)</td>
<td>8 (25)</td>
</tr>
<tr>
<td>Sphericity index</td>
<td>0.59±0.07</td>
<td>0.58±0.09</td>
</tr>
<tr>
<td>Mitral annular diameter, mm</td>
<td>35±3</td>
<td>34±4</td>
</tr>
<tr>
<td>Coaptation height, mm</td>
<td>5.7±2.9</td>
<td>4.0±2.4</td>
</tr>
<tr>
<td>LA diameter, cm</td>
<td>32±6</td>
<td>31±6</td>
</tr>
<tr>
<td>Mitral regurgitation, n (%)</td>
<td>None or trace 26 (63) 24 (75)</td>
<td>0.42</td>
</tr>
<tr>
<td>Mild 9 (22)</td>
<td>8 (25)</td>
<td></td>
</tr>
<tr>
<td>Moderate 6 (15)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Severe 0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations as in Table 3.

PapMI on LV Volume and MR

MR was present in 34 of 118 patients (28.8%). The regurgitant orifice area was 0.15±0.03 and 0.27±0.04 cm² in patients with mild (n=27) and moderate (n=7) regurgitation, respectively. MRI and echocardiographic data for patients with anterior PapMI, posterior PapMI, and without PapMI are shown in Table 3. There were no significant differences in terms of infarct size and the presence of MR among these groups, whereas the coaptation height was significantly greater in the posterior PapMI group (P<0.01).

In patients with anterior MI, there were no significant differences in any parameters, regardless of the presence of PapMI. Table 4 gives the MRI and echocardiographic data of patients with nonanterior MI (LCx and RCA lesions). In the nonanterior MI group, patients with PapMI had higher LV end-systolic volume, lower LVEF, larger infarct size, and greater coaptation height than patients without PapMI.

Determinants of Presence and Severity of MR

Patients with MR had larger infarct size, larger LV end-systolic volume, larger sphericity index, and greater coaptation
presence and laterality of PapMI ($P=0.18$), were significantly associated with the severity of MR. Microvascular obstruction of the LV was not associated with the presence and severity of MR ($P=0.96$). The direction of regurgitant jets was central in 81.3% and 88.9% of patients with and without PapMI ($P=0.65$), respectively.

### LV Volume and MR at the 8-Month Follow-Up
In 104 of 118 patients (88.1%), the second MRI and echocardiography were performed 8 ± 1 months after the MI. Infarct size by MRI was reduced from 17.5% to 14.3% of the LV (18.3% reduction) during the 8-month follow-up period. In terms of LV morphology, 21 patients (20%) demonstrated >15% increase and 26 patients (25%) showed >15% decrease in LV end-diastolic volume at the 8-month follow-up. Presence of PapMI was not associated with LV remodeling in patients with nonanterior MI or in all patients ($P=0.28$ and $P=0.31$, respectively). Infarct size correlated positively with LV end-diastolic volume ($r=0.41$, $P<0.001$) and inversely with LVEF ($r=-0.66$, $P<0.001$) at the 8-month follow-up. During the follow-up period, MR grade improved in 20 patients and deteriorated in 4 patients. The change in MR grade correlated significantly with the change in LV end-diastolic volume in all patients ($r=0.40$, $P<0.001$) and in patients without PapMI ($r=0.51$, $P<0.001$). In patients with PapMI, however, there was no significant correlation between the change in MR and LV volume in nonanterior MI ($P=0.24$) or in all patients ($P=0.15$). Furthermore, no patients with PapMI demonstrated deterioration of MR grade despite the larger infarct size ($P<0.001$) and lower LVEF ($P<0.001$) in the nonanterior MI group at baseline.

### Discussion
This study is the first to demonstrate, using LGE-MRI, the frequency of the mitral PapMI, its relationship to LV function, and the prevalence of MR for each culprit vessel in patients with STEMI. Papillary muscles were involved in up to 40% of patients with STEMI, and 71% of the patients had infarctions in the posterior papillary muscle. PapMI was encountered more frequently in patients with LCx and RCA lesions compared with LAD lesions. The presence of PapMI was not associated with MR and LV remodeling at the 8-month follow-up.

### PapMI With and Without Rupture After STEMI
It is widely recognized that papillary muscle is prone to necrosis in ischemic events because the central artery of papillary muscle is an end artery.2 The frequency of papillary muscle rupture in MI has been reported at 0.4% to 0.9% on the basis of autopsies.19 Rupture of the posterior papillary muscle occurred almost 3 times more frequently than rupture of the anterior papillary muscle in the analysis of 22 autopsies (73% and 27%, respectively).2

On the other hand, papillary muscle necrosis without rupture was documented in 19% to 32% of MI patients in autopsies.20 Coma-Canella et al21 reported that the posterior papillary muscle was involved most frequently (13 cases, 52%), followed by the anterior papillary muscle (8 cases, 16%) and both papillary muscles (8 cases, 32%), in a total of 133 acute MI cases with autopsy.

Noninvasive detection of PapMI without rupture has been difficult premortem and seems to be challenging. Conventional echocardiography can detect only fibrosis and calcification of papillary muscles.22 Strain analysis of papillary muscle requires special echocardiography equipment and good echocardiographic images. Conventional nuclear medicine equipment lacks sufficient spatial resolution to visualize the papillary muscle reliably except in patients with hypertrophic cardiomyopathy.23 Multidetector computed tomography seems to be a promising modality to assess the viability and perfusion of papillary muscles, but it requires double radiation exposure and an ionizing contrast agent as an adjunctive evaluation of coronary artery.

On the other hand, LV function and myocardial viability can be assessed noninvasively by cardiac MRI in the clinical settings. Gadolinium is used as a positive contrast agent to assess the myocardial viability in the LV wall. Necrosis of the papillary muscle can be also identified with LGE-MRI. Hombach et al24 reported that PapMI was seen in 26% of patients with STEMI. However, they did not demonstrate a relationship between the infarct-related artery and PapMI. Furthermore, the clinical significance of PapMI without rupture has been unclear.

In the present study, the LGE in papillary muscle could be identified among 40% of STEMI patients. The posterior papillary muscle was involved ≈3 times more frequently than the anterior papillary muscle, which was consistent with previous reports.21 22
Blood Supply of Papillary Muscles

Perfusion patterns of the papillary muscles have been evaluated in some clinical studies using contrast echocardiography. Lim et al. injected contrast agents into both the RCA and LCA during coronary angiography and analyzed the blood supply of the papillary muscles using echocardiography. In their report, the anterior papillary muscle was supplied by the LCA, and the posterior papillary muscle was opacified by either the RCA or LCA. Voci et al. assessed the perfusion of papillary muscles by injecting contrast agents into bypass grafts during coronary artery bypass surgery. They reported that the anterior papillary muscle was often perfused by a dual blood supply from the first diagonal branch of the LAD and the obtuse marginal branches of the LCx, whereas the posterior papillary muscle had mainly a single blood supply from either the RCA or the posterolateral branch of the LCx. These different perfusion patterns of each papillary muscle could explain the vulnerability of the posterior papillary muscle in infarction.

In the present study comparing angiographic and LGE-MRI findings, the supply artery to the anterior papillary muscle was confirmed to be the first diagonal branch of the LAD and the obtuse marginal branches of the LCx, and that of the posterior papillary muscle was the segment 4 atrioventricular branch of the RCA and the posterolateral branch of the LCx.

PapMI and MR

The role of papillary muscles in ischemic MR, especially in the acute phase of MI, has previously been unclear. In animal models, isolated papillary muscle dysfunction without LV remodeling failed to cause ischemic MR. Furthermore, papillary muscle dysfunction even attenuated ischemic MR by reducing its longitudinal contraction and tethering papillary muscle in previous experimental and clinical studies. From these investigations, it is now widely accepted that the main cause of ischemic MR is the tethering of the mitral leaflet by outward displacement of the papillary muscle resulting from LV remodeling in patients with prior MI. In the present study, PapMI was not associated with the presence and severity of MR in the acute phase, and the change of MR grade correlated with the change in LV volume, but not the PapMI, at the 8-month follow-up.

As it has been demonstrated that revascularization therapy reduced infarct size by scintigraphy, our 8-month follow-up data also showed a reduction in infarct size and LV volume. In addition, PapMI had no statistically significant influences on MR and LV remodeling. The 8-month follow-up data may not completely represent all the remodeling that may occur after the onset of STEMI because all patients underwent primary percutaneous coronary intervention and optimal medical therapy such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and β-blockers.

Study Limitations

The presence of papillary muscle necrosis was not confirmed with histological examination in this study. However, LGE-MRI is a well-established method to detect myocardial necrosis, and its sensitivity has been confirmed by histology in animal models, even in small and subendocardial necrosis that is missed by other imaging methods. In this study, 3-dimensional LGE-MRI was performed with a spatial resolution of $0.68 \times 0.68 \times 5$ mm³ after reconstruction, which would be enough to detect PapMI. Quantification of the extent of PapMI is needed, and further technical advances would enable us to assess the extent of necrosis on papillary muscle quantitatively.

Reperfusion time, preconditioning and postconditioning, and adjunctive medical therapy may affect the prevalence of PapMI and subsequent LV remodeling and MR in STEMI. Some of the subgroup analysis might not have had enough power to detect significant differences because the sample size was relatively small in the present study.

Clinical Implications

PapMI can be identified noninvasively by LGE-MRI in the clinical setting. Infarction of papillary muscle was identified in up to 40% of patients, mainly in nonanterior MIs. The presence of PapMI was not associated with MR and LV remodeling at the 8-month follow-up. Previous studies by echocardiography demonstrated that scarred and stretched papillary muscle attenuated tethering force and reduced MR in patients with prior MI. This discrepancy might be explained by additional larger-scale studies performing longer serial observations of papillary muscle morphology and LV function, beginning with the acute postinfarction state and following through to the remodeled, chronic infarction state.

Conclusions

PapMI is present more frequently in patients with STEMI than previously thought yet appears to have significant clinical latency. The size of the MI seems to affect LV remodeling, and PapMI is not obligatorily associated with MR and LV remodeling at the 8-month follow-up. Although longer-term follow-up data are not available, our data seem to support the concept that changes associated with remodeling are likely the strongest factors affecting whether a patient will develop MR.

Disclosures

None.

References

Tanimoto et al  Papillary Muscle Infarction by MRI  2287

routine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study.  


11. Effect of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: results of the TIMI IIIB Trial: Thrombolysis in Myocardial Ischemia.  


18. Madu EC, Cruz IA. The vital role of papillary muscles in mitral and ventricular function: echocardiographic insights.  


22. Schwenger FT. Papillary muscle calcification after inferoposterior myocardial infarction.  

23. Steinmetz AP, Maisey MN, Hardoff R. Patterns of papillary muscle ischemia in myocardial PET.  


J Cardiol. 2008;51:145–156.

27. McCallister BD Jr, Christian TF, Gersh BJ, Gibbons RJ. Prognosis of myocardial infarctions involving more than 40% of the left ventricle after acute reperfusion therapy.  

Go to http://cme.ahajournals.org to take the CME quiz for this article.
Prevalence and Clinical Significance of Papillary Muscle Infarction Detected by Late Gadolinium-Enhanced Magnetic Resonance Imaging in Patients With ST-Segment Elevation Myocardial Infarction

Takashi Tanimoto, Toshio Imanishi, Hironori Kitabata, Nobuo Nakamura, Keizo Kimura, Takashi Yamano, Kohei Ishibashi, Kenichi Komukai, Yasushi Ino, Shigeho Takarada, Takashi Kubo, Kumiko Hirata, Masato Mizukoshi, Atsushi Tanaka and Takashi Akasaka

_Circulation_. published online November 15, 2010;
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/early/2010/11/15/CIRCULATIONAHA.109.935338

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/