Increase in serum cardiac myosin light chain I associated with elective percutaneous transluminal coronary angioplasty in patients with ischemic heart disease

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Changes in serum myosin light chain I (MLCI) due to elective percutaneous transluminal coronary angioplasty (PTCA) were studied after PTCA (0, 8 and 48 hours) in 57 patients with old myocardial infarction (MI group) and 20 patients with angina pectoris (AP group). The AP group showed no increase after PTCA. In contrast, in the MI group there were 16 patients in whom MLCI at 48 hours was increased by 1.0 ng/ml or more (MI1 group) and another group of 41 patients who showed no increase in MLCI (MI2 group). The MI1 group had a significantly higher incidence of (1) non-Q wave myocardial infarction (62.5% vs. 17.1%, p<0.01), (2) 99% stenosis of a coronary artery (50.0% vs. 12.2%, p<0.01), and (3) redistribution in a hypoperfusion area found in the delayed image of resting thallium-201 (T201) myocardial scintigraphy (85.7% vs. 15.8%, p<0.01). The left ventricular ejection fraction (LVEF) was significantly improved in the MI1 group, 3 to 4 months later (from 0.49±0.12 to 0.58±0.11, p<0.01), in contrast to the patient of MI2 group who did not show any improvement. The AP group was not considered to have a bulk of myocardium impaired enough to show a release of MLCI due to PTCA-associated transient coronary occlusion. In the MI1 group, however, MLCI was probably released from the chronically underperfused, but still salvageable, portion of the myocardium. This is consistent with the improvement in LVEF observed 3 to 4 months after the relief of severe coronary stenosis. These findings suggest that the MI1 group had a large amount of "hibernating myocardium."

Key words: myosin light chain I, PTCA, hibernating myocardium

INTRODUCTION

Many markers of the degree of myocardial damage have been examined, including creatine kinase (CK), glutamate oxaloacetate transaminase (GOT), lactate dehydrogenase (LDH) and myoglobin (Mb). Recently it has become possible to measure serum levels of myosin light chain I (MLCI), a myocardial structural protein, as an indicator of myocardial necrosis.

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Serial changes in serum MLCI have been reported to be more useful in the assessment of myocardial infarct size than CK which can be released even in the case of solely enhanced permeability of the cell membrane.1,2

In experimental animals, it has been reported that an approximately 20 minutes coronary occlusion does not cause myocardial necrosis.3-5 In humans, percutaneous transluminal coronary angioplasty (PTCA) provides a useful model in studying the myocardial damage due to a brief coronary occlusion. Changes in CK, CK-MB (MB isoyme of CK) and Mb associated with elective PTCA have been reported,6-9 but to date, no studies on changes in MLCI have been published. To investigate PTCA-associated
myocardial damage,4,7 we studied changes in serum MLCI following elective PTCA and their possible pathophysiological significance.

**MATERIALS AND METHODS**

**Patients**
Seventy-seven patients who underwent successful PTCA were examined. The study group consisted of 57 patients with old myocardial infarctions who underwent PTCA on the infarct-related coronary artery (MI group), and 20 patients without previous myocardial infarction but with angina pectoris (AP group) (Table 1). There was no difference between the two groups in age, gender, the number of coronary lesions, location of the PTCA-targeted coronary artery, or the percentage of coronary stenosis.

**Blood sampling**
Peripheral blood samples were drawn four times: before PTCA, and immediately, 8 and 48 hours after PTCA. Serum MLCI, CK and Mb levels were determined.

**Measurements of MLCI**
Measurement of MLCI were made with the “Yamsa”, Myosin LI Assay Kit (Nihon Medi-Physics Co., Hyogo, Japan), using an immunoradiometric assay (IRMA) with iodine-125 (125I). For the measurement of radioactivity, a well-type scintillation counter (Auto well gamma system ARC-1000M, Aloka, Co., Tokyo, Japan) was used. The standard curve was provided

with the kit (Fig. 1). To provide a standard curve for concentrations less than 2.5 ng/ml, standard solution was diluted to produce concentrations of 1.25, 0.625 and 0.313 ng/ml. Samples were incubated for 20 hours at 22°C. The detection limit of the system was 0.625 ng/ml. The coefficient of variation (CV) increased at the concentration of the standard solution less than 1.0 ng/ml (Fig. 2). The detection limit was comparable to those described by Suehiro et al.10

![Image](image_url)

**Table 1** Clinical features of the subjects studied

<table>
<thead>
<tr>
<th></th>
<th>Group MI (n=57)</th>
<th>Group AP (n=20)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)*</td>
<td>60.4±13.6</td>
<td>61.9±9.8</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>45/12</td>
<td>13/7</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-vessel</td>
<td>22</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Multivessel</td>
<td>35 (61.4%)</td>
<td>6 (30.0%)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Two-vessel</td>
<td>19</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Three-vessel</td>
<td>16</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Target coronary artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>32</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>LCX</td>
<td>7</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>RCA</td>
<td>18</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary % stenosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>10</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>99%</td>
<td>13</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>90%</td>
<td>23</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>75%</td>
<td>11</td>
<td>8</td>
<td>NS</td>
</tr>
</tbody>
</table>

LAD=left anterior descending coronary artery; LCX=left circumflex artery; NS=not significant; RCA=right coronary artery. * Values are mean± standard deviation.

![Image](image_url)

**Fig. 1** Standard curve for measurement of MLCI (myosin light chain I). C=net binding count; T=total count.

![Image](image_url)

**Fig. 2** Precision profile in this study. X axis indicates the logarithmic values of the concentration of the standard solution. CV=coefficient of variation.

![Image](image_url)

**Fig. 3** Changes in MLCI (myosin light chain I) with cardiac catheterization. B=before PTCA; ΔMLCI=differences of MLCI between pre- and post-PTCA.

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Examination of significant variations in MLCI
Changes in MLCI with cardiac catheterization were examined in five patients with old myocardial infarction and five patients with angina pectoris serving as control subjects (Fig. 3). The change in MLCI after catheterization was 0.1 ± 0.5 ng/ml (mean ± SD; standard deviation). On the basis of this result, any change more than twice the SD, i.e., more than 1.0 ng/ml, was judged to be significant.

Factors examined
To clarify the factors which influence MLCI changes, the following factors were examined before PTCA: electrocardiogram (ECG) findings, the extent of stenosis of the PTCA-targeted coronary artery based on the classification of the American Heart Association, collateral circulation, and degree of myocardial wall motion abnormalities in the target area. PTCA balloon inflation time was taken as an index of the duration of the coronary occlusion.

Electrocardiographic evaluation
From the serial ECGs, all infarcts were classified as Q wave myocardial infarction (QMI) or non Q wave myocardial infarction (NQMI). The diagnosis of QMI was based on Q waves 0.04 second or greater in duration and amplitude greater than 25% of following R wave, associated with evolving ST segment and T wave changes in the same lead. Q waves in lead III alone were not considered adequate for diagnosis of inferior wall Q wave infarction. In the case of posterior infarction, the presence of R waves 0.04 second or greater in duration with RV1/SV1 and/or RV2/SV2 greater than 1 associated with evolving ST segment and T wave changes in lead V1 and/or V2 was required. ECG criteria for NQMI included persistent ST or T wave changes without development of diagnostic Q waves.

Resting 201Th myocardial scintigraphy
Resting thallium-201 (201Tl) myocardial scintigraphy was performed in 26 patients. The patients were injected intravenously with 148 MBq (4 mCi) of 201Tl while seated. They were then placed supine on a scintigraphic imaging table. Single photon emission computed tomography (SPECT) imaging was carried out with a 180° imaging arc (45° right anterior oblique to 45° left posterior oblique) and 18 acquisitions of 50 second each. Data were acquired with a large field-of-view rotating gamma camera (ZLC-7500, Siemens Gammasonics, Inc., Chicago, USA) equipped with a high resolution collimator, and stored in an on-line computer system (Scintipac 2400, Shimadzu Co., Ltd., Kyoto, Japan). Initial and delayed myocardial imagings were carried out 10 minutes and 2 hours, respectively, after the injection of 201Tl. Each projection was stored as a 64 x 64 matrix in a dedicated computer. The pixel size was adjusted so that the actual thickness of the slice was 6 mm/pixel. Six tomographic projection images (i.e. transverse, coronal, sagittal, vertical long axial, horizontal long axial and short axial) in each initial and delayed acquisition were reconstructed for visual interpretation, jointly by three experienced physicians. Redistribution was considered to have occurred when there was “filling in” of the defects or an improvement in the hypoperfusion in delayed SPECT images.

Cardiac catheterization
Coronary arteriograms were obtained in multiple projections by means of either Judkins or Sones technique. Left ventriculography (LVG) was performed at the projection of 30° right anterior oblique and 45° left anterior oblique for evaluation of abnormal wall motion and calculation of the left ventricular ejection fraction (LVEF). Wall motion abnormalities were classified into the following four: normal, reduced, none, dyskinetic without reference of the scintigraphic data. LVEF was calculated by the area-length method.11 Grades of collateral filling from the contralateral vessel were: absent; poor = filling of side branches of the artery to be dilated via collateral channels without visualization of the epicardial segment; good = filling of the epicardial segment of the artery being dilated via collateral channels. The angioplasty procedure was performed by the femoral approach according to the standard technique. Balloon dilatation catheters and guide wires of various sizes were used as clinically indicated. Angiographic success was defined as a final stenosis of less than 50%. None of the patients developed complications such as coronary dissection, acute coronary occlusion, side branch occlusion, or distal embolization. No perfusion catheter was used in any of the subjects.

In the 46 patients who were restudied 3 to 4 months after PTCA, LVG was done to assess the impact of revascularization. Restenosis was defined as a luminal narrowing of more than 75% at the previously dilated site.

Statistical analysis
Data are expressed as the mean ± SD. Statistical comparisons were performed by appropriate t-test. Chi-square test and Fisher's exact test were also used to determine the significance of difference in observed rates of occurrence when appropriate. Namely, when the expected frequencies were less than five, Fisher's exact test was substituted. Differences of p < 0.05 were considered significant.
RESULTS

Serial change in serum MLCI due to PTCA
No patient in the AP group had a significant increase in their serum MLCI level (Fig. 4). In the MI group,

16 of the 57 patients (28.0%) had an increase in serum MLCI of 1.0 ng/ml or more (from 1.3±1.0 to 3.1±1.2 ng/ml) after PTCA (Fig. 5): MI1 group. The remaining 41 patients showed no significant increase: MI2 group (Fig. 6). All of the patients in the MI1 group had the highest serum MLCI at 48 hours among the three post-PTCA sera. When compared with pre-PTCA levels, MLCI increased by less than 1.0 ng/ml immediately and 8 hours after PTCA, but by 1.0 ng/ml or more 48 hours after PTCA.

Clinical features of the MI1 and MI2 groups
Tables 2 and 3 show the clinical features of the MI1 and MI2 groups. There were no differences between the MI1 and MI2 groups in age, gender or length of time from the onset of myocardial infarction to elective PTCA. However, the MI1 group contained significantly more patients with NQMI than the MI2 group (10 of 16 (62.5%) vs. 7 of 41 (17.1%), p<0.01

Table 2 Comparison of clinical features between the MI1 and MI2 groups

<table>
<thead>
<tr>
<th></th>
<th>MI1:</th>
<th>MI2:</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMLCI ≥ 1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)*</td>
<td>64.4±9.4</td>
<td>61.4±7.6</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/7</td>
<td>32/9</td>
<td>NS</td>
</tr>
<tr>
<td>Interval between AMI and PTCA (days)*</td>
<td>107±85</td>
<td>181±186</td>
<td>NS</td>
</tr>
<tr>
<td>ECG</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q wave MI</td>
<td>6 (37.5%)</td>
<td>34 (82.9%)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>non-Q wave MI</td>
<td>10 (62.5%)</td>
<td>7 (17.1%)</td>
<td></td>
</tr>
<tr>
<td>T inversion</td>
<td>11 (68.8%)</td>
<td>20 (46.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary % stenosis</td>
<td>100%</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>99%</td>
<td>0</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>90%</td>
<td>8 (50.0%)</td>
<td>5 (12.2%)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>75%</td>
<td>7</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Collaterals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>11</td>
<td>23</td>
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</tr>
<tr>
<td>Poor</td>
<td>4</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Good</td>
<td>1 (6.3%)</td>
<td>14 (34.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Wall motion (LVG)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Reduced</td>
<td>8</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>None</td>
<td>6</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Dyskinetic</td>
<td>1</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>(Aneurysmal)</td>
<td>(0)</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td>Inflation time of PTCA balloon (sec)*</td>
<td>394±192</td>
<td>453±329</td>
<td>NS</td>
</tr>
<tr>
<td>201TI scintigraphy redistribution</td>
<td>6/7 (85.7%)</td>
<td>3/19 (15.8%)</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

AMI=acute myocardial infarction; ECG=electrocardiogram; LVG=left ventriculography; MI=myocardial infarction; MLCI=myosin light chain 1; NS=not significant; PTCA=percutaneous transluminal coronary angioplasty. * Values are mean±standard deviation.
Table 3  Summary of clinical characteristics of 16 cases in the M1 group

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/Sex</th>
<th>ECG</th>
<th>Target CA</th>
<th>Stenosis (%)</th>
<th>Collateral development</th>
<th>Wall motion (LVG)</th>
<th>201TI scintigraphy</th>
<th>MLCI (ng/ml) B/A</th>
<th>LVEF B/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40/M</td>
<td>NQ</td>
<td>13</td>
<td>99</td>
<td>Absent</td>
<td>None</td>
<td>RD (+)</td>
<td>1.2/2.8</td>
<td>0.39/0.49</td>
</tr>
<tr>
<td>2</td>
<td>67/M</td>
<td>NQ</td>
<td>13</td>
<td>99</td>
<td>Absent</td>
<td>Reduced</td>
<td>RD (+)</td>
<td>1.7/3.1</td>
<td>0.47/0.59</td>
</tr>
<tr>
<td>3</td>
<td>64/M</td>
<td>NQ</td>
<td>7</td>
<td>99</td>
<td>Absent</td>
<td>Reduced</td>
<td>RD (+)</td>
<td>0.0/3.0</td>
<td>0.63/0.68</td>
</tr>
<tr>
<td>4</td>
<td>71/F</td>
<td>NQ</td>
<td>7</td>
<td>90</td>
<td>Good</td>
<td>Reduced</td>
<td>ND</td>
<td>2.1/3.3</td>
<td>0.48/0.69</td>
</tr>
<tr>
<td>5</td>
<td>78/F</td>
<td>NQ</td>
<td>11</td>
<td>90</td>
<td>Absent</td>
<td>Reduced</td>
<td>ND</td>
<td>1.9/4.0</td>
<td>0.61/0.69</td>
</tr>
<tr>
<td>6</td>
<td>57/M</td>
<td>Q</td>
<td>1</td>
<td>90</td>
<td>Poor</td>
<td>Reduced</td>
<td>ND</td>
<td>2.6/3.6</td>
<td>0.56/0.56</td>
</tr>
<tr>
<td>7</td>
<td>69/M</td>
<td>NQ</td>
<td>7</td>
<td>99</td>
<td>Absent</td>
<td>None</td>
<td>ND</td>
<td>0.0/1.3</td>
<td>0.55/0.59</td>
</tr>
<tr>
<td>8</td>
<td>56/F</td>
<td>Q</td>
<td>4</td>
<td>90</td>
<td>Absent</td>
<td>Dyskinetic</td>
<td>ND</td>
<td>0.0/3.7</td>
<td>0.24/0.33</td>
</tr>
<tr>
<td>9</td>
<td>56/F</td>
<td>Q</td>
<td>7</td>
<td>99</td>
<td>Absent</td>
<td>None</td>
<td>ND</td>
<td>3.5/5.9</td>
<td>0.33/0.51</td>
</tr>
<tr>
<td>10</td>
<td>74/F</td>
<td>Q</td>
<td>1</td>
<td>99</td>
<td>Absent</td>
<td>Reduced</td>
<td>ND</td>
<td>0.0/1.6</td>
<td>0.57/0.68</td>
</tr>
<tr>
<td>11</td>
<td>66/M</td>
<td>NQ</td>
<td>6</td>
<td>75</td>
<td>Absent</td>
<td>Reduced</td>
<td>ND</td>
<td>0.9/2.3</td>
<td>0.51/0.52</td>
</tr>
<tr>
<td>12</td>
<td>72/M</td>
<td>NQ</td>
<td>15</td>
<td>90</td>
<td>Poor</td>
<td>None</td>
<td>RD (+)</td>
<td>2.1/3.4</td>
<td>0.37/ND</td>
</tr>
<tr>
<td>13</td>
<td>63/F</td>
<td>Q</td>
<td>2</td>
<td>99</td>
<td>Poor</td>
<td>None</td>
<td>RD (+)</td>
<td>1.2/2.4</td>
<td>0.39/0.53</td>
</tr>
<tr>
<td>14</td>
<td>59/M</td>
<td>Q</td>
<td>2</td>
<td>90</td>
<td>Absent</td>
<td>Reduced</td>
<td>ND</td>
<td>1.9/5.1</td>
<td>0.65/0.69</td>
</tr>
<tr>
<td>15</td>
<td>78/F</td>
<td>NQ</td>
<td>7</td>
<td>99</td>
<td>Poor</td>
<td>None</td>
<td>RD (+)</td>
<td>0.9/2.6</td>
<td>0.36/0.48</td>
</tr>
<tr>
<td>16</td>
<td>61/M</td>
<td>NQ</td>
<td>6</td>
<td>90</td>
<td>Absent</td>
<td>Normal</td>
<td>ND</td>
<td>0.7/1.8</td>
<td>0.54/0.74</td>
</tr>
</tbody>
</table>

A = after PTCA; B = before PTCA; CA = coronary artery defined by the American Heart Association committee report; ECG = electrocardiogram; LVEF = left ventricular ejection fraction; LVG = left ventriculography; MLCI = myosin light chain I; ND = not done; NQ = non-Q wave myocardial infarction; Q = Q wave myocardial infarction; RD = redistribution.

Table 4 Changes in serum CK and Mb during pre-and post-PTCA in the M1 group

<table>
<thead>
<tr>
<th></th>
<th>Before PTCA</th>
<th>After PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 hours</td>
<td>8 hours</td>
</tr>
<tr>
<td>CK (IU/l)</td>
<td>67±30</td>
<td>59±20</td>
</tr>
<tr>
<td>Mb (ng/ml)</td>
<td>36±20</td>
<td>37±20</td>
</tr>
</tbody>
</table>

CK = creatine kinase; Mb = myoglobin; PTCA = percutaneous transluminal coronary angioplasty. Upper limit of normal is 195 IU/l in men and 180 IU/l in women for CK; 60 ng/ml for Mb. Values are mean ± standard deviation.

201TI image and improvement in LVEF
On the delayed images with resting 201TI myocardial scintigraphy obtained in 26 patients, redistribution in the hypoperfusion area was noted in 6 of the 7 patients in the M1 group (85.7%), significantly more frequent than in the M1 group (3 of 19 patients, 15.8%, p<0.01 by Fisher's exact test) (Table 2).

Fifteen patients in the M1 group had a significant improvement in LVEF (from 0.49±0.12 to 0.58±0.11, p<0.01). In 11 patients who did not develop restenosis, there was a 5% or greater improvement in LVEF. In the remaining 4 patients, LVEF improvement was less than 5% of pre-PTCA levels, and 2 of the 4 patients developed restenosis. In contrast, LVEF did not improve in the 31 patients in the M2 group (from 0.53±0.13 to 0.54±0.12) although only 1 patient developed restenosis (Fig. 7).

Correlation of change in MLCI with CK and Mb
None of the patients had abnormalities in CK or Mb values (Table 4).

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DISCUSSION

Release of MLCI after PTCA

As to the PTCA for angina of effort, it has been
reported that unstable angina, coronary spasm and
intimal tear lead to the release of CK but that in
successful PTCA, no release of CK was noted.9
Measurement of CK-MB at 4 hour intervals after
PTCA failed to demonstrate either complications or
CK-MB release despite the high incidence of tran-
sient chest pain and ECG changes. It has therefore
been reported that PTCA does not cause myocardial
injury.6 However, in their study with Mb, Pauletto
et al.7 noted the release of Mb as well as CK-MB,
suggesting myocardial injury at the intramyocardial
Mb structural level. Such divergence in the findings
regarding the release of intramyocardial substances
may be attributed to the following reasons: the
changes in CK, CK-MB and Mb after PTCA are
slight, if any; and the release reaches a peak in a
very short time (4-8 hours for CK and 2-4 hours for
Mb). We regard the changes in MLCI as a more
reliable index of myocardial necrosis. This study
demonstrated that MLCI increased in the MI group
but not in the AP group.

In the AP group, no myocardial wall motion
abnormalities were noted in the area dominated by
the PTCA-targeted coronary artery. The patients
appeared to have a “normal” myocardium. In these
patients, MLCI did not increase significantly follow-
ing PTCA, and this result is compatible with
previous findings. In other words, this supports the
hypothesis8-5 that a brief (from several seconds to
minutes) coronary occlusion associated with PTCA
do not cause injury to the normal myocardium.

However, in the MI group, most of the patients
had increased MLCI 48 hours after the PTCA-
related brief coronary occlusion without detection of
CK or Mb release. Whereas the AP group consisted
almost entirely of patients with coronary stenosis of
90% or less, the MI group contained patients with
99% stenosis, and their myocardium was therefore
thought susceptible to myocardial injury by PTCA.

The release of MLCI may be attributable to myo-
cardial injury due to (1) transient coronary artery
occlusion, (2) reperfusion injury associated with
relief of a severe stenosis, or (3) microembolism. If
the release of MLCI occurs as described in the first
hypothesis, this may correspond with the observation
that MLCI increases approximately 48 hours after
the onset of acute myocardial infarction.1,2 How-
ever, in experimental infarction, it has been observed
that MLCI release results from a decrease in myo-
fibrillar ATPase activity about 48 hours after the
start of ischemia.12,18 It was also assumed that
PTCA-associated localized lesions might lead to
intracoronary thrombus formation. But, in view of
the absence of cases with increased serum MLCI in
the AP group, this possibility seems remote.

With elective PTCA in patients with 100% steno-
sis, no significant changes in MLCI were noted. The
following reasons may be considered: myocardial
necrosis was completed in the dominant area of 100%
stenosis without any viable myocardium which can
be saved with reperfusion therapy; the remaining
myocardium was not so ischemic even if reper-
fusion was not conducted; or the PTCA-associated
coronary occlusion was minor due to the develop-
ment of collateral circulation.

Furthermore, the fact that MLCI increases regard-
less of the duration of the coronary occlusion sug-
gests that the release of MLCI is related with the
extent of stenosis in the targeted coronary artery and
the condition of the myocardium. Two patients in
the MI1 group (Nos. 6 and 9 in Table 3) had high
MLCI (>2.5 ng/ml) before PTCA, and they might
have had severe silent myocardial ischemia.

Possible pathophysiological significance

It has also been demonstrated that NQMI is closely
related to non-transmural and subendocardial infarc-
tion.14 Ischemic areas that are not completely
necrotized have been found in cases of NQMI.15 This
has been demonstrated by means of 201Tl myocardial
cintigraphy. Typically, it has been shown that 201Tl
redistribution cintigraphy appears to reliably distin-
guish viable from nonviable asynergic myocardial
zones,16,17 and predicts the response of these seg-
ments to coronary arterial bypass grafting18,19 or
PTCA.20 Therefore, the myocardium of the MI1
group subjects may contain predominantly viable
muscle.

Furthermore, in the MI1 group revascularization
with PTCA had produced an improvement in LVEF
when examined 3 or 4 months afterwards. Braunwald
et al.21 proposed the term “hibernating myocar-
dium”: ischemic myocardium results from months
or years of ischemia and ventricular dysfunction
persists until the blood flow is restored. The ischemia
can be relieved with bypass surgery or coronary
revascularization such as PTCA, followed by an
improvement in systolic function. Cohen et al.22
noted that successful PTCA was useful in salvaging
chronic ischemic myocardium. The serum MLCI
increased after PTCA was thought to be released
from the chronically underperfused but still sal-
vageable bulk of the myocardium.

Repeated ischemic episodes cause derangement
of membrane permeability in the area perfused by
the coronary artery with 99% stenosis.4,9 This
suggests that if coronary occlusion during PTCA results in
new ischemia, intracellular dissociation of MLCI

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is likely to occur. This hypothesis may be in disagreement with the theory of ischemic preconditioning. However, in an animal experiment, transient ischemia is produced by occlusion of the intact coronary artery. Therefore, the results of that experiment may not be identical to the hibernating myocardium. Although ischemic preconditioning in human beings has also been described, the MI group consisted mainly of patients with 99% stenosis of the coronary artery. Furthermore, it remains unclear whether the ischemic preconditioning exists in hibernating myocardium in the adjacent area to the infarcted myocardium.

It will now be important to examine when the hypoperfusion seen in Tl myocardium scintigraphy improves after PTCA as compared with before PTCA and whether CK or Mb release can be detected in a shorter period of blood collection than in the present study.

CONCLUSIONS

In the MI group, 16 of the 57 patients (28.0%) had an increase in serum MLCI of 1.0 ng/ml or more after PTCA. There was a higher incidence of NQMI, 99% stenosis of the PTCA-targeted coronary artery, and redistribution in hypoperfusion areas in the delayed images with resting Tl scintigraphy.

REFERENCES


