Characteristics of the Pathological Images of Coronary Artery Thrombi According to the Infarct-Related Coronary Artery in Acute Myocardial Infarction

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Background  Unstable plaque and coronary arterial thrombi sometimes induce a no-reflow phenomenon after intervention whereby there is insufficient reperfusion. The greater susceptibility of the right coronary artery to development of large thrombi makes successful reperfusion more difficult, therefore the characteristics of the pathological images of coronary arterial thrombi according to the infarct-related coronary artery were investigated.

Methods and Results  Coronary arterial thrombi were extracted from 77 patients with acute myocardial infarction (AMI) using a thrombectomy catheter. The 36 patients had a thrombus containing atherosclerotic cells. Platelets, fibrin, and neutrophils were seen in all cases. The mean ratios of structural components of thrombi were 51.0±29.5% (mean±SD) of the platelet component, 19.9±25.7% of the erythrocyte component and 11.9±22.5% of atherosclerosis component. Erythrocyte-rich thrombi and mixed thrombi mainly composed of erythrocytes were seen in 14 of the 30 cases involving the right coronary artery, 6 of the 35 cases in the left anterior descending artery, 2 of the 11 cases of the left circumflex artery, and in the 1 case of saphenous vein bypass graft. There was significantly more erythrocyte component in the thrombi from the right coronary artery (28.7±30.1%) than in those from the left coronary artery (12.1±18.4%).

Conclusion  Coronary artery thrombi in AMI are composed principally of platelets. Atherosclerotic cells were identified within thrombi from some patients. In the right coronary artery there were many more thrombi that were rich in erythrocytes than in thrombi from the left coronary artery. (Circ J 2004; 68: 308–314)

Key Words:  Acute myocardial infarction; Coronary artery thrombus; Thrombectomy

Percutaneous coronary intervention (PCI) is an effective treatment in the early phase of acute myocardial infarction (AMI),1–3 but the unstable plaque and coronary arterial thrombi that are involved in the onset of AMI sometimes induce the no-reflow phenomenon after PCI whereby there is insufficient reperfusion.4 There is a high incidence of the no-reflow phenomenon or slow flow in AMI in which the right coronary artery (RCA) is the culprit lesion.4–6 The greater susceptibility of the RCA to developing large thrombi makes successful reperfusion more difficult, therefore the characteristics of the pathological images of coronary arterial thrombi according to the infarct-related coronary artery were investigated.

Methods

Subjects  Subjects were 231 patients with AMI who had sought treatment at Toyama Prefectural Central Hospital during a 30-months period from September 2000 to February 2003 and who had undergone emergency coronary angiography. AMI was diagnosed when chest pain persisted for at least 30 min and the 12-lead ECG confirmed ST elevation of at least 2 mm in at least 2 leads in succession, and there was confirmation by initial coronary angiography of occlusion or sub-occlusion of the infarct-related artery. Of the 199 patients indicated for PCI, 129 underwent thrombectomy. Patients who were scheduled for coronary bypass surgery (multivessel disease and left main trunk lesion), patients who could not undergo coronary arterial thrombectomy because of serious complications (fatal arrhythmia, cardiogenic shock, and pulmonary edema), and patients who had undergone thrombolytic therapy before emergency coronary angiography were excluded from the study. Of the 129 patients who underwent coronary arterial thrombectomy, there were 77 cases in which the coronary artery thrombi could be extracted for study within 24 h of the onset of AMI.

Cardiac Catheterization and Coronary Intervention  Written informed consent was obtained from all patients, after the patients and their families were informed of the
Intracoronary Thrombus of AMI

All patients received our standard treatment: isosorbide dinitrate, heparin (7,000–10,000 IU), and aspirin (162–200 mg/day).

Coronary angiography was performed via insertion of a 7Fr guiding catheter into the right femoral artery and was interpreted by experienced angiographers using a caliper method based on the criteria proposed by the American Heart Association. When a thrombotic occlusion or subocclusion was seen at the culprit lesion, coronary arterial thrombectomy was performed as the subsequent procedure. After a 0.014-inch PCI guide wire was passed through the lesion site, a 4.5Fr thrombectomy catheter (Rescue PT system®, Boston, MA, USA) was inserted into the coronary artery. While applying negative pressure of 650 mmHg, the thrombectomy catheter was inserted anterior to the thrombus toward the periphery, and the substance within the coronary artery was aspirated. After repeated intra-arterial aspiration, angioplasty was also repeated to reduce the degree of residual stenosis in all regions of the infarct-related artery vessel to <25% with thrombolysis in myocardial infarction (TIMI) grade 3 flow.

Pathologic Examination

Thrombi that were aspirated and placed in a collection bottle were fixed in formalin buffer solution and pathology samples were prepared. These materials were stained with hematoxylin and eosin, azan and KP-1. Each sample was observed under a light microscope, and the platelet compo-

![Fig 1. Pathological findings of a coronary artery thrombus. (A) Platelet component (hematoxylin and eosin (H&E), ×100); (B) erythrocyte component, (H&E, ×100); (C) atherosclerosis component (KP-1, ×200); (D) conglomeration of leukocytes (H&E, ×100).](image)

![Fig 2. A case of 77 year-old female. A thrombotic occlusion was seen in the segment 6 left anterior descending artery. When the coronary arterial thrombi were aspirated using a thrombectomy catheter, blood flow recovered to TIMI grade 3. The extracted thrombi were 13×2 mm in size.](image)
nent (Fig 1A), erythrocyte component (Fig 1B), atherosclerosis component (Fig 1C), and edematous component were evaluated and the ratios determined. An edematous component was classified as the lack of both the atherosclerosis and blood corpuscle components. A platelet-rich thrombus was defined as that in which the platelet component was at least twice that of the erythrocyte component, an erythrocyte-rich thrombus was defined as that in which the erythrocyte component was at least twice that of the platelet component, and all others were defined as a mixed thrombus. The amounts of leukocytes (Fig 1D) and fibrin in each thrombus were classified as one of 3 levels: low, moderate and high. The level was classified as low when the leukocytes in the thrombus were scattered, moderate when there was some cell conglomeration, and high when there were many conglomerations of cells.

Statistical Analysis
Data are presented as mean value±SD. The comparison of characteristics of the thrombi of the infarct-related coronary arteries was obtained by Student’s t-test or by chi-square test for independent samples. All calculations were performed on a personal computer using the statistical package Stat View (Abacas Concepts, Inc, Berkeley, CA, USA; 1995). A p-value <0.05 was considered significant.

Results

Case Presentation
Fig 2 shows the coronary angiogram findings and extracted thrombus sample from a 77 year-old female. A thrombotic occlusion was seen in segment 6 of the left anterior descending artery (LAD). When the coronary arterial thrombi were aspirated using a thrombectomy catheter, blood flow recovered to TIMI grade 3. The extracted thrombi were 13×2 mm in size.

Characteristics of the Subjects
The clinical characteristics of subjects are shown in Table 1. The vessel responsible for the infarct was the RCA in 30 cases, the LAD in 35 cases, the left circumflex artery (LCX) in 11 cases, and a saphenous vein bypass graft in 1 case. The TIMI grade of coronary blood flow at the time of initial angiography was grade 0 in 59 cases, grade 1 in 14 cases, and grade 2 in 4 cases. The 6 LAD cases and 1 saphenous vein bypass graft case were treated with either an anticoagulant or an antiplatelet drug (aspirin or cilostazol). These drugs were administered significantly more often to the LAD group than to the RCA and LCX groups. The mean time from chest pain to thrombectomy in the LCX group was slightly but insignificantly shorter than those of the RCA and LAD groups.

Table 1 Characteristics of the Subjects With Acute Myocardial Infarction

<table>
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<tr>
<th></th>
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<th>RCA</th>
<th>LAD</th>
<th>LCX</th>
<th>SVG</th>
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<td>35</td>
<td>11</td>
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<tr>
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<td>62±11</td>
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Table 2 Structural Components of the Coronary Artery Thrombi

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<th>LAD</th>
<th>LCX</th>
<th>SVG</th>
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<td>Platelet component (%)</td>
<td>51.0±29.5</td>
<td>44.3±30.5*</td>
<td>59.6±27.1</td>
<td>44.5±30.2</td>
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<td>Erythrocyte component (%)</td>
<td>19.9±25.7</td>
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<td>Edematous component (%)</td>
<td>17.1±19.7</td>
<td>19.3±22.4</td>
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<tr>
<td>Atherosclerosis component (%)</td>
<td>11.9±22.5</td>
<td>7.7±16.9</td>
<td>12.6±21.5</td>
<td>22.3±35.8</td>
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RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; SVG, saphenous vein bypass graft.
*p<0.05 compared with LAD group.
Table 2 shows the characteristics of the infarct-related arteries and thrombi in the cases studied. The mean ratios of structural component of thrombi were 51.0±29.5% of the platelet component and 19.9±25.7% of the erythrocyte component. In the RCA group, the erythrocyte component was significantly more and the platelet component was significantly less than in the LAD group. Thirty-six of the 77 cases (47%) were thrombi containing atherosclerotic cells in which cholesterin, foam cells, collagen fiber, and elastic fiber were evident. The mean ratio of the atheroscle-
rosis component of the thrombi was 11.9±22.5%. Fibrin and leukocytes were seen in the thrombi from all patients, and the leukocytes were mainly neutrophils.

Figs 3–5 show the results of an investigation into the properties of the thrombi in each case based on the microscopic samples. There were 54 cases of platelet-rich thrombi, 14 cases of erythrocyte-rich thrombi, and 9 cases of mixed thrombi (Table 3). In particular, thrombi made up of at least 50% of the platelet component were predominant (41 cases). The size of the platelet-rich thrombi ranged from 0.5 to 8 mm. There were 13 cases of platelet-rich thrombi that were at least 4 mm, but most (41 cases) were small thrombi of less than 4 mm. Of the erythrocyte-rich thrombi and mixed thrombi there were 8 cases of thrombi less than 4 mm, 15 cases of thrombi of at least 4 mm and 6 cases of large thrombi of 10–40 mm.

Erythrocyte-rich thrombi and mixed thrombi occurred in 14 of 30 RCA cases (46.7%), 6 of 35 LAD cases (17.1%), 2 of 11 LCX cases (18.1%), and the 1 saphenous vein bypass graft case (Table 3). The thrombi in the RCA and saphenous vein bypass graft had a high erythrocyte component ratio (Table 2), with many large thrombi of 11–40 mm seen (Fig 3, Fig 5). Thrombi in the left coronary artery (LCA) were primarily composed of platelets, and most were small thrombi of no more than 10 mm (Fig 4, Fig 5).

**Characteristics of the Thrombi and Coronary Artery Narrowing Before Intervention**

Table 3 shows the characteristics of the coronary artery thrombi and grade of coronary narrowing in this study. In terms of the degree of coronary artery narrowing, there were 59 cases of total occlusion and 18 cases of sub-occlusion (≤99%). Platelet-rich thrombi occurred in 40 of 59 cases of total occlusion (67.8%) and 14 of 18 cases of sub-occlusion (77.8%). Erythrocyte-rich thrombi and mixed thrombi occurred in 19 of 59 cases of total occlusion (32.2%) and 4 of 18 cases of sub-occlusion (22.2%). There tended to be more cases of total occlusion than sub-occlusion among patients with erythrocyte-rich thrombi and mixed thrombi, but the difference was not significant.

![Fig 5. Pathological characteristics of coronary artery thrombi (left circumflex artery and saphenous vein bypass graft).](image-url)
Intracoronary Thrombus of AMI

Right Coronary Artery and Left Coronary Artery

Table 4 shows the ratios of the structural components of the RCA and LCA thrombi in this study. The LAD cases that received an anticoagulant drug or antiplatelet drug were excluded from this analysis. In the RCA group (N=30), the platelet component was 44.3±30.5% and the erythrocyte component was 28.7±30.1%. In the LCA group (N=40), the platelet component was 56.6±27.4% and the erythrocyte component was 12.1±18.4%. The erythrocyte component was significantly more in the RCA group than in the LCA group.

Fig 6 shows the comparison of the structural components and size of the thrombi in this study. Of the small thrombi of less than 4 mm, the erythrocyte component was significantly more in the RCA group than in the LCA group (RCA: 18.1±25.0%, LCA: 7.2±7.4%, p=0.006). Of the large thrombi of at least 4 mm, the platelet component was significantly less in the RCA group than in the LCA group (RCA: 25.0±15.2%, LCA: 51.9±23.1%, p=0.039). Of these, the RCA group had a more erythrocyte component than did the LCA group, but no significant difference was evident (RCA: 44.6±28.5%, LCA: 22.3±18.0%, p=0.074).

Discussion

One of the important causes of the onset of acute coronary syndrome, based on the pathology images of autopsy cases13,14 or coronary angiograms15-17 is thrombogenesis accompanied by atheroma rupture. We have previously observed by light microscopy the coronary arterial thrombi that were extracted using thrombectomy, and we investigated pathologically the components of those coronary artery thrombi. As a result, we reported that many thrombi in the early phase of AMI had a more platelet component11. In the present study we further confirmed that coronary artery thrombi in the RCA are rich in erythrocytes.

In acute coronary syndrome, inflammatory cells promote platelet thrombus formation through plaque non-stabilization18,19 and P-selectin activation20. The fact that the leukocytes identified within the coronary artery lumen were principally neutrophils suggests the presence of inflammation within the coronary artery in acute coronary syndrome. It is possible that neutrophils conglomerating in the thrombi promote thrombus growth after plaque rupture. In the present study there were no differences in the inflammatory cells according to the infarct-related coronary artery.

Recently, Kotani et al reported that no-reflow after PCI may be caused by the gruel that forms from the atheroma attributable to mechanical plaque disruption during the intervention10,21. In the present study, many coronary artery thrombi contained atherosclerotic cells and there was some plaque that had partially ruptured. Therefore, it is possible that the atherosclerotic cells become the cause of the no-reflow phenomenon after PCI.

After the plaque has ruptured, a thrombus began to form. The small thrombi extracted in the present study were mostly platelet-rich thrombi, whereas the erythrocyte-rich thrombi and mixed thrombi were large. This is thought to reflect a process whereby a small platelet thrombus forms because of platelet adherence and aggregation, and then a secondary thrombus develops from deposition of erythrocytes following a decrease in coronary blood flow. The fact that antiplatelet drugs such as aspirin, ticlopidine, and GP IIb/IIIa receptor inhibitor prevent the onset of AMI indicates the importance of platelets in the thrombogenesis in the coronary arteries22,23. Identification of a platelet component in all cases of coronary artery thrombi in the present study supports the importance of antiplatelet therapy.

Platelet-rich thrombi composed chiefly of platelets and fibrin were seen often in the LCA when it was the infarct-related coronary artery. It became clear that in the RCA,
compared with the LCA, the volume of thrombus was large and there was a more erythrocyte component. Indications are that erythrocyte-rich thrombi that form because of a reduction in coronary blood flow after platelet thrombogenesis are more likely to occur in the RCA. The one case of thrombus in a saphenous vein bypass graft had a more erythrocyte component, but as this was a single case, it will not be referred to in the present investigation.

In the thrombi from the RCA, the erythrocyte component was more than in those from the LCA and this increased erythrocyte component was already beginning to emerge in the small thrombi. In large thrombi, there was a significantly less platelet component in the RCA group compared with the LCA group and this decreased platelet component was the consequence of the increased erythrocyte component. It has been reported that in cases of deterioration of coronary blood flow after PCI, the coronary artery responsible was the RCA and that is was related to the diameter thickness of the coronary artery.24 Furthermore, Nakano et al reported that the predictive factors for massive thrombus in the RCA were coronary artery diameter and elapsed time.25 The RCA has fewer branching vessels and a thicker vessel lumen than the LCA so it is likely that once the coronary occlusion occurs, erythrocyte-rich thrombi would be prone to develop and the thrombus volume would be prone to increase. It is possible that such an erythrocyte-rich massive thrombus becomes the cause of slow flow after PCI.

Study Limitations
In the present study microscopic observations were conducted to evaluate the structural components of the coronary arterial thrombi, but there were some patients in whom it was difficult to aspirate all of the thrombus within the coronary artery using the Rescue PT system. Therefore, it cannot be ruled out that in patients in whom only some of the coronary artery thrombus was evaluated, the structural components of the sample might differ from the actual thrombus. A sample of a thrombus that had ruptured during catheter aspiration could also be included. However, at our institution we confirm by coronary angiography that aspiration of the thrombus has been sufficient, without administering thrombolytic drugs before emergency PCI, and so any effects on the determination of the structural components within the thrombus are thought to be minimal.

Conclusion
Coronary artery thrombi in AMI are composed principally of platelets. Atherosclerotic cells were identified within the thrombi in some patients when the plaque rupture has occurred. We also showed that in AMI in which the culprit lesions were in the RCA, there were many large thrombi principally made up of erythrocytes.

References