The role of intracoronary thrombus in unstable angina: angiographic assessment and thrombolytic therapy during ongoing anginal attacks

Koichi Gotoh, M.D., Takazo Minamino, M.D., Ph.D., Osamu Katoh, M.D., Yutaka Hamano, M.D., Sugao Fukui, M.D., Ph.D., Masatsugu Hori, M.D., Ph.D., Hideo Kusuoka, M.D., Ph.D., Masayoshi Mishima, M.D., Ph.D., Michitoshi Inoue, M.D., Ph.D., and Takenobu Kamada, M.D., Ph.D.

ABSTRACT Intracoronary thrombus is regarded as a potentially important factor in the etiology of unstable angina, but the incidence of intracoronary thrombus in unstable angina has not been clearly defined. To determine the occurrence of intracoronary thrombus during ongoing angina pectoris, coronary angiography was performed during spontaneous ischemic attacks in 37 patients with prolonged rest angina. All patients exhibited significant (>50%) stenoses of at least one major coronary artery. Of the 37 patients, 21 (57%) had intracoronary thrombus in major coronary arteries, whereas 14 (38%) had fixed narrowings without evidence of intracoronary thrombus and two exhibited coronary spasm. ST segment elevation was observed in 16 of 21 patients with thrombus and in all of the patients with coronary spasm, but all the patients with organic stable obstruction showed ST segment depression. Twenty of the 21 patients with thrombus improved after thrombolytic therapy with intracoronary injection of urokinase; obstructed arteries were reopened, or narrowings were attenuated, with relief of ischemic symptoms. In patients with fixed obstructions, the rate-pressure product during active symptoms was significantly higher than during an asymptomatic period, indicating that a transient increase in myocardial oxygen demand may contribute to the ischemic attack in these patients. A high incidence (71%) of recurrent symptoms was observed in patients with intracoronary thrombus even after successful thrombolysis, in contrast to a much lower incidence (36%) in those without intracoronary thrombus. Myocardial infarction within 4 weeks after catheterization was observed more frequently in patients with intracoronary thrombus (24%) than in those without thrombus (7%). Thus our results indicate that the incidence of intracoronary thrombus is quite high during ongoing attacks of unstable angina, although a transient increase of myocardial oxygen demand also plays an important etiologic role. It is also suggested that patients with thrombus fare less well than those with organic stable obstruction.


Recent angiographic studies have suggested that intracoronary thrombus plays an important etiologic role not only in myocardial infarction1–5 but also in unstable angina.6–14 Nevertheless, there is considerable variation in the reported incidence of coronary thrombus in patients with unstable angina, with figures varying from 1%7 to 85%8 in several reports.6–14 This inconsistency in the reported incidence of thrombus may be partly attributable to variability in the timing of angiographic study with respect to the last anginal attack; a relatively low incidence of thrombus (1% to 12%) was reported in patients catheterized 30 to 90 days after the last attack,6, 7, 9, 10, 12 whereas the incidence was higher (52% to 85%) when angiography was performed soon after active symptoms.8, 13, 14 Angioscopy performed during coronary artery bypass surgery also revealed a high incidence of intracoronary thrombus in patients with a history of unstable angina.15 Since intracoronary thrombus can form rapidly and resolve spontaneously, the possible role of coronary thrombus in the etiology of unstable angina should be evaluated during ongoing anginal attacks. This has not been evaluated systematically in earlier studies, so that the incidence of
in intracoronary thrombus during active symptoms remains unclear.

In the present study, to elucidate the role of coronary thrombus as a cause of recurrent prolonged rest angina, coronary angiography was performed during ongoing attacks in the patients with unstable angina; the incidence of intracoronary thrombus and the degree of coronary narrowings were assessed at the time of chest pain. Intracoronary urokinase was then given to determine the efficacy of thrombolytic therapy during an acute attack. We also investigated whether a transient increase in myocardial oxygen demand might contribute to the episodes of prolonged chest pain attack in patients with severe coronary stenosis not accompanied by thrombus.

Materials and methods

Of 202 consecutive patients during 42 months (from December 1982 to May 1986) who were diagnosed as having unstable angina and admitted to the coronary care unit in Sakurabashi Watanabe Hospital within 48 hr of prolonged rest anginal attacks, 37 were selected according to the following criteria: (1) recurrent prolonged (30 to 60 min) anginal attacks had occurred within 3 weeks before admission, without recent acute myocardial infarction, and refractory to medical treatment with nitrates, calcium antagonists, and $\beta$-blockers; (2) coronary angiography could be performed during a spontaneous anginal attack without any provocation such as ergonovine maleate; (3) the attack during coronary angiography was similar to prior ones in severity and duration of chest pain and electrocardiographic changes; (4) neither an increase in serum creatine kinase level (to more than twice the normal upper limit) nor a new abnormal Q wave were observed at the time of, or within 12 hr after, coronary angiography. In this study, the coronary angiography either happened to be performed during an episode of unstable angina or patients were actually taken to the catheterization laboratory during a prolonged symptomatic period. Finally, 150 patients were excluded from the study because angiography could not be performed during spontaneous ongoing attacks of unstable angina (due to resolution of the attack before catheterization), and 15 patients were excluded because of emergency treatment with percutaneous transluminal coronary angioplasty or coronary artery bypass surgery. Of the patients selected, 27 were men and 10 were women, with an average age of 61 years (range, 38 to 80 years). Informed consent was obtained from all patients who participated in the study.

Coronary angiography was performed from a brachial or femoral approach by standard catheterization techniques. Immediately after vascular access was achieved, heparin (6000 U) was administered intravenously. In the first coronary angiogram obtained during ongoing angina pectoris, all patients showed significant coronary artery stenoses (>50%). The angiogram was repeated after intracoronary injection of 0.3 mg of nitroglycerin. Relief of the stenosis by infusion of nitroglycerin (>50%) was interpreted as evidence for coronary vasospasm. When the lesion was not affected by nitroglycerin, urokinase (24,000 U/min for 10 to 40 min) was subselectively injected into the ischemia-related vessel (see below for the definition), and repeat coronary angiography was performed every 10 min up to 60 min. The patients who received urokinase were then heparinized (10,000 to 20,000 U/day) and intravenous urokinase, which was tapered over 3 days. Oral anticoagulation therapy with warfarin (controlled to 20% of normal by the thrombostest) was initiated and continued for at least 1 month. Some of the patients who revealed intracoronary thrombus were treated with aspirin (250 mg/day orally) after the catheterization. Thirty of 37 patients were restudied by angiography 4 weeks later to check for changes in the degree of coronary stenosis. Three patients could not be recruited for restudy because of noncardiac (panperitonitis, pneumonia) or cardiac sudden death. Four patients refused restudy.

The coronary angiograms were reviewed by two experienced angiographers independently and blindly. The most severe stenotic lesion of the ischemia-related artery was analyzed from multiple cineprojections, including cranial and caudal angulation projections. The diameter of the stenotic lesion was measured on images projected onto a screen ($\times$30) at 0.1 mm resolution, and stenosis was reported as percent reduction of the diameter of the normal proximal juxtaposed segment. The ischemia-related vessel was defined as the occluded or significantly stenosed vessel that corresponded most closely to the ischemic area determined by electrocardiography. Intracoronary thrombus was determined by the following criteria after the method of Vetrovec et al: (1) total coronary artery occlusion with convex, irregular, or hazy distal margins and postinjection contrast retention or staining in the absence of adjacent branches to maintain run-off or (2) nontotal occlusion with (a) shaggy or irregular margins or (b) a filling defect at or adjacent to a significant coronary stenosis seen in at least two projections. When the coronary lesion in the ischemia-related vessel could not be attributed to coronary spasm or thrombus, it was determined to be a fixed obstruction.

Data are presented as mean ± SEM. Statistical analysis was performed with the paired or nonpaired t test or the chi-square test where appropriate. The results were considered significant when the p value was less than .05.

Results

Intracoronary thrombus. Figure 1 depicts typical coronary angiograms from a patient with intracoronary thrombus. In the initial angiogram (figure 1, A) taken during an anginal attack (note the ST segment elevation shown in the inset), the left circumflex artery was totally obstructed with a frayed border, indicating the presence of intracoronary thrombus. After a 20 min infusion with 480,000 U of urokinase, the coronary obstruction was partially relieved, but a filling defect persisted (figure 1, B); the symptoms of chest pain ceased with normalization of the ischemic ST change (inset). Coronary angiography was repeated 4 weeks after thrombolysis, and the contour of the narrowed vessel was found to be smooth and regular (figure 1, C); this suggests that urokinase did not dissolve the thrombus completely, but the residual thrombus was eventually lysable.

Of the 37 patients in this study, 21 (57%) showed angiographic changes similar to those discussed above, with intracoronary thrombus identified as a contributor to the ischemic attack; four patients showed a total occlusion with frayed border and/or with staining of contrast medium. Eleven patients showed nontotal occlusion with a filling defect at or adjacent to a sig-
significant stenosis seen in at least two projections. Six patients showed nontotal occlusions with shaggy or irregular margins. Table 1 summarizes the features of the patients in this group. The distribution of intracoronary thrombus in all 21 cases of thrombus was as follows: 11 in the left anterior descending coronary artery, five in the left circumflex coronary artery, and five in the right coronary artery. Only one patient in this group failed to respond to infusion of urokinase (total of 960,000 U). The extent of coronary narrowings was improved immediately after infusion of urokinase (from 94.1 ± 1.1% [mean ± SEM] to 75.8 ± 2.9%). Despite the favorable response to urokinase, recurrent chest pain occurred in 15 patients in this group (71%) within 48 hr after thrombolysis (table 1).

In 18 patients with evidence of intracoronary thrombus, follow-up angiography was performed 4 weeks after thrombolysis. Recurrent prolonged rest angina had disappeared at the latest within 10 days of the initial angiography, and thrombus could no longer be detected angiographically in any of the patients.

**Organic stable obstruction.** Figure 2 demonstrates representative coronary angiograms from a patient whose anginal attack was caused by fixed obstruction without thrombus. Thrombus was not detected angiographically in the initial angiogram obtained during an anginal attack (figure 2, A). The subtotal obstruction and the delayed antegrade flow in the left anterior descending coronary artery were improved neither by the intracoronary injection of 0.3 mg of nitroglycerin nor by thrombolytic treatment with 960,000 U of urokinase for 60 min (figure 2, B). However, anginal pain and ST

---

**FIGURE 1.** Representative coronary angiograms demonstrating intracoronary thrombus during prolonged rest angina and reopening after thrombolysis. A, The initial appearance of the left coronary artery during chest pain. The left circumflex coronary artery is completely occluded. Contrast dye outline is convex with a ground glass appearance (arrow). The inset shows ischemic ST segment elevation in the ECG (lead V7). B, Reopening of the coronary artery with endoluminal filling defect (arrow) during intracoronary infusion of urokinase (480,000 U, 20 min). Symptoms were relieved with an normalization of ST segment change (inset). C, The narrowed vessel has a smooth and regular contour 4 weeks after thrombolytic treatment (arrow).
segment depression in lead V4 disappeared spontaneously in association with a decrease in the rate-pressure product (10,800 mm Hg/min at the initial angiography and 7300 mm Hg/min during the second angiogram). At follow-up angiography performed 4 weeks later, the obstruction was unchanged (figure 2, C). These results suggest a role for an increase in myocardial oxygen demand in the subset of unstable angina patients having a stable organic obstruction without thrombus. This relationship between oxygen demand and unstable angina is discussed later.

Of 37 patients in this study, 14 (38%) exhibited this pattern and were diagnosed as having organic stable obstructions without thrombus. None of the 14 patients showed improvement in the severity of coronary stenosis after intracoronary injection of nitroglycerin or urokinase, in contrast to the group that exhibited thrombus, in which the extent of coronary narrowings was improved immediately after infusion of urokinase. The distribution of the lesions in the patients with fixed obstructions was as follows: six in the left anterior descending coronary artery, four in the left circumflex coronary artery, and four in the right coronary artery.

In all 37 patients, transient ST segment alterations were observed during ongoing anginal attacks while the initial angiography was being performed. ST segment elevation was present in 16 of 21 patients with intracoronary thrombus, whereas all patients with organic stable obstruction showed ST segment depression (tables 1 and 2).

Late change in coronary stenosis. Tables 1 through 3 show the results of coronary arteriography in all 37 patients. Intracoronary thrombus was observed in 21 patients (57%), whereas organic stable obstruction without intracoronary thrombus was observed in 14 patients (38%). Vasospasm was diagnosed in two patients in whom intracoronary injection of nitroglycerin relieved the chest pain and reopened total occlusions to less than 50% residual stenosis without thrombus.

The degree of coronary stenosis was severe in most patients during spontaneous anginal attacks. The distributions of coronary stenoses in patients with or without intracoronary thrombus at initial angiography were statistically identical (p > .20; figure 3). Thrombolytic therapy improved coronary stenosis in the patients with

### TABLE 1

Features of the patients with intracoronary thrombus

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>% stenosis in initial angiogram</th>
<th>Changes in ST segment</th>
<th>Changes in clinical symptoms during thrombolytic therapy</th>
<th>Utilization of aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>M</td>
<td>100</td>
<td>D</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>M</td>
<td>100</td>
<td>E</td>
<td>Worsened +</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>M</td>
<td>100</td>
<td>E</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>M</td>
<td>100</td>
<td>E</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>77</td>
<td>F</td>
<td>99</td>
<td>D</td>
<td>Worsened</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>59</td>
<td>M</td>
<td>99</td>
<td>E</td>
<td>Unchanged</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>74</td>
<td>F</td>
<td>99</td>
<td>D</td>
<td>Worsened</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>M</td>
<td>95</td>
<td>E</td>
<td>Worsened</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>80</td>
<td>M</td>
<td>94</td>
<td>E</td>
<td>Improved</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>M</td>
<td>94</td>
<td>D</td>
<td>Worsened</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>52</td>
<td>M</td>
<td>94</td>
<td>E</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>73</td>
<td>M</td>
<td>93</td>
<td>E</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>74</td>
<td>F</td>
<td>92</td>
<td>D</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>50</td>
<td>F</td>
<td>92</td>
<td>E</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>47</td>
<td>M</td>
<td>91</td>
<td>E</td>
<td>Worsened</td>
<td>+</td>
</tr>
<tr>
<td>16</td>
<td>63</td>
<td>M</td>
<td>90</td>
<td>E</td>
<td>Improved</td>
<td>+</td>
</tr>
<tr>
<td>17</td>
<td>65</td>
<td>M</td>
<td>90</td>
<td>E</td>
<td>Unchanged</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>70</td>
<td>F</td>
<td>90</td>
<td>E</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>38</td>
<td>M</td>
<td>90</td>
<td>E</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>53</td>
<td>F</td>
<td>85</td>
<td>E</td>
<td>Disappeared</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>50</td>
<td>M</td>
<td>82</td>
<td>E</td>
<td>Improved</td>
<td></td>
</tr>
</tbody>
</table>

D = depression; E = elevation.

*Clinical symptoms were evaluated by the frequencies of prolonged rest anginal attacks before and within 48 hr after catheterization. Frequencies after catheterization that increased or decreased by 30% of that before catheterization are defined as "worsened" and "improved," respectively. When the attack did not occur again after catheterization, it was displayed as "disappeared." Otherwise, the cases were expressed as "unchanged."
intracoronary thrombus, whereas no improvement was observed in patients with stable organic obstruction.

Eighteen of 21 patients with intracoronary thrombus were evaluated angiographically 4 weeks later. A variety of outcomes was evident. Six patients showed progression of coronary narrowings; two patients showed reobstruction and the four others exhibited coronary narrowings that had progressed by more than 10%. In four patients, stenosis had regressed by more than 10%. Eight patients remained at the same degree as immediately after thrombolysis (figure 3, A). Ten of 14 patients with organic stable obstruction without thrombus were also evaluated angiographically 4 weeks later. None demonstrated any obvious changes in the follow-up angiography (figure 3, B).

Five of the patients with intracoronary thrombus had developed acute myocardial infarction during the 1 month follow-up period. Three of these five patients demonstrated progression of coronary stenosis at re-study. In the group of patients with organic stable obstruction, only one patient had developed an acute myocardial infarction during the follow-up phase of 1 month, but repeat coronary angiography showed no further change in the degree of stenosis. The occurrence of acute myocardial infarction during the 1 month follow-up period was somewhat greater in patients with intracoronary thrombus (5/21, 24%) than in the patients with organic stable obstruction (1/14, 7%); this difference approached but did not quite reach statistical significance (p = .20).

**FIGURE 2.** Representative coronary angiograms in a patient with organic stable obstruction without thrombus. Insets show the ECG (lead V₄) obtained during each angiographic assessment. A, The initial appearance of the left coronary arteries during chest pain; the angiogram shows the eccentric segmental narrowing (arrow) in the proximal left anterior descending coronary artery with delayed distal filling. B, The coronary arterial appearance after a 60 min infusion of urokinase (960,000 U). Although chest pain was relieved, no change was noted in the appearance of contrast outline (arrow). The rate-pressure product was decreased (7300 mm Hg/min during the asymptomatic period vs 10,800 mm Hg/min during active symptoms). C, The follow-up angiogram obtained 4 weeks after the initial assessment shows an unaltered angiographic appearance of the coronary lesion (arrow).
None of the patients who underwent follow-up angiography had a prolonged rest anginal attack when they were restudied. The coronary narrowings were significantly improved in the group of patients with intracoronary thrombus (% stenosis = 77.7 ± 5.2%) compared with the initial angiogram taken during active symptoms (94.0 ± 1.3%; n = 18, p < .05), whereas no patients in the group with stable organic obstruction showed such improvement (98.9 ± 0.7% vs 98.1 ± 0.9%; n = 10, p > .20). Taken together, these results strongly suggest that the prolonged attacks of rest angina were caused by intracoronary thrombosis in some patients, but the cause for unstable angina in the group with stable organic obstruction requires further consideration.

Change in rate-pressure product in the patients with stable organic obstruction. The patients with stable organic obstruction showed significantly higher rate-pressure products during active symptoms (13,900 ± 800 mm Hg/min) than during asymptomatic periods (9400 ± 500 mm Hg/min; p < .05). Five of these patients suffered recurrent episodes of prolonged rest angina again within 48 hr after the angiographic examination (table 2), and again showed higher rate-pressure products during anginal attacks (14,000 ± 1000 mm Hg/min; p < .05) as compared with symptom-free periods. In contrast to the patients with organic stable obstructions, the patients with intracoronary thrombi or coronary spasm showed no significant difference in the rate-pressure product during active symptoms (9900 ± 400 mm Hg/min) as compared with asymptomatic periods (9400 ± 400 mm Hg/min; p > .05). An increase in myocardial oxygen demand has been proposed as a mechanism for recurrent ischemic symptoms.19 Our results also suggest that an increase in myocardial oxygen demand, as indicated by an increase in the rate-pressure product, may play an important role in rest angina even in the absence of a dynamic stenosis such as intracoronary thrombosis or vasospasm. The underlying mechanism of the increase in oxygen demand, however, is still unclear; emotional stress or other undefined factors may be involved in this episodic event.

Discussion

Incidence of intracoronary thrombus. Several reports have emphasized the importance of intraluminal coronary artery thrombus in unstable angina.6–17 although the reported incidence of intracoronary thrombus in this syndrome has varied widely.5–15 The major origin of the inconsistencies may be due to differences in the delay between active symptoms and angiography. When coronary angiography was performed more than 30 days after the last symptom, the incidence of thrombus was low (1% to 12%).6, 7, 9, 10, 12), whereas the incidence was much higher (52% to 85%) when angiography was performed within 2 weeks of active symptoms.8, 13, 14 Such a correlation has been noted previously.12 The evanescence of intracoronary thrombus has also been reported during coronary angiography in patients with unstable angina.9 It was also suggested that spontaneous lysis of intracoronary thrombus often occurs within 24 hr after acute myocardial infarction.1 Therefore the role of intracoronary thrombus in unstable angina should be evaluated during the occurrence of symptoms.

In the present study, intracoronary thrombus was identified in 57% of patients catheterized during attacks of rest angina. This incidence was compatible with a report in which coronary angiography was performed within 24 hr after the last attack (52%13) and with our previous study in which angiography was performed within 50 hr of the last attack (55%14). The extent of coronary obstruction caused by thrombus may also change as a function of the duration after the last attack.

### TABLE 3

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>% stenosis in initial angiogram</th>
<th>Changes in ST segment</th>
<th>Changes in clinical symptoms after catheterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>49</td>
<td>M</td>
<td>100</td>
<td>E</td>
<td>Disappeared</td>
</tr>
<tr>
<td>37</td>
<td>54</td>
<td>M</td>
<td>100</td>
<td>E</td>
<td>Disappeared</td>
</tr>
</tbody>
</table>

Abbreviations and explanations as in table 1.
Sherman et al.\textsuperscript{15} recently reported that the thrombi frequently observed at intraoperative angioscopy of patients with unstable angina were not identified by prior angiography. Our ability to detect a high incidence of thrombus angiographically is not necessarily inconsistent with the report. The patients studied intraoperatively by Sherman and co-workers had undergone catheterization at some point before surgery, but not necessarily during ongoing attacks of unstable angina. Thrombus formation some time after angiography may have induced the recurrent attacks, which were refractory to medical therapy. Our observation indicates that the incidence of thrombi is much higher in patients with refractory anginal attacks than in patients during asymptomatic periods. The timing of the angiography was not mentioned, but a significant delay between the last attack of angina and the angiography might explain the discrepancy between the findings obtained by angiography and angioscopy.

In this study, intracoronary thrombus was confirmed both by morphology and by responsiveness to thrombolytic therapy. The angiographic criteria for thrombus followed earlier reports.\textsuperscript{1-3, 5-14, 16} Intracoronary injection of urokinase was used for therapeutic diagnosis of thrombus; anginal pain was found to disappear when intracoronary urokinase attenuated the stenosis.

There is a limitation in the functional diagnosis of thrombus by means of urokinase, because the injection of urokinase was not effective in one patient with angiographic findings characteristic of thrombus. Nevertheless, our results suggest that active ischemic symptoms resulted at least partially from subtle morphologic changes induced by thrombosis, superimposed on underlying atherosclerotic lesions.

Earlier angiographic studies demonstrated that the extent of coronary obstruction in patients with unstable angina was similar to that in the patients with stable angina.\textsuperscript{20, 21} Previously, we reported that only 10 of 29 patients (34\%) with unstable angina showed more than 90\% coronary narrowing when they were examined within 50 hr after the last attack.\textsuperscript{14} In contrast to our previous report, the initial angiography in this study always showed critically severe narrowings in at least one coronary artery; in fact, 34 of 37 patients (92\%) demonstrated more than 90\% narrowing during anginal attacks. The extent of coronary narrowing in this study was significantly more severe than in our previous reports (p < .001). The discrepancy in the extent of coronary narrowing between our two studies may be attributable to the time relationship between active symptoms and coronary angiography, given the evanescent nature of intracoronary thrombus.

\textbf{FIGURE 3.} The extent of coronary stenosis during active symptoms, immediately after the trial of coronary thrombolytic therapy, and in the follow-up angiography performed 4 weeks later. A, Patients with intracoronary thrombus (n = 21). B, Patients with stable organic obstruction (n = 14). Follow-up coronary angiography was not performed in seven patients (\%). Six patients (–); five in panel A, one in panel B) developed acute myocardial infarction during the follow-up period of 1 month.
Progression of intracoronary thrombus. In our study, 15 of 21 patients (71%) with intracoronary thrombus had recurrent symptoms even after successful thrombolysis, and five patients (24%) developed acute myocardial infarction within 28 days. In contrast, only one of 14 patients (7%) with stable organic stenosis without thrombus developed acute myocardial infarction after the angiographic study, although recurrent symptoms were observed in five of 14 patients (36%).

The difference in the incidence of myocardial infarction approached but did not quite reach statistical significance (p = .20). This may be due to the relatively small population size. The ST segment was elevated in 16 of 21 patients with intracoronary thrombus, whereas all patients with organic stable stenosis showed depression of ST segments. These findings are consistent with earlier reports in which a characteristic electrocardiographic pattern (ST segment elevation and T wave inversion) was observed in high-risk patients with unstable angina. These differences between the patients with or without thrombus may be attributable to the dynamic formation and lysis of intracoronary thrombus, as has been demonstrated in the experimental models. Platelet aggregation in partially obstructed canine coronary arteries causes a cyclic reduction in coronary flow.

Recurrent thrombus formation after thrombolysis has been also reported.

In our study, only five patients developed myocardial infarction, and the incidence of myocardial infarction was not significantly different in patients with and without aspirin (29% vs 21%; p > .20). However, beneficial effects of aspirin on the incidence of myocardial infarction or coronary death in patients with unstable angina have been observed in many reports. The lack of a demonstrable benefit here may well be due to the limited sample size. Thus the patient with unstable angina due to intracoronary thrombus may profit from intensive anticoagulant therapy for a long period after thrombolytic treatment to prevent the development of myocardial infarction, although this has not yet been demonstrated.

Limitations of the study. In the present study we performed angiography in patients having ongoing attacks of unstable angina, and we have gathered direct evidence of a high incidence of intracoronary thrombus. However, the limitation regarding the sensitivity in identification of intracoronary thrombus by angiographic criteria should be kept in mind. In autopsy specimens of patients dying after a bout of unstable angina, a part of the intracoronary thrombus was found to be organized and layered. Such small, thin-layered thrombus may be indistinct angiographically if it is adjacent to atherosclerotic lesions. However, we focused on fresh thrombus in this study as an etiologic factor in prolonged rest angina. In this respect, organized old thrombus that may be resistant to urokinase has no special significance in the promotion of unstable angina.

In conclusion, we have demonstrated that intracoronary thrombus was quite frequent during spontaneous anginal attacks in patients with prolonged rest angina. The coronary arteries were totally or subtotally obstructed in most patients with this syndrome; dynamic occlusion with intracoronary thrombus was observed in 21 (57%) of 37 patients, whereas 14 (38%) of the patients had severe stable narrowings. Five of 21 patients with intracoronary thrombus developed myocardial infarction even after thrombolysis, whereas only one of 14 with organic stable obstruction progressed to infarction. Thus these results suggest that intracoronary thrombus and organic stable obstruction have different clinical features, both in etiology and prognosis. Our data also suggest that, despite thrombolytic therapy and anticoagulation, patients with thrombus fare less well than those with a simple increase of myocardial oxygen demand and stable narrowings.

We thank Dr. Eduardo Marban for his helpful comments on the manuscript.

References
The role of intracoronary thrombus in unstable angina: angiographic assessment and thrombolytic therapy during ongoing anginal attacks.

K Gotoh, T Minamino, O Katoh, Y Hamano, S Fukui, M Hori, H Kusuoka, M Mishima, M Inoue and T Kamada

_Circulation_. 1988;77:526-534
doi: 10.1161/01.CIR.77.3.526

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 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/77/3/526

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/