Incidence, Morphology, Angiographic Findings, and Outcomes of Intramural Hematomas After Percutaneous Coronary Interventions
An Intravascular Ultrasound Study

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Background—Intramural hematomas during percutaneous coronary intervention (PCI) have not been well studied.

Methods and Results—We used intravascular ultrasound to determine the incidence, morphology, and clinical features of post-PCI intramural hematomas. In 905 patients with 1025 consecutive native coronary artery, non–in-stent restenosis lesions undergoing PCI, 72 hematomas were detected in 69 arteries in 68 patients. The incidence of intramural hematomas per artery was 6.7% (69 of 1025); 36% (26 of 72) involved the proximal reference artery, 18% (13 of 72) were confined to the lesion, and 46% (33 of 72) involved the distal reference artery. The entry site from the lumen into the hematoma was identified in 86% of hematomas (62 of 72) and had the appearance of a dissection into the media. Conversely, a re-entry site was identifiable in only 8% (6 of 72). The axial extension of the hematoma was distal in 63% and proximal in 37%. In 60% of the hematomas (42 of 72) the angiogram had the appearance of a dissection; in 11% (8 of 72), it appeared to be a new stenosis; and in 29% (22 of 72), no significant abnormality was detected. Non–Q-wave myocardial infarctions occurred in 26% of patients (17 of 65). In 3 patients, the creatine kinase-MB was not measured during the hospital stay. Repeat revascularization occurred in 2 patients in-hospital, 2 additional patients at 1 month, and 8 additional patients at 1 year. There were 3 sudden deaths at 1 year.

Conclusions—Intravascular ultrasound identified intramural hematomas after 6.7% of PCIs. The mechanism appeared to be a dissection into the media where blood accumulated because of a lack of re-entry. A third of ultrasound-identified hematomas showed no angiographic abnormalities. There was a high rate of non–Q-wave myocardial infarction, need for repeat revascularization, and sudden death in patients with hematomas. (Circulation. 2002;105:2037-2042.)

Key Words: hematoma ■ ultrasonics ■ circulation

In the era of balloon angioplasty, the rate of periprocedural occlusions was reportedly ≈5% and was strongly related to the severity of the residual dissection.1–3 Stents have dramatically reduced this ischemic complication; however, several case reports have shown a different type of dissection morphology suggestive of an intramural hematoma.4–7 Recently, the American College of Cardiology Task Force on Clinical Expert Consensus Documents reported the standards for the acquisition, measurement, and reporting of intravascular ultrasound (IVUS) studies. This report defined an intramural hematoma after a percutaneous coronary intervention (PCI) as an accumulation of blood within the medial space displacing the internal elastic membrane inward and the external elastic membrane outward, with or without identifiable entry and exit points. The purpose of the present study was to determine the incidence, morphology, angiographic appearance, and clinical features of intramural hematoma detected by IVUS during various interventions. It was our hypothesis that a significant percentage of intramural hematomas were angiographically silent.

Methods

Patient Population
From January 1998 to August 1998, 905 patients with 1025 native artery, non–in-stent restenosis lesions underwent percutaneous intervention with IVUS imaging. The IVUS studies of these patients were reviewed, and 72 intramural hematomas in 69 arteries in 68 patients were identified.
Clinical Demographics
Patient demographics were confirmed by hospital chart review, and outcome was determined by contact with patients or physicians at 1, 6, and 12 months. Coronary risk factors included diabetes mellitus (diet-controlled, oral agent, and insulin-treated), hypertension (medication-treated only), and hypercholesterolemia (medication-treated or a measurement $>240 \text{ mg/dL}$). Unstable angina was defined as new-onset severe angina, accelerated angina, or angina at rest. Previous myocardial infarction, coronary bypass grafting, and percutaneous interventional therapies were identified. Postprocedure target vessel revascularization, myocardial infarction, and cardiac death were evaluated. Non-Q-wave myocardial infarction was defined as creatine kinase-MB isoenzymes $>3$ times the upper limit of normal without new Q waves.

Angiographic Analysis
All angiograms were reviewed independently (A.B.B.) without knowledge of clinical and IVUS data. Significant stenosis was defined as a diameter stenosis $>50\%$. Dissections were classified using the National Heart, Lung, and Blood Institute criteria (type A through F). A new stenosis was defined as a new narrowing without adjacent dissection that persisted after the administration of intracoronary nitroglycerin. Staining was defined as persistent evidence of contrast in the vessel wall after contrast washed out from the remaining portion of the vessel.

IVUS Imaging and Analysis
A commercially available IVUS system (Boston Scientific Corporation/SciMed) was used. All IVUS studies were performed after the intracoronary administration of $200 \mu g$ of nitroglycerin. The IVUS catheter was advanced distal to the lesion, and imaging was performed retrograde through the proximal reference artery at a pull-back speed at 0.5 mm/s automatically. When the first run was ambiguous, additional manual pull-backs, typically with contrast or saline injection, were performed. IVUS studies were recorded onto a high-resolution, half-inch, s-VHS tape for later analysis.

Qualitative Analysis
Intramural hematomas were identified according to the criteria of the American College of Cardiology Clinical Expert Consensus document on IVUS and confirmed by comparing pre- versus post-interventional IVUS studies. Intramural hematomas were typically crescent-shaped, with straightening of the internal elastic membrane (Figures 1 to 3). The accumulation of blood was usually homoge neous and hyperechoic and, especially on static images, visually continuous with the intima (or plaque) and adventitia.

The location of hematoma relative to the preintervention lesion, any dissection planes, branch points, or the edge of an implanted stent was evaluated. “Normal vessel wall” was defined as having $<0.3 \text{ mm}$ of intimal thickness. Entry/re-entry (exit) sites were defined as communications between the lumen and the hematoma, which were typically located at the ends of the hematoma. If there was only one communication, we considered this to be the entry site. If there were two communications, we considered these to be the entry and re-entry sites, but we could not define which site was entry and which was re-entry.

Figure 1. Example of angiographic dissection. Angiography showed type C dissection. The IVUS study is shown in duplicate: one un labeled and one labeled with numbers. It corresponds to the black arrow on the post-balloon angiogram. Image slices are 1 mm apart. There is evidence of an entry site (1) at the junction of the plaque and adjacent normal arterial wall; this dissection extends distally (2). The hematoma (3) is 4 mm in length, and there is evidence of flow into the hematoma (4). In addition, there is an echolucent area at the distal end of the hematoma (5).

Figure 2. Example of angiographic new narrowing. Although angiography showed insignificant stenosis, IVUS showed severe calcified tight stenosis (minimum lumen area of 2.9 mm$^2$). After stenting, a new narrowing was appreciated distal to the stent edge. IVUS demonstrated intramural hematoma. A, Minimum lumen site before intervention; B, the site before intervention where the hematoma formed after stent implantation; C, intramural hematoma (arrowheads). Arrows on angiograms indicate location of corresponding IVUS images.
Quantitative Analysis
The image slice with the largest hematoma area, the image slice with the minimum lumen cross-sectional area (CSA), and the proximal and distal reference sites were identified and measured. The reference sites were the most normal-looking cross sections within 5 mm proximal and distal to the lesion site. Using planimetry software (TapeMeasure, INDEC Systems Inc), the following measurements were made: external elastic membrane CSA (mm²), lumen CSA (mm²), hematoma CSA (mm²), percent hematoma CSA (hematoma CSA divided by external elastic membrane CSA), and the length of the hematoma (calculated from the known pullback speed). An eccentric plaque had a maximum/minimum plaque thickness >2.0.

Reproducibility of IVUS Analysis
The agreement of 2 independent observers (A.M. and G.S.M.) was assessed regarding the identification of the hematomas, entry/re-entry sites, and echolucent areas within the hematomas. The rate of agreement for hematoma was 95% (72 of 76). Four cases with disagreement were excluded from the analysis. The rate of agreement for entry/re-entry sites was 99%, and that for echolucent area within the hematoma was 100%. When the maximum hematoma site was chosen and analyzed independently, the intraclass correlation coefficient 5 months apart for repeated measurement of the external elastic membrane CSA was 0.96, that for the lumen CSA was 0.93, that for the hematoma CSA was 0.95, and that for the hematoma length was 0.98. The interclass correlation coefficient for the measurement of the external elastic membrane was 0.93, that for the lumen CSA was 0.88, that for the hematoma CSA was 0.92, and that for the hematoma length was 0.97.

Statistics
Statistical analysis was performed using StatView 5.0 (SAS Institute). Continuous variables (presented as mean±SD) were compared using a paired Student’s t test or ANOVA. Categorical variables (presented as frequencies) were compared using χ² statistics or Fisher’s exact probability test. P<0.05 was considered significant.

Results
A total of 72 hematomas were detected in 69 arteries of 68 patients. The incidence of intramural hematoma per artery was 6.7% (69 of 1025). Baseline clinical demographics are shown in Table 1. Hematomas occurred more often in diabetic patients and those with less advanced coronary artery disease. Most hematomas (96%; 69 of 72) occurred in de novo lesions. The location of the hematomas was the right coronary artery in 47% (34 of 72), left anterior descending artery in 29% (21 of 72), and left circumflex artery in 24% (17 of 72). In 3 right coronary arteries, there were 2 separate intramural hematomas. The hematoma was located in the proximal portion of the artery in 50% (36 of 72), the mid portion in 22% (16 of 72), distal position in 20% (14 of 72), and the ostium in 8% (6 of 72).

Thirty-four hematomas occurred after nonstent strategies (balloon only in 25 and rotablator with or without adjunct balloon in 9). In the nonstented group, the hematoma was located only within the lesion in 38% of patients (13 of 34), in both the lesion and the reference in 41% of patients (14 of 34), and only within the reference artery in 21% of patients (7 of 34). In the nonstented group, 9 of 34 hematomas were proximal and 12 of the 34 hematomas were distal to the lesion. Thirty-eight hematomas were detected after stenting. In the stented lesions, all hematomas were located at the edge of the stent (distal edge in 55% [21 of 38] and proximal edge in 45% [17 of 38]). Thus, overall, combining nonstent and stent interventions, 36% of the hematomas (26 of 72) involved the proximal reference artery, 18% (13 of 72) were confined to the lesion, and 46% (33 of 72) involved the distal reference artery. The location of the largest hematoma was in a normal segment of artery in 18% (13 of 72), at the site of an eccentric plaque in 61% (44 of 72), and at the site of concentric plaque in 21% (15 of 72). When located at the site of an eccentric plaque, the hematoma involved the normal arc of arterial wall in 68% (30 of 44), both normal and diseased...
The entry site from the lumen into the hematoma was identified in 86% (62 of 72) and had the appearance of a dissection into the media. In 56% of hematomas (40 of 72), there was evidence of flow from the true lumen into the hematoma. Conversely, a re-entry site was identifiable in only 6 of the hematomas. The axial extension of the hematoma was distal to the entry site in 63% and proximal to the entry site in 37%. Excluding hematomas that were adjacent to and presumably limited by a stent edge, the extension of a hematoma was limited by plaque in 63% and/or a branch in 37%. Conversely, the hematoma ended within a nonbranching normal segment of artery in only 8%.

In 7 of 72 hematomas (9.7%), there were sharply demarcated echoluent areas within the hyperechoic hematoma, usually at the end opposite to the entry site.

**Angiographic Findings**

In 60% of the hematomas (42 of 72), there was an angiographic appearance of a dissection. Dissections were type B in 24% (10 of 42), type C in 52% (22 of 42), and type D in 24% (10 of 42). In 11% of the hematomas (8 of 72), there was an angiographic appearance of a new stenosis. In 29% of the hematomas (22 of 72), there was no significant angiographic abnormality. Examples are shown in Figures 1 to 3. Six of the 7 cases that had echoluent areas within the hematoma on IVUS imaging had evidence of angiographic staining supporting the supposition that these echoluent areas contained retained contrast or saline.

A comparison of the IVUS findings according to the angiographic appearance is shown in Table 2. The percent hematoma CSA tended to be larger in the new stenoses group (42±17%) compared with the dissection group (32±12%) or with arteries with no significant angiographic abnormalities (30±13%).

**Treatment**

Individual operators determined both the treatment strategy and the end point. Forty-seven patients with 51 hematomas sites were treated by stents, 10 patients with 10 hematomas were treated by additional balloon angioplasty, and 11 patients with 11 hematomas were not treated. Only one patient was treated with a glycoprotein IIb/IIIa inhibitor. Post-treatment IVUS imaging was available in 62 of 72 hematoma sites (86%). The final lumen area according to intervention strategy is shown in Table 3.

In the stent-treated group, there was an increase in the lumen area at the hematoma site from 4.3±1.8 to 8.2±3.4 mm² (P<0.0001). In these cases, the entire hematoma (including the entry site) was covered by the stent.

All arteries in the balloon-treated group had residual hematomas after additional balloon angioplasty. However, the lumen area at the hematoma site increased from 4.5±1.2 to 6.3±1.8 mm² (P=0.02). Five cases had a new re-entry site created by additional balloon angioplasty.

**Outcome**

Non-Q-wave myocardial infarctions related to the procedure occurred in 26% of patients (17 of 65); the peak creatine kinase-MB was 45±61 ng/mL (normal is <4 ng/mL). In 3 patients, the creatine kinase-MB was not measured during the hospital stay. (The frequency of non-Q-wave myocardial infarction was similar to the concurrent non-hematoma cohort at 25%.) During the hospital stay, there were 2 repeated target vessel revascularizations, both in nonstented patients with residual hematomas after PCI. The first patient had mild chest discomfort after the procedure. Because of worsening of symptoms, this patient returned to the catheterization laboratory, where recoil of the site was treated by additional stenting. The second patient did well for 36 hours but developed progressive chest pain with ST elevation related to the treated vessel. The patient was treated with emergent coronary bypass grafting.

In the subsequent month, there were 2 additional target vessel revascularization events (at 8 and 21 days), both in nonstented patients. One had a repeat percutaneous intervention and the other had coronary artery bypass grafting. In both patients, there were residual hematomas at the time of the original intervention; in one patient, there was also a residual

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**TABLE 2. Quantitative IVUS Analysis According to Angiographic Findings**

<table>
<thead>
<tr>
<th></th>
<th>New Stenosis (n=8)</th>
<th>Dissection (n=42)</th>
<th>No Abnormality (n=22)</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen CSA, mm²</td>
<td>4.2±3.1</td>
<td>4.5±1.8</td>
<td>4.6±1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Hematoma CSA, mm²</td>
<td>4.8±2.5</td>
<td>5.1±3.0</td>
<td>4.9±4.4</td>
<td>1.0</td>
</tr>
<tr>
<td>% Hematoma CSA</td>
<td>42±17</td>
<td>32±12</td>
<td>30±13</td>
<td>0.08</td>
</tr>
<tr>
<td>Hematoma length, mm</td>
<td>4.7±3.9</td>
<td>5.4±6.3</td>
<td>4.5±2.4</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Values are mean±SD.

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**TABLE 3. Final IVUS Measurements According to Treatment Strategy**

<table>
<thead>
<tr>
<th></th>
<th>Stent</th>
<th>Additional PTCA</th>
<th>No Further Therapy</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean reference lumen CSA, mm²</td>
<td>8.2±2.6</td>
<td>8.0±2.5</td>
<td>7.8±3.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Hematoma site lumen CSA, mm²</td>
<td>8.2±3.4</td>
<td>6.3±1.8</td>
<td>6.5±2.8</td>
<td>0.15</td>
</tr>
<tr>
<td>Minimal lumen CSA, mm²</td>
<td>6.6±1.9</td>
<td>5.1±1.3</td>
<td>6.4±2.1</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Values are mean±SD. PTCA indicates percutaneous transluminal coronary angioplasty.
hematoma detected by IVUS at 21 days. A total of 66 patients were discharged on ticlopidine or clopidogrel and aspirin. None of the 4 patients with repeat target vessel revascularization in-hospital or within 1 month had evidence of thrombus by IVUS, angiography, and/or operative findings. The cumulative (in-hospital and 1-month) target vessel revascularization rates were higher in patients with hematomas than for the concurrent nonhematoma cohort (1.9%; P = 0.046).

One-year follow-up was available in 93% of patients (63 of 68). At 1 year, there were 3 cardiac deaths, no myocardial infarctions, and a total of 8 additional revascularizations. All 3 late deaths were sudden and occurred outside the hospital at 78, 149, and 163 days in patients with moderate-to-severe left ventricular dysfunction. All 3 late deaths and 7 of the 8 repeat target vessel revascularizations occurred in patients with hematomas treated with stent implantation. The late outcomes were similar to those in the concurrent nonhematoma cohort (Table 4).

### Discussion

The main findings of the current study are consistent with the above operative and pathological observations. These features include the following: (1) an entry site that was a dissection to the media, (2) propagation of the hematoma that was more often distal than proximal, and (3) propagation of the hematoma into more normal segments or arcs of arterial wall.

### Possible Mechanism of Intramural Hematoma Formation After PCI

In 1984, Murphy et al. reported 4 patients who underwent emergent coronary bypass surgery after intervention; all 4 had false lumens with bloody fluid, suggesting a dissecting hematoma. Zack et al. reported a patient with progression of an asymptomatic intimal tear to an occlusive dissection 4 weeks after angioplasty; at operation, there was a liquefied hematoma between the intima and the adventitia. Werner et al. showed 7 intramural hematoma cases detected by IVUS. In one case, the hematoma extended to the left main artery and was discovered at emergent surgery. Pathologically, Block et al. reported a patient who died 90 hours after balloon angioplasty and who had a dissecting hematoma beginning at the angioplasty site and extending distally. The operative or pathological findings in these cases indicate that an intramural hematoma begins as a dissection to the media and propagates along the medial plane into more normal arterial segments but does not re-enter the lumen.

One common location of dissection after angioplasty is at the junction of the thinnest plaque and adjacent normal arterial wall. During PCI, the stiffer atherosclerotic plaque resists circumferential expansion more than the normal site and high shear stresses are generated at their interface, causing a dissection. Similarly, after stent implantation, dissection occurs at the edge of a stent that is the transition point between the rigid stent and unstented reference segment. Once medial dissection occurs, hematoma formation and expansion seem to require a normal segment or arc of arterial wall. Waller et al. have reported that the thickness of the media behind atherosclerotic plaque is less than half that of the normal wall and is accompanied by scarring and loss of smooth muscle cells. Because the “diseased” media is more scarred, it may prevent propagation of the medial dissection. In the present study, the patients with hematoma had less advanced coronary artery disease compared with a contemporary nonhematoma cohort. Furthermore, in autopsy studies after angioplasty, approximately half of the arteries had medial disruption and healing; this may explain the observation in the current study that intramural hematomas were rare in restenotic lesions.

### IVUS Appearance

The IVUS features of a post-PCI intramural hematoma in the current study are consistent with the above operative and pathological observations. These features include the following: (1) an entry site that was a dissection to the media, (2) propagation of the hematoma that was more often distal than proximal, and (3) propagation of the hematoma into more normal segments or arcs of arterial wall.

By IVUS, an intramural hematoma appeared as a homogeneous, hyperechoic, crescent-shaped area. The echogenicity of blood depends on the flow rate, red cell aggregation, and fibrin content. Yamada et al. reported that the backscatter intensity of blood increased dramatically with stagnant flow. Van der Heiden et al. showed that the increase in backscatter intensity depended on red cell aggregation. In an animal model, Fowlkes et al. showed that whole-blood thrombus increased its echogenicity over time and that this was related to the fibrin content. According to these studies, the IVUS appearance in the current study could represent stagnant blood, coagulating blood, or solid hematoma, depending on time factors.

Intramural hematomas can also contain distinct echolucent zones within the hyperechoic areas (Figure 1). These echolucent zones have distinct borders and often occur at the end of the hematoma opposite the site of entry. Presumably, these echolucent areas represent accumulation of radiographic contrast or saline within the hematoma space, as was suggested.
by the finding in the current study that most were associated with angiographic staining.

Clinical Implications
Because one third of the intramural hematomas showed no angiographic abnormalities, IVUS may be the only tool to identify the existence of post-PCI intramural hematomas. Because this is an intramural pathological process, the lumen surface is still smooth. In fact, 10% of the intramural hematomas in the current study had the appearance of a new stenosis or spasm. In the current study, there was IVUS evidence of flow from the true lumen into the hematoma in only half of the patients. When flow into the intramural hematoma is minimal, there may not be angiographic evidence of a dissection.

The proper management of intramural hematomas has not been well-defined. However, short-term complications (non–Q-wave MI and need for repeat revascularization within 1 month) and long-term outcomes (death and need for repeat revascularization at 1 year) were troublesome. In the present study, early (within 1 month) complications occurred mainly in the nonstented group, whereas the late (1 month to 1 year) complications occurred mainly in the stented group. Because the number of patients in the current study was small and because this was a retrospective analysis, the best way to treat post-PCI intracoronary hematomas is presently unclear. However, it seems that most of the adverse events related to the development of intramural hematomas occur early, either in-hospital or within 1 month.

Limitations
We excluded patients with in-stent restenosis. Despite the fact that this is a large consecutive series of patients undergoing IVUS imaging during percutaneous intervention, there may be selection bias. Therefore, the exact frequency of intramural hematoma accumulation may be unknown. However, these data were collected from a high-volume laboratory that uses IVUS during most interventional procedures. Similarly, because multiple devices were used, it is difficult to assign rates of intramural hematoma formation to individual treatment strategies. Only one of the patients was treated with a glycoprotein IIb/IIIa inhibitor; therefore, we cannot determine the effect of glycoprotein IIb/IIIa inhibitors in this scenario.

Conclusions
IVUS identified intramural hematomas after 6.7% of PCIs. The mechanism seemed to be a dissection into the media where accumulation occurred because of a lack of re-entry. A third of IVUS-identified hematomas showed no angiographic abnormalities. There was a high rate of non–Q-wave myo-

References
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