Significance of Coronary Arterial Thrombus in Transmural Acute Myocardial Infarction

A Study of 54 Necropsy Patients

FRANK C. BROSU III, M.D., AND WILLIAM C. ROBERTS, M.D.

SUMMARY In 54 necropsy patients with transmural acute myocardial infarction (AMI) and coronary arterial thrombi, histologic sections of coronary arteries that contained the thrombi were examined by videoplanimetry to determine if the amount of luminal narrowing caused by thrombi was comparable to that produced by underlying atherosclerotic plaques, and to determine the amount of luminal narrowing by plaques immediately proximal and distal to the thrombi. The 54 coronary arteries in the 54 patients were narrowed 33–98% (mean 81%) by atherosclerotic plaque alone in cross-sectional area at the site of the thrombus (occlusive in 47 and nonocclusive in seven), from 26–98% (mean 75%) within the 2-cm segment proximal to the thrombus, and from 43–98% (mean 79%) within the 2-cm segment distal to the thrombus. Of the 54 arteries, 52 (96%) were narrowed 76–98% in cross-sectional area by atherosclerotic plaque alone at or immediately proximal or distal to the thrombus and 26 (48%) were narrowed 91–98% by plaque alone. The thrombi were 0.1–6.0 mm² (mean 1.4 mm²) in cross-sectional area and the underlying atherosclerotic plaques were 3.0–21.0 mm² (mean 8.7 mm²). Thus, among necropsy patients with transmural AMI, coronary thrombi occur at sites already severely narrowed by atherosclerotic plaques.

THROMBI in coronary arteries of necropsy patients with transmural acute myocardial infarction (AMI) have been observed in numerous studies. Herrick, in 1912 and 1919, found them in four patients with fatal AMI, and for many decades thrombi were believed to have precipitated AMI. They were considered so important in causing this acute event that the term “coronary thrombosis” was used for years to describe the event that most physicians now call “acute myocardial infarction.” In recent years the primary role of coronary thrombus in precipitating AMI has been questioned. To evaluate the significance of coronary thrombus in AMI, we examined in detail the coronary arteries containing thrombi in 54 necropsy patients with transmural AMI. Several previously undescribed observations on coronary thrombi resulted, which clarify the significance of coronary thrombi in AMI.

Patients and Methods

All necropsy patients with transmural AMI accessioned in the Pathology Branch, National Heart, Lung, and Blood Institute, were reviewed. Of 235 such patients, 99 had histologic sections available from each 5-mm segment of each of the four major coronary arteries (right, left main, left anterior descending and left circumflex). Movat-stained histologic sections, approximately 55 per patient, were reviewed, and a thrombus was found in one of the four major coronary arteries in 54 patients (55%). These 54 patients constitute the study group.

In each patient, the coronary artery that contained the thrombus was examined. The maximal degree of
Cross-sectional area narrowing by atherosclerotic plaque was determined at the site of the thrombus, in the 2-cm portion of artery proximal to the proximal portion of the thrombus, and in the 2-cm segment of coronary artery distal to the distal site of attachment of the thrombus (fig. 1). The length of the thrombus was determined by the number of 5-mm-long segments of coronary artery that contained thrombus. Thus, if three sections prepared from three 5-mm-long coronary segments contained thrombus, the thrombus was judged to be 1.5 cm long.

A coronary arterial thrombus was defined as a collection of fibrin (with or without engulfed erythrocytes) or platelets or both within the residual lumen and attachment of the fibrin/platelets to the luminal surface of the artery (fig. 2). Among the 54 patients with fatal AMI, this luminal surface always was the surface of an underlying atherosclerotic plaque. The thrombus was always attached to the intimal surface in its distal portion, but in a few patients it was not attached in its most proximal portion. The thrombus was considered occlusive when it occupied the residual lumen of the artery, i.e., the portion not occupied by atherosclerotic plaque (fig. 2). In many patients, the occlusive thrombi were detached from the surface of the underlying plaque in some areas, but this detachment was considered artifactual, the result of processing the artery through dehydrating solutions (alcohol and xylene) during the processing of the tissues for histologic sectioning. The thrombus was considered nonocclusive when it filled a relatively small portion of the residual lumen, with no evidence of previous circumferential attachment to the surface of the underlying atherosclerotic plaque (fig. 2).

The maximal degrees of cross-sectional area narrowing by atherosclerotic plaque were determined at the site of the coronary thrombus and within the 2-cm portions of the artery proximal and distal to the thrombus by means of a video-based, computer-linked system described elsewhere. Briefly, Movat-stained sections of coronary artery were positioned on the stage of a projection-light microscope. The image was then magnified ×650 onto opaque white paper and a pencil tracing was made of the artery's original lumen (denoted by the black-staining internal elastic membrane), the area occupied by atherosclerotic plaque, and, in the case of nonocclusive thrombi, the area occupied by the thrombus (fig. 2). The area of the occlusive thrombus was the difference between the area of the original lumen and the area of the atherosclerotic plaque. In the case of nonocclusive thrombus, the area of the thrombus was determined directly by tracing the borders of its projected image. Also, in the case of nonocclusive thrombus, the

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**Figure 1.** Diagram of an "average" coronary artery with an occlusive thrombus. The four 5-mm segments of coronary artery proximal (P) to the thrombus (T) were narrowed an average of 75% in cross-sectional area by atherosclerotic plaque (AP), the four segments with an occlusive thrombus were narrowed an average of 81% by plaque, and the four segments distal (D) to the thrombus were narrowed an average of 79% by plaque.
residual lumen was the difference between the artery's original lumen and the sum of the area occupied by atherosclerotic plaque plus the area occupied by the nonocclusive thrombus (fig. 2). In the sections of coronary artery proximal and distal to the thrombus, the residual lumen was the difference between the artery's original lumen and the area occupied by atherosclerotic plaque. The percent of cross-sectional area narrowed by atherosclerotic plaques and by thrombi (in the case of nonocclusive thrombi) was calculated. The area of each artery enclosed by the internal elastic membrane (original lumen), the area of the atherosclerotic plaque and that of the nonocclusive thrombus provided by videoplanimetry were converted into actual area.

All patients had had AMIs that involved the entire inner half of the left ventricular wall and a portion or all of the outer half of the left ventricular wall. In addition to these acute left ventricular infarcts, 20 patients had one or more transmural scars. The 54 patients ranged in age from 38–92 years (mean 62 years); 41 were men and 13 were women.

Results

The major morphologic findings in the 54 coronary arteries containing thrombi are summarized in tables

### Table 1. Data in the 54 Autopsy Patients: Coronary Thrombi

<table>
<thead>
<tr>
<th>Coronary artery with T</th>
<th>No. of pts</th>
<th>Distance (cm) of T from origin of coronary artery</th>
<th>Length (cm) of T</th>
<th>Duration (days) from clinical onset of AMI to death</th>
<th>Maximal narrowing (%) at site of T</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>proximal to death</td>
<td></td>
<td>Proximal 2 cm to T</td>
<td>By AP only</td>
</tr>
<tr>
<td>Occlusive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>19</td>
<td>0.5–15.5 (4.8)</td>
<td>0.5–10.0 (2.4)</td>
<td>1–18 (5.7)</td>
<td>56–98</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>19</td>
<td>0.0–6.0 (2.1)</td>
<td>0.5–5.0 (1.4)</td>
<td>1–25 (6.9)</td>
<td>26–94</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>9</td>
<td>0.0–5.0 (2.3)</td>
<td>0.5–1.5 (1.1)</td>
<td>1–45 (9.6)</td>
<td>59–90</td>
</tr>
<tr>
<td>Subtotals</td>
<td>47</td>
<td>0.0–15.5 (3.2)</td>
<td>0.5–10.0 (1.8)</td>
<td>1–45 (6.9)</td>
<td>26–98</td>
</tr>
<tr>
<td>Nonocclusive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>0</td>
<td>0.5–2.0 (1.2)</td>
<td>0.5–1.0 (0.7)</td>
<td>1–7 (4.3)</td>
<td>50–91</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>3</td>
<td>0.5–3.0 (1.5)</td>
<td>0.5–1.0 (0.8)</td>
<td>1–28 (8.0)</td>
<td>82–92</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>4</td>
<td>0.5–3.0 (1.4)</td>
<td>0.5–1.0 (0.7)</td>
<td>1–28 (8.4)</td>
<td>50–92</td>
</tr>
<tr>
<td>Subtotals</td>
<td>7</td>
<td>0.5–3.0 (1.4)</td>
<td>0.5–1.0 (0.7)</td>
<td>1–28 (8.1)</td>
<td>50–92</td>
</tr>
<tr>
<td>Totals</td>
<td>54</td>
<td>0.0–15.5 (2.9)</td>
<td>0.5–10.0 (1.6)</td>
<td>1–45 (6.8)</td>
<td>26–98</td>
</tr>
</tbody>
</table>

Abbreviations: T = thrombus; AMI = acute myocardial infarction; AP = atherosclerotic plaque.
TABLE 2. Total Numbers of the Three Major Coronary Arteries Showing Five Categories of Narrowing

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of coronary arteries with maximal narrowing (%) by atherosclerotic plaque alone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(0-25)</td>
</tr>
<tr>
<td>Proximal 2 cm to thrombus</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(12%)</td>
</tr>
<tr>
<td>At site of thrombus</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(4%)</td>
</tr>
<tr>
<td>Distal 2 cm to thrombus</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(6%)</td>
</tr>
<tr>
<td>Either at, or proximal or distal</td>
<td>0</td>
</tr>
<tr>
<td>to thrombus</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1-3 and illustrated in figures 1 and 2. The thrombi were occlusive in 47 patients (87%) and nonocclusive in seven (13%). The coronary arterial systems containing thrombi were left anterior descending in 22 (41%), right in 19 (35%), and left circumflex in 13 (24%). In one of the 19 patients with a thrombus in the right coronary system, the thrombus was present only in the posterior descending branch of the right coronary artery. In one of the 13 patients with a thrombus in the left circumflex system, the thrombus was present in the left obtuse marginal branch rather than the left circumflex proper. Of the 13 patients with a thrombus in the left circumflex system, this artery was the dominant posterior perfusing artery in seven: in six of nine patients with occlusive thrombi and in one of four with nonocclusive thrombi (table 1).

The coronary thrombi ranged from 0.5-10 cm long (mean 1.6 cm) (table 1). The occlusive thrombi were 0.5-10 cm long (mean 1.8 cm) and the nonocclusive thrombi were 0.5-1.0 cm long (mean 0.7 cm). The mean lengths of occlusive thrombi in the right coronary artery were longer than the mean lengths of occlusive thrombi in the left anterior descending and left circumflex coronary arteries ($p < 0.025$) (table 1). In the case of the right coronary artery, the length of the thrombus increased directly as the intervals increased between onset of AMI and death; such was not the case, however, with thrombi in the left anterior descending and left circumflex coronary arteries.

The distance from the origin of a coronary artery (aorta for the right and left main for the left anterior descending and left circumflex) to the most proximal portion of a coronary thrombus ranged from 0-15.5 cm (mean 2.9 cm). This mean distance was 3.2 cm (range 0-15.5 cm) for the occlusive thrombi and 1.4 cm (range 0.5-3.0 cm) for the nonocclusive thrombi (NS). The mean distance of an occlusive thrombus from the aorta in the right coronary artery, however, was significantly ($p < 0.01$) greater than the mean distance of either an occlusive or nonocclusive thrombus from the left main in either the left anterior descending or left circumflex coronary arteries.

The amount of luminal narrowing by atherosclerotic plaques and by thrombus proximal, at, and distal to the coronary thrombus is summarized in tables 1-3. The maximal luminal narrowing by atherosclerotic plaques alone at the site of the thrombus varied from 33-98% (mean 81%); the maximal coronary luminal narrowing by thrombus alone varied

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**Table 3. Areas of Minimal Residual Lumen of Coronary Artery**

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of coronary arteries with minimal residual luminal area*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;2 mm²</td>
</tr>
<tr>
<td>Proximal 2 cm to thrombus</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>(42%)</td>
</tr>
<tr>
<td>At site of thrombus</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>(28%)</td>
</tr>
<tr>
<td>Distal 2 cm to thrombus</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(11%)</td>
</tr>
<tr>
<td>Either at, or proximal or distal</td>
<td>1</td>
</tr>
<tr>
<td>to thrombus</td>
<td>(2%)</td>
</tr>
</tbody>
</table>

*Represents area not occupied by atherosclerotic plaque; ignores further occlusion by thrombus.
from 2–67% (mean 19%) in the 47 patients with occlusive thrombi and from 2–24% (mean 7%) in the seven patients with nonocclusive thrombi. The maximal luminal narrowing by atherosclerotic plaques in the 2 cm of coronary artery proximal to the thrombus ranged from 26–98% (mean 75%), and in the 2 cm distal to the distal site of attachment of the thrombus from 43–98% (mean 79%). No significant differences were noted in the amount of maximal luminal narrowing at, proximal, or distal to the thrombus between the 47 patients with occlusive thrombi and the seven with nonocclusive thrombi (table 1). Likewise, no significant differences were observed in the amount of maximal luminal narrowing at, proximal or distal to the coronary thrombus in the three major coronary arteries (table 1).

The absolute area occupied by atherosclerotic plaques, the area occupied by thrombus, and the area of the residual coronary lumens for the sites of maximal narrowing at, proximal and distal to coronary artery thrombi were as follows. At the site of maximal luminal narrowing of the coronary artery at the site of the thrombus, the area occupied by atherosclerotic plaque ranged from 1.5–15.0 mm² (mean 7.2 mm²); the area occupied by occlusive thrombus, from 0.1–6.0 mm² (mean 1.5 mm²); and that occupied by nonocclusive thrombus, from 0.1–1.5 mm² (mean 0.5 mm²). The area of the original coronary lumen (that enclosed by internal elastic membrane) at the site of the thrombus ranged from 3–21 mm² (mean 8.7 mm²); proximal to the thrombus, from 2.8–13.6 mm² (mean 8.7 mm²); and distal to the thrombus, from 0.8–13.5 mm² (mean 5.1 mm²). The maximal area occupied by atherosclerotic plaque proximal to the thrombus ranged from 2.2–12.1 mm² (mean 6.5 mm), and distal to the thrombus, from 0.4–11.8 mm² (mean 4.0 mm²).

No significant differences in mean areas between the 47 patients with occlusive and nonocclusive coronary thrombi were observed in the original size of the coronary artery or in the amount of lumen obliterated by atherosclerotic plaque proximal, at, or distal to the coronary thrombus. Likewise, we found no differences in mean areas among the three major coronary arteries in the 47 patients with occlusive thrombi or in the seven with nonocclusive thrombi.

The amount of coronary luminal narrowing in cross-sectional area by atherosclerotic plaques in five categories of narrowing at, proximal and distal to thrombi are summarized in table 2. In 52 (96%) of the 54 coronary arteries with thrombi, the lumens of the arteries at, proximal or distal to the thrombi were already narrowed 76–100% in cross-sectional area by atherosclerotic plaques: in 27 of 42 arteries (64%) examined proximal to the thrombus (in 12 arteries the thrombi began at or virtually at the origin of the coronary artery from the aorta or left main coronary artery), in 35 (66%) of 53 arteries examined distal to the distal site of attachment of the thrombus, and in 41 (76%) of the 54 coronary arteries (or patients) at the site of attachment of the thrombus. Furthermore, in 26 (48%) of the 54 coronary arteries, the lumens of the arteries at, proximal or distal to the thrombi were narrowed 91–98% in cross-sectional area by atherosclerotic plaques. In 16 (30%) of 54 coronary arteries with thrombi, the site of most severe narrowing by atherosclerotic plaque in the portion of artery examined was within the 2 cm proximal to the thrombus: in 25 of 54 (46%) it was at the site of the thrombus and in 13 of 54 (24%) it was in the 2-cm segment distal to the thrombus. The site of most severe narrowing in coronary arteries was not significantly different between occlusive and nonocclusive thrombi.

The areas in three categories of the coronary arteries not occupied by atherosclerotic plaques proximal and distal to and at the site of attachment of the thrombus are summarized in table 3.

At the site of attachment of thrombi, the underlying atherosclerotic plaques contained extravasated erythrocytes in 21 (39%) of the 54 patients: in 18 (38%) of 47 with occlusive thrombi and in three of seven with nonocclusive thrombi. In none of the 21, however, did the hemorrhage into the pultaceous debris of the plaque appear to compromise the lumen.

**Discussion**

The relationship of coronary thrombi to AMI has received considerable attention in recent years. Some investigators believe that thrombi precipitate transmural AMI,1 3 23 33 primarily because coronary thrombi are frequently found in patients with fatal AMI and, when found, they are located in the artery that perfuses the area of infarcted left ventricular myocardium. Others believe that coronary thrombi follow the AMI, resulting from the slowed flow (in the coronary artery) produced by the infarct itself.6 15 17 20 This view is based primarily on the absence of coronary thrombi in a significant percentage of patients with fatal transmural AMI,4 10 12 14 18 their absence in patients with fatal coronary events other than transmural AMI (sudden coronary death,16 24 36 subendocardial infarcts14 and angina pectoris98), their increased frequency in patients with relatively longer durations of survival after AMI,5 10 and their high frequency in patients with severe congestive heart failure or cardiogenic shock with AMI,11 12 37 38 However, surprisingly little detailed information is available on the status of a coronary artery containing a thrombus in patients with fatal AMI.

The results of the present study raise questions regarding the importance of coronary thrombi in patients with fatal transmural AMI. The major finding in our study is that among patients with fatal AMI, thrombi are found in major coronary arteries that already are severely narrowed by old atherosclerotic plaques at, immediately proximal and/or immediately distal to the site of thrombosis. The lumen of the coronary artery containing the thrombus was already narrowed an average of 79% (range 26–98%) in cross-sectional area by atherosclerotic plaque alone at and within 2 cm proximal and distal to the thrombus; i.e., an "average" coronary artery with a thrombus was severely narrowed (79% in cross-sectional area) at three sites (at, proximal and distal to the
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thrombus). The "average" coronary arterial narrowing at the site of thrombus, however, actually underestimates the true severity of the narrowing in the vicinity of the thrombus. The site of most severe narrowing in the approximately 6-cm portion of artery examined was within the 2 cm proximal to the thrombus in 16 of 54 (30%) coronary arteries, at the site of thrombus in 25 (46%), and within the 2-cm segment distal to the thrombus in 13 (24%). At the site of most severe narrowing, 96% of the coronary arteries were narrowed 76–98% in cross-sectional area by atherosclerotic plaque, and half were narrowed 91–98%. In contrast, the percent of coronary lumen narrowed by thrombus alone averaged 19% of the original cross-sectional area of the artery (range 2–67%) in the 47 patients with occlusive thrombi, and 7% (range 2–24%) in the seven patients with nonocclusive thrombi. Thus, if thrombus were the only luminal material, the amount of thrombus within the coronary artery, with a few exceptions, probably would not by itself diminish or slow blood flow. A corollary to this statement is that among necropsy patients with fatal AMI, the coronary thrombus, when present, is always superimposed on an atherosclerotic plaque. The exception is coronary embolism, when clot may be present without underlying atherosclerotic plaque.14, 28 (Patients with coronary emboli, however, an infrequent cause of fatal AMI, were excluded from our study.)

Others15, 26, 29 have reported that thrombi, when present in a coronary artery in necropsy patients with AMI, most often are found in the more proximal portions of the major coronary arteries. Our study confirmed this observation, at least in regard to the two major branches of the left main coronary artery; but we also found thrombi to be more proximal in the case of nonocclusive than occlusive thrombi. Among the 47 patients with occlusive thrombi, the distance from the origin of the coronary artery to the proximal portion of the thrombus averaged 3.2 cm (range 0–15.5 cm), and among the seven patients with nonocclusive thrombi, 1.4 cm (range 0.5–3 cm). Of the 28 patients with occlusive thrombi in either the left anterior descending or left circumflex coronary artery, this distance averaged 2.1 cm (range 0–6 cm) and with the right coronary artery, 4.8 cm (range 0.5–15.5 cm). Thus, thrombi in the right coronary artery tend to be in its middle third more often than the proximal third.

The length of coronary thrombi in necropsy patients with fatal AMI has been described previously.15, 26 Of 91 patients studied by Sinapius,26 the average coronary thrombus was 2.0 cm long. Of 12 patients studied by Erhardt and colleagues,15 the average coronary thrombus was 2.7 cm long (range 0.4–8.5 cm). Among our 54 study patients, the average coronary thrombus was 1.6 cm long (range 0.5–10 cm); the occlusive thrombi were longer than the nonocclusive thrombi, 1.8 vs 0.7 cm. Also, occlusive thrombi in the right coronary arteries tended to be longer than those in the left anterior descending and left circumflex coronary arteries (2.4 vs 1.4 and 1.1, p < 0.025). Because the right and left anterior descending coronary arteries in adults are over 10 cm long and the left circumflex is usually about 6 cm long, the actual length of a coronary artery occupied by thrombus is small, and in no patient was the entire length of a coronary artery occupied by thrombus. In the right coronary artery, there was a weak, but significant, positive correlation between the length of an occlusive thrombus and the duration of survival of a patient between the time of AMI and death (p < 0.05). This relation suggests that thrombi may lengthen or "grow" with time. This finding supports the work of Erhardt and associates,15, 18 who demonstrated growth of thrombi after AMI by their uptake of 125I-labeled fibrinogen.

In seven of 13 patients, the left circumflex coronary artery with a thrombus was also the dominant posterior artery (i.e., the artery that crossed the crux of the heart and supplied the artery to the atrioventricular node). The left circumflex coronary artery is the dominant posterior artery in only about 12% of a random sample from a large population.40 The left circumflex appears to be more prone to thrombosis when it is the dominant posterior artery.

Finally, not all thrombi occupy the entire residual lumen of a coronary artery. In seven of our 54 patients (13%), the coronary thrombus was nonocclusive. It occupied on an average only 7% of the cross-sectional area of the coronary artery (range 2–24%) and was an average of 0.7 cm long (range 0.5–1.0 cm). These nonocclusive thrombi probably have little, if any, capacity to interfere with coronary arterial blood flow.

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