Histologic Studies in Percutaneous Transluminal Coronary Angioplasty for Chronic Total Occlusion: Comparison of Tapering and Abrupt Types of Occlusion and Short and Long Occluded Segments

MASAYUKI KATSURAGAWA, MD, HISAYOSHI FUJIWARA, MD, MASAMI MIYAMAE, MD, SHIGETAKE SASAYAMA, MD, FACC
Kyoto, Japan

Objectives. The purpose of this study was to examine the histologic-angiographic correlates of chronic total coronary occlusion and to explain why a tapering type of occlusion and short occluded segments are favorable for percutaneous transluminal coronary angioplasty.

Background. Coronary angioplasty is less successful for vessels with chronic total occlusion than for highly stenotic but patent vessels. Several clinical and angiographic factors determining the rate of initial success have been investigated, but the underlying histologic features are not clear.

Methods. Ten autopsy hearts that showed chronic total coronary occlusion on cineangiography performed <3 months before death were selected. In all, the estimated duration of occlusion was >1 year. At autopsy, postmortem angiography was performed and hearts were fixed with 10% buffered formalin. Occluded segments were sectioned transversely and serially into slices 10 μm thick. Every five slices were stained in hematoxylin-eosin and elastic van-Gieson.

Results. Ten hearts with chronic total coronary occlusion were angiographically classified into five with a tapering and five with an abrupt type of occlusion and seven with a short (≤15 mm) and three with a long (>15 mm) occluded segment. Histologically, the occluded segment was composed of loose or dense fibrous tissue, atheroma, small vascular channels and calcified tissue. Reconstruction of the serial preparations showed that small lumen recanalized areas (diameter 160 to 230 μm) with surrounding loose fibrous tissue penetrated the occluded segment in four hearts with occlusion of the tapering type and a short occluded segment. In these four cases, the lack of antegrade flow on cineangiography could be explained by the presence of rich collateral flow. In three cases of the abrupt type of occlusion with a short occluded segment, a mass of loose fibrous tissue penetrated the occluded segment. In hearts with a long occluded segment (one with a tapering type of occlusion and two with an abrupt type), there was no recanalization and loose fibrous tissue was dispersed in the occluded segment.

Conclusions. Chronic total coronary occlusion of the tapering type or with a short occluded segment, or both, is possibly favorable for angioplasty, because small lumen recanalized areas or loose fibrous tissue penetrates the occluded segment and may form a route for successful angioplasty.

(J Am Coll Cardiol 1993;21:604-11)

In the early experience with percutaneous transluminal coronary angioplasty, the favorable indications for the procedure were single vessel disease and proximal and discrete lesions without calcification (1). However, developments in catheter technique and equipment have made angioplasty possible for more complicated lesions, including acute or chronic total coronary occlusion (2). In cases of acute or recent myocardial infarction, occluding thrombus is not organized, is relatively soft and is easily crossed with a guide wire. In contrast, in chronic total coronary occlusion, occluding thrombus is organized and replaced by fibrous tissue; therefore, the success rate of coronary angioplasty for chronic total occlusion is low compared with that of acute or recent occlusion. The initial success rate is <60% when the duration of occlusion is >3 months (3-5) and the restenosis rate is ≥40% (6-9). The initial success rate has been reported to be mainly determined by the following factors (5,10): duration of the occlusion, presence of a tapering or abrupt type of occlusion, length of the occluded segment, presence of collateral circulation and presence of a vessel stump. However, the histologic features of chronic total occlusion are rarely studied, although these are believed to be important.

The present study was designed 1) to define the histologic differences between tapering and abrupt types of occlusion and between short and long occluded segments in coronary arteries with chronic total occlusion, and 2) to analyze the possible factors that might predict successful angioplasty.
Methods

Case selection (Table 1). Ten consecutive autopsy hearts from our cardiac pathology laboratory were studied. All had chronic total coronary occlusion without anterior graft flow of ≥ 3 months' before death (≤ 2 days in Case 2 and Case 6). The indication for coronary angiography was angina pectoris in eight patients and acute or recent myocardial infarction in two. In the cases with acute or recent infarction, chronic total occlusion was found in major coronary arteries other than the infarct-related artery. In all cases the patient had a clinical history of old myocardial infarction from 1 to 10 years before death, and the old infarct-related arteries showed total occlusion. Therefore, the interval from coronary occlusion to death was estimated to be > 1 year. The causes of death are listed in Table 1.

Cineangiography and postmortem angiography. Coronary cineangiography was performed with a Toshiba Cas-Up Angiexex System. Angiography of each coronary artery was performed in five to three projections in the right coronary artery and five projections in the left coronary artery) by injection of 0.5 ml of contrast medium in 3 to 5 s with recording on 35-mm cinefilm.

At autopsy, 8F polyethylene tubes were inserted into the right and left coronary orifices of each heart ≤ 3 h after death. Postmortem coronary angiography was performed with a barium-gelatin mixture that was infused at a pressure of 100 mm Hg. Low voltage (<50 kV) roentgenograms were taken by a Softex CMB-2. After fixation in 10% buffered formalin solution, major epicardial coronary arteries were removed from the epicardial surface. Low voltage roentgenograms of these coronary arteries were taken.

The following variables were examined on the cineangiogram: 1) the site of the occlusion and the length of the occluded segment. 2) presence of a tapering type of occlusion; 3) presence of collateral circulation; 4) presence of a side branch at the occluded segment; 5) presence of vessel stump beyond the last side branch. The method described by Kereiakes et al. (11) was used to quantitate the length of the nonvisualized occluded segment. Briefly, the segment from the point of total occlusion to the most proximal point of distal vessel visualization by collateral contrast filling was measured by using a transparent ruler on the 8 × 10-in. (20.3 × 25.4 cm) magnification (Elk Cap-35B, Elmo) angiogram. These estimations were made from a view perpendicular to the direction of flow in the vessel to minimize the effects of foreshortening.

Histologic examination. Removed coronary arteries including the cineangiographically occluded segment were decalcified, and sectioned transversely and serially into 2-mm slices. The slices were inspected, sketched and then embedded in paraffin. The slice of the occluded segment and one to two slices proximal and distal to them were sectioned transversely and serially into slices 10 μm thick. Hematoxylin-eosin and elastic-van Gieson stains were performed on every fifth slice. Other slices were stained if necessary. These specimens were examined by light microscopy.

Statistics. Histologic data were expressed as mean value ± SD. Statistical comparison was performed by Student's t test and Fisher exact test. A p value of < 0.05 was considered significant.
**Results**

Cineangiographic and postmortem angiographic findings. In all 10 cases, premortem cineangiograms and postmortem angiograms showed almost similar findings regarding the contour of the occluded segment. However, in each case, small vascular channels that were not visualized on the premortem study were visualized in the occluded segment on the postmortem angiogram (Fig. 1).

Angiographic findings of chronic total coronary occlusion are summarized in Table 2. Ten cases of chronic total coronary occlusion (five of the left anterior descending, three of the left circumflex and two of the right coronary artery) were classified as tapering or abrupt types of occlusion (five coronary arteries each) (Fig. 2). Side branches at the proximal site of occlusion were seen in only one of five cases with a tapering type of occlusion, but in four of five cases with an abrupt type. A vessel stump beyond the last side branch was seen in each heart with a tapering type of occlusion, but in only one with the abrupt type. The length of the occluded segment was 10 ± 9 mm in tapering occlusions and 14 ± 12 mm in abrupt occlusions (p = NS). There was no significant difference in the estimated duration of occlusion between the tapering and abrupt types or between the short (≤15 mm) and long (>15 mm) occluded segments.

Microscopic findings. Histologically, the segments with chronic total coronary occlusion were composed of loose or dense fibrous tissue, atheroma (foam cells or pultaceous debris), small vascular channels, calcified tissue and focal lymphocyte infiltrate (12). There was no evidence of fresh thrombus in any of them. Some loose fibrous tissue contained foam cells. Reconstruction of vascular channels using serial sections revealed that small recanalized areas penetrated the occluded segment from proximal lumen to distal lumen in four cases; the minimal diameter of these areas ranged from 160 to 230 μm. In all four cases the occlusion...
was of the tapering type (Fig. 2 and 3). In coronary arteries without small lumen recanalized areas, vascular channels extended to the small side branches or vasa vasorum within the occluded segment (Fig. 2 and 4). The length of the occluded segments was ≤8 mm in four cases with small lumen recanalization (6 ± 2 mm), and 16 ± 12 mm in six cases without it (p < 0.05).

From the reconstruction of the fibrous tissue, the cases were classified into two types. In type 1, a loose fibrous tissue mass penetrating continuously from the proximal to the distal site of the occluded segment (Fig. 2 and 4). Four of five coronary arteries with a tapering type of occlusion, each of which had small lumen recanalized areas, and three of five coronary arteries with the abrupt type of occlusion belonged to type 1. In each case with small lumen recanalized areas, the loose fibrous tissue of type 1 was present around the small lumen recanalized area. In type 2, penetrating loose fibrous tissue was not seen (Fig. 2 and 5A). Three occluded coronary arteries, one with a tapering type of occlusion and two with an abrupt type of occlusion, belonged to type 2. The length of the occluded segment was ≤9 mm in seven coronary arteries with type 1 (6 ± 2 mm) and >20 mm in each of three arteries with type 2 (26 ± 7 mm) (p < 0.05).

Foam cells, pultaceous debris and calcified tissue were found in each of 10 cases. Large massive pultaceous debris was found in five cases, 4 with a tapering type of occlusion

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Table 2. Cinseangiographic Findings of Chronic Total Coronary Occlusion

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Occluded Segment</th>
<th>Length of Occlusion (mm)</th>
<th>Collateral Vessels</th>
<th>Side Branch</th>
<th>Vessel Stump</th>
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<tr>
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<td>LCX</td>
<td>7</td>
<td>+</td>
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<td>8</td>
<td>+</td>
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<tr>
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<td>14 ± 4</td>
<td>5 ± 0</td>
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<td>Mean ± SD</td>
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<td>5 ± 2</td>
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*Significant difference between groups. LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; ← = absent; + = present.

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Figure 2. Clinical and histologic classification of chronic total coronary occlusion of the tapering type (left) and abrupt type (right). Left. In four of the five cases of the tapering type of occlusion, small recanalized areas penetrated the occluded segment. In these four cases, the occluded segment was short. Loose fibrous tissue (hatched areas) penetrating the occluded segment (type 1) was seen around the area of recanalization. Each had large pultaceous debris. In the fifth case of the tapering type, multiple and dispersed loose fibrous tissue masses were seen (type 2) and the occluded segment was long. There was no evidence of recanalization, although small vascular channels (asterisks) were observed in the occluded segment. Right, Recanalization was not seen in any heart with the abrupt type of occlusion. In two of these hearts, loose fibrous tissue of type 2 was present and the occluded segment was long. In the other three cases, loose fibrous tissue of type 1 was present and the occluded segment was short. Large pultaceous debris (cross-hatched areas) was present in one.
and 1 with an abrupt type. All five cases had a short occluded segment (Fig. 2, 3 and SB).

The estimated duration of occlusion did not differ significantly between the hearts with and without recanalization, or between the cases with loose fibrous tissue of type 1 and type 2.

Discussion

Cineangiographic features of chronic total coronary occlusion favorable for percutaneous transluminal coronary angioplasty are a tapering rather than an abrupt type of occlusion (IO), a short (<1.5 cm) rather than a long occluded segment (12), presence of collateral circulation and of a vessel stump beyond the last side branch (4,5). For successful dilation of arteries with chronic total coronary occlusion, it is necessary for the guide wire to cross the occluded segment, which is filled with organized thrombus (13). The guide wire would go through the least resistant part of the occluded segment (14,15).

Advantages of tapering type of occlusion, small lumen recanalization, surrounding loose fibrous tissue and vessel stump. The present study revealed that in hearts with the tapering type of occlusion, small lumen recanalized areas and surrounding loose fibrous tissue were frequently seen. The average diameter of the recanalized lumen was 200 μm, which was just slightly smaller than the size of current available guide wires. The presence of surrounding loose fibrous tissue might help the crossing of the guide wire through the recanalized lumen. In addition, the arteries of these hearts had a shorter occluded segment and had a vessel stump. These features would explain why the tapering type of occlusion is favorable for angioplasty. In many hearts with an abrupt type of occlusion, the main lumen was occluded just distal to the branching point of a side branch and the lumen extended smoothly to the side branch. As a result, no vessel stump was seen. In addition, recanalization was rare in hearts with an abrupt type of occlusion. Therefore, the guide wire would easily enter the side branch but be unable to enter the occluded segment. A possible route of the angioplasty wire in the abrupt type of occlusion may be the loose fibrous tissue penetrating the occluded segment. This route was taken in three of five coronary arteries with the abrupt type of occlusion. In these hearts, the length of the occluded segment was relatively short. A short occluded segment was seen only in coronary arteries with a tapering type of occlusion with small lumen recanalized areas or with an abrupt type of occlusion with loose fibrous tissue penetrating the occluded segment. Thus, the tapering type of occlusion or a short occluded segment, or both, is favorable for angioplasty because of the presence of a vessel stump, a short segment and favorable histologic features.

In each occluded segment, small vascular channels were observed. Some of these extended from the proximal to the distal lumen (recanalization), but others extended to the small side branch or vasa vasorum (no recanalization). If the
guide wire or balloon catheter, or both, enters the recanalized vascular channel, angioplasty would be successful. However, if either enters the vascular channel that extends to the small side branch or vasa vasorum, a subintimal false lumen may be formed and perforation may occur. Even if the guide wire and catheter go through the false lumen and return to the distal true lumen, dilation may result in acute redilation.

Intracoronary thrombus formation after the rupture of an atherosclerotic plaque extends distal and proximal to the rupture site (16–18). In the present study, the special feature of the tapering type of occlusion was the presence of a vessel stump and recanalization; that of the abrupt type was the presence of a side branch, no vessel stump and no recanalization. These findings suggest that the arteries that are recanalized after thrombotic occlusion will manifest the tapering type of vessel occlusion with a vessel stump. The arteries that are not recanalized will manifest the abrupt type. In these cases, thrombus formation extends to the proximal site and reaches to the branching point of the large side branch, and a vessel stump is not formed.

Generally, stenotic lesions of coronary arteries without occlusion were classified as short (≤5 mm), tubular (5 to 20 mm) or long (≥20 mm) according to the length of the lesion (19). In the present study, a short occluded segment (≤9 mm) showed recanalization or penetrating loose fibrous tissue, or both, on histologic study. However, we do not know whether these histologic features were the cause or the result of shortness of the occluded segment. In long occluded segments, massive loose fibrous tissues were multiple, suggesting the importance of repeated multiple thrombotic events in the pathogenesis. In addition, short or long stenotic lesions preceding thrombotic occlusion may also be one of the important factors for short or long occluded segments.

Methodologic problems. In the present study, 4 of 10 hearts with cineangiographic total occlusion had recanalization, although we excluded hearts with functional occlusion (delayed flow) and selected only those with chronic total occlusion (no anterograde flow). Generally, it is difficult to detect a coronary artery <300 μm in diameter with coronary cineangiography (20). The diameter of the recanalized arter-
ies in this study was <230 μm. The postmortem angiogram showed the presence of small vascular channels in the cineangiographically occluded segment in each of 10 coronary arteries. However, it was difficult to define the three-dimensional structure of each vascular channel from the postmortem angiogram. Therefore, the presence of the recanalization was confirmed by histologic reconstruction.

On premortem cineangiography, each heart had a rich collateral flow; in this setting, anterograde flow through the stenotic segment may disappear, decreasing the pressure gradient across the stenotic segment. In addition, the interval between premortem coronary cineangiography and autopsy was ≤3 months, and only 1 and 2 days, respectively, in two of four cases. The estimated duration of occlusion in these four cases was >2 years. These observations indicate that the discrepancy between cineangiographic and histologic findings cannot be explained by assuming that the occluded segment was recanalized after cineangiography; rather, it is due to the limitation of cineangiography. Some cases seen as chronic total occlusion with rich collateral circulation on cineangiography had small lumen recanalization at autopsy.

The duration of occlusion is usually considered the key factor determining the initial success of angioplasty in chronic total occlusion. A short duration of occlusion (≤3 months) is favorable, whereas a long duration of occlusion (>3 months) is unfavorable. Because it is difficult to collect many hearts with both various durations of occlusion and coronary cineangiography performed ≤3 months before death, the present study focused on cases with an occlusion duration >1 year, thereby excluding the factor of duration of occlusion in comparing the histologic and the angiographic variables. Under these conditions, we found no macroscopic and histologic variables associated with the estimated duration of occlusion. Further investigation of this factor is warranted.

Conclusions. Chronic total coronary occlusions of the tapering type or with a short occluded segment often had small lumen recanalized areas or a loose fibrous tissue mass penetrating the occluded segment, or both. These histologic features are probably important factors in successful angioplasty.

We thank Yumiho Yamamoto and Miwa Yoshida for assistance in preparing this manuscript.

References