Intravascular Ultrasound Analysis of Infarct-Related and Non–Infarct-Related Arteries in Patients Who Presented With an Acute Myocardial Infarction

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**Background**—Previous studies have reported diffuse destabilization of atherosclerotic plaques in acute myocardial infarction (AMI).

**Methods and Results**—We used intravascular ultrasound (IVUS) to assess 78 coronary arteries (38 infarct-related arteries [IRAs] with culprit and nonculprit lesions and 40 non-IRAs) from 38 consecutive AMI patients. IVUS analysis included qualitative and quantitative measurements of reference and lesion external elastic membrane (EEM), lumen, and plaque plus media (P&M) area. Positive remodeling was defined as lesion/mean reference EEM >1.0. Culprit lesions were identified by a combination of ECG, wall motion abnormalities (ventriculogram or echocardiogram), scintigraphic perfusion defects, and coronary angiogram. Culprit lesions contained more thrombus (23.7% versus 3.4% in nonculprit IRA plaques and 3.1% in non-IRA plaques; \(P=0.0011\)). Culprit lesions were predominantly hypoechoic (63.2% versus 37.9% of nonculprit IRA plaques and 28.1% of non-IRA plaques; \(P=0.0022\)). Culprit lesions were longer (17.5±10.1, 9.8±4.0, and 10.3±5.7 mm, respectively; \(P<0.0001\)) had larger EEM area (15.0±6.0, 11.5±5.7, and 12.6±5.6 mm², respectively; \(P=0.0533\)) and P&M area (13.0±6.0, 7.5±3.7, 9.3±4.3 mm², respectively; \(P<0.0001\)), smaller lumens (2.0±0.9, 4.1±3.1, and 3.4±2.5 mm², respectively; \(P=0.0009\)), and more positive remodeling (79.4%, 59.0%, and 50.8%, respectively; \(P=0.0155\)). The frequency of plaque rupture/dissection was greater in culprit, nonculprit IRA, and non-IRA plaques in AMI patients than in a control group of chronic stable angina patients with multivessel IVUS imaging.

**Conclusions**—Culprit plaques have more markers of instability (thrombus, positive remodeling, and large plaque mass); however, these markers of instability are not typically found elsewhere. This suggests that the vascular event in AMI patients is determined by local pre-event lesion morphologies. (*Circulation.* 2003;107:2889-2893.)

**Key Words:** myocardial infarction ■ plaque ■ ultrasonics

Acute myocardial infarction (AMI) is caused by plaque disruption (or erosion) and secondary thrombosis. Previous studies have reported diffuse destabilization of atherosclerotic plaques, leading to the concept of “pancoronaritis” in AMI patients. Intravascular ultrasound (IVUS) can assess vessel wall architecture and remodeling in a way not possible with angiography or angioscopy. In the present study, we investigated the characteristics of the “culprit plaque” in comparison with nonculprit plaques of both infarct-related artery (IRA) and non-IRA in AMI patients.

**Methods**

**Patient Population**

Between April 1997 and May 2000, IVUS was performed in 2 or more native arteries in 38 patients within 1 week from onset of a myocardial infarction. All patients had documented ST-segment changes and creatine kinase >3 times normal. The IRA and the culprit lesion were identified by the combination of ECG findings, left ventricular wall motion abnormalities (left ventriculography or echocardiography), scintigraphic defects, and angiographic lesion morphology. In selecting a second or third artery to image, the ones with the more severe angiographic disease were studied. Using IVUS, 3 types of plaques were identified and compared: IRA culprit plaques, IRA nonculprit plaques, and non-IRA plaques.

As a control group, we examined 48 consecutive chronic stable angina patients with multivessel IVUS imaging. There were 91 plaques in 48 ischemia-related arteries and 77 plaques in 51 non–ischemia-related arteries.

**Angiographic Analysis**

All angiograms were analyzed with an automated edge-detection algorithm (CAAS II, Pie Medical) by an independent angiographic core laboratory using standard protocols. Because some nonculprit plaques were completely undetectable by angigram, information from the IVUS study was sometimes necessary to identify the plaque location.

**IVUS Imaging**

All IVUS examinations were performed before any intervention and after intracoronary administration of 100 to 200 μg of nitroglycerin using a commercially available IVUS system that incorporated a 30- or 40-MHz transducer within a short monorail imaging sheath (Boston Scientific...
Corporation/SciMed). The IVUS catheter was advanced distal to the target, and imaging was performed retrograde back to the aorto-ostial junction at an automatic pullback speed of 0.5 mm/s.

**IVUS Qualitative Analysis**

Qualitative analysis was performed according to criteria of the American College of Cardiology clinical expert consensus document on IVUS and the Study Group on Intracoronary Imaging of the Working Group of Coronary Circulation and of the Subgroup on IVUS of the Working Group of Echocardiography of the European Society of Cardiology.6,7 Identification of 2 separate plaques in the same artery (ie, IRA culprit versus nonculprit plaques) required a ≥5-mm reference segment between them; if not, they were considered to be part of one long lesion.

Calcium was brighter than the adventitia with acoustic shadowing. The location (superficial, deep, or mixed) was noted, and the arc (in degrees) and length (in millimeters) were measured. Calcified plaque had an arc >90°. Hyperechoic plaque was as bright or brighter than the adventitia without shadowing. Hypoechoic plaque was less bright than the adventitia. When there was no dominant plaque composition, the plaque was considered “mixed.” The identification of thrombus required at least 2 of the following: distinct hypoechoic mass, brightly speckled plaque, channeling within the plaque, evacuated plaque cavity, or detached mobile mass.

A ruptured plaque contained a cavity that communicated with the lumen with an overlying residual fibrous cap fragment. A dissection was a longitudinal tear in the plaque parallel to the vessel wall.

**IVUS Quantitative Analysis**

Using planimetry software (TapeMeasure, INDEC Systems Inc), lesion and proximal and distal references were analyzed as follows: external elastic membrane cross-sectional area (EEM CSA, in millimeters squared), lumen CSA (in millimeters squared), and plaque and media CSA (P&M =EEM minus lumen, in millimeters squared). Plaque burden (percent) was calculated as P&M divided by EEM CSA. The reference segments were the most normal-looking cross sections within 5 mm proximal and distal to the lesion but before any side branch. A remodeling index was calculated as the lesion divided by the mean reference EEM. Positive remodeling was defined as a remodeling index >1.0.1 Eccentricity was minimum/maximum P&M thickness.

**Statistical Analysis**

Statistical analysis was performed with StatView 5.0 (SAS Institute). Categorical variables are presented as frequencies and compared by χ² statistics or Fisher’s exact test. Continuous variables are presented as mean±1SD and compared by unpaired t test or ANOVA (with post hoc comparisons using Fisher’s protected least significant difference test). P<0.05 was considered statistically significant.

**Results**

**Patient Population**

Mean duration from onset of AMI to IVUS was 4±2 days. Sixteen patients (42.1%) had ST-segment elevation. Seventeen patients (44.7%) were treated with thrombolysis before IVUS examination, and no patient received glycoprotein IIb/IIIa receptor blocker agents. The other 21 patients underwent primary angioplasty. Patient background is summarized in Table 1.

The IRA (n=38) was left anterior descending in 10, left circumflex in 13, and right coronary in 15. The nonculprit IRA plaques were proximal to the culprit in 12 of 29 arteries and distal in 17 of 29 arteries. The non-IRA (n=40) was diagonal in 2, left anterior descending in 16, left circumflex in 13, and right coronary in 10. An example is shown in the Figure. Quantitative angiographic analysis is shown in Table 2. Culprit plaques had smaller minimum lumen diameters and larger diameter stenoses than IRA nonculprit plaques and non-IRA plaques.

**TABLE 1. Patient and Lesion Characteristics**

<table>
<thead>
<tr>
<th>Patients, n</th>
<th>38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62±11</td>
</tr>
<tr>
<td>Gender, male/female, n</td>
<td>24/14</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>50.6±10.8</td>
</tr>
<tr>
<td>Hypertension, n</td>
<td>18</td>
</tr>
<tr>
<td>Diabetes mellitus, n</td>
<td>4</td>
</tr>
<tr>
<td>Family history, n</td>
<td>18</td>
</tr>
<tr>
<td>Current smoker, n</td>
<td>17</td>
</tr>
<tr>
<td>Cholesterol level, mg/dL</td>
<td>199±51</td>
</tr>
<tr>
<td>Infarct area, n (%)</td>
<td>38 (100)</td>
</tr>
<tr>
<td>Arterial wall (including apex)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Lateral wall</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Inferolateral wall</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Inferior wall</td>
<td>12 (31.6)</td>
</tr>
<tr>
<td>Arteries (including IRA and non-IRA), n (%)</td>
<td>78 (100)</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>25 (32.1)</td>
</tr>
<tr>
<td>Diagonal</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>26 (33.3)</td>
</tr>
<tr>
<td>Right coronary</td>
<td>25 (32.1)</td>
</tr>
</tbody>
</table>

**Qualitative IVUS Findings**

Qualitative IVUS findings are shown in Table 3. In the IRA, there were 38 culprit and 29 nonculprit plaques. In the non-IRA, there were 64 distinct plaques. Therefore, there were 1.8±0.6 IRA plaques per patient (range 1 to 3) and 1.5±0.5 non-IRA plaques per patient (range 1 to 3). Thrombi were more common in culprit plaques than in IRA nonculprit plaques or non-IRA plaques. Ruptured/dissected plaques were similar in frequency in all 3 locations. Multiple plaque ruptures were seen in 4 IRAs; however, no non-IRA contained multiple plaque ruptures.

Only 2 (4.2%) of 48 ischemia-related lesions of the control (chronic stable angina) group had ruptured/dissected plaques (P=0.1 compared with culprit lesions of AMI patients). None of the 43 nonculprit plaques in ischemia-related arteries of the control group contained rupture/dissected plaques (P=0.0231 versus nonculprit plaques of IRAs in AMI patients). Only 1 of the 77 lesions in the non–ischemia-related arteries of the control group contained a ruptured/dissected plaque (1.3% versus 9.4% in the AMI group; P=0.0466). Multiple ruptures were seen more frequently in AMI patients (10.5%) than in control patients (0%; P=0.0348).

**Quantitative IVUS Findings**

Quantitative IVUS findings are shown in Table 4. Culprit lesions were longer, had larger EEM and P&M CSA and smaller CSA, and more often presented with positive remodeling than did IRA nonculprit plaques and non-IRA plaques. There was a trend for culprit plaques to be less eccentric than nonculprit plaques (0.4±0.3, 0.3±0.2, and 0.3±0.3, respectively; P=0.08).

**Characteristics of Angiographic “Occult” Lesions**

Five (17.2%) of the nonculprit plaques in the IRAs and 4 (6.3%) of the non-IRA plaques were not evident angiographically. IVUS lesion location data (ie, the distance from a major branch to the plaque) was used to perform quantitative angiography. The diameter stenosis (28.1±5.0%) and the minimal lumen diameter
(1.8±0.6 mm) of these plaques were less severe than those of other nonculprit plaques (54.1±15.2%, \( P<0.0001 \) and 1.2±0.6 mm, \( P=0.0117 \), respectively). IVUS analysis of these plaques showed more plaque eccentricity (0.3±0.3 versus 0.2±0.1; \( P=0.0438 \)) than other angiographically detectable nonculprit plaques. The other quantitative and qualitative findings were similar.

**Discussion**

The present study showed that culprit plaques in AMI are distinct from nonculprit plaques in the same artery and plaques in non-IRA arteries. The 2 “control groups” (the nonculprit plaques in the IRAs and the non-IRA plaques) were similar. The frequency of plaque rupture/dissection was greater in AMI patients than in a control group of patients with chronic stable angina.

### Difference Between Culprit Plaques and Nonculprit Plaques

The characteristics of the culprit plaques were (1) more positive remodeling and larger EEM and P&M CSA, (2) more hypoechoic plaque and lesser amounts of other (hyperechoic/mixed/calcific) plaque types, and (3) more evidence of thrombus. The IRA nonculprit plaques and the non-IRA plaques had similar IVUS lesion morphologies, and culprit and nonculprit plaques (whether in IRAs or non-IRAs) had a similar frequency of plaque rupture.

Previous reports have studied differences between culprit versus nonculprit plaques in specific subsets of ACS patients and between target lesions in ACS patients versus chronic stable angina patients. The present study extends these observations to patients who present with ST-segment elevation myocardial infarction (MI). Most (83.3%) of the plaque ruptures of non-IRAs in the present study were observed in ST-elevation MI patients.

Rioufol et al \(^4\) reported plaque ruptures somewhere other than the culprit lesion in 79% of patients with acute coronary syndrome (ACS). When they compared culprit lesions (of which only 37.5% showed evidence of rupture) with remote ruptured plaques, they found a smaller lumen CSA, larger plaque burden, longer lesion length, and more calcium in the culprit lesions but similar remodeling response in culprit and nonculprit ruptured plaques. \(^4\) They did not compare culprit lesions with nonculprit plaques regardless of the presence of plaque rupture or with non-IRA plaques regardless of the presence of plaque rupture, as was done in the present analysis. Asakura et al \(^2\) performed angioscopy in 20 MI patients. They showed residual yellowish plaque in 90% of culprit lesions; yellowish plaque was observed diffusely (3.2±1.7 per artery) in all major arteries. Von Birgelen et al \(^8\) compared ruptured plaques versus nonruptured plaques in the same artery and versus another group of patients with computer-matched control plaques. The greatest ec-

### TABLE 2. Angiographic Findings

<table>
<thead>
<tr>
<th></th>
<th>IRAs (n=67)</th>
<th>Culprit Plaques (n=38)</th>
<th>Nonculprit Plaques (n=29)</th>
<th>Non-IRA Plaques (n=64)</th>
<th>P, ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference, mm</td>
<td>2.7±0.6</td>
<td>2.4±0.7</td>
<td>2.7±0.7</td>
<td>2.7±0.7</td>
<td>0.4</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.6±0.5*</td>
<td>1.3±0.5</td>
<td>1.3±0.7</td>
<td>1.3±0.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DS, %</td>
<td>79.6±15.3*</td>
<td>42.2±17.0</td>
<td>51.1±17.0</td>
<td>51.1±17.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

MLD indicates minimal lumen diameter; DS, diameter stenosis. \(^*P<0.01\) vs others.
centricity, positive remodeling, and hypoechoic plaque morphologies were seen in ruptured plaques; these findings occurred with decreasing frequency in nonruptured plaques (in the same artery) and in matched control plaques in other patients, respectively. Earlier reports compared patients with different coronary syndromes (eg, patients with ACS, AMI, or stable angina). These reports showed more plaque disruption, more hypoechoic plaque, and more positive remodeling in target lesions in patients with unstable coronary syndromes versus patients with stable angina.9,10 11

Finally, a study by Hoffmann et al13 showed patient and local influences between lesion morphologies in the same patient. Changes of the lesion site secondary to the event could theoretically account for some of the findings. Only future large-scale, prospective studies will allow definitive assessment of plaque vulnerability.

Frequency of Plaque Rupture

The frequency of nonculprit plaque ruptures was lower in the present study than the one previous report.4 Although the reasons for this difference are not entirely clear, a lower frequency of remote plaque rupture would influence strategies to detect multiple vulnerable plaques in unstable patient subsets.

Multiple plaque ruptures were seen in only 10.5% of the patients in the present study. This is in sharp contrast with the study by Rioufol et al,4 which showed multiple plaque rupture in 79% of

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TABLE 4. Quantitative IVUS Findings

<table>
<thead>
<tr>
<th>IRA Plaques (n=67)</th>
<th>Culprit (n=38)</th>
<th>Nonculprit (n=29)</th>
<th>Non-IRA (n=64)</th>
<th>P, ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEM CSA, mm²</td>
<td>14.8±6.4</td>
<td>11.9±5.2</td>
<td>13.9±6.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Lumen CSA, mm²</td>
<td>7.6±3.6</td>
<td>6.9±3.5</td>
<td>7.3±3.8</td>
<td>0.8</td>
</tr>
<tr>
<td>P&amp;M CSA, mm²</td>
<td>7.2±3.8</td>
<td>4.9±2.8</td>
<td>6.5±4.0</td>
<td>0.0576</td>
</tr>
<tr>
<td>Calcium arc, °</td>
<td>90.4±40.5</td>
<td>80.2±38.6</td>
<td>93.1±16.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Calcium length, mm</td>
<td>3.7±1.1</td>
<td>2.6±1.1</td>
<td>2.7±1.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Length, mm</td>
<td>17.5±10.1†</td>
<td>9.8±4.0</td>
<td>10.3±5.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EEM CSA, mm²</td>
<td>15.0±6.0†</td>
<td>11.5±5.7</td>
<td>12.6±5.6</td>
<td>0.0353</td>
</tr>
<tr>
<td>Lumen CSA, mm²</td>
<td>2.0±0.9*</td>
<td>4.1±3.1</td>
<td>3.4±2.5</td>
<td>0.0009</td>
</tr>
<tr>
<td>P&amp;M CSA, mm²</td>
<td>13.0±6.0*</td>
<td>7.5±3.7</td>
<td>9.3±4.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positive remodeling, %</td>
<td>79.4*</td>
<td>50.0</td>
<td>50.8</td>
<td>0.0155</td>
</tr>
<tr>
<td>Calcium arc, °</td>
<td>75.4±35.1</td>
<td>93.1±46.1</td>
<td>80.2±38.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Calcium length, mm</td>
<td>2.5±1.5</td>
<td>2.7±1.2</td>
<td>2.6±1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Distal reference</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEM CSA, mm²</td>
<td>11.0±4.8</td>
<td>11.4±5.5</td>
<td>10.3±5.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Lumen CSA, mm²</td>
<td>5.5±2.2</td>
<td>6.5±3.5</td>
<td>5.6±2.9</td>
<td>0.2</td>
</tr>
<tr>
<td>P&amp;M CSA, mm²</td>
<td>5.6±3.6</td>
<td>4.9±3.2</td>
<td>4.7±3.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Calcium arc, °</td>
<td>60.2±26.6</td>
<td>116.8±78.5†</td>
<td>69.1±34.2</td>
<td>0.0492</td>
</tr>
<tr>
<td>Calcium length, mm</td>
<td>2.6±1.3</td>
<td>5.2±3.8†</td>
<td>2.2±1.4</td>
<td>0.0490</td>
</tr>
</tbody>
</table>

*P<0.01 vs others; †P<0.05 vs others.
patients. There is no easy way to explain this difference. However, 
Rioufol et al4 studied all 3 coronary arteries, whereas in the present 
study, only 2 patients had IVUS imaging of all 3 arteries; they 
included patients with a broad range of acute coronary syndromes; 
and they studied patients up to 4 weeks after symptom onset.

The diagnosis of plaque rupture may be affected by the presence 
and size of a coronary thrombus; the presence and size of a 
thrombus may, in turn, be affected by the time from symptom onset 
to imaging. Most previous IVUS and/or angiographic studies that 
assessed both IRAs and non-IRAs studied patients in the relatively 
subacute phase (up to 4 to 6 weeks) after the onset of an MI.14,15 
The time from symptom onset to imaging in the study by Rioufol et 
al4 was 3 days to 1 month (mean 2.3±1.5 weeks). Rioufol et al4 did 
not include the critical stage of unstable angina, such as Braun-
wald’s classification class III (rest angina within 48 hours) or the 
acute phase of AMI, even though their study included ST-elevation 
MI patients. The angiographic study by Asakura et al2 was per-
fomed 1 month after the onset of MI. Detection of a ruptured 
plaque may also be affected by the healing response, which 
presumably is also related to the interval between symptom onset 
and imaging.

The pharmacological treatment between symptom onset and 
image might affect both the amount of thrombus and the healing 
response of the ruptured plaque. The IVUS analysis in the present 
study showed no difference between patients with and without 
thrombolysis before imaging: EEM CSA, lumen CSA, P&M CSA, 
plaque burden, and the frequency of plaque rupture/dissection were 
similar.

The diagnosis of thrombus by IVUS is presumptive. Therefore, 
no definitive relationship between interval, therapy, thrombus bur-
den, and IVUS findings of plaque rupture is possible. Finally, a 
previous study reported patients who had sudden death due to 
coronary thrombosis without evidence of plaque rupture.16

**Study Limitations**

This study was retrospective. Not all arteries were imaged. The 
issues of the diagnosis of thrombus by IVUS have been discussed. 
Arteries were, in general, diffusely diseased. The selection of the 
nonculprit plaques and the second, non-IRA to image may have 
cluded some bias. Finally, the insertion of the IVUS catheter 
through a subtotal occlusion could have caused changes in lesion 
gometry that may have contributed to the findings.

**Conclusions**

Although both IRAs and non-IRAs showed similar numbers of 
atherosclerotic plaques, culprit plaques were distinctly different 
from nonculprit plaques whether the nonculprit plaques occurred in 
the same or a different artery. This suggests that the vascular event 
in AMI patients is determined by pre-event lesion morphologies.

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