Frequency and Location of Yellow and Disrupted Coronary Plaques in Patients as Detected by Angioscopy

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Background: Clarification of frequency and distribution of yellow plaques and disrupted plaques will increase understanding of acute coronary syndrome (ACS) onset.

Methods and Results: Consecutive patients with ACS (n=75) or without ACS (n=90) who received coronary angioscopic examination were studied. Distance from ostium to yellow plaques, diameter stenosis and vessel wall irregularity at the site of yellow plaques, their yellow color grade (grade 1–3) and if they had thrombus were analyzed. Yellow plaques with thrombus were regarded as disrupted. Average number of yellow plaques, grade-3 yellow plaques and disrupted yellow plaques per vessel was 4.0, 0.87 and 1.0, respectively. The number of grade-3 yellow plaques and disrupted yellow plaques per vessel were larger in ACS than in non-ACS patients. Yellow plaques were distributed diffusely in the right coronary artery but more in mid-segments in the left anterior descending coronary artery and left circumflex coronary artery. Diameter stenosis in the non-culprit segments was severer at disrupted than at non-disrupted yellow plaques. Vessel wall irregularity was detected more frequently at disrupted than at non-disrupted yellow plaques.

Conclusions: Approximately 4 yellow plaques, 1 grade-3 yellow plaque and 1 disrupted yellow plaque were detected per vessel. About 25% of detected yellow plaques were disrupted. More grade-3 yellow plaques and disrupted yellow plaques were detected in ACS than in non-ACS patients. These findings strengthen the association between yellow plaques detected by angioscopy and ACS events. (Circ J 2011; 75: 603–612)

Key Words: Acute coronary syndrome; Angioscopy; Disrupted yellow plaque; Yellow plaque

Vulnerable plaques are supposed to cause acute coronary syndrome (ACS) by their disruption and subsequent thrombus formation. Many efforts have been made so far to identify vulnerable plaques by various methodologies; and thin-cap fibroatheroma (TCFA) observed by pathological studies is regarded as vulnerable plaque and the target for clinical diagnostic tools. Angioscopy can detect both the yellow color of plaque that is associated with high thrombogenic potential and the thin fibrous cap, and thus high vulnerability of the plaque. Furthermore, angioscopically-detected disrupted yellow plaques would include both ruptured and eroded plaques, because >90% of ACS culprits are yellow by angioscopy, whereas 70% of them are pathologically ruptured and 30% eroded. However, silent plaque ruptures have been detected widely in the non-culprit segments of coronary arteries of patients with or without ACS by intravascular ultrasound, optical coherence tomography and pathological studies. However, angioscopy would be most suitable to detect intracoronary thrombus in living humans, and thus, fresh disruption of plaque that has thrombus can be detected by angioscopy, differentiating it from the old disruption that has already healed and does not have fresh thrombus anymore. Therefore, in the present study, we have examined the frequencies and distributions of yellow plaques that are regarded vulnerable and unhealed disrupted yellow plaques that still have thrombus, and also we have compared the frequencies of those plaques between patients with ACS and those without ACS who have no history of prior ACS.

Methods

Study Patients
Consecutive patients with ACS (n=75) or without ACS (n=90) who received coronary angioscopic examination were studied. Distance from ostium to yellow plaques, diameter stenosis and vessel wall irregularity at the site of yellow plaques, their yellow color grade (grade 1–3) and if they had thrombus were analyzed. Yellow plaques with thrombus were regarded as disrupted. Average number of yellow plaques, grade-3 yellow plaques and disrupted yellow plaques per vessel was 4.0, 0.87 and 1.0, respectively. The number of grade-3 yellow plaques and disrupted yellow plaques per vessel were larger in ACS than in non-ACS patients. Yellow plaques were distributed diffusely in the right coronary artery but more in mid-segments in the left anterior descending coronary artery and left circumflex coronary artery. Diameter stenosis in the non-culprit segments was severer at disrupted than at non-disrupted yellow plaques. Vessel wall irregularity was detected more frequently at disrupted than at non-disrupted yellow plaques.

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ACS, n=90) who received successful coronary angiographic examination were analyzed. Patients without ACS but with the history of prior ACS were excluded from the analysis. Therefore, 24 patients were excluded.

Although we included all the consecutive patients who received successful angioscopic examination during the period from May 2007 to April 2008, angioscopic examination was performed for the following reasons: (1) to identify and evaluate the culprit lesions in ACS patients; (2) to evaluate the stabilization/healing of the disrupted culprit plaques in the follow-up of ACS patients; (3) to evaluate the percutaneous coronary intervention (PCI) target lesions in patients with stable effort angina or silent myocardial ischemia; (4) to evaluate the stabilization/healing of the PCI site in the follow-up of patients with stable effort angina or silent myocardial ischemia; (5) to examine if the patient has disrupted yellow plaque and thrombus formation in the suspected ACS patients without significant coronary stenosis; and (6) to evaluate the neointima over drug-eluting stent.

Oral aspirin (200 mg) and clopidogrel (300 mg) were given to patients with an acute myocardial infarction (MI) during their emergency care. Intravenous heparin (100 U/kg) was administered at the beginning of catheterization, and an additional dose was repeated at the time of PCI as a component of standard care. GP-IIIb/IIa inhibitors were not used for any patients, because they were not approved in Japan at the time of the study.

ACS includes acute MI with ST elevation (STEMI) or without ST elevation (NSTEMI) as defined by The Joint European Society of Cardiology/American College of Cardiology Committee. Unstable angina was defined according to the Braunwald classification. Among 75 ACS patients, 35 patients were diagnosed as STEMI, 12 patients as NSTEMI, and 28 patients as unstable angina. Hypertensive patients were defined as those with systemic arterial pressure >140/90 mmHg or those already taking anti-hypertensive drugs. Diabetic patients were defined as those with fasting blood glucose >126 mg/dl or those already taking oral drugs for diabetes mellitus or receiving insulin therapy. Obesity was defined as a body mass index (BMI = weight (kg)/[height (m)]^2) >26.4. Written informed consent was acquired from all patients. The protocol was approved by the Osaka Police Hospital Ethical Committee.

**Table 1. Clinical Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>ACS</th>
<th>Non-ACS</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>165</td>
<td>75</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>134 (81)</td>
<td>63 (84)</td>
<td>71 (79)</td>
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<tr>
<td>Age, years</td>
<td>63.2±10.7</td>
<td>63.4±10.4</td>
<td>63.3±11.0</td>
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<td>Risk factors, n (%)</td>
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<td></td>
<td></td>
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<tr>
<td>DM</td>
<td>57 (35)</td>
<td>24 (32)</td>
<td>33 (37)</td>
<td>0.71</td>
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<tr>
<td>HT</td>
<td>132 (80)</td>
<td>61 (81)</td>
<td>71 (79)</td>
<td>0.77</td>
</tr>
<tr>
<td>Smoking</td>
<td>100 (61)</td>
<td>51 (68)</td>
<td>49 (54)</td>
<td>0.11</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24.4±3.1</td>
<td>24.6±2.8</td>
<td>24.3±3.4</td>
<td>0.50</td>
</tr>
<tr>
<td>Lipid profile, mg/dl</td>
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<tr>
<td>TC</td>
<td>201.5±40.8</td>
<td>204.4±43.5</td>
<td>199.0±38.5</td>
<td>0.41</td>
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<td>HDL-C</td>
<td>47.0±10.6</td>
<td>45.9±9.7</td>
<td>47.9±11.3</td>
<td>0.21</td>
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<td>TG</td>
<td>198.3±159.9</td>
<td>191.6±162.3</td>
<td>203.8±158.5</td>
<td>0.63</td>
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<tr>
<td>LDL-C</td>
<td>121.8±34.0</td>
<td>132.5±36.3</td>
<td>113.0±29.4</td>
<td>&lt;0.001</td>
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<td>HbA1c</td>
<td>5.88±1.35</td>
<td>6.13±1.67</td>
<td>5.68±0.97</td>
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<td>Target vessel, n (%)</td>
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<tr>
<td>LAD</td>
<td>79 (48)</td>
<td>32 (43)</td>
<td>47 (52)</td>
<td></td>
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<tr>
<td>LCX</td>
<td>26 (16)</td>
<td>11 (15)</td>
<td>15 (17)</td>
<td></td>
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<tr>
<td>RCA</td>
<td>60 (36)</td>
<td>32 (43)</td>
<td>28 (31)</td>
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<tr>
<td>No. of diseased vessel, n (%)</td>
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<tr>
<td>0</td>
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<td>7 (9)</td>
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<td>1</td>
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<td>3</td>
<td>28 (17)</td>
<td>17 (23)</td>
<td>11 (12)</td>
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<tr>
<td>Medications, n (%)</td>
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<tr>
<td>Statins</td>
<td>65 (39)</td>
<td>13 (17)</td>
<td>52 (58)</td>
<td>&lt;0.001</td>
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<tr>
<td>Aspirin</td>
<td>104 (63)</td>
<td>24 (32)</td>
<td>80 (89)</td>
<td>&lt;0.001</td>
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<tr>
<td>Clopid/Ticlo</td>
<td>94 (57)</td>
<td>14 (19)</td>
<td>80 (89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACEI/ARB</td>
<td>68 (41)</td>
<td>15 (20)</td>
<td>53 (59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ca blocker</td>
<td>45 (27)</td>
<td>15 (20)</td>
<td>30 (33)</td>
<td>0.056</td>
</tr>
<tr>
<td>β-blocker</td>
<td>48 (29)</td>
<td>12 (16)</td>
<td>36 (40)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome; DM, diabetes mellitus; HT, hypertension; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; Clopid/Ticlo, clopidogrel or ticlopidine; ACEI/ARB, angiotensine converting enzyme inhibitor/angiotensine II receptor blocker; Ca blocker, calcium channel blocker.

*ACS vs. non-ACS.
Figure 1. Distributions of yellow plaques of each yellow color grade are shown. Mean numbers of yellow plaques of color grade 1, 2 and 3 were separately presented for left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), and right coronary artery (RCA). Yellow color grade is known to be correlated with cap thickness and grade-3 yellow plaques are regarded as thin-cap fibroatheroma.
Figure 2. Comparison between number and mean number of yellow plaques are shown. The number and the mean number of yellow plaques should diverge in the segments where observed number of vessel is small. Therefore, without this standardization, we would mistakenly regard the number smaller in those segments. Divergence was observed in the distal segments that were examined in a smaller number of patients. The scales were adjusted so that the height of both bars became same at the segment 21–25 mm (*). LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.
Figure 3. Distributions of yellow plaques and disrupted yellow plaques are shown. Mean numbers of yellow plaques and of disrupted yellow plaques were presented for left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), and right coronary artery (RCA). Disrupted plaques include both ruptured and eroded plaques.
Angiographic Examination and Evaluation

Catheterization was performed by a femoral, brachial, or radial artery approach using a 6- or 7-Fr sheath and catheters. The coronary angiogram was recorded by the Advantx medical system (GE Yokogawa, Tokyo, Japan) and quantitative coronary angiographic analysis was also performed with the system to measure the %diameter stenosis of the segment where each yellow plaque was detected. Lesion length was determined for the lesion with significant stenosis for which PCI was performed. The presence of non-smooth vessel wall characteristics such as irregularity, haziness, fissuring, ulceration or filling defect was determined on the angiogram for each site of yellow plaque as were associated with ruptured plaque or thrombus in Ambrose type criteria. We angiographically classified all detected yellow plaques into 5 categories: (1) yellow plaques at culprit segment of ACS (PCI performed); (2) yellow plaques in the segment of additional stenosis in ACS patients (PCI performed); (3) yellow plaques in the non-culprit segments in ACS patients (PCI not performed); (4) yellow plaques in the segment of target stenosis in non-ACS patients (PCI performed); and (5) yellow plaques in the non-target segments in non-ACS patients (PCI not performed). For each yellow plaque detected, the distance from ostium of the vessel to the plaque was determined. The number of plaques was counted for each 5 mm coronary segment and the mean number of plaques per observed vessels was calculated.

Angioscopic Examination and Evaluation

Angioscopic examination was performed in the culprit vessel after the PCI procedure. The angioscope RX-3310A & MV-5010A (Machida, Tokyo, Japan) and optic fiber DAG-2218LN (Machida) were used. The angioscopic observations were made while blood was cleared from the viewing field by the injection of 3% dextran-40 as previously reported. The intensity of yellow detected was classified into 3 grades (1: slight yellow, 2: yellow, 3: intensive yellow) by comparison with standard colors, as previously reported. Thrombus was defined as white or red material with cotton-like or ragged appearance or with fragmentation with or without protrusion into the lumen or adherent to the luminal surface. For each yellow plaque detected, its yellow color grade and whether or not it had thrombus on it were determined. Yellow plaques with thrombus were defined as disrupted. Angioscopic evaluations were made by 2 angioscopic specialists blinded to the patients’ characteristics. In the case of a disagreement, a third reviewer served as an arbitrator. The inter- and intra-observer reproducibility for the interpretation of angioscopic images was 85% and 95% for plaque color, and 90% and 100% for thrombus, respectively.

Statistical Analysis

Continuous data were presented as mean±SD. Comparisons between groups were done by unpaired Student’s t-test, ANOVA with Scheffe’s post-hoc comparison or chi-square test. A P-value <0.05 was regarded as statistically significant.

Results

Distribution of Yellow Plaques and Disrupted Plaques

Patients’ characteristics are shown in Table 1. The time from onset of symptom to angioscopic examination was 7.1±5.8 h and 180±184 h in acute MI and unstable angina patients, respectively. In the present study, 651 yellow plaques were detected in 165 patients; and 4.0±2.3 yellow plaques and 0.87±1.4 grade-3 yellow plaques were detected per vessel. Grade-3 yellow plaques accounted for 22.1% of all yellow plaques. The distribution in the mean number of yellow plaques of each yellow color grade in each coronary vessel is shown in Figure 1. Yellow plaques distributed diffusely in the right coronary artery but more in mid-segments in the left anterior descending coronary artery and left circumflex coronary artery. Because proximal vessels were examined by angiography more frequently than distal segments, the number of yellow plaques was lower in the distal segments (Figure 2). Therefore, it was necessary to standardize the calculations by the number of vessels observed. Among all yellow plaques detected, 168 (25.8%) were disrupted (Figure 3), and 1.0±1.4 disrupted yellow plaques were detected per vessel.

Frequencies of Yellow Plaques and Disrupted Plaques in ACS and Non-ACS Patients

Although the number of yellow plaques per vessel (4.3±2.5 vs. 3.7±2.2, P=0.08) was not statistically different between

<table>
<thead>
<tr>
<th>Table 2. Angiographic and Angioscopic Findings of Culprit/Non-Culprit Plaques in ACS/Non-ACS Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACS patients</strong></td>
</tr>
<tr>
<td>Culprit</td>
</tr>
<tr>
<td>Add stenosis</td>
</tr>
<tr>
<td>Non-culprit</td>
</tr>
<tr>
<td>Non-target vessels</td>
</tr>
<tr>
<td><strong>Non-ACS patients</strong></td>
</tr>
<tr>
<td>Culprit</td>
</tr>
<tr>
<td>Non-culprit</td>
</tr>
</tbody>
</table>

ACS, acute coronary syndrome; Add stenosis, additional stenosis; %DS, diameter stenosis by QCA; Disrupted, prevalence of disrupted plaques; G3YP, prevalence of grade-3 yellow plaques; Irregularity, prevalence of non-smooth vessel wall characteristics such as irregularity/haziness/fissuring/ulceration/filling defect.

Percutaneous coronary intervention (PCI) was performed for culprit and additional stenosis. Lesion length (Length) was determined for the lesions with significant stenosis for which PCI was performed.

*P<0.05 vs. non-culprit of non-ACS patients. †P<0.05 vs. non-culprit of ACS patients. §Maximum diameter stenosis and the prevalence of vessel wall irregularity in the non-target vessels in which angioscopic examination was not performed.
ACS and non-ACS patients, the number of grade-3 yellow plaques (1.2±1.7 vs. 0.6±0.9, \(P=0.007\)) and the number of disrupted yellow plaques (1.5±1.4 vs. 0.6±1.2, \(P<0.001\)) per vessel were significantly larger in ACS than in non-ACS patients. The number of significant (>50%) stenosis without yellow plaque was 0.1±0.3 and 0.1±0.3 per vessel, and the number of mild stenosis (≤50%) without yellow plaque was 0.6±0.9 and 0.6±0.7 per vessel in ACS and non-ACS patients, respectively.

Among ACS patients, the number of yellow plaques (4.5±2.1 vs. 4.3±2.9 vs. 4.0±2.7, \(P=0.69\)), the number of grade-3 yellow plaques (1.3±1.7 vs. 0.9±1.3 vs. 1.1±1.9, \(P=0.78\)) and the number of disrupted yellow plaques (1.7±1.4 vs. 1.7±1.2 vs. 1.2±1.4, \(P=0.34\)) per vessel were not different between STEMI, NSTEMI, and unstable angina patients.

ACS patients had 101 yellow plaques at culprit lesions of ACS that received PCI, 12 yellow plaques at additional stenotic lesions that received PCI, and 209 yellow plaques in the non-culprit segments. Non-ACS patients had 56 yellow plaques at culprit lesions that received PCI and 273 yellow plaques in the non-culprit segments. Angioscopic and angio graphic findings of these yellow plaques were presented in Table 2. About half of the yellow plaques at culprit lesions were disrupted and one-third of them were grade-3, similar in ACS and non-ACS patients. The incidence of disruption among yellow plaques in non-culprit segments was twice as high in ACS than in non-ACS patients. The diameter stenosis in the non-culprit segments was severer at the disrupted than at the non-disrupted yellow plaques (23±30% vs. 16±25%, \(P=0.04\)). The vessel wall irregularity was detected more frequently at the disrupted yellow plaques than at the non-disrupted yellow plaques (22.0% vs. 5.7%, \(P<0.001\)). Positive and negative predictive value of the vessel wall irregularity to detect disrupted plaque was 86.1% and 42.8%, respectively.

**Discussion**

Although the disruption of a vulnerable plaque is widely considered to be the cause of most ACS, many plaque ruptures are silent and do not cause an ACS.\(^9,9,13–15\) The frequency and distribution of TCFA (suspected to be vulnerable plaques) and disrupted plaques have been precisely determined in a study of human coronary autopsy specimens;\(^9\) however, the distribution of such plaques as determined by angioscopy, which permits observations in living patients, has not been reported. In the present study, we elucidated the frequencies and distributions of yellow plaques, grade-3 yellow plaques and disrupted yellow plaques in the patients with or without ACS, and compared the frequencies of those plaques between patients with ACS and those without ACS. Furthermore, we focused on the yellow plaques and disrupted plaques in the culprit or non-culprit segments to clarify the frequency of silent plaque disruptions.

**Frequencies of Yellow Plaques, Grade-3 Yellow Plaques and Disrupted Plaques**

We have found approximately 4 yellow plaques, 1 grade-3 yellow plaque and 1 disrupted plaque per vessel. Although we examined only 1 vessel per patient, the number of yellow plaques was not different between culprit and non-culprit vessels according to our previous report.\(^7\) According to an optical coherence tomography study,\(^18\) grade-3 yellow plaques are compatible with TCFA and all yellow plaques generally have fibrous cap thickness <300 \(\mu\)m. Because the disruption of plaques was defined as to have thrombus on the plaques, disrupted plaques should include both ruptured plaques and eroded plaques, and possibly the plaques with antithrombotic dysfunction. Therefore, our study population would have approximately 1 TCFA and 1 ruptured or eroded plaque per vessel. These numbers should change according to the characteristics of study population.

More grade-3 yellow plaques and disrupted yellow plaques were detected in ACS patients than in non-ACS patients. Because we compared ACS patients and non-ACS patients without prior history of ACS, ACS patients were supposed to have more advanced atherosclerosis and actually had larger number of grade-3 yellow plaques and disrupted yellow plaques than non-ACS patients. Formation and disrup-
Figure 5. Distributions of plaques comparing with those from previous pathologic report are shown. Distributions of thin-cap fibroatheroma (TCFA) and ruptured plaques was similar with those of Grade-3 yellow plaques and disrupted yellow plaques in the proximal to mid segments; however, in the mid to distal segments, TCFA or ruptured plaques were not detected by pathology but grade-3 yellow plaques and disrupted yellow plaques were detected by angioscopy. LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery.
tion of vulnerable plaques shown by the numbers of grade-3 yellow plaques and disrupted yellow plaques were not different between STEMI, NSTEMI, and unstable angina patients, while they were significantly different between ACS and non-ACS patients. Although what determines whether or not the disrupted plaques lead to STEMI, NSTEMI, or unstable angina or remain asymptomatic is left for future investigations, some factor other than the formation or disruption of vulnerable plaques (ie, vulnerable blood) might be an important factor. Another possible explanation for the higher prevalence of disrupted plaques in ACS than in non-ACS patients would be that higher thrombogenic potential of blood or higher level of whole vessel inflammation in ACS patients might have enhanced the formation of thrombus.

Judging from the data in Table 2, thrombus formation appears to be enhanced by the presence of grade-3 yellow plaques or moderate to severe stenosis. The presence of grade-3 yellow plaques, ie, vulnerable plaques, might be associated with the high rate of plaque disruption, and the presence of stenosis might be associated with the enhanced thrombus formation due to blood flow disturbance.

Because we classified yellow plaques into 5 categories by the angiogram, more than 2 yellow plaques could be classified as those in the culprit segment, and thus, some of them would be disrupted and others would not. Therefore, the prevalence of disrupted plaques at the ACS culprit became as low as 55%, and the disrupted plaque in the culprit segment would be the ‘culprit of culprit’ that caused the ACS event.

When the outcomes of plaque disruptions are considered (Figure 4), our data suggests that 26% of yellow plaques are disrupted and 35% of disrupted plaques are associated with acute symptom of ACS. The rest of the disrupted plaques are not associated with acute symptom of ACS: 19% of disrupted plaques are associated with severe coronary stenosis that requires PCI and 48% of disrupted plaques are completely silent without significant stenosis or vessel wall irregularity. Disruption of vulnerable plaques followed by thrombus formation and their organization has been supposed to contribute to the progression of luminal stenosis. Furthermore, in the present study, the stenosis was severer at disrupted plaques than at non-disrupted plaques in the non-culprit segments. As many as 0.6 silent plaque disruptions were detected per vessel, which might contribute to the progression of coronary stenosis and development of stable angina.

Comparison With Previous Report on Vulnerable and Ruptured Plaques

We compared our results with a previous report on vulnerable and ruptured plaques evaluated pathologically (Figure 5). Intensively yellow plaque is known to have a thin fibrous cap, and thus in this comparison, we compared grade-3 yellow plaques (angiscopy) with TCFA (pathology) and disrupted yellow plaque (angiscopy) with ruptured plaque (pathology). There seemed to be some differences in our results compared with the pathologic results: (1) plaques of all types were detected more by angiscopy than by pathology; (2) plaques of all types were distributed more in the proximal segments in pathologic study than in the angioscopic study; and (3) disrupted yellow plaques were detected more in the mid to distal segments by angiscopy than the ruptured plaques detected by pathology. These differences might be caused by the different examination methodologies and different study populations. The reasons for these differences might be that: (1) some thick-cap fibroatheroma and diffuse depositions of lipid without necrotic core should also look yellow and are detected as yellow plaques by angiscopy; (2) plaques with erosive thrombosis are also regarded as disrupted and thus the number of disrupted plaques by angiscopy becomes larger than that of ruptured plaques by pathology; (3) the number of examined samples (Figure 2) might be smaller in mid to distal segments than in proximal segments; and (4) the study population might be different between these 2 studies. However, the most important finding for the investigation of vulnerable plaques and of mechanisms for ACS occurrence is that there are so many ruptured/disrupted plaques that have failed to cause ACS in the coronary arteries; pathology has detected 0.45 ruptured plaques/heart, angiscopy has detected 1.0 disrupted plaques/vessel in the present study, and intravascular ultrasound has detected 0.70 ruptured plaques/patient. These findings mean that majority of patients with coronary heart disease have a very high risk of having disrupted plaques but has luckily escaped from suffering ACS. Was it truly by chance that the disruption of plaque did not cause ACS? Some additional factors (ie, thrombogenic potential of blood, thrombogenic potential of necrotic core that would be exposed to blood by plaque rupture, underlying stenosis or stenosis caused by the protrusion of necrotic core at the site of plaque rupture, and vasoconstriction) must be required for the disrupted plaque to cause ACS.

For the prevention of ACS, stabilization of vulnerable plaques is an important target, which has been well studied with statins, however, clarifying and intervening the mechanisms how some disrupted plaques cause ACS and others remain silent should be the next important target.

Study Limitations

There are some limitations in the present study. First, our study population is limited to those who received angioscopic examination for a clinical indication, ie, suspected ACS, immediately after PCI, or follow-up after PCI/MI/medication, and thus a selection bias is possible. Our findings should be confirmed by future studies in a larger population. Second, the angioscopic image was not acquired for all segments of coronary arteries, because we did not examine all 3 coronary vessels, nor did we examine segments not suitable for angioscopic examination, ie, small vessel diameter or severe tortuosity. Therefore, the distal segments were less frequently observed than the proximal segments; however, we standardized the number of plaques by the number of observed vessels to reduce the effect of this limitation. Third, angioscopy might not acquire a complete circumferential view in a large vessel with high blood flow, which might be one of the reasons for the different distribution results between our angioscopic study and a pathologic study. Fourth, we did not include white plaques associated with a thrombus although such lesions were quite rare. Fifth, some yellow plaques counted as different ones by angiscopy would be pathologically the different parts of a same plaque. Sixth, we cannot completely exclude the influence of PCI on the angioscopic findings, although PCI usually does not change the yellow color grade or presence/absence of thrombus at the target lesions. Seventh, patients without ACS but with a history of prior ACS were not included in this study. However, only a few patients met this criterion. Eighth, we defined plaques with thrombus as disrupted and did not differentiate rupture from erosion as the cause. This can also be viewed as a strength of the study because erosive thrombosis can also cause ACS. Finally, although we tried to measure the distance of yellow plaques on the angi-
graphic view in which the vessel looked the longest, the results would be dependent on the view angle.

Conclusions

Approximately as many as 4 yellow plaques, 1 grade-3 yellow plaque, and 1 disrupted yellow plaque per vessel were detected. About 25% of detected yellow plaques were disrupted. More grade-3 yellow plaques and disrupted plaques were detected in ACS than in non-ACS patients. Non-ACS patients had as many as 0.6 disrupted plaques per vessel, which was not associated with acute symptom but might contribute to the progression of coronary stenosis and development of stable angina.

Disclosures


References

1. Raffel OC, Merchant FM, Tearney GJ, Chia S, Gauthier DD, None. J. E. Muller, CEO of IntrarExx, Inc, a company that has developed a NIR spectroscopic coronary imaging device.


