Incidence and Predictors of Plaque Rupture in the Peripheral Arteries

Hiroyuki Okura, MD; Koichiro Asawa, MD; Tomoichiro Kubo, MD; Haruyuki Taguchi, MD; Iku Toda, MD; Minoru Yoshiyama, MD; Junichi Yoshikawa, MD; Kiyoshi Yoshida, MD

**Background**—Plaque rupture may be present in the peripheral arteries of the patients at high risk for cardiovascular events and is possibly associated with vascular vulnerability.

**Methods and Results**—One hundred one iliofemoral arteries from 101 patients undergoing angioplasty were studied. Intravascular ultrasound imaging was performed before intervention. Plaque rupture was defined as presence of a cavity that communicated with the lumen with an overlying residual fibrous cap fragment. Incidence, numbers, and location of the plaque rupture were investigated. Plaque rupture was found in 42 of 101 arteries (42%). Patients with plaque rupture had significantly higher prevalence of acute coronary syndrome than did patients without plaque rupture (42% vs 16%, P=0.01). By multivariable logistic regression analysis, acute coronary syndrome (P=0.004) and male sex (P=0.01) were independent clinical correlates of plaque rupture. During follow-up (median, 14.7 months), the incidence of major adverse cardiac or cerebrovascular events (death, myocardial infarction, and ischemic stroke) was similar between the 2 groups. The incidence of major adverse cardiac or cerebrovascular events plus peripheral vascular events (unplanned vascular intervention and amputation) was significantly higher in patients with plaque rupture than in patients without plaque rupture (46% vs 21%, P=0.008). By multivariable Cox regression analysis, plaque rupture (hazard ratio=2.80, 95% CI: 1.23 to 6.37, P=0.01) and Fontaine stage IV (hazard ratio=3.50, 95% CI: 1.58 to 7.71, P=0.002) were independent predictors of major adverse cardiac or cerebrovascular events plus peripheral vascular events.

**Conclusions**—Ruptured plaque of the iliofemoral arteries is a common finding. Patients with plaque rupture had a higher prevalence of history of acute coronary syndrome and lower major adverse cardiac or cerebrovascular events plus peripheral vascular event-free survival. (Circ Cardiovasc Interv. 2010;3:63-70.)

**Key Words:** intravascular ultrasound ■ peripheral vascular disease ■ revascularization ■ vessels ■ vascular intervention

Postmortem pathological examinations showed that =60% to 70% of the culprit lesions for acute coronary syndrome (ACS) demonstrated plaque rupture. Several intravascular ultrasound (IVUS) studies revealed the presence of plaque rupture in 14% to 66% of the culprit lesions from patients with ACS in vivo. Moreover, recent 3-vessel IVUS studies have also revealed that plaque rupture may be present not only in the culprit lesion but also in nonculprit lesions. Those multiple plaque ruptures have been reported in 16% to 79% of the patients with ACS, suggesting the presence of pan-coronary artery vulnerability, possibly as a result of systemic inflammation. Although a possible link between coronary arterial vulnerability and carotid arterial instability was suspected, the incidence and clinical significance of plaque rupture in the peripheral arteries have not been fully investigated.

We hypothesized that plaque rupture may be present in the peripheral arteries of the patients at high risk for cardiovascular events and is possibly associated with vascular vulnerability. Therefore, this study was conducted to investigate the incidence and clinical significance of plaque rupture in the peripheral arteries of patients with peripheral arterial disease (PAD).

**Clinical Perspective on p 70**

**Methods**

**Study Population**

A total of 126 patients with PAD of the iliofemoral territory underwent the first percutaneous transluminal angioplasty (PTA) at Bell Land General Hospital. IVUS could not cross the lesion before intervention in 22 lesions, and the guide wire did not cross the lesion.
in 3 lesions. Finally, 101 lesions (28 common iliac, 27 external iliac, and 46 superficial femoral arteries) from 101 patients were enrolled for analysis in this study. There were 79 male and 22 female patients with a mean age of 70±10 years. Clinical characteristics including age, sex, coronary risk factors (hypertension, hyperlipidemia, diabetes mellitus, and smoking), history of coronary artery bypass grafting, history of stable angina pectoris, history of ACS, history of ischemic stroke, and hemodialysis were investigated and compared. ACS includes acute myocardial infarction (both ST elevation and non-ST elevation) and unstable angina pectoris. Clinical indications for intervention were classified according to the Fontaine stage.13,14 Ankle-brachial index was calculated before PTA.14 A blood sample was obtained 1 day before the PTA procedure.

**Angiographic and IVUS Procedures**

Angiography and PTA were performed according to the standard femoral approach. All patients received intravenous heparin (100 U/kg) before the procedures. After diagnostic angiography, IVUS imaging was performed at baseline and repeated after PTA. By using an automated pullback device, IVUS pullback imaging was performed at a rate of 1.0 mm/s. IVUS imaging was performed in the diseased vessel alone. After a diagnostic IVUS examination, PTA (balloon angioplasty and/or stenting) was performed in a usual manner to achieve percent diameter stenosis of <25%. After PTA, patients were maintained on a regimen of aspirin (100 mg daily) plus ticlopidine (200 mg daily) or cilostazol (200 mg daily) for at least 4 weeks. For the common iliac artery and external iliac artery lesions, IVUS pullback imaging was performed from the ostial common iliac artery to the distal end of the external iliac artery, covering the entire part of the iliac artery. For the superficial femoral artery lesions, IVUS pullback imaging was performed from the popliteal artery to the ostial superficial femoral artery, covering the entire part of the superficial femoral artery. As a result, 55 common iliac arteries, 55 external iliac arteries, and 46 superficial femoral arteries were imaged.

**Ultrasound Imaging Protocol**

In this study, we used 1 of 3 commercially available IVUS systems. The first incorporated a single-element 30-MHz transducer (Ultracross; CVIS/Boston Scientific Corp, San Jose, Calif) mounted on the tip of a flexible shaft that was rotated at 1800 rpm within a short monorail imaging sheath to form planar cross-sectional images in real time; with this system, the transducer was withdrawn automatically at 1.0 mm/s to perform the imaging sequence. The second incorporated a single-element 25-MHz transducer rotated at 1800 rpm within a short monorail imaging catheter (Intrafocus; Terumo Corp, Tokyo, Japan); with this system, the catheter was withdrawn automatically at 1.0 mm/s to perform the imaging sequence. The third phased-array catheters (Eagle Eye Gold; Volcano Corp, Rancho Cordova, Calif) incorporated a 64-element phased-array 20-MHz transducer within an imaging catheter; the transducer was withdrawn automatically at 1.0 mm/s to perform the imaging sequence. Ultrasound images were recorded on half-inch, Super-VHS videotape or on CD/DVD disc as a DICOM format for off-line analysis.

**Angiographic Analysis**

Angiographic images were reviewed and evaluated for qualitative parameters by an analyst blinded to the clinical and IVUS information. The following lesion characteristics were defined according to the previously used criteria for coronary arterial lesion.13 Thrombus was defined as abrupt vessel cutoff with persistence of contrast or an

![Figure 1. Distribution of plaque rupture in the iliofemoral arteries is shown. In each arterial segment, a clear clustering pattern of the plaque rupture to the proximal thirds is demonstrated. Horizontal axis represents total number of plaque ruptures in each segment. CIA indicates common iliac artery; EIA, external iliac artery; SFA, superficial femoral artery.](http://circinterventions.ahajournals.org/Downloaded_from)
intraluminal filling defect in a patent vessel within or adjacent to a stenotic region with surrounding homogeneous contrast opacification. Plaque ulceration was defined as a small crater consisting of a discrete luminal widening with luminal irregularity.16

Qualitative and Quantitative IVUS Analyses
All ultrasound images were reviewed and evaluated qualitatively and quantitatively by an analyst blinded to the clinical and angiographic information according to the American College of Cardiology (ACC) clinical expert consensus document.17 Morphometric parameters consisted of external elastic membrane (EEM) and lumen cross-sectional areas (CSAs). The EEM CSA was defined as the area within the media or adventitial border (ie, including lumen, plaque, and media). Plaque plus media CSA was calculated as EEM CSA minus lumen CSA. Plaque burden was calculated as plaque plus media CSA/EEM CSA × 100. Morphological parameters consisted of plaque type, presence or absence of thrombus, and plaque rupture. Plaque was divided into 1 of the following 3 types: fibrous, fibrofatty, or calcified. Fibrous plaque was defined as bright as or brighter than the adventitia without shadowing. Fibrofatty plaque was defined as less bright than the adventitia. Calcified plaque was defined as brighter than the adventitia with acoustic shadowing. Intravascular thrombus was defined as (1) distinct hypoechoic mass, brightly speckled plaque, channeling within the plaque, and evacuated plaque cavity or (2) detached mobile mass.1 Plaque rupture was defined as the presence of a cavity that communicated with the lumen with an overlying residual fibrous cap fragment.3,18 IVUS measurements were performed at the narrowest cross-sections in the target segment. IVUS measurements were also performed at the nonsignificant or nontarget cross-sections with plaque rupture in the iliofemoral arteries. Identification of 2 separate plaques in the same artery (ie, target lesion versus nontarget lesion) required a cross-section with plaque rupture in the iliofemoral arteries. Identification of 2 separate plaques in the same artery (ie, target lesion versus nontarget lesion) required a cross-section with plaque rupture in the iliofemoral arteries.

Clinical Follow-Up
Prespecified clinical events including death, myocardial infarction, unplanned peripheral arterial revascularization (angioplasty or bypass surgery), ischemic stroke, and amputation (major or minor) were reviewed by either a medical record check or a telephone contact. Clinical end points were adjudicated by an investigator blinded to the baseline IVUS findings. Patients were followed up by each primary care physician every 1 to 2 months.

Statistical Analysis
Quantitative data were presented as a mean value ± SD, and qualitative data were presented as frequencies. Continuous variables were compared with unpaired t tests or the Mann-Whitney U test, as appropriate. Binary variables were examined by the use of Fisher exact and χ² tests. Statistical significance was a value of P<0.05. To identify clinical correlates of plaque rupture in the iliofemoral arteries or target lesion plaque rupture, multivariable logistic models were used. Variables entered into the logistic models were those with a univariable P value of <0.10. Cumulative cardiovascular event-free survival curves during the follow-up in patients with plaque rupture in the iliofemoral arteries versus without plaque rupture were obtained by the Kaplan-Meier method with a log-rank test. To identify predictors of major adverse cardiac or cerebrovascular events (MACCE) plus peripheral vascular events, Cox regression analysis was used. All statistical analyses were performed with the Statview version 5.0 (SAS Institute, Cary, NC).

Results
Clinical Characteristics
Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Plaque Rupture (+) (n=42)</th>
<th>Plaque Rupture (−) (n=59)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>70.0±8.3</td>
<td>70.7±11.1</td>
<td>0.70</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>38/4</td>
<td>41/18</td>
<td>0.01</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>27 (64)</td>
<td>41 (69)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>29 (69)</td>
<td>43 (75)</td>
<td>0.28</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>25 (61)</td>
<td>27 (73)</td>
<td>0.23</td>
</tr>
<tr>
<td>Fontaine stage (I/II/III/IV)</td>
<td>0/27/7/8</td>
<td>0/38/6/15</td>
<td>0.40</td>
</tr>
<tr>
<td>ABI</td>
<td>0.63±0.14</td>
<td>0.62±0.16</td>
<td>0.96</td>
</tr>
<tr>
<td>History of stable angina, n (%)</td>
<td>9 (21)</td>
<td>17 (29)</td>
<td>0.40</td>
</tr>
<tr>
<td>History of ACS, n (%)</td>
<td>18 (43)</td>
<td>10 (17)</td>
<td>0.004</td>
</tr>
<tr>
<td>UAP/NSTEMI, n (%)</td>
<td>6 (14)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>STEMI, n (%)</td>
<td>12 (29)</td>
<td>9 (15)</td>
<td></td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>6 (14)</td>
<td>5 (8)</td>
<td>0.36</td>
</tr>
<tr>
<td>Hemodialysis, n (%)</td>
<td>3 (7)</td>
<td>5 (8)</td>
<td>0.81</td>
</tr>
<tr>
<td>Ischemic stroke, n (%)</td>
<td>11 (26)</td>
<td>11 (19)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

| ABI indicates ankle-brachial index; CABG, coronary artery bypass grafting; NSTEMI, non-ST elevation myocardial infarction; PR, plaque rupture; STEMI, ST-elevation myocardial infarction; UAP, unstable angina pectoris. |

Plaque rupture (55% vs 25%, P<0.0001).

Clinical and angiographic findings are shown in Table 3. Plaque ulceration was detected more frequently in patients with plaque rupture in the iliofemoral arteries than in patients without plaque rupture (55% vs 25%, P<0.0001).

Laboratory Data and Medications
Table 2 shows laboratory data and medications. There were no significant differences in laboratory data between the 2 groups. Statin was similarly prescribed in both groups.

Angiographic and IVUS Findings
Angiographic findings are shown in Table 3. Plaque ulceration was detected more frequently in patients with plaque rupture in the iliofemoral arteries than in patients without plaque rupture (55% vs 25%, P<0.0001).
IVUS findings of the target lesion are also shown in Table 3. Plaque type did not differ between groups. Also, thrombus was similarly detected in the 2 groups. Quantitative IVUS results are also summarized in the Table 3. Target lesion EEM CSA, lumen CSA, and plaque plus media CSA were significantly larger in patients with plaque rupture than in patients without plaque rupture.

By univariable analysis, history of ACS \((P=0.004)\) and male sex \((P=0.01)\) were clinical correlates \((P<0.10)\) of plaque rupture in the iliofemoral arteries. By multivariable logistic regression analysis, both history of ACS \((\chi^2=8.1, \text{odds ratio} [\text{OR}]=4.1, 95\% \text{ CI: } 1.55 \text{ to } 10.80, P=0.004)\) and male sex \((\chi^2=6.1, \text{OR}=4.8, 95\% \text{ CI: } 1.390 \text{ to } 16.39, P=0.01)\) were independent clinical correlates of plaque rupture in the iliofemoral arteries. Figure 2 demonstrates an angiogram and IVUS images from a patient with multiple plaque rupture in the iliofemoral arteries.

### Clinical Follow-Up
Clinical follow-up data are available for 97 of 101 patients (96%; Table 5). The median follow-up period was 14.2
stroke, unplanned vascular intervention, and amputation) was significantly higher in patients with plaque rupture in the iliofemoral arteries than in patients without plaque rupture (46% vs 21%, \(P=0.008\)).

MACCE-free survival rate was similar between the 2 groups (log rank, \(P=0.37\)). On the other hand, MACCE plus peripheral vascular event-free survival rate was significantly lower in patients with plaque rupture than in patients without plaque rupture (log rank, \(P=0.007\); Figure 3). Plaque rupture in the iliofemoral arteries \((P=0.008)\), Fontaine stage IV \((P=0.04)\), and diabetes mellitus \((P=0.04)\) were univariable predictors \((P<0.10)\) of MACCE plus peripheral vascular events. By multivariable Cox regression analysis, plaque rupture in the iliofemoral arteries \((\chi^2=6.0, \text{OR}=2.80, 95\% \text{ CI}: 1.23 \text{ to 6.37}, P=0.01)\) and Fontaine stage IV \((\chi^2=9.6, \text{OR}=3.50, 95\% \text{ CI}: 1.58 \text{ to 7.71}, P=0.002)\) were independent predictors of MACCE plus peripheral vascular events. On the other hand, diabetes mellitus \((\chi^2=3.5, \text{OR}=2.53, 95\% \text{ CI}: 0.95 \text{ to 6.75}, P=0.06)\) was a borderline predictor of MACCE plus peripheral vascular events.

**Discussion**

This IVUS study demonstrates the following: (1) Plaque rupture of the iliofemoral arteries is documented in 42% of the patients with PAD. (2) A history of ACS and male sex are clinical correlates of plaque rupture in the iliofemoral arteries. (3) Plaque burden predicts plaque rupture in the target lesion. (4) Plaque rupture in the iliofemoral arteries is the only independent predictor of MACCE plus peripheral vascular events in the patients with PAD after PTA.

Rothwell et al\(^{11}\) reported that \(\approx50\%\) of patients with ischemic stroke exhibited irregular unstable plaques at angiography in the contralateral nonculprit carotid artery, and they were more likely to have fatal and nonfatal cardiac events than were patients with smooth carotid plaques. Lombardo et al\(^{12}\) reported that complex carotid plaque was found in 23.2% of the unstable angina pectoris and 3.2% of the stable angina pectoris patients who underwent coronary artery bypass grafting. Our results showing that ACS was an independent clinical correlate of iliofemoral arterial plaque rupture may also suggest the possible link between coronary arterial disease and peripheral arterial instability. A previous autopsy study demonstrated the presence of panarterial in-

**Table 4. IVUS Results Between Target and Nontarget Plaque Ruptures**

<table>
<thead>
<tr>
<th></th>
<th>Target Lesion Plaque Rupture ((n=26))</th>
<th>Nontarget Lesion Plaque Rupture ((n=16))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM CSA, (\text{mm}^2)</td>
<td>69.1±32.9</td>
<td>63.8±28.1</td>
<td>0.62</td>
</tr>
<tr>
<td>(P+M) CSA, (\text{mm}^2)</td>
<td>60.8±28.9</td>
<td>43.6±18.8</td>
<td>0.06</td>
</tr>
<tr>
<td>Lumen CSA, (\text{mm}^2)</td>
<td>8.3±5.7</td>
<td>19.4±11.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plaque burden, %</td>
<td>88.0±5.8</td>
<td>68.4±9.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cavity CSA, (\text{mm}^2)</td>
<td>16.2±16.8</td>
<td>8.8±6.0</td>
<td>0.15</td>
</tr>
</tbody>
</table>

PR indicates plaque rupture; \(P+M\), plaque plus media.
flammation in patients with symptomatic atherosclerosis. Fleiner et al. showed high intimal macrophage infiltration in apparently intact common iliac, common carotid, and renal arteries in patients with symptomatic atherosclerosis. Our present in vivo study further extended these observations to in vivo evidence of advanced vulnerable plaque rather than early atherosclerotic changes in symptomatic patients with PAD.

Systemic inflammation as assessed by C-reactive protein (CRP) was reported higher in patients with ACS and coronary plaque rupture. However, we did not find differences in CRP level between those with and without plaque rupture in the iliofemoral arteries. This discordant result may be attributed to the fact that our study patients may be in a chronic and relatively stable stage after development of the plaque rupture in the iliofemoral arteries. Hong et al. reported that an increased CRP level was an independent predictor of plaque rupture in patients with acute myocardial infarction but not in patients with stable angina pectoris. Despite the chronic nature of the clinical presentation, overall CRP levels of our study population were relatively higher than in patients with coronary plaque rupture reported previously. Because of this high baseline inflammation status, it is possible that the presence of local plaque rupture did not significantly affect the systemic CRP level.

Male sex was another independent predictor of plaque rupture of the iliofemoral arteries in our study population. This is quite concordant with a previous postmortem pathological coronary study of patients with acute myocardial infarction. According to the report by Arbustini et al., plaque rupture of the culprit coronary lesion was more frequently found in male patients than in female patients.

As previously reported from coronary IVUS studies, plaque rupture does not always cause symptomatic vascular events. Our IVUS examination showing that greater plaque burden was associated with symptomatic stenotic or occlusive lesion is quite in agreement with a previous report. Also, spatial distribution of the plaque rupture showing a clustering pattern to the proximal part of each vessel is quite consistent with the previous angiographic and IVUS coronary studies. These results may suggest that plaque instability is related to its location in peripheral arteries. On the other hand, our results did not show an association between plaque rupture and plaque composition based on gray-scale IVUS. Radiofrequency signal–derived tissue characterization might be useful to clarify a specific plaque component that is prone to rupture.

Higher cardiovascular event rate was found in patients with plaque rupture in the iliofemoral arteries. This is quite in concordance with previous coronary IVUS studies. However, this result should be carefully interpreted. The difference mainly comes from the higher incidence of unplanned vascular interventions because of nontarget lesion progres-

<table>
<thead>
<tr>
<th>No.</th>
<th>Age, y</th>
<th>Sex</th>
<th>Plaque Rupture at Baseline</th>
<th>Time to Revascularization, d</th>
<th>Treated Lesion</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74</td>
<td>M</td>
<td>+</td>
<td>490</td>
<td>Target lesion+ nontarget lesion</td>
<td>Surgery</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>M</td>
<td>+</td>
<td>231</td>
<td>Contra lateral artery</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>3</td>
<td>84</td>
<td>M</td>
<td>+</td>
<td>45</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>M</td>
<td>+</td>
<td>235</td>
<td>Target lesion+ nontarget lesion</td>
<td>Surgery</td>
</tr>
<tr>
<td>5</td>
<td>74</td>
<td>M</td>
<td>+</td>
<td>31</td>
<td>Target lesion+ nontarget lesion</td>
<td>Surgery</td>
</tr>
<tr>
<td>6</td>
<td>63</td>
<td>M</td>
<td>+</td>
<td>28</td>
<td>Contralateral artery</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>M</td>
<td>+</td>
<td>98</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>M</td>
<td>+</td>
<td>95</td>
<td>Contralateral artery</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>M</td>
<td>+</td>
<td>353</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>10</td>
<td>71</td>
<td>M</td>
<td>+</td>
<td>35</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>11</td>
<td>71</td>
<td>F</td>
<td>–</td>
<td>350</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>12</td>
<td>67</td>
<td>M</td>
<td>–</td>
<td>353</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>13</td>
<td>60</td>
<td>M</td>
<td>–</td>
<td>168</td>
<td>Ipsilateral artery, nontarget lesion</td>
<td>Angioplasty</td>
</tr>
<tr>
<td>14</td>
<td>64</td>
<td>M</td>
<td>–</td>
<td>81</td>
<td>Contralateral artery</td>
<td>Angioplasty</td>
</tr>
</tbody>
</table>

Figure 3. Kaplan-Meier curves comparing patients with and without plaque rupture in the iliofemoral arteries. A, MACCE-free survival curve shows only a weak trend toward lower event-free survival rate in patients with plaque rupture (log rank, \( P=0.374 \)). B, MACCE plus peripheral vascular event-free survival curve shows that patients with plaque rupture were associated with worse clinical outcome.
ision or target lesion restenosis in patients with plaque rupture in the iliofemoral arteries than in patients without plaque rupture. Therefore, this study may be underpowered to demonstrate the impact of plaque rupture on “hard” end points, such as myocardial infarction, ischemic stroke, and cardiac death. As mentioned, it took 3.7 years between prior ACS events and the current PTA procedures. Therefore, a long-term follow-up will be necessary to clarify the impact on the hard end points.

Limitations

There are several limitations in this study. First, this is a single-center report with a relatively small number of patients. Second, the use of statins may be lower for the high-risk profile of the study population. Because some of the patients did not have any prior vascular events at the time of study entry, they might have been treated as patients at low or intermediate risk. More aggressive lipid-lowering strategy with a higher dose of statins may affect the prognostic impact of plaque rupture. Third, intracoronary ultrasound imaging was not performed. Therefore, whether patients with peripheral arterial plaque rupture in the iliofemoral arteries had rupture or vulnerable plaque in their coronary arteries is unknown. Fourth, IVUS examination was not performed in the contralateral vessels. Therefore, incidence of plaque rupture in the iliofemoral arteries may be underestimated. Finally, the true incidence of thrombus or plaque rupture may be also underestimated because of the limited resolution of the current IVUS system compared with optical coherence tomography.

Conclusions

In conclusion, IVUS imaging revealed the presence of plaque rupture in 42% of the patients with iliofemoral arterial disease. Those who have plaque rupture in the iliofemoral arteries had a higher prevalence of history of ACS. The presence of plaque rupture in the iliofemoral arteries may be associated with subsequent cardiovascular events, suggesting that plaque rupture of peripheral arteries is related to vascular vulnerability.

Disclosures

None.

References

1. van der Wal AC, Becker AE, van der Loos CM, Das PK. Site of intimal rupture or erosion of thrombosed coronary atherosclerotic plaques is characterized by an inflammatory process irrespective of the dominant plaque morphology. Circulation. 1994;89:36–44.
This study investigated the incidence and clinical significance of the plaque rupture in the iliofemoral arteries detected by intravascular ultrasound in 101 patients with peripheral artery disease. Overall, plaque rupture of the iliofemoral arteries were detected in 42 of 101 arteries (42%), and a history of acute coronary syndrome and male gender were independent predictors of the plaque rupture. Importantly, major adverse cardiac or cerebrovascular events (death, myocardial infarction, and ischemic stroke) plus peripheral vascular event-free (unplanned vascular intervention and amputation) survival rate was significantly higher in patients with plaque rupture than in patients without plaque rupture (46% versus 21%, \( P=0.008 \)). By multivariable analysis, plaque rupture and Fontaine stage IV were independent predictors of major adverse cardiac or cerebrovascular events plus peripheral vascular events. Therefore, even in the peripheral arterial territory, plaque rupture in the peripheral arteries is not a rare finding. Furthermore, the presence of plaque rupture in the peripheral arteries may suggest the presence of the coronary and peripheral vascular vulnerability. According to the results, clinicians should consider patients with peripheral arterial disease and plaque rupture as patients at a higher risk, and therefore, aggressive risk factor management may be indicated.
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Supplemental Material
**Video 1** Pre angioplasty IVUS pullback image of multiple plaque ruptures from a patient with left common iliac artery stenosis are shown (same patient as Figure 3). IVUS pullback started from the ostial left common iliac artery and ended at the proximal left external iliac artery (pullback speed 1.0 mm/sec). IVUS pullback image shows a plaque rupture in both target and non-target lesions.