A Possible Association Between Coronary Plaque Instability and Complex Plaques in Abdominal Aorta


Objective—Coronary plaque instability causes myocardial infarction (MI). Angiographic lesions with such instability are complex lesions. Complex carotid plaques were reported to be prevalent in unstable angina. We investigated associations between coronary plaque instability, such as MI and angiographic complex coronary lesions, and aortic plaques.

Methods and Results—Aortic MRI was performed in 146 patients undergoing coronary angiography, of whom 108 had coronary artery disease (CAD) and 44 also had MI. Prevalence of plaques in thoracic and abdominal aortas was higher in patients with than without CAD (73% and 94% versus 32% and 79%), but it was similar in CAD patients with and without MI. Notably, complex plaques in abdominal aorta were more prevalent in CAD patients with than without MI (36% versus 14%; P<0.025). In multivariate analysis, abdominal complex plaques were associated with MI (odds ratio [OR], 4.5; 95% CI, 1.5 to 13.8). Among patients without MI, thoracic and abdominal complex plaques were more prevalent in patients with than without complex coronary lesions (22% and 33% versus 2% and 7%; P<0.05). Abdominal complex plaques were also associated with complex coronary lesions (OR, 9.8; 95% CI, 1.1 to 85.9).

Conclusion—Complex plaques in abdominal aorta were associated with MI and complex coronary lesions, suggesting a link between coronary and aortic plaque instability.

Key Words: aorta ■ coronary artery disease ■ myocardial infarction ■ MRI

Plaque instability is a main cause of acute coronary syndrome, such as myocardial infarction (MI).1 Angiographic features of coronary lesions associated with plaque instability are sharp overhanging edge, irregular border, and intraluminal lucency, so-called complex lesions.2,3 Although angiographic complex coronary lesions are seen in 10% to 20% of patients with stable angina,2 such lesions are known to be common in acute coronary syndrome and to be predictive of coronary events.2,4,5 Recently, complex plaques in carotid arteries were reported to be more prevalent in patients with unstable angina than in those with stable angina, suggesting a link between coronary and carotid plaque instability.6 Plaque instability in patients with coronary artery disease (CAD) may not be confined to coronary arteries, but it may also involve other arteries. Complex plaques in thoracic aorta, detected by transesophageal echocardiography (TEE), were reported to be associated with systemic embolic events.7,8 However, the association between coronary plaque instability and complex aortic plaques has not yet been elucidated.

Recently, MRI became a useful tool for noninvasively detecting plaques in both thoracic and abdominal aortas.9,10 We11,12 and others13 showed the good correlations for plaque morphology and characterization in the aortas between in vivo and ex vivo MRI findings and histopathology in animal models. In humans, we reported that MRI evaluations of thoracic aorta closely correlated with TEE findings.9 Using MRI, we previously reported the association between the severity of coronary stenosis and the extents of aortic plaques in 102 patients undergoing coronary angiography.10 In the present study, we investigated the association between coronary plaque instability, such as MI and angiographic complex coronary lesions, and complex plaques in thoracic and abdominal aortas. Because MRI can visualize a lipid-rich core9,11 and because plaques with a large lipid-rich core are recognized to be prone to rupture,14 we also evaluated the prevalence of aortic plaques with a lipid-rich core.

Methods

Study Patients

The 372 consecutive patients (78% male; mean age 64±9 years; range 40 to 80 years) undergoing elective coronary angiography for suspected or known CAD at National Defense Medical College Hospital were eligible for our study. However, only 116 patients...
agreed to have aortic MRI at Iruma Heart Hospital because they had to pay its cost and to go to the hospital far from our college for MRI and because patients who underwent angiography followed by stenting were canceled to have MRI. Among the 129 consecutive patients (84% male; 63 ± 9 years of age) undergoing coronary angiography for acute coronary syndrome, 30 patients (25 with acute MI and 5 with unstable angina at rest) also agreed to have MRI. As a result, our study patients consisted of 146 patients (76% male; 64 ± 9 years of age), of whom 102 were included in our previous study. Excluded were patients with a history of cardiovascular surgery, aortic diseases, valvular or congenital heart disease, infectious or autoimmune diseases, or neoplasma. Our study was approved by the institutional ethics committee. After informed consent was obtained, MRI was performed within 2 weeks of angiography in 121 of 146 patients. However, of the 23 patients with acute MI, 13 had MRI in 1 to 3 months after the onset of MI, and 12 did it in 4 to 8 months because of stent implantation.

Of the 146 study patients, 108 (74%) had CAD (>50% stenosis), of whom 44 also had MI. MI was confirmed by the documentation of coronary stenosis plus either elevations of cardiac enzymes or diagnostic changes on electrocardiograms. The diagnosis of acute and old MI was given to 25 and 19 patients, respectively. Of the 146 patients, 85 (58%) had hypertension (blood pressures ≥ 140/90 mm Hg or on drugs), of whom 68 were on drugs, and 79 (54%) had hyperlipidemia (total cholesterol level > 240 mg/dL or on drugs), of whom 57 were taking statin. Diabetes mellitus (fasting plasma glucose level ≥ 126 mg/dL or on treatment) was present in 36 (25%) patients, and 67 (46%) were smokers (>10 packs per year). Fasting blood samples were taken on the day of angiography. Serum lipid levels were measured by standard laboratory methods. Plasma high sensitivity C-reactive protein (hsCRP) levels were measured by a BNII nephelometer (Dade Behring).

Coronary Angiography

Angiograms were recorded using the Judkins technique and a cineangiogram system (Toshiba). All angiograms were evaluated by Y.M., blinded to MRI data. CAD was defined as ≥1 coronary artery having > 50% luminal diameter stenosis. The degree of stenosis in each segment was evaluated by 5 grades (< 25%, 26% to 50%, 51% to 75%, 76% to 90%, and > 90% stenosis). Coronary segments were defined by CASS classification. Complex coronary lesions were defined as 1 with sharp overhanging edges, irregular borders, or intraluminal lucency.

MRI of Aortas

MRI was performed on Sigma 1.5T Cvi scanner using a phased-array body coil (GE Medical Systems). Transverse proton density-weighted (PDW) and T2-weighted (T2W) images of thoracic descending and abdominal aortas were obtained using ECG-gated, double-inversion-recovery fast spin-echo sequence. Imaging parameters were repetition time = 2 RR intervals, echo time = 10 ms (PDW) and 60 ms (T2W), 20-cm field of view, 4-mm slice thickness, 8-mm interslice gap, 256 × 256 acquisition matrix, and 32 echo-train. As in our previous studies, 9 slices of thoracic aorta and 9 slices of abdominal aorta were obtained at 12-mm intervals, which each covered ~10-cm portions of thoracic aorta below the arch and 10-cm portions of abdominal aorta above the bifurcation of common iliac artery.

Plaques were defined as a clearly identified luminal protrusion with focal wall thickening. Among plaques, complex plaques were defined as 1 with maximal wall radial dimension > 4 mm and irregular surface with or without a pedunculate component, referring to the definition on TEE (Figure 1).1,12,13 In each slice, the presence and morphology of plaque was evaluated by 2 observers, and discrepancy was resolved by consensus. In our study, plaque characterization was based on the signal intensities of plaque on PDW and T2W images.9,14 Lipid components were identified as hyperintense on PDW and hypointense regions on T2W images. Fibrocellular components were identified as hyperintense regions on both images. Plaque with a lipid-rich core was identified as 1 with a hypointense region in its center on T2W image. T1W images were reported to add little additional information beyond that from PDW and T2W images because the tissue contrast of PDW and T1W images was similar.13 Because of improved flow suppression and higher signal-to-noise ratio of PDW images with double-inversion-recovery fast spin-echo sequence compared with T1W with conventional spin-echo sequence, T1W images were omitted to reduce examination time. Total examination time was ~ 40 minutes.

Statistical Analysis

Differences between 2 groups were evaluated by unpaired t test for parametric variables, by Mann–Whitney U test for nonparametric variables, and by χ2 test for categorical variables. Differences among 3 groups were evaluated by ANOVA with Scheffe test for parametric variables, by Kruskal–Wallis rank test for nonparametric variables, and by χ2 test for categorical variables. Multiple logistic regression analysis was used to elucidate associations between aortic plaques and CAD or MI. A P value of < 0.05 was considered statistically significant. Results are presented as mean ± SD, except for hsCRP levels that are presented as the median value.

Results

Of the 146 patients, 62% (n = 91) and 90% (n = 132) had plaques in thoracic and abdominal aortas by MRI, respectively. Plaques were more prevalent in abdominal than in thoracic aorta (P < 0.001). Of the 274 thoracic aortic plaques, 7% and 2% were complex ones and ones with a lipid-rich core, respectively. Of the 575 abdominal aortic plaques, 8% and 1% were complex ones and ones with a lipid-rich core.
As a result, complex plaques in thoracic and abdominal aortas were present in 6% (n=9) and 18% (n=27) of patients. Plaques with a lipid-rich core in thoracic and abdominal aortas were present in 3% (n=5) and 3% (n=4) of patients. However, of the 9 patients having plaques with a lipid-rich core, 7 also had complex plaques.

CAD was present in 108 patients. Compared with 38 patients without CAD, 108 with CAD had lower high-density lipoprotein cholesterol and higher hsCRP levels (Table 1). Patients with CAD more often had plaques in thoracic (73% versus 73%) and abdominal (93% versus 95%) aortas than those without CAD (P<0.025). Complex plaques in abdominal aortas were also more prevalent in patients with CAD (23% versus 5%; P<0.05). However, multivariate analysis revealed plaques in thoracic aorta to be an independent factor associated with CAD (odds ratio [OR], 9.8; 95% CI, 1.1 to 85.9), whereas abdominal aortic plaques or complex plaques were not (Table 2). The prevalence of thoracic aortic plaques for predicting CAD were 73%, 68%, 87%, and 76%, respectively.

Of the 108 patients with CAD, 44 had MI. The diagnosis of acute and old MI was given to 25 and 19 patients, respectively. In patients with MI, MRI was performed in 17 patients within 6 months and in 27 patients >6 months after the onset of MI (median 6 months; range 1 month to 5 years). Between CAD patients with and without MI, there was no difference in risk factors except for smoking (Table 1). The prevalence of plaques in thoracic (73% versus 73%) and abdominal (93% versus 95%) aortas was similar in CAD patients with and without MI (P=NS; Figure 2). Notably, abdominal complex plaques were more prevalent in patients with MI than in CAD patients without MI (36% versus 14%; P<0.025). The prevalence of abdominal complex plaques was 41% in patients with MI within 6 months and 33% with MI >6 months previously. There was no difference in the prevalence of thoracic complex plaques or plaques with a lipid-rich core between CAD patients with and without MI. Multivariate analysis showed abdominal complex plaques to be an independent factor associated with MI (OR, 4.5; 95% CI, 1.5 to 13.8; Table 2). The sensitivity, specificity, and positive and negative predictive values of the presence of abdominal complex plaques for predicting MI were 36%, 89%, 59%, and 76%, respectively.

Of the 64 CAD patients without MI, 6 had de novo effort angina, 5 had worsening effort angina, and 5 had unstable angina at rest. However, 18 patients showed complex coronary lesions on angiograms. Between CAD patients with and without complex coronary lesions, there was no difference in risk factors and hsCRP levels (Table 3). Although there was no difference in the prevalence of plaques in thoracic and abdominal aortas, complex plaques in thoracic (22% versus 2%; P<0.05) and abdominal (33% versus 7%; P<0.025) aortas were more prevalent in patients with complex coronary lesions than without complex coronary lesions (Figure 3). Plaques with a lipid-rich core tended to be more prevalent in patients with complex coronary lesions. Multivariate analysis in 102 patients without MI revealed abdominal complex plaques to be an independent factor associated with complex coronary lesions (OR, 9.8; 95% CI, 1.1 to 85.9), whereas
thoracic complex plaques were not (Table 2). The sensitivity, specificity, and positive and negative predictive values of the presence of abdominal complex plaques for predicting complex coronary lesions were 33%, 94%, 55%, and 87%, respectively.

### Discussion

Using MRI, we investigated the associations between thoracic and abdominal aortic plaques and CAD, MI, or complex coronary lesions in 146 patients undergoing coronary angiography. The prevalence of plaques in thoracic and abdominal aortas was higher in patients with CAD than without CAD. Although plaques were more prevalent in abdominal than in thoracic aorta, plaques in thoracic aorta, but not in abdominal aorta, were an independent factor for CAD. However, the

### TABLE 2. Associations Between Aortic Plaques and the Presence of CAD, MI, or Complex Coronary Lesions (Multiple Logistic Regression Analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3.7 (1.4–9.9)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Low HDL cholesterol (&lt;40 mg/dL)</td>
<td>4.7 (1.1–22.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thoracic aortic plaques</td>
<td>5.7 (2.1–15.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abdominal aortic plaques</td>
<td>1.2 (0.3–5.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Thoracic complex plaques</td>
<td>0.3 (0.1–2.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal complex plaques</td>
<td>3.8 (0.7–20.8)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>MI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>3.2 (1.2–9.0)</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>hsCRP (per 1.0 mg/L increase)</td>
<td>1.3 (1.1–1.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Thoracic aortic plaques</td>
<td>2.0 (0.7–5.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal aortic plaques</td>
<td>0.4 (0.1–2.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Thoracic complex plaques</td>
<td>0.2 (0.1–1.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal complex plaques</td>
<td>4.5 (1.5–13.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Complex coronary lesions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>8.9 (1.5–52.2)</td>
<td>&lt;0.025</td>
</tr>
<tr>
<td>Thoracic aortic plaques</td>
<td>1.5 (0.3–6.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal aortic plaques</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Thoracic complex plaques</td>
<td>1.4 (0.1–23.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal complex plaques</td>
<td>9.8 (1.1–85.9)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The dependent variables were CAD, MI, and complex coronary lesions. This analysis included age, gender, hypertension, hyperlipidemia, low HDL cholesterol, diabetes, smoking, hsCRP, thoracic plaque, thoracic complex plaque, abdominal plaque, and abdominal complex plaque.

HDL indicates high-density lipoprotein.
prevalence of plaques in thoracic and abdominal aortas did not differ between CAD patients with and without MI. Notably, complex plaques in abdominal aorta were more prevalent in CAD patients with MI than without MI. Among patients without MI, complex aortic plaques were more prevalent in patients with complex coronary lesions than without complex coronary lesions. Complex aortic plaques, especially in abdominal aorta, were found to be associated with MI and complex coronary lesions.

In 2004, Lombardo et al.6 investigated carotid plaques using ultrasonography in patients scheduled for coronary bypass surgery (181 unstable and 92 stable angina). The prevalence of carotid plaques was similar in patients with unstable (75%) and stable angina (65%), but complex carotid plaques were more prevalent in patients with unstable (23%) than stable angina (3%). In line of evidence, Saito et al.19 evaluated carotid plaques using ultrasonography in 63 patients with angina and documented complex carotid plaques to be associated with complex coronary lesions. Rothwell et al.20 reported patients having carotid stenosis with angiographic irregular surface to more often have a history of MI than those having carotid stenosis with smooth surface. These suggest that plaque instability in patients with CAD may not be confined to coronary arteries but may also involve carotid arteries.

A recent postmortem study21 demonstrated high intimal macrophage infiltration at all 3 arterial sites (iliac, carotid, and renal arteries) in patients experiencing cardiovascular events, suggesting that plaque instability may be attributable to a widespread process throughout all vascular beds. Although aortic plaques were reported to be more strongly associated with CAD than carotid plaques,22 the association between coronary and aortic plaque instability has not yet been elucidated. Amanullah et al.16 investigated plaques in ascending aorta and arch in 127 patients referred for TEE. They showed complex plaques to be a predictor for cardiac events. Varga et al.23 reported plaques in thoracic descending aorta to be associated with cardiovascular events. However, an autopsy study showed plaques in abdominal aorta, but not in thoracic aorta, to be more severe in patients with cardiac catastrophe than without it.24 TEE provides high-resolution images of thoracic aorta; but it cannot assess abdominal aorta. MRI can detect plaques in both thoracic and abdominal aortas.9,10 Using MRI, we assessed plaques in thoracic and abdominal aortas in 146 patients undergoing coronary angiography. Complex plaques, especially in abdominal aorta, were prevalent in patients with MI and in patients with complex coronary lesions. Abdominal complex plaques were associated with MI and complex coronary lesions. Because MI is mainly attributable to coronary plaque instability and because complex coronary lesions are recognized to be lesions associated with plaque instability,1–3 complex plaques in abdominal aorta may thus be linked to coronary plaque instability, which leads to the development of MI and complex coronary lesions.

As we reported previously,10 plaques in thoracic and abdominal aortas were more prevalent in patients with CAD than without CAD. Complex plaques in abdominal aorta were also more prevalent in patients with CAD. However, thoracic aortic plaques were an independent factor associated with CAD, but abdominal aortic plaques or complex plaques were not. The association between CAD and thoracic aortic plaques has often been reported using TEE.17,25 In line with our results, Takasu et al.26 showed that thoracic aortic plaques were more closely associated with CAD than abdominal aortic plaques by computed tomography. These suggest that thoracic aortic plaques may be a better marker of coexisting CAD than abdominal aortic plaques. However, complex plaques in abdominal aorta may be a better marker of coronary plaque instability than any plaques in thoracic aorta.

The mechanism of different associations of thoracic and abdominal aortic plaques with CAD has not yet been clarified, but some differences in their structures have been reported. The aortic diameter tapers geometrically from thoracic to abdominal aorta, and abdominal aorta usually has higher blood pressures than thoracic aorta.27 Vasa vasorum is
common in thoracic aorta but rare in abdominal aorta, suggesting that the oxygen and nourishment of abdominal aorta is mainly provided by diffusion from aortic lumen. These factors may be the reason why plaque complexes are more prevalent in abdominal than in thoracic aorta.

Study Limitations
First, in thoracic aorta, we did not evaluate ascending aorta or arch to reduce examination time. Because complex plaques are much more prevalent in thoracic descending aorta (6%) than in arch (2%) and ascending aorta (0.2%) and because plaque complexes in descending aorta are a stronger factor associated with CAD than those in arch or ascending aorta, we evaluated only descending aorta. Second, MRI was used to evaluate aortic plaques, but angiography was used to evaluate coronary lesions. Angiography cannot visualize plaques and only shows lumen characteristics. MRI can detect lipid-rich core. In our study, only 6% of patients had aortic plaque with a lipid-rich core. Because 37% of our patients were taking statin and lipid-lowering therapy decreases lipid-rich cores and because in-plane resolution was 0.78×0.78 mm, small lipid-rich cores may have not been detected. Moreover, T1W images were omitted to reduce examination time. This may have caused some misdiagnosis of certain plaque components. Third, our study was performed in Japanese patients referred for angiography. Our results may not be applicable to general population and other ethnicities. Moreover, only 30% of patients undergoing angiography agreed to have MRI because they had to pay its cost and to go to the affiliated hospital far from our college for MRI. Patients with a history of cardiovascular surgery were also excluded. These may have caused some selection bias. Our study included only 5 patients with unstable angina at rest. To clarify the association between acute coronary syndrome and aortic plaques, further study in a large number of patients with unstable angina is needed. Finally, our study is cross-sectional. Such a study cannot establish causality. However, little attention has been paid to the importance of abdominal aortic plaques. Our study first demonstrated the association of MI and complex coronary lesions with complex plaques in abdominal aorta, suggesting a link between coronary and abdominal aortic plaque instability. This hypothesis is worth of further study in a prospective manner.

Conclusions
The prevalence of plaques in thoracic and abdominal aortas was high in patients with CAD, but it was similar between CAD patients with and without MI. However, the prevalence of complex plaques in abdominal aorta was characteristically high in patients with MI and in patients with complex coronary lesions. Abdominal complex plaques were found to be associated with MI and complex coronary lesions, suggesting a possible link between coronary and abdominal aortic plaque instability.

References


A Possible Association Between Coronary Plaque Instability and Complex Plaques in Abdominal Aorta

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/early/2006/01/19/01.ATV.0000204637.00865.87.citation