Atheromatous plaques of the aorta have been regarded as a potential source of emboli. As transesophageal echocardiography (TEE) provides clear images of the aorta, the thickness, morphology, and mobility of the plaques can be evaluated by TEE. However, there are few reports about the frequency and prognosis of patients with thoracic aortic plaques and about the relationship between aortic plaque morphology and prognosis of patients, especially, there are no reports with regard to the long-term follow-up data among the Japanese population.

The purpose of this study was to clarify the frequency and prognosis of patients with severe atheromatous plaques in the thoracic aorta and the impact of aortic plaque morphology on the survival rate and on the incidence of subsequent embolic events.

**Background:** There are no reports about the long-term follow-up data of patients with aortic plaques among the Japanese population. The purpose of this study was to clarify the frequency of patients with severe aortic plaques and the impact of aortic plaque morphology on the prognosis.

**Methods and Results:** We retrospectively investigated 1,570 consecutive patients who underwent transesophageal echocardiography. Survival rate and subsequent embolic event rate were compared between patients with severe aortic plaque (>5 mm in thickness) and control patients. The relationship between aortic plaque morphology and prognosis was also estimated according to the presence of ulceration, calcification, hypoechoic plaques, and mobile plaques. The mean follow-up period was 8.7 years. Among 1,570 patients, severe aortic plaque was detected in 92 patients (5.9%). These 92 patients showed a significantly low survival rate and high subsequent embolic event rate compared to control patients (5-year survival rate: 69% vs 94%; 5-year embolic event free rate: 52% vs 95%). Among patients with severe aortic plaque, only ulceration was associated with a low survival rate (hazards ratio: 2.4, 95% confidence interval (CI): 1.1–5.2) and only mobile plaque was associated with a high embolic event rate (hazards ratio: 2.2; 95%CI: 1.1–5.1).

**Conclusions:** Aortic plaque >5 mm in thickness was a predictor of poor prognosis. In the presence of aortic plaque >5 mm, ulceration was a predictor of a low survival rate and mobile plaque was a predictor of a high embolic event rate. (Circ J 2010; 74: 2152–2157)

**Key Words:** Aortic plaque; Embolic event; Prognosis; Survival rate; Transesophageal echocardiography
Aortic Plaque and Prognosis

Aortic Plaque and Prognosis

and thoracic aortic aneurysm were also excluded. After these exclusions, the presence of severe diffuse plaque in the thoracic aorta and its morphology were examined in 1,570 patients (948 male, mean age: 62 years (30–92 years)). Control patients were randomly selected from the patients who showed little or no plaque by TEE and they were matched by age, gender, risk factor of atherosclerosis and examination period with the patients with severe aortic plaque.

Patients’ survival and embolic events during the follow-up period were examined by medical chart review and telephone contact.

First, the survival rate and subsequent embolic event rate were compared between patients with severe aortic plaque and control patients without aortic plaque. Next, the risk of death and subsequent embolic events in the patients with severe aortic plaque were estimated according to plaque morphology such as ulceration, calcification, hypoechoic plaques, and mobile plaques. The primary end-point in evaluating the subsequent embolic event rate was an embolic event, including stroke, transient ischemic attack, bowel infarction, renal infarction, acute ischemia of a limb and cholesterol emboli, and/or sudden death that was likely to have occurred as a result of an embolic event in the patient’s clinical history.

The study protocol was approved by the institutional’s ethics committee at Tenri Hospital.

Evaluation of the Atheromatous Plaques in the Thoracic Aorta

Transesophageal echocardiography examination was performed using a Toshiba SSH 140A Ultrasonic Unit with a 5 MHz multiplane or biplane transducer. We observed the horizontal and longitudinal views of the descending thoracic aorta and aortic arch through TEE.

Severe aortic plaque was defined as fixed protruding plaque more than 5 mm in thickness. The thickness of atheromatous plaque was defined as the distance between the medial-adventitial border and the lumen of the aorta, and it was measured at its maximal site. Ulceration was defined as plaque, which appears like a crater that was >2 mm in depth and width. Calcification was defined as focal increased echo density within the aortic plaque accompanied by an acoustic shadow. Hypoechoic plaque was defined as plaque that contains an echolucent area. Mobile plaque was defined as plaque that protrudes into the aortic lumen and presents any degree of mobility. Figure 1 shows representative cases of each morphology.

Statistical Analysis

Statistical analysis was performed using JMP version 6. Values were expressed as mean±SD. Survival rate and the incidence of subsequent embolic event in the groups was compared by using Kaplan-Meier survival analysis and a log-
rank test. The Cox proportional hazards method was used to assess the contribution of aortic plaque morphologies to the development of death and subsequent embolic event during follow up. Relative risks were calculated with 95% confidence interval (CI). Statistical significance was set at a P value of less than 0.05.

Results

Frequency and Clinical Characteristics of Patients With Severe Atheromatous Plaques in the Thoracic Aorta

Among 1,570 patients, severe aortic plaque more than 5 mm in thickness was detected in 92 patients (5.9%). Among these 92 patients, 76 patients were male and 77% of the patients had a smoking history. One-hundred and nine control patients were randomly selected, as mentioned previously. Table 1 shows clinical characteristics of 92 patients with severe aortic plaque and 109 control patients.

Comparison of Prognosis Between Patients With Severe Aortic Plaques and Control Patients

The mean follow-up period was 8.7 years (interquartile range: 5.2–12.4 years).

Patients with severe aortic plaque showed a significantly lower survival rate and higher subsequent embolic event rate than control patients (P<0.0001). The 5-year survival rate after TEE was 69% in patients with severe aortic plaque but 94% in control patients. The 5-year embolic event-free rate after TEE was 52% in patients with severe aortic plaque but 95% in control patients (Figure 2).

Among the 62 patients with severe aortic plaque who died during the follow-up period, death occurred at a mean of 66 months after TEE. Sudden death was a cause of death for 12 patients, embolic events for 9 patients, cardiac disease for 15 patients, and other causes, such as cancer and pneumonia for 26 patients.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of Study Patients</th>
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<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Risk factors of atherosclerosis</td>
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<tr>
<td>Smoking</td>
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<td>Hyperlipidemia</td>
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<td>Diabetes</td>
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Figure 2. Survival rate and subsequent embolic event rate in patients with severe aortic plaque and control patients. Patients with severe aortic plaque showed a significantly lower survival rate and higher subsequent embolic event rate than control patients. Pts, patients.
Aortic Plaque and Prognosis

Impact of Aortic Plaque Morphology in the Presence of Severe Plaque

Among the 92 patients with severe aortic plaque, ulceration was present in the thoracic aorta in 58 patients, calcification was present in 20 patients, hypoechoic plaque was present in 46 patients and mobile plaques were present in 36 patients.

Patients with ulceration showed a significantly lower survival rate than patients without ulceration (Figure 3). However, calcification, hypoechoic plaques, and mobile plaques were not related to a lower survival rate. In multivariate Cox model analysis, only ulceration was independently associated with a lower survival rate (Table 2). Hazards ratio for the presence of ulceration was 2.4 and a 95%CI was from 1.1 to 5.2.

Patients with mobile plaques showed a significantly higher incidence of subsequent embolic events than those without mobile plaques (Figure 4). However, plaques with ulceration, calcification, and hypoechoic plaques were not related to a higher embolic event rate. Only mobile plaque was independently associated with a high embolic event rate. Hazards ratio for the presence of mobile plaques was 2.2 and a 95%CI was from 1.1 to 5.1 (Table 3).

Discussion

Previous Studies

As several studies demonstrated the relationship between aortic atheromatous plaques and embolic events in the 1990s, atheromatous plaques in the thoracic aorta have been thought to be a potential source of emboli.

Several studies mentioned the relationship between plaque morphology and embolic event rate. A study with a large number of patients showed that increasing plaque thickness was related to high risk of emboli, and plaque thickness of >4 mm was a significant risk factor for stroke. In addition, the presence of mobile lesions and ulceration, and the absence of calcification have been recognized to be related to a high embolic risk.

Furthermore, there have been a few prospective studies regarding the risk of future vascular events in patients with protruding aortic plaques. One study demonstrated that aortic atheromatous plaque more than 4 mm in thickness was a significant predictor of recurrent vascular events during the mean 2.4-year follow-up period. The mean follow-up period in these previous studies was 1 to 4 years. There are no reports regarding long-term follow-up data of patients with aortic atheromatous

Table 2. Relative Risk of Death

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95%CI</th>
<th>P value</th>
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<tbody>
<tr>
<td>Ulceration</td>
<td>2.4</td>
<td>1.1–5.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Calcification</td>
<td>1.3</td>
<td>0.6–2.8</td>
<td>0.57</td>
</tr>
<tr>
<td>Hypoechoic plaque</td>
<td>0.8</td>
<td>0.4–1.7</td>
<td>0.58</td>
</tr>
<tr>
<td>Mobile plaque</td>
<td>1.4</td>
<td>0.7–2.8</td>
<td>0.33</td>
</tr>
</tbody>
</table>

HR, hazards ratio; CI, confidence interval.
Prognosis and Aortic Plaque Morphology

Our long-term follow-up study demonstrated that patients with severe aortic plaque showed a significantly lower survival rate and higher subsequent embolic event rate than control patients. Concerning the relationship between plaque morphology and prognosis among patients with severe aortic plaque, ulceration was a predictor of a low survival rate and mobile plaque was a predictor of a high embolic event rate.

In the present study, mobile lesions were regarded as mobile plaques, but according to some previous studies, the aortic mobile lesions were considered as superimposed thrombi. Some mobile lesions have been reported to disappear during anticoagulant therapy or thrombolytic agents. In contrast, a previous report showed that aortic atheromatous plaques became ulcerated and the flailed segments developed mobile lesions over a 1-year course. Another study showed the relationship between ulceration or echolucency within the aortic plaque and mobile lesions. These findings demonstrated that some mobile lesions in the aorta were disrupted atheromatous plaques. Because it is difficult to distinguish with certainty between a thrombus and a flailed segment of a ruptured plaque through TEE, mobile lesions were regarded as mobile plaques in the present study.

Figure 4. Subsequent embolic event rate in patients with severe aortic plaque according to plaque morphology. Mobile plaque was a predictor of a high embolic event rate.

Clinical Implications

Detecting severe atheromatous plaques through TEE has multiple clinical implications. First, detection of severe aortic plaque through TEE assists us to consider whether we should perform cardiac catheterization or not, because embolic events, such as cholesterol emboli, often develop after cardiac catheterization in patients with mobile plaques.

Second, we can determine which patients need intensive treatment for risk factors. Intensive treatment through cholesterol lowering therapy for patients with severe aortic plaque might result in improving their prognosis. Previous reports showed a favorable effect of intensive cholesterol-lowering therapy on regression of aortic atheroma. Anticoagulant therapy for patients with severe aortic plaque remains controversial. According to a previous retrospective study, anticoagulant therapy was effective in preventing stroke in patients with mobile lesions. However, another study demonstrated that statin use has an independent protective effect on recurrent embolic events with severe aortic atheromatous plaque, but anticoagulant or antiplatelet drugs did not show a beneficial effect on recurrent embolic events.

Finally, mobile plaques detected by TEE might become a
hint in making a diagnosis of cholesterol emboli. As symptoms of cholesterol emboli are non-specific, it is sometimes difficult to diagnose. 

**Study Limitations**

The present study has some limitations. First, because the present study is retrospective, all patients were not systematically followed. Second, the study population consisted of consecutive patients who were clinically referred for TEE, but it is inevitable that there is a selection bias in patients who underwent TEE. This selection bias might have affected our results regarding the frequency of patients with severe aortic plaque, which might be different from that among the general population. Third, we did not evaluate the influence of other clinical factors on patients’ prognosis, such as coronary risk factors, underlying disease and medication. Finally, there is a possibility that plaque morphology might change during the follow-up period. For example, hypochoic plaque might be easily ruptured, resulting in the formation of ulceration, and some parts of ruptured plaque showed flailed segments, that is, mobile plaques. However, we didn’t take this possibility into consideration for this study, which might have affected our results.

**Conclusions**

In conclusion, aortic plaque more than 5 mm in thickness was detected in 5.9% of the consecutive patients who underwent TEE. Aortic plaque more than 5 mm in thickness was a predictor of a low survival rate and a high embolic event rate. Among patients with severe aortic plaque, ulceration was a predictor of a low survival rate and mobile plaque was a predictor of a high embolic event rate.

**References**