Atherosclerosis of the Aorta in Patients With Acute Thoracic Aortic Dissection

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Background  The role of atherosclerosis in thoracic aortic dissection has not been established yet. Transesophageal echocardiography (TEE) is an imaging modality widely used in the diagnostic evaluation of thoracic aortic dissection, and it can detect aortic atherosclerotic plaques and assess their size and specific characteristics.

Methods and Results  One hundred consecutive patients with thoracic aortic dissection and adequate imaging of the thoracic aorta by TEE were studied. The type of dissection (proximal or distal) and the presence and the degree of aortic atherosclerosis were defined. Proximal aortic dissection (Stanford type A) was found in 64 patients. Patients with proximal dissection were younger than those with distal (type B; 58±13 vs 67±11 years, p<0.001). The prevalence of arterial hypertension was higher in patients with distal dissection compared with those with proximal. Aortic atherosclerosis was present in less patients with proximal than with distal dissection (67% vs 94%, p<0.002). Logistic regression analysis revealed that patients with severe atherosclerosis were 7.6-fold more probable to have type B than type A dissection (p<0.001).

Conclusion  Aortic atherosclerosis is more associated with distal than with proximal aortic dissection. (Circ J 2008; 72: 1773–1776)

Key Words: Aortic atherosclerosis; Aortic dissection; Transesophageal echocardiography

Dissection of the thoracic aorta is a life threatening situation with high mortality rates in the early phase and in the long term.1–4 Risk factors for thoracic aortic dissection include (1) inherited connective tissue disorders (eg, Marfan syndrome, Ehlers-Danlos syndrome), (2) familial forms of aortic dissection, and (3) acquired conditions, mainly chronic hypertension, but also smoking, dyslipidemia, inflammatory diseases, and cocaine abuse.5–7 Although atherosclerosis has been reported to contribute to the pathogenesis of aortic dissection,8 its role in thoracic aortic dissection has not yet been established.9 According to Stanford’s classification, there are 2 types of thoracic aortic dissection, type A and type B, different in pathogenesis, prognosis, and treatment.10–15

Transesophageal echocardiography (TEE) is a useful imaging modality widely used in the diagnostic evaluation of thoracic aortic dissection10,11 and other aortic pathological entities13 It is able to detect aortic atherosclerotic plaques and assess their size and specific characteristics.14–18 The aim of this study was to compare the degree of atherosclerosis of the aorta in patients with type A and type B acute thoracic aortic dissection, using TEE.

Methods

Study Population  Our study population comprised 104 consecutive patients with acute thoracic aortic dissection (patients with intramural hematomas were excluded). All patients underwent TEE as part of their diagnostic evaluation. Although both the diagnosis and the type of dissection were established by TEE, more than 1 imaging technique was used in most cases: computed tomography (33 patients, 32%) and cardiac catheterization–aortography (27 patients, 26%). Four patients were excluded because of inadequate imaging of the entire thoracic aorta. The remaining 100 patients (age 61±13 years, 72 males) were studied. Of them, 16 had had prior surgery involving the aorta for the following reasons: aortic aneurysm (5 patients, 2 of whom had Marfan syndrome), prior aortic dissection (2 patients, coronary artery bypass grafting (2 patients), coarctation of aorta (1 patient), and aortic valve replacement (6 patients, 4 of whom had a bicuspid aortic valve). In total, 6 patients had Marfan syndrome and 7 had a bicuspid aortic valve. In all patients, several characteristics were recorded, such as history of smoking, hypertension (systolic blood pressure (BP) ≥140 and/or diastolic BP ≥90 mmHg, or taking antihypertensive drugs), hypercholesterolemia (>240 mg/dl, or taking hypolipidaemic agents) diabetes mellitus (fasting glucose level ≥126 mg/dl, or taking antidiabetic drugs), and family history of premature coronary artery disease. All patients gave informed written consent and the study was approved by the institutional ethics committee.

Echocardiography  TEE was performed in the echocardiography laboratory with 2 ultrasound imagers (Sonos 2500, and Sonos 5500,
to the Stanford Classification (type A: proximal, or type B: distal). Type A means the dissection involves the ascending aorta, whereas type B dissection does not.

Aortic diameter was measured using 2-dimensional images at 4 sites: sinuses of Valsalva, ascending aorta, aortic arch, and descending aorta. The maximum diameter among these 4 was defined as the "maximum" aortic diameter.

Aortic atherosclerosis was assessed as previously described. In brief, the thicknesses of the intimal and medial layers of the far wall were measured during systole in 3 aortic segments: the descending aorta, the aortic arch, and the ascending aorta. If the wall thickness was less than 1 mm, this was considered to represent no atherosclerosis. If atherosclerotic plaques were found, their maximal thickness was measured (Fig 1A). If there was plaque at the site of the intimal flap, the maximal thickness between its 2 surfaces was measured (Fig 1B). Mild atherosclerosis was defined as plaque thickness 1 mm or more, but less than 4 mm, and severe atherosclerosis as plaque thickness 4 mm or more.

Statistical Analysis

Numerical data are expressed as the mean±SD, and frequencies are expressed as percentages. Differences between the 2 groups were evaluated using 2-tailed t-test and chi-square test. Multivariable logistic regression analysis was used to estimate the likelihood of having proximal aortic dissection (dependent variable) according to the presence of severe atherosclerosis in any of the segments of the aorta (main independent variable), taking into account all clinical characteristics of the patients. A p-value <0.05 was considered statistically significant. Data analysis was performed using the SPSS statistical package for Windows (version 10.0, SPSS Inc, Chicago, IL, USA).

Results

Proximal aortic dissection (type A) was found in 64 patients, and distal (type B) was found in 36 patients. Patients with type A dissection were younger than patients with type B. In the univariate analysis, the prevalence of arterial hypertension was higher in patients with distal aortic dissection compared with patients with proximal dissection, but no difference was found in the prevalence of hypercholesterolemia, diabetes mellitus, smoking, or family history of coronary heart disease (Table 1).

Patients with type A aortic dissection had a higher diameter of the Valsalva sinus and ascending aorta, and lower values for the descending aorta diameter, but no difference in aortic arch diameter or in the "maximum" aortic diameter was found between the 2 groups of patients (Table 1). As expected, a greater percentage of patients with type A dissection also had aortic regurgitation than patients with type B dissection (Table 1). Aortic atherosclerosis was present in fewer patients with type A than with type B dissection (Table 1). The same was true when only severe atherosclerosis was compared between the 2 groups (20% in type A vs 72% in type B, p<0.001).

When we stratified our analysis according to the presence of severe atherosclerosis in any of the 3 segments of the thoracic aorta (ascending, arch, and descending), after taking into account all clinical characteristics (ie, age, gender, smoking, hypercholesterolemia, diabetes mellitus, hypertension, family history of coronary artery disease), we found a significant association between severe atherosclerosis and type B dissection. In fact, patients with severe...
Aortic dissection and atherosclerosis were 7.6-fold more likely to have type B than type A dissection (p<0.001, Table 2). A significant association was also found between hypertension and type B dissection. Hypertensive patients were 4.1-fold more likely to have type B than type A aortic dissection (p<0.05, Table 2).

The same results as those in the total population were observed when patients with the Marfan syndrome or with a bicuspid aortic valve were excluded from the analyses, and even when patients with prior surgery involving the aorta were subsequently excluded.

**Discussion**

This is the first study to use TEE to evaluate the presence of aortic atherosclerosis in patients with acute dissection of the thoracic aorta. The results demonstrate that type B dissection of the aorta is much more associated with aortic atherosclerosis than the type A dissection and this association was not altered when patients with known structural deficiencies, such as Marfan syndrome or a bicuspid aortic valve, were excluded from analyses.

The central pathophysiological event leading to the development of aortic dissection is the dedifferentiation of vascular smooth muscle cells. This process commonly occurs because of enhanced elastolysis caused by genetic alterations, or from longstanding hypertension. On the other hand, atherosclerosis induces intimal thickening and thus hypoxia of the media, which, facilitated by increases in wall stress from hypertension, leads to a weakening of the aortic wall, and a decrease in elastin content. This, in turn, makes the aortic wall vulnerable to shear stress forces, which ultimately may lead to dissection. 

TEE has very good sensitivity and specificity for the diagnosis of aortic dissection, comparable with magnetic resonance imaging and computed tomography and far superior to transthoracic echocardiography. It can be performed quickly at the bedside with minimal risk, and it is the imaging modality of choice in critically ill patients. In contrast to magnetic resonance imaging and to computed tomography, it typically takes only 10–15 min to complete and requires neither arterial access nor intravenous contrast.

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**Table 1 Clinical Characteristics and Ultrasound Findings of the Study Population According to the Type of Dissection**

<table>
<thead>
<tr>
<th>Type of dissection</th>
<th>Type A (n=64)</th>
<th>Type B (n=36)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.9±13.0</td>
<td>67.4±11.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>47 (73%)</td>
<td>25 (69%)</td>
<td>0.669</td>
</tr>
<tr>
<td>Smoking</td>
<td>29 (45%)</td>
<td>12 (33%)</td>
<td>0.242</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35 (55%)</td>
<td>32 (89%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>22 (34%)</td>
<td>17 (47%)</td>
<td>0.206</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (16%)</td>
<td>4 (11%)</td>
<td>0.532</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>5 (8%)</td>
<td>2 (6%)</td>
<td>0.671</td>
</tr>
<tr>
<td>Marfan syndrome</td>
<td>5 (8%)</td>
<td>1 (3%)</td>
<td>0.309</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>6 (9%)</td>
<td>1 (3%)</td>
<td>0.215</td>
</tr>
<tr>
<td>Prior aortic surgery</td>
<td>13 (20%)</td>
<td>3 (8%)</td>
<td>0.117</td>
</tr>
<tr>
<td>Aortic diameter, mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valsalva sinus</td>
<td>43.9±9.1</td>
<td>38.0±5.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ascending</td>
<td>59.3±13.5</td>
<td>40.9±6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arch</td>
<td>40.0±10.3</td>
<td>37.2±8.7</td>
<td>0.363</td>
</tr>
<tr>
<td>Descending</td>
<td>37.7±12.2</td>
<td>54.0±15.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum</td>
<td>60.4±13.0</td>
<td>55.7±14.6</td>
<td>0.098</td>
</tr>
</tbody>
</table>

Categorical variables are expressed as absolute and relative frequencies; age is expressed as mean±SD; p values by the student's t-test for independent variables or by the chi-square test.

**Table 2 Results of Multiple Logistic Regression Analysis Evaluating the Relative Risk of a Participant Having Type B Aortic Dissection (Dependent Variable) According to His/Her Characteristics**

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>Exp(B)</th>
<th>95%CI for Exp(B)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.965</td>
<td>0.912–1.022</td>
<td>0.222</td>
</tr>
<tr>
<td>Gender</td>
<td>0.645</td>
<td>0.194–2.142</td>
<td>0.474</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.000</td>
<td>0.319–3.131</td>
<td>1.000</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.770</td>
<td>0.253–2.344</td>
<td>0.646</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.466</td>
<td>0.107–2.018</td>
<td>0.307</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.106</td>
<td>1.096–15.382</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>0.874</td>
<td>0.089–8.591</td>
<td>0.908</td>
</tr>
<tr>
<td>Severe atherosclerosis</td>
<td>7.605</td>
<td>2.414–23.960</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI, confidence interval. Other abbreviation see in Table 1.
or ionizing radiation. TEE is also the imaging modality of choice for the detection of aortic plaques. Although it is difficult to visualize the distal ascending aorta and proximal arch, TEE is superior to dual-helical computed tomography and magnetic resonance angiography in aortic atherosclerosis assessment. Furthermore, those 2 imaging modalities are inferior to TEE in the characterization of plaque mobility and in the visualization of superimposed mobile thrombi.

In the present study, we used a cut-off point of 4 mm of plaque thickness for severe atherosclerosis, which is in line with previous studies that have associated aortic atherosclerosis with coronary atherosclerosis and have demonstrated that severe atherosclerosis (plaques ≥4 mm) of the aortic arch carry a high risk for stroke.

In our univariate analysis the prevalence of hypertension was higher in patients with a distal aortic dissection, a finding that was confirmed in the multivariate analysis. This has been reported before although not confirmed in all studies. On the other hand, although patients with distal aortic dissection were older than patients with proximal aortic dissection, in the multivariate analysis age was not found to be a predictor of the type of dissection.

**Study Limitations**

TEE may have difficulties in accurately assessing the degree of atherosclerosis at the site of dissection (intimal flap), which could have resulted in underestimation of aortic atherosclerosis in our study group. The external aortic diameters were measured, so the false lumen was also included in the measurements. We decided to do so in order to avoid underestimating the diameters should we have measured the internal diameter or the diameter just proximal to the intimal flap. Although this choice could have confounded the results concerning the aortic diameters prior to dissection, it does not confound the association of type B dissection with atherosclerosis.

The clinical characteristics of our study population were entered as categorical variables. More analytical data (ie, the duration and control of hypertension and the degree of hyperlipidemia) have not been taken account in the analyses, because these data were not available for the whole population.

Although our study shows that distal aortic dissection is much more associated with aortic atherosclerosis than is proximal dissection, further studies are needed to establish a direct causal link between atherosclerosis and aortic dissection.

**Conclusion**

Aortic atherosclerosis is more frequent in patients with distal (type B) than with proximal (type A) aortic dissection. This finding may provide new insights into the possible role of atherosclerosis in the pathogenesis of aortic dissection, especially that of the descending aorta.

**References**


