Aortic Aneurysm

Long-Term Predictors of Descending Aorta Aneurysmal Change in Patients With Aortic Dissection

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Objectives
We sought to demonstrate the long-term natural course of descending aorta dilation after acute aortic dissection (AD) and identify early predictors for late aneurysmal change.

Background
Aneurysmal dilation of the aorta is a critical late complication in AD patients.

Methods
Contrast-enhanced computed tomography (CT) was performed during the acute phase in 100 AD patients, comprising 51 type 1 who underwent ascending aorta surgery and 49 type 3 AD patients. Clinical observation was conducted for 53 ± 26 months, and CT was repeated for 31 ± 27 months.

Results
Aneurysm (diameter ≥60 mm) occurred in 14.4%, 8.2%, 4.1%, and 3.1% of patients at the upper descending thoracic aorta (UT), mid descending thoracic aorta (MT), lower descending thoracic aorta (LT), and abdominal aorta (AA), respectively. Of 53 patients in whom CT was repeated for ≥2 years, the rates of aorta diameter enlargement at the UT, MT, LT, and AA levels were 3.43 ± 3.66 mm/year, 3.21 ± 2.70 mm/year, 2.62 ± 2.19 mm/year, and 1.93 ± 3.13 mm/year, respectively (p < 0.01), and aneurysm developed in 15 (28%). The initial false lumen diameter at the UT, the aorta diameter at the MT, and Marfan syndrome were independent predictors of late aneurysm. A ≥22-mm initial false lumen diameter at the UT predicted late aneurysm with a sensitivity of 100% and a specificity of 76%. The patients with initial UT false lumen diameter ≥22-mm (n = 42) showed higher event rate (aneurysm or death) than others (n = 58) (p < 0.001).

Conclusions
The UT is the major site of late aneurysmal dilation. A large UT false lumen diameter on the initial CT portends late aneurysm and adverse outcome warranting early intervention. (J Am Coll Cardiol 2007;50:799–804)

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Aneurysmal dilation of the aorta is one of the most critical late complications causing a poor long-term outcome in patients with type 3 aortic dissection (AD) (1–4) and type 1 AD after ascending aorta surgery (5–7). Close long-term clinical monitoring involving imaging studies is essential for both prevention of aortic rupture and for undertaking of timely surgical or percutaneous interventions (2,3,5).

Recently, stent-grafting has been reported as a safe and optimal therapeutic option for patients with distal AD (8–10), and it has provided favorable results compared with results of surgery in some reports (4,11). It has been suggested that stent-grafting to the distal AD could protect the dissected aorta from delayed dilation and rupture by closing the major intimal tear site (9). However, in terms of stent-graft implantation, treatment of acute AD was reported to result in poorer clinical outcomes than was treatment of chronic AD (11). Some patients with distal AD do not develop late aortic aneurysms and are successfully managed for many years with medical treatment only. Therefore, choosing optimal patients and times for intervention is important. To address this issue, we investigated the long-term natural course of distal aorta dilation after acute event and identified early predictors for late aneurysmal change in AD patients.

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Methods

Patient population. A total of 100 patients with AD involving descending thoracic aorta (age 53 ± 13 years, 40
CT and imaging follow-up. The CT scans were performed with a variety of scanners obtaining axial images with contiguous 2.5- to 10-mm thick sections from the top of the aortic arch to the iliac bifurcation. All CT examinations were performed with and without contrast material enhancement. The CT angiography was performed with a bolus injection of 100 to 120 ml of contrast agent at a rate of 3 ml/s via an automated injector.

Using CT images, the aorta diameter was measured at the aortic arch, upper descending thoracic aorta (UT), mid descending thoracic aorta (MT), and lower descending thoracic aorta (LT), and abdominal aorta (AA) at the level of the midaortic arch, just distal to the aortic arch, pulmonary artery bifurcation, the center of the left atrium, and periumbilicus, respectively. The maximum false lumen diameter was also measured at the UT, MT, LT, and AA. True and false lumens were determined by evaluating continuity with normal aorta lumen. If the intimal flap was shown as 2 lines on the CT image due to wavering, the midportion between the 2 lines was defined as the intimal flap position. The ratio of the false lumen diameter to the aorta diameter was also calculated. The CT was repeated for a period of 31 ± 27 months. In 9 patients comprising 2 type 1 AD and 7 type 3 AD patients who underwent surgery on the descending aorta during the follow-up period after the initial CT, CT performed before surgery was included and CT after surgery was excluded from the analysis. The rate of aorta dilation was calculated using the aorta diameter measurements on the initial and the final follow-up CT and the follow-up period: (follow-up diameter – initial diameter)/follow-up duration. On the follow-up CT, an aorta diameter ≥60 mm was defined as an aneurysmal change (2,12,13), and obliteration of the false lumen with a false lumen diameter ≤3 mm was defined as complete resorption (14). Follow-up CT was performed for ≥24 months in 53 patients (27 type 1 and 26 type 3 AD patients).

Clinical follow-up. Clinical observation was conducted for 53 ± 26 months. Data were obtained during patient visits to the hospital or by telephone interview conducted by a trained cardiologist. Clinical events were defined as “aneurysmal change at any part of the aorta” and “death.”

Statistical analysis. Statistical analysis was performed using SPSS 12.0 (SPSS Inc., Chicago, Illinois). Numerical values are expressed as mean ± standard deviation. Student unpaired t tests were used to assess differences between groups. Fisher exact test was used to compare frequency ratios between groups. A 1-way analysis of variance (ANOVA) was used to determine significant differences in the aorta dilation rate among the 3 types of ascending aorta surgery in type 1 AD patients. Comparison of the aorta dilation rates in multiple locations was performed using repeated-measures ANOVA. Comparisons of variables between the initial and follow-up CT were evaluated using paired t tests. Multiple stepwise logistic regression analysis was used to identify independent predictors of late aneurysmal change. A receiver-operating characteristics curve analysis was performed to determine the best cutoff value for predicting a late aneurysm. Kaplan-Meier analysis was used to determine the event-free survival rate, and the difference between groups was analyzed using log-rank test. A p value <0.05 was considered significant.

Results

Natural course and aneurysmal change of distal AD. Of 51 type 1 AD patients after ascending aorta surgery, 8 showed aneurysmal change in the distal aorta, and 3 died 16, 21, and 71 months after the onset of acute AD. Complete resorption of the false lumen occurred in 6 patients with type 1 AD. Of 49 type 3 AD patients, there were 2 in-hospital deaths. During the follow-up period, 12 patients showed aneurysmal change, and 1 patient died 36 months later. Complete resorption of the false lumen occurred in 3 patients with type 3 AD. The incidences of aneurysmal change were 3.1% (0% in type 1 and 6.5% in type 3) at the aortic arch, 14.4% (15.7% in type 1 and 13.0% in type 3) at the UT, 8.2% (7.8% in type 1 and 8.7% in type 3) at the MT, 4.1% (2.0% in type 1 and 6.5% in type 3) at the LT, and 3.1% (2.0% in type 1 and 4.3% in type 3) at the AA (Fig. 1). Nine patients who showed complete resorption during the follow-up period tended to have smaller initial false lumen diameters at the UT (17 ± 7 mm vs. 21 ± 7 mm, p = 0.14), MT (17 ± 7 mm vs. 20 ± 7 mm, p = 0.18), and LT (16 ± 8 mm vs. 20 ± 7 mm, p = 0.17) compared with others, although there was no statistical significance. This tendency was more prominent in type 3 AD patients, at the UT (12 ± 11 mm vs. 22 ± 8 mm, p = 0.08), MT (12 ± 11 mm vs. 21 ± 8 mm, p = 0.09), and LT (12 ± 11 mm vs. 20 ± 8 mm, p = 0.11).

Predictors of long-term aneurysmal change. Of the 53 patients who underwent imaging follow-up for ≥24 months, the rates of aorta diameter enlargement at the UT, MT, LT, and AA levels were 3.43 ± 3.66 mm/year, 3.21 ± 2.70 mm/year, 2.62 ± 2.19 mm/year, and 1.93 ± 3.13 mm/year, respectively (p < 0.01). The rates of aorta dilation...
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Baseline Characteristics and Initial Measurements of Patients With and Without Late Aneurysmal Change Among Patients in Whom Imaging Was Repeated for ≥24 Months

<table>
<thead>
<tr>
<th>Variable</th>
<th>Aneurysm (+) (n = 15)</th>
<th>Aneurysm (−) (n = 38)</th>
<th>Univariate p Value</th>
<th>Multivariate p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>50 ± 5</td>
<td>52 ± 10</td>
<td>0.60</td>
<td></td>
</tr>
<tr>
<td>Female gender (%)</td>
<td>27</td>
<td>39</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>Marfan syndrome (%)</td>
<td>20</td>
<td>2.6</td>
<td>0.06, &lt;0.05</td>
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<tr>
<td>Hypertension (%)</td>
<td>47</td>
<td>55</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>13</td>
<td>0</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Imaging follow-up period (months)</td>
<td>56 ± 28</td>
<td>48 ± 18</td>
<td>0.31</td>
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</tr>
</tbody>
</table>

Initial CT measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Aneurysm (+) (n = 15)</th>
<th>Aneurysm (−) (n = 38)</th>
<th>Univariate p Value</th>
<th>Multivariate p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UT diameter (mm)</td>
<td>42 ± 6</td>
<td>37 ± 5</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>UT false lumen (mm)</td>
<td>26 ± 4</td>
<td>19 ± 5</td>
<td>&lt;0.001</td>
<td>&gt;0.005</td>
</tr>
<tr>
<td>MT diameter (mm)</td>
<td>38 ± 6</td>
<td>34 ± 3</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MT false lumen (mm)</td>
<td>22 ± 4</td>
<td>18 ± 4</td>
<td>&lt;0.005</td>
<td></td>
</tr>
<tr>
<td>LT diameter (mm)</td>
<td>33 ± 4</td>
<td>31 ± 4</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>LT false lumen (mm)</td>
<td>21 ± 5</td>
<td>18 ± 4</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>AA diameter (mm)</td>
<td>25 ± 9</td>
<td>21 ± 3</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>AA false lumen (mm)</td>
<td>13 ± 10</td>
<td>9 ± 5</td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

AA = abdominal aorta; CT = contrast-enhanced computed tomography; LT = lower descending thoracic aorta; MT = mid descending thoracic aorta; UT = upper descending thoracic aorta.

AA = abdominal aorta; CT = contrast-enhanced computed tomography; LT = lower descending thoracic aorta; MT = mid descending thoracic aorta; UT = upper descending thoracic aorta.

at the UT, MT, LT, and AA levels were 3.79 ± 4.14, 3.54 ± 2.87, 2.79 ± 2.66, and 2.55 ± 3.91 mm/year, respectively, in 27 type 1 AD patients (p = 0.22), and were 3.05 ± 3.12, 2.87 ± 2.53, 2.45 ± 1.61, and 1.28 ± 1.92 mm/year, respectively, in 26 type 3 AD patients (p < 0.005). The rates were not significantly different between the 2 AD types at any location. For type 1 AD patients, there was no significant difference in the rate of aorta dilation at any part of the aorta among the 3 different types of ascending aorta surgery. At the UT, the rate of aorta dilation significantly correlated with the initial false lumen diameter (r = 0.38, p < 0.005), but not with the initial aorta diameter (r = 0.05, p = 0.73). Of the 53 patients who underwent imaging follow-up for ≥24 months, 15 (28%) showed aneurysmal change. In those 15 patients showing late aneurysmal change, compared with the initial CT, the ratio of the false lumen diameter to aorta diameter significantly increased at the UT (0.63 ± 0.10 to 0.74 ± 0.09, p < 0.005) and MT (0.60 ± 0.13 to 0.72 ± 0.09, p < 0.01) according to follow-up CT, whereas the ratio did not significantly change at either the UT (0.52 ± 0.12 to 0.51 ± 0.28, p = 0.93) or MT (0.55 ± 0.12 to 0.54 ± 0.28, p = 0.95) in 38 patients without late aneurysmal change. Those 15 patients with late aneurysmal change tended to have higher proportion of Marfan syndrome and diabetes than the 38 patients without late aneurysmal change (Table 1). The 15 late aneurysmal change patients had significantly larger initial aorta diameters and false lumen diameters at the UT and MT, and larger initial false lumen diameters at the LT than the 38 patients without aneurysmal change. Multiple stepwise logistic regression analysis including these variables showed that Marfan syndrome (p < 0.05), a large initial false lumen diameter at the UT (odds ratio [OR] 1.50, 95% confidence interval [CI] 1.15 to 1.95, p < 0.005), and a large aorta diameter at the MT (OR 1.77, 95% CI 1.08 to 2.90, p < 0.05) were independent predictors for late aneurysmal change. The initial false lumen diameter at the UT showed a larger area under the curve on the receiver-operating characteristics curve for predicting late aneurysmal change (0.91, 95% CI 0.83 to 0.98) than the initial aorta diameter at the UT and the initial false lumen diameter and aorta diameter at the MT (Fig. 2). A ≥22-mm false lumen diameter at the UT on the initial CT predicted a late aneurysm with a sensitivity of 100% and a specificity of 76% (Figs. 2 and 3). The best cutoff values in type 1 and type 3 AD patients were 22 mm and 21 mm, respectively. Of the 53 patients who underwent imaging...
follow-up for ≥24 months, the 24 patients with a ≥22-mm false lumen diameter at the UT on the initial CT showed significantly higher rates of aorta dilation at the UT (5.04 ± 4.32 mm/year vs. 2.16 ± 2.40 mm/year, p < 0.005) and MT (4.44 ± 2.64 mm/year vs. 2.16 ± 2.40 mm/year, p < 0.005) than the 29 patients with a <22-mm initial false lumen diameter at the UT (Fig. 4). In a total of 100 patients, 42 patients with a ≥22-mm initial false lumen diameter at the UT tended to have a higher mortality (17% vs. 5%, p = 0.09) and showed significantly higher incidence of aneurysmal change (42% vs. 5%, p < 0.001) than 58 patients with a <22-mm initial false lumen diameter at the UT. The former patients had a significant lower event-free survival rate than the latter patients by the log-rank test (p < 0.001) (Fig. 5).

Discussion

Rate of aorta dilation. In terms of dilation location, the present study found that the rate of aorta dilation was highest at the UT, and the most common site of aneurysmal change was also UT. The study found no significant difference between type 1 and type 3 AD patients in terms of the rate of distal aorta dilation, even though tearing sites in the ascending aorta were removed by surgery in type 1 patients. This result might explain a previous observation
that late survival after discharge from the hospital was similar for patients with all types of AD and modes of therapy (15), and suggests that a late aorta aneurysm is a long-term complication of distal AD irrespective of AD type or ascending aorta surgery. Such a finding must be attributed, at least in part, to the observation that in distal aorta it is very common for the false lumen patency to be maintained even after ascending aorta surgery in type 1 AD patients (5,6). In the present study, all except 6 (12%) type 1 AD patients who showed complete false lumen resorption had a patent false lumen after surgery according to follow-up CT. It was reported that a total arch replacement for acute type 1 AD might decrease the risk of late complications related to the false lumen, and lead to excellent long-term survival (16,17). However, we could not find any statistical difference in the rate of aorta dilation among 3 different surgery types according to aorta surgery extent in type 1 AD patients.

Predictors of late aneurysmal change. It has been reported that the initial descending thoracic aorta diameter is an independent determinant of late aneurysmal formation in patients with type 1 AD after ascending aorta surgery (6). The current study found that the initial false lumen diameter at the UT and initial aorta diameter at the MT were independent predictors of late aneurysmal change in patients with type 1 and type 3 AD. Multiple logistic regression and receiver-operating characteristics curve analyses showed that the initial false lumen diameter at the UT was the most powerful predictor and was better than the initial aorta diameter in terms of predicting late aneurysmal change. The study also demonstrated that the initial false lumen diameter, but not the aorta diameter, correlated with the rate of aorta dilation at the UT, and that the ratio of the false lumen diameter to aorta diameter increased at the UT and MT in late aneurysmal change patients according to follow-up CT. These results suggest that an initial large false lumen at the UT is not only a cause of accelerated aorta dilation but is also the main aorta compartment undergoing dilation. This would likely explain why the initial false lumen diameter is a better predictor of late aneurysmal...
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change than the initial aorta diameter at the UT. A large false lumen probably reflects high false lumen pressure, which may play a critical role in dilating the false lumen itself and generating an aorta aneurysm.

The present study also found that Marfan syndrome was an independent predictor of late aneurysmal change. This result may explain a previous observation that despite satisfactory early results, long-term survival of AD patients with Marfan syndrome was suboptimal (18).

Clinical events. It has been reported that false lumen patency and the location of the most-dilated aortic segment at the distal arch were independent risk factors for poor outcome in type 3 AD patients and postasending aorta surgery type 1 AD patients (17,19). Consistent with those reports, we have demonstrated that patients with a large initial false lumen diameter at the UT (≥22 mm) showed a higher rate of aorta dilation and a higher incidence of clinical events including development of aortic aneurysm and death compared with those with a smaller initial false lumen diameter. This result suggests that a large false lumen diameter at the UT on the initial CT can be used as a single variable determining late aneurysmal change and poor clinical prognosis. Furthermore, a finding in this study that the initial false lumen diameter tended to be smaller in patients showing complete resorption during the follow-up period suggests that a small initial false lumen diameter might be a predictor of a more favorable outcome, especially in type 3 AD patients.

Study limitations. The present study was conducted in a single center and had a relatively small study population. The study focused on the baseline characteristics and initial CT measurements as predictors of late aneurysmal change and clinical outcome, but the effects of medication and blood pressure control were not considered. However, in most patients, multiple antihypertensive agents, including beta-blockers, were used, and blood pressure was well controlled. Finally, genetic and molecular susceptibility to the aneurysmal dilation could not be evaluated in this study (20).

Clinical implications. According to our data, we suggest that early surgical or percutaneous intervention such as stent-grafting might be considered for patients with a large (≥22 mm) initial false lumen at the UT, since such patients are more likely to show accelerated aorta dilation, develop aorta aneurysms, and suffer catastrophic clinical events. A further prospective randomized study of aggressive versus conservative management guided by the initial false lumen size would be necessary to identify the optimal time for interventional treatment and to confirm the clinical advantage of early intervention in these selected patients.

Conclusions

The UT is the major site of late aneurysmal change. A large false lumen diameter at the UT on the initial CT portends late aneurysm and adverse outcome warranting early intervention.