Improved Prognosis of Thoracic Aortic Aneurysms

A Population-Based Study

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Context.—Managing thoracic aortic aneurysms identified incidentally by increased use of computed tomography, echocardiography, and magnetic resonance imaging is problematic, especially in the elderly.

Objective.—To ascertain whether the previously reported poor prognosis for individuals with thoracic aortic aneurysms has changed with better medical therapies and improved surgical techniques that can now be applied to aneurysm management.

Design.—Population-based cohort study.

Setting and Patients.—All 133 patients with the diagnosis of degenerative thoracic aortic aneurysms among Olmsted County, Minnesota, residents between 1980 and 1994 compared with a previously reported cohort of similar patients between 1951 and 1980.

Main Outcome Measures.—The primary clinical end points were incidence, cumulative rupture risk, rupture risk as a function of aneurysm size, and survival.

Results.—In contrast to abdominal aortic aneurysms, for which men are affected predominately, 51% of thoracic aortic aneurysms were identified in women who were considerably older at recognition than men (mean age, 75.9 vs 62.8 years, respectively; P = .01). The overall incidence rate of 10.4 per 100 000 person-years (95% confidence interval [CI], 8.6-12.2) between 1980 and 1994 was more than 3-fold higher than the rate from 1951 to 1980. The cumulative risk of rupture was 20% after 5 years. Seventy-nine percent of ruptures occurred in women (P = .01). The 5-year risk of rupture as a function of aneurysm size at recognition was 0% for aneurysms less than 4 cm in diameter, 16% (95% CI, 4%-28%) for those 4 to 5.9 cm, and 31% (95% CI, 5%-56%) for aneurysms 6 cm or more. Overall 5-year survival improved to 56% (95% CI, 48%-66%) between 1980 and 1994 compared with only 19% between 1951 and 1980 (P < .01).

Conclusions.—In this population, elderly women represent an increasing portion of all patients with clinically recognized thoracic aortic aneurysms and constitute the majority of patients whose aneurysm eventually ruptures. Overall survival for thoracic aortic aneurysms has improved significantly in the past 15 years.
Table 1.—Operative Mortality and Morbidity of Thoracic Aortic Aneurysms

<table>
<thead>
<tr>
<th>Range, %</th>
<th>Incident per 100 000 Person-Years</th>
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<tbody>
<tr>
<td>Operative mortality</td>
<td>Ascending aorta</td>
</tr>
<tr>
<td></td>
<td>Aortic arch</td>
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<tr>
<td></td>
<td>Descending aorta</td>
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<tr>
<td></td>
<td>Thoracoabdominal aorta</td>
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<tr>
<td>Neurologic complication</td>
<td>Stroke</td>
</tr>
<tr>
<td></td>
<td>Paraparesis/paraplegia*</td>
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<tr>
<td></td>
<td>Renal failure†</td>
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<td></td>
<td>Cardiac event (myocardial infarction, arrhythmia, congestive failure)</td>
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</table>

*Generally associated with descending or thoracoabdominal aneurysms.
†Defined as need for assisted ventilation for more than 72 hours.

models. The Cox model was also used for multivariate assessment of risk factors for rupture, including time-dependent risk factors.

Results

Clinical Spectrum.—Between January 1, 1980, and December 31, 1994, 133 Olmsted County residents were diagnosed as having a degenerative (nondissecting) thoracic aortic aneurysm. Etiology of the aneurysms was diverse, but medial degeneration and atherosclerosis predominated. The anatomic location was delineated as ascending aortic or aortic arch disease alone in 40%, descending thoracic aortic disease alone in 31%, and both in 29%. Sixty-five (49%) were men and 68 (51%) were women. The average age at diagnosis was 69.0 years, but women were significantly older at their initial diagnosis than men (75.9 ± 12.7 years vs 62.8 ± 17.3 years, P < .01). The mean diameter (±SD) of these degenerative aneurysms was 4.9 ± 0.2 cm (median, 4.7 cm). Size at diagnosis did not differ by sex (mean, 4.9 ± 1.2 cm among the women and 4.9 ± 1.6 cm among the men). Seventy-nine percent of the 105 aneurysms were less than 6 cm at initial diagnosis, while 21% of the 28 aneurysms were 6 cm or larger.

Incidence.—The 133 Olmsted County residents with thoracic aortic aneurysms were identified from a population averaging about 100 000. The overall incidence rate, age- and sex-adjusted to the 1990 US white population, was 10.4 per 100 000 person-years (95% CI, 8.6-12.2). Incidence rates increased dramatically with age, and age-adjusted rates were greater for men than women. After the 1980 to 1984 study, age-adjusted incidence rates increased more than 3-fold compared with our previous study from 1951 to 1980 (Figure 1).

Rupture Risk.—Rupture occurred in 28 (21%) of the 133 cases. The 5-year cumulative probability of rupture was 20% (95% CI, 12%-28%), ie, survival free of rupture was 80% at 5 years. In only 4 patients (3%), the aneurysm was diagnosed initially at the time of rupture. Of the 24 aneurysms that ruptured subsequent to diagnosis, the interval between initial diagnosis and rupture was 4.3 ± 0.7 years. Seventy-nine percent of the ruptures were in women. The 5-year cumulative probability of rupture was 33% (95% CI, 19%-47%) for women and 9% (95% CI, 1%-17%) for men (P < .01).

Of the variables examined in univariate analyses, eventual development of dissection within the aneurysm, female sex, symptoms at diagnosis, and age at diagnosis were related significantly to aneurysm rupture (Table 2). Hypertension was of borderline significance. Smoking, chronic obstructive pulmonary disease, hyperlipidemia, family history of aneurysm, and saccular configuration were not related significantly to rupture.

When the 3 significant factors at diagnosis (sex, symptoms, and age) were placed in a Cox multivariate model, the factors that remained associated with increased rupture risk were female sex (risk ratio, 6.8; 95% CI, 2.3-19.9; P = .01) and symptoms at recognition (risk ratio, 7.0; 95% CI, 2.56-19.3; P = .01). Age at diagnosis was not associated with rupture risk when included in the multivariate model (risk ratio, 1.03; 95% CI, 0.99-1.07; P = .16).
Risk of Rupture in Relation to Initial Aneurysm Size.—The relationship of size to the cumulative probability of rupture did not achieve statistical significance in the univariate analysis (P = .48), but the observed probabilities of rupture risk were consistent with increasing risk with increasing size (Figure 2). The cumulative probability of rupture at 5 years was 0% for those with aneurysms less than 4 cm in diameter, 16% (95% CI, 4%-28%) for those with aneurysm diameters between 4 and 5.9 cm, and 51% (95% CI, 5%-56%) in those with diameters 6 cm or larger (Figure 3). Mean aneurysm diameter documented prior to rupture was 6.3 ± 0.3 cm.

Survival.—Eighty deaths occurred among the 133 patients with degenerative thoracic aortic aneurysms, for a 5-year survival rate of 56% (95% CI, 48%-66%) compared with an expected survival of 78% (Figure 3). This survival rate was significantly better than the 5-year survival of 19% between 1951 and 1980 (P < .01). Median survival was 6.6 years. The leading cause of death in this cohort was rupture of the thoracic aortic aneurysm, which accounted for 30% of the deaths. Cardiac events accounted for another 25%, along with pulmonary causes in 15%, cancer in 10%, stroke in 4%, and various other causes of death in 16%.

Operative Intervention.—Among the 133 patients in this study, 35 procedures were performed in 32 patients, for an operative intervention rate of 24%. The 5-year cumulative probability of any operation (elective or emergent) was 29% (95% CI, 16%-41%) for men and 19% (95% CI, 7%-32%) for women (P = .31). The 5-year cumulative probability for elective aneurysm repair was 25% (95% CI, 13%-37%) for men and 13% (95% CI, 2%-23%) for women (P = .14). Time from diagnosis to operation averaged 2.9 ± 0.6 years. Thirty-day case-fatality rates were 8% and 57%, respectively, for elective compared with emergent operations.

Comment

This population-based study identifies several important changes in the natural history of thoracic aortic aneurysms. First, the incidence of this condition has increased more than 3-fold in the past 4 decades. Second, we have found a strong independent correlation of female sex with ruptures. Finally, survival for patients with a thoracic aortic aneurysm has improved in the past 2 decades. Multiple factors have contributed to these trends, which now have new implications for current and future clinical management. The dramatic increase in overall incidence was associated with enhanced recognition of thoracic aneurysms by the introduction of computed tomography and 2-dimensional echocardiography in the 1970s and early 1980s, respectively. Many of these aneurysms are small and consequently have been observed. Second, the association between female sex and rupture risk remains unexplained by our current understanding of aneurysm pathogenesis. Although the mean age at diagnosis was 13 years older for women than men, the mean size at recognition was similar. However, the surgical intervention rate in women was one half the rate for men. Because women were on average 76 years old at diagnosis compared with men who were only 63 years old, advanced age may have influenced the decision for less operative intervention in the female cohort.

Finally, one of the most reassuring findings of this study was the improved 5-year survival of patients diagnosed as having a thoracic aortic aneurysm. What factors may be contributing to an improved outlook in recent years? First, there may be a lead-time bias since smaller aneurysms than what had been previously detected were recognized in the current study. Earlier detection may also account in part for the higher elective operative rate in this study compared with our population-based report from 1951 to 1980 (11% between 1951-1980 vs 24% between 1980-1994). Second, better antihypertensive therapies

<table>
<thead>
<tr>
<th>Variable</th>
<th>P Value</th>
<th>Risk Ratio</th>
<th>95% CI*</th>
</tr>
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<tbody>
<tr>
<td>Female sex</td>
<td>.001</td>
<td>4.91</td>
<td>1.98-12.19</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>.004</td>
<td>1.06</td>
<td>1.02-1.10</td>
</tr>
<tr>
<td>Hypertension</td>
<td>.12</td>
<td>2.58</td>
<td>0.78-8.60</td>
</tr>
<tr>
<td>Smoking</td>
<td>.98</td>
<td>0.99</td>
<td>0.44-2.21</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>.22</td>
<td>1.63</td>
<td>0.69-4.84</td>
</tr>
<tr>
<td>Family history of aneurysm</td>
<td>.68</td>
<td>0.74</td>
<td>0.18-3.13</td>
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<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>.73</td>
<td>1.16</td>
<td>0.51-2.64</td>
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<tr>
<td>Size†</td>
<td>.48</td>
<td>1.13</td>
<td>0.81-1.57</td>
</tr>
<tr>
<td>Symptoms at diagnosis</td>
<td>.008</td>
<td>3.25</td>
<td>1.37-7.73</td>
</tr>
<tr>
<td>Subsequent dissection</td>
<td>&lt;.001</td>
<td>15.76</td>
<td>7.31-34.05</td>
</tr>
<tr>
<td>Sacular</td>
<td>.52</td>
<td>0.62</td>
<td>0.15-2.64</td>
</tr>
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</table>

*CI indicates confidence interval.
†Of the 84 patients sized within 35 days of diagnosis, there were 15 events.

Figure 2.—Cumulative probability of rupture of thoracic aortic aneurysms based on maximum aneurysm diameter at initial diagnosis. Only patients who had serial aneurysm measurements are included (n = 78); 18 with an aneurysm larger than 6.0 cm, 48 had one between 4.0 and 5.9 cm, and 12 less than 4 cm.

Figure 3.—Overall survival of Olmsted County, Minnesota, residents with degenerative thoracic aortic aneurysms comparing 2 time periods. The first was between 1951 and 1980 and the second was between 1980 and through 1994.
may have played an important role. This current study showed a trend that hypertension was a prognostic factor for rupture. Since β-blockers appear to slow aneurysm expansion rates, their more prevalent use may have delayed or averted rupture in some patients.\(^2\)\(^,\)\(^3\) Third, earlier recognition and more aggressive management of coronary heart disease is likely to have had a salutary influence on patient survival in the past 15 years.\(^4\)\(^,\)\(^5\) Finally, operative techniques and perioperative care have also improved.

With the increasing number of elderly patients, the trends revealed by this population-based study are likely to continue. The relatively high incidence of thoracic aortic aneurysms among women and the aneurysms’ propensity to rupture are important factors to be considered in future management strategies. Decreasing rupture rates in women would require an increased rate of elective surgery, a strategy that may or may not be appropriate in the very elderly. The risks of surgery and the lack of randomized trials for managing small thoracic aneurysms also discourage mass screening of the elderly.

Currently, 3 general guidelines are suggested for all patients with clinically recognized thoracic aortic aneurysms. Hypertension\(^2\) is one risk factor that is known to increase rupture risk and a factor that can be controlled in most patients. Second, symptomatic aneurysms and those complicated by dissection are more likely to rupture and should be evaluated urgently for repair. Finally, asymptomatic thoracic aortic aneurysms with diameters of 6 cm or greater are at increased risk of eventual rupture and should be considered for elective repair in acceptable surgical candidates.

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### References