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 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 predominantly, 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.

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THERE IS renewed clinical interest in the prognosis of thoracic aortic aneurysms.1 With the advent of computed tomography and 2-dimensional echocardiography, recognition of such aneurysms has increased. Many of these aneurysms are relatively small at diagnosis (<6 cm in diameter), raising the critical question of when surgical or endovascular repair should be recommended.

Most of the current information on the prognosis of thoracic aortic aneurysms is provided by selected referral populations and tertiary surgical series.1 The applicability of such data to the initial management of thoracic aneurysms that present in community practice is uncertain. An earlier population-based study from Rochester, Minn, reported a dismal outlook for these patients, but it was performed prior to routine use of computed tomography and echocardiography and prior to recent advances in medical and surgical management.2 In addition, the indications for elective repair of thoracic aneurysms remain debatable because morbidity and mortality are higher than for repair of abdominal aortic aneurysms3-6 (Table 1). In particular, spinal cord and cerebral and visceral ischemia contribute to these risks.7,8 However, no recent data are available on the risk of rupture of thoracic aortic aneurysms among unselected patients from the community at large.

Therefore, we used the resources of the Rochester Epidemiology Project to conduct a population-based study of thoracic aortic aneurysm incidence, prognosis, operative intervention, and survival among the residents of Olmsted County, Minnesota. In addition, we investigated factors that were associated with an increased risk of rupture. Key findings were compared with results from an earlier study in this population that covered from between 1951 and 1980.2

Methods

This population-based study was possible because all Olmsted County residents with a recognized thoracic aortic aneurysm could be identified, and their complete (outpatient and inpatient) medical records could be retrieved for review.2 All medical records were reviewed for each resident of Olmsted County in whom a diagnosis of thoracic aortic aneurysm was initially made between January 1, 1980, and December 31, 1994. A diagnosis of thoracic aortic aneurysm was accepted if a focal aortic dilation (1.5 times larger than normal lo-
The anatomic aorta was identified and confirmed by radiographic studies, operation, or autopsy. Acute aortic dissections, traumatic aortic lacerations, annular dilatation without ascending aortic enlargement, and penetrating atheromatous lesions without aneurysmal change were excluded.

We obtained from the medical records data regarding patient demographic characteristics, clinical presentation, maximal diameters of the aneurysms, cardiovascular risk factors, operative indication, surgical outcome, and survival. All patients were followed up through their complete medical records until death, emigration from the community, or to February 1, 1997, to identify aneurysm repair, rupture, or death.

Incident cases were defined as persons who were residents of Olmsted County on the date of the diagnosis of thoracic aortic aneurysm. Detailed age- and sex-specific population figures for 1980 through 1994 were derived by linear interpolation of decennial census figures for 1980 and 1990. With these denominators, age- and sex-specific incidence rates for thoracic aortic aneurysm were calculated for both overall and 5-year periods from 1980 through 1994. Summary rates were directly adjusted to the (5-year) age distribution of the white population of the United States in 1990. Ninety-five percent confidence intervals (CIs) were calculated around the summary rates with Poisson regression.

The Kaplan-Meier method was used to estimate survival and to ascertain the cumulative probability of rupture, which was estimated as a function of time following initial diagnosis of the aneurysm. Expected survival rates were calculated from life tables of the Minnesota white population. Survival curves were compared with log-rank tests. Associations between continuous risk factors and rupture risk were evaluated with Cox proportional hazards 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 7-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).
Table 2.—Risk Factors for Rupture of Thoracic Aortic Aneurysms Excluding Acute Dissections (N = 133 With 28 Ruptures) Among Olmsted County, Minnesota, Residents From 1980 Through 1994

<table>
<thead>
<tr>
<th>Variable</th>
<th>P Value</th>
<th>Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<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>1.83</td>
<td>0.69-4.64</td>
</tr>
<tr>
<td>Family history of aneurysm</td>
<td>.88</td>
<td>0.74</td>
<td>0.18-3.13</td>
</tr>
<tr>
<td>Chronic obstructive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pulmonary disease</td>
<td>.73</td>
<td>1.16</td>
<td>0.51-2.64</td>
</tr>
<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>Saccular</td>
<td>.52</td>
<td>0.62</td>
<td>0.15-2.64</td>
</tr>
</tbody>
</table>

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

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 31% (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. Cardiovascular 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 thoracic aortic aneurysms 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...
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. 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. 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 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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Table 3.—Rupture Risk and Surgical Intervention Rates Related to Anatomic Extent of Thoracic Aortic Aneurysm Among Olmsted County, Minnesota, Residents From 1980 Through 1994.*

*CI indicates confidence interval.

<table>
<thead>
<tr>
<th>Location of Aneurysm</th>
<th>Ascending (n = 52)</th>
<th>Descending (n = 42)</th>
<th>Both (n = 39)</th>
<th>Total (N = 133)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, No. (%)</td>
<td>33 (64)</td>
<td>14 (33)</td>
<td>18 (46)</td>
<td>65 (49)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>19 (36)</td>
<td>28 (67)</td>
<td>21 (54)</td>
<td>68 (51)</td>
</tr>
<tr>
<td>5-y rupture risk, % (95% CI)</td>
<td>9 (1-18)</td>
<td>26 (8-44)</td>
<td>29 (13-46)</td>
<td>20 (12-28)</td>
</tr>
<tr>
<td>5-y operative intervention rate, % (95% CI)</td>
<td>28 (14-42)</td>
<td>27 (9-46)</td>
<td>16 (3-29)</td>
<td>24 (16-33)</td>
</tr>
</tbody>
</table>

References