# WHAT IS THE APPROPRIATE SIZE CRITERION FOR RESECTION OF THORACIC AORTIC ANEURYSMS?

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**Although many articles have described techniques for resection of thoracic aortic aneurysms, limited information on the natural history of this disorder is available to aid in defining criteria for surgical intervention. Data on 230 patients with thoracic aortic aneurysms treated at Yale University School of Medicine from 1985 to 1996 were analyzed. This computerized database included 714 imaging studies (magnetic resonance imaging, computed tomography, echocardiography). Mean size of the thoracic aorta in these patients at initial presentation was 5.2 cm (range 3.5 to 10 cm). The mean growth rate was 0.12 cm/yr. Overall survivals at 1 and 5 years were 85% and 64%, respectively. Patients having aortic dissection had lower survival (83% 1 year; 46% 5 year) than the cohort without dissection (89% 1 year; 71% 5 year). One hundred thirty-six patients underwent surgery for their thoracic aortic aneurysms. For elective operations, the mortality was 9.0%; for emergency operations, 21.7%. Median size at time of rupture or dissection was 6.0 cm for ascending aneurysms and 7.2 cm for descending aneurysms. The incidence of dissection or rupture increased with aneurysm size. Multivariable regression analysis to isolate risk factors for acute dissection or rupture revealed that size larger than 6.0 cm increased the probability by 32.1 percentage points for ascending aneurysms ($p = 0.005$). For descending aneurysms, this probability increased by 43.0 percentage points at a size greater than 7.0 cm ($p = 0.006$). If the median size at the time of dissection or rupture were used as the intervention criterion, half of the patients would suffer a devastating complication before the operation. Accordingly, a criterion lower than the median is appropriate. We recommend 5.5 cm as an acceptable size for elective resection of ascending aortic aneurysms, because resection can be performed with relatively low mortality. For aneurysms of the descending aorta, in which perioperative complications are greater and the median size at the time of complication is larger, we recommend intervention at 6.5 cm. (J Thorac Cardiovasc Surg 1997;113:476-91)**

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Thoracic aortic aneurysms are serious conditions that frequently necessitate surgical intervention owing to the threat of dissection or rupture. The natural history of aortic aneurysm is often related to the specific location and the primary cause of the disease. Patients with Marfan's syndrome have aneurysms of the ascending aorta with chronic aortic regurgitation and aortic root dissection and rupture, which are the primary causes of their reduced life expectancy.[1] In patients with atherosclerotic aneurysms of the ascending aorta, rupture is the most common cause of death.[2] The law of Laplace predicts that as the aneurysm size increases, the wall tension rises as well.[3] The inherent disease progression usually consists of self-propagating incremental expansion and possible rupture.

Unfortunately, the size-rupture correlation that is well established for abdominal aortic aneurysms does not hold true for the thoracic aorta. The decision-making process is further complicated by the greater risks of replacing the thoracic aorta than the abdominal aorta. Resection and graft replacement of ascending aortic aneurysms often requires significant additional surgery such as coronary artery bypass grafting and aortic valve replacement, and descending thoracic aortic replacement carries the ever-present risk of spinal cord paraplegia. Joyce and associates[4] in 1964 found that approximately 50% of patients with thoracic aortic aneurysm died within 5 years of the diagnosis. They found that the presence of associated coronary, cerebral, or other peripheral arterial occlusive or aneurysmal disease had a negative impact on survival. The 5-year survival was approximately 26.9% for symptomatic aneurysms and 58.3% for asymptomatic aneurysms.

Pressler and McNamara[5] in 1985 reported that the natural history of thoracic aortic aneurysms not treated surgically involved rupture in 47% of patients. With increasing surgical management, they reported a decrease in operative mortality to 5% for elective resections and to 16% for emergency resections.

In developing management protocols for appropriate patient selection for surgery, it is essential to study risk factors that may influence the natural history of the disease. The specific objective is to select patients for whom the operative risks are justified. The current recommendations for surgical intervention are based largely on clinical judgment, with a paucity of hard scientific and statistical data regarding the appropriate size criterion for surgical intervention. The current study involves data collected from a series of 230 patients with thoracic aortic aneurysms followed up at the Center for Thoracic Aortic Disease at Yale University during the period October 1985 to March 1996. This analysis aims to define scientific criteria for surgical intervention on the basis of the natural history available from this group of patients.

## Patients and methods

Patients were enrolled in the study after a computerized search had been conducted of all patients undergoing magnetic resonance imaging, computed tomographic scanning, or echocardiography of the thoracic aorta at Yale–New Haven Hospital from October 1985 to March 1996. The search was formatted to exclude patients with ascending or descending thoracic aortas of less than 3.5 cm in diameter and patients younger than 16 years of age. A search was also conducted to identify patients undergoing aortic operations, and autopsy records were examined for all patients who died of aortic disease during this time period. A hospital chart review was then conducted on every identified patient. Data recovered from hospital records and computer files were cross-checked with hospital discharge abstract data monitored by the Connecticut Hospital Association and Connecticut State Mortality Records. This computerized database is maintained as part of ongoing studies at the Yale Center for Thoracic Aortic Disease, a major referral center for New England.

The database includes 714 radiographic studies (250 computed tomographic scans, 147 magnetic resonance imaging scans, and 317 echocardiograms) performed on 230 patients with thoracic aortic aneurysms. Dinsmore and associates[6] reported an extremely high correlation among magnetic resonance imaging, computed tomographic scans, and echocardiograms in the measurement of thoracic aortic aneurysms. Thus in the present study we have elected to combine these imaging modalities. The thoracic aorta was considered aneurysmal if it attained a maximal diameter of 3.5 cm or greater. Of these 230 patients, 138 are male and 92 are female. The average age is 62.0 years, with a range of 16 to 92 years. There are 25 patients with Marfan's syndrome in this series.

Of the 230 patients with thoracic aortic aneurysms who were followed up, there was a core group of 174 patients who were observed serially. This group of patients consisted of 111 individuals with aneurysms of the ascending aorta, 11 with aneurysms of the aortic arch, 41 with aneurysms of the descending aorta, and 11 with thoracoabdominal aneurysms. Serial information on aneurysm sizes was obtained in 79 patients who did not undergo aortic graft surgery. The period of follow-up ranged from 1 to 106 months, with a mean of 25.9 months. These patients were followed up longitudinally, and this sample was used to estimate aneurysm growth rates and to identify risk factors affecting aneurysm growth in a multivariable model. A similar multivariable model was used to study factors that affect aneurysm rupture or dissection and overall survival.

A total of 136 patients underwent surgical treatment for their thoracic aortic aneurysms over the 11-year period. Overall, there were 67 elective and 69 emergency operations. Operations included 86 ascending or arch aneurysms (47 elective and 39 emergency) and 50 descending or thoracic aortic aneurysms (21 elective and 29 emergency).

Operations on the ascending aorta were performed with the use of cardiopulmonary bypass with myocardial preservation by systemic hypothermia, topical hypothermia with iced saline solution, and cold crystalloid or blood cardioplegia. Deep hypothermia and circulatory arrest were used uniformly for arch replacements and liberally for the distal anastomosis of ascending aortic replacements. The circulatory arrest times ranged from 14 to 64 minutes.

Since 1987, operations on the descending aorta have been performed routinely with the use of left atrial–femoral artery bypass with a centrifugal pump without an oxygenator, except when the patient's condition was not

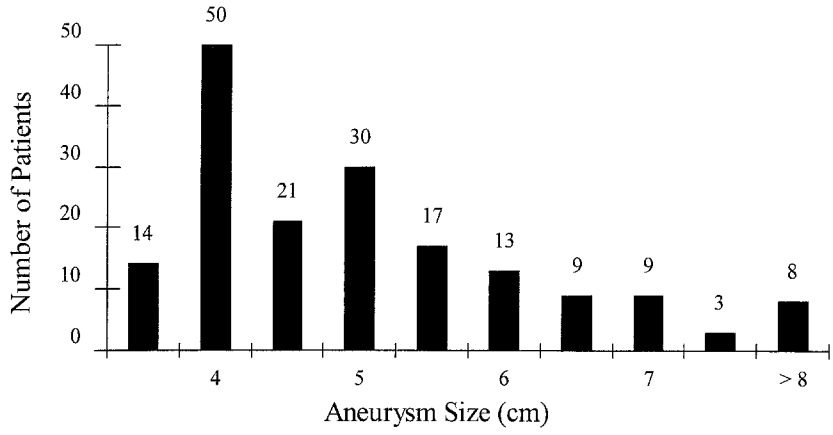


**Fig. 1.** Distribution of patients with thoracic aortic aneurysms by initial aneurysm size.

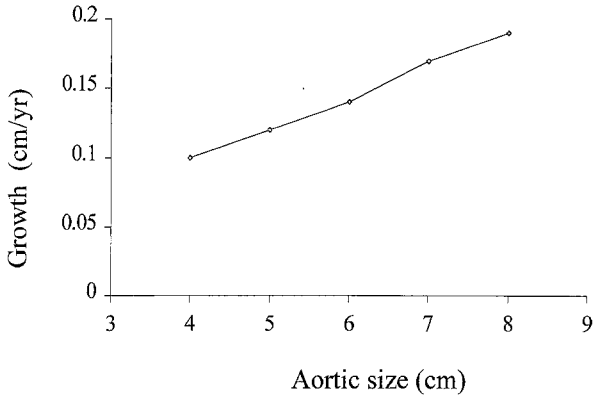


**Fig. 2.** Absolute change in growth as a function of initial size of aneurysm.

stable enough for cannulation; in this case the operation was done by the "clamp-and-sew" technique.

**Statistical method.** Statistical methods were used to identify and estimate risk factors for the following outcomes: annual growth rates of aneurysms, rates of major complications (acute dissection and rupture), operative mortality, and long-term survival.

*Aneurysm growth rates.* Serial information on aneurysm size was available for 79 patients. These patients formed the sample for our growth rate estimates. Once patients underwent surgical repair, their subsequent imaging measurements were excluded from growth rate estimates. These estimates were obtained by means of multivariable regression analysis in which aneurysm growth followed an exponential path. In particular, the natural logarithm of the last measured size to the first measured size was related to the time interval between the two tests and interactions between this time variable and risk factors (see the appendix).[7, 8] Initial risk factors analyzed included chronic dissection, aneurysm size (<4.0 cm, 4 to 4.9 cm, 5 to 5.9 cm, and >6.0 cm), Marfan's syndrome, aneurysm location (ascending aorta or arch vs descending or thoracoabdominal aorta), age, smoking history, hypertension (diastolic blood pressure >95 mm Hg), and sex. The models presented herein include the following risk factors: chronic dissection, aneurysm location, age, and sex. Preliminary statistical analysis revealed that initial aneurysm size, smoking history, Marfan's syndrome, and hypertension were not predictive of aneurysm growth rate, and these factors were eliminated from the final estimates. We estimated separate growth equations for ascending or arch aneurysms and descending or thoracoabdominal aneurysms.

*Complication rates.* The incidence of acute dissections or ruptures (or both) was evaluated by both descriptive and multivariable analyses. The multivariable analysis specifies a logistic regression model relating occurrence of rupture or acute dissection to each of the following: initial aneurysm size, aneurysm location (ascending or arch vs descending or thoracoabdominal), age, and sex.

*Operative mortality.* We present both descriptive and multivariable evidence on operative mortality. A logistic regression model was estimated relating operative mortality to the following: emergency/nonemergency status, aneurysm location, and acute dissection or rupture (or both) at the time of the operation.

*Survival analysis.* Five-year survival estimates were calculated by life-table analysis (Kaplan-Meier). Differences in survival were tested by means of the LIFEREG procedure in SAS version 6.07, 1994 (SAS Institute, Inc., Cary, N.C.). In particular, a Weibull distribution was fitted to failure-time data. The specific factors tested for survival differences included chronic dissection on enrollment, aneurysm location, prior operation, and initial aneurysm size on enrollment in the study.

## Results

**Aneurysm size.** The mean and median sizes of the thoracic aorta were 5.2 cm and 5.0 cm, respectively. Fig. 1 demonstrates the distribution of thoracic aortic aneurysms by initial size at presentation.

**Table I.** *Multivariable estimates of aneurysm growth rates*

| *Patient category* | *Annual growth rate according to initial aneurysm size** | | | | | |
|---|---|---|---|---|---|---|
| | *4.0 cm* | *5.0 cm* | *6.0 cm* | *7.0 cm* | *8.0 cm* | *5.2 cm (sample mean)* |
| All ($n$ = 79) | 0.10 cm/yr (0.05-0.14) | 0.12 cm/yr (0.06-0.18) | 0.14 cm/yr (0.07-0.21) | 0.17 cm/yr (0.09-0.25) | 0.19 cm/yr (0.10-0.28) | 0.12 cm/yr (0.06-0.18) |
| Dissection status | | | | | | |
| Chronic dissection ($n$ = 16) | 0.28 cm/yr (0.10-0.47) | 0.35 cm/yr (0.13-0.59) | 0.42 cm/yr (0.15-0.70) | 0.49 cm/yr (0.18-0.82) | 0.56 cm/yr (0.20-0.94) | 0.37 cm/yr (0.13-0.61) |
| No dissection ($n$ = 63) | 0.07 cm/yr (0.02-0.11) | 0.08 cm/yr (0.03-0.14) | 0.10 cm/yr (0.03-0.17) | 0.12 cm/yr (0.04-0.20) | 0.14 cm/yr (0.04-0.23) | 0.09 cm/yr (0.03-0.15) |
| Location of aneurysm | | | | | | |
| Ascending or arch ($n$ = 54) | 0.08 cm/yr (0.03-0.12) | 0.10 cm/yr (0.04-0.15) | 0.11 cm/yr (0.05-0.18) | 0.13 cm/yr (0.06-0.21) | 0.15 cm/yr (0.06-024) | 0.10 cm/yr (0.04-0.16) |
| Descending or thoracic aorta ($n$ = 25) | 0.23 cm/yr (0.07-0.39) | 0.28 cm/yr (0.08-0.49) | 0.34 cm/yr (0.10-0.59) | 0.40 cm/yr (0.12-0.69) | 0.45 cm/yr (0.13-0.79) | 0.29 cm/yr (0.09-0.51) |

*95% Confidence interval is given in parentheses.

**Growth rates.** Growth rates for aneurysms of the thoracic aorta were calculated as described earlier. The exponential model assumed that aneurysm growth increases with initial size. Thus, for the average aneurysm size in our sample (5.2 cm), the annual growth rate was estimated to be 0.12 cm/yr. Larger aneurysms were estimated to grow by greater increments.

Table I shows the estimated aneurysm growth rates in relation to initial aneurysm size, chronic dissection, and location. Annual growth varied from 0.10 cm/yr for small (4.0 cm) aneurysms to 0.19 cm/yr for large (8.0 cm) aneurysms. This relationship is depicted graphically in Fig. 2. The annual growth rates for patients with chronic dissections are significantly higher, ranging from 0.28 cm/yr for small (4.0 cm) aneurysms to 0.56 cm/yr for large (8.0 cm) aneurysms. For ascending aortic aneurysms, the annual growth rate was 0.10 cm, and for descending aortic aneurysms, 0.29 cm.

**Complication rates.** Fig. 3 displays the incidence of acute dissection or rupture according to aneurysm size. The incidence of these complications increases with larger aortic size. At less than 4 cm, 4.0 to 4.9 cm, 5.0 to 5.9, and more than 6.0 cm, the incidence of acute dissection or rupture was 7.1%, 8.5%, 12.8%, and 45.2%, respectively. Similar increases were observed for the incidence of acute dissection alone and rupture alone, as illustrated in Figs. 4 and 5.

The median thoracic aortic sizes at the time of rupture or dissection are shown in Table II. In patients who had a rupture or acute dissection, the median aortic size was 6.0 cm. Descending or thoracoabdominal aneurysms, however, ruptured or dissected at a median size of 7.2 cm. Ascending or arch aneurysms ruptured or dissected at a median size of 6.0 cm. Three of 25 patients with Marfan's syndrome in our series had acute dissections or ruptures at aneurysm sizes less than 5 cm in diameter.

Table III shows the results of a multivariable regression analysis predicting the probability of a dissection or rupture. Table III indicates that the odds of incurring a rupture or acute dissection are 8.84 times greater for patients with aneurysms of 6 to 6.9 cm than for patients with aneurysms of 4.0 to 4.9 cm ($p$ = 0.005). A similar pattern occurs for patients with aneurysm diameters of 7.0 cm or larger.

Additional multivariable analyses were performed to estimate the probability of rupture or acute dissection in relation to aneurysm location. The effects of initial aneurysm size and location on these complications are summarized in Table IV. As Table IV indicates, the probability of rupture or dissection is 36.2% in patients with ascending or arch aneurysms larger than 6.0 cm ($p$ = 0.005) and 47.1% in patients with descending aneurysms larger than 7.0 cm ($p$ = 0.006). The increase in probability of dissection or rupture relative to the 4.0 to 4.9 cm reference cohort is depicted in Figs. 6 and 7 for ascending and descending aneurysms, respectively. Fig. 6 illustrates the estimated increase in the probability of incurring a dissection or rupture as a function of ascending aneurysm size. Relative to the 4.0 to 4.9 cm cohort, the probability of incurring a dissection or rupture is 32.1 percentage points higher in the 6.0 to 6.9 cm cohort ($p$ = 0.005). Similarly, Fig. 7 shows that

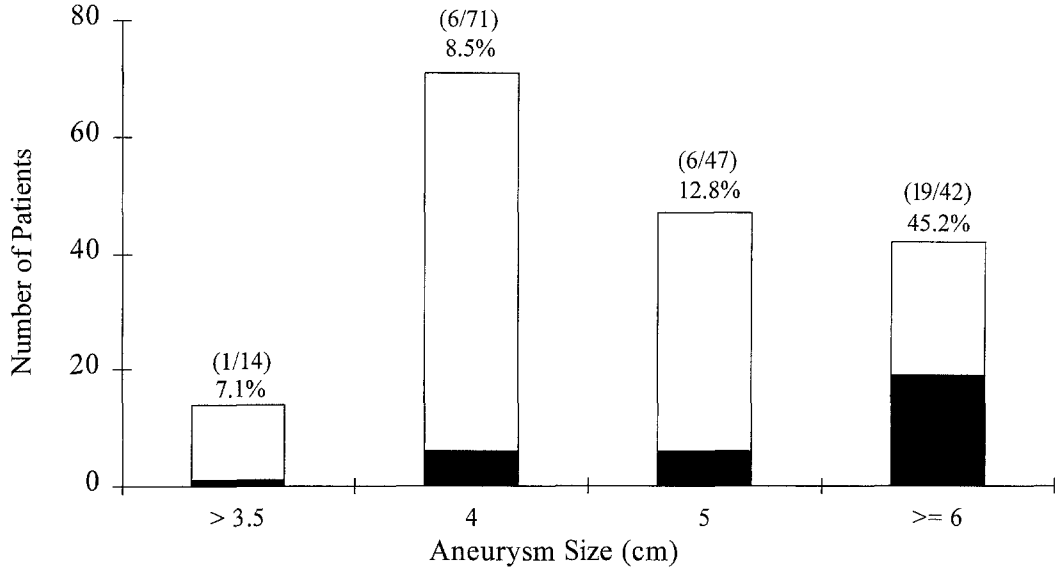


**Fig. 3.** Incidence of acute dissection or rupture as a function of initial aneurysm size. The entire column indicates the total number of patients with thoracic aortic aneurysms in each size range. The *black area* indicates the number of patients who incurred an acute dissection or rupture of the aneurysm.

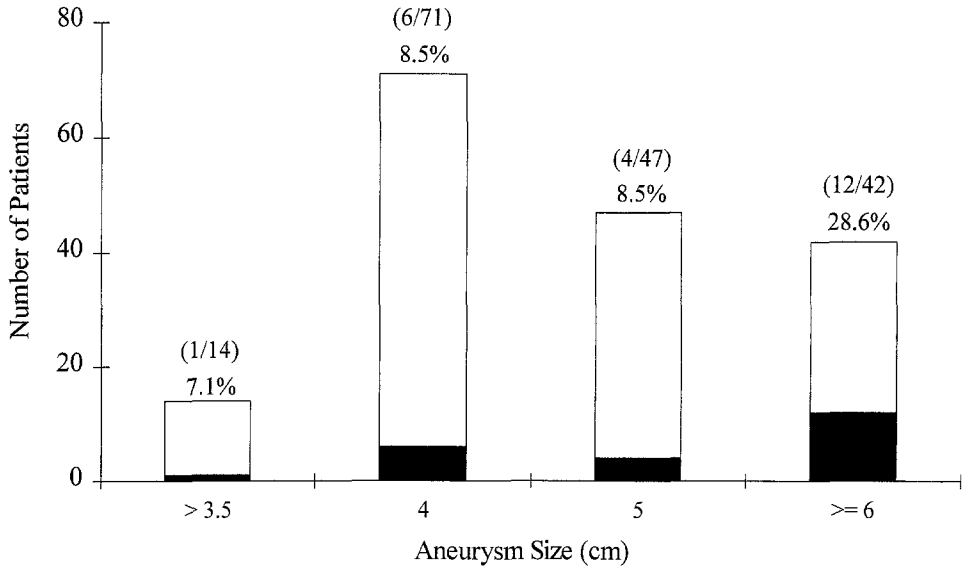


**Fig. 4.** Incidence of acute dissection as a function of initial aneurysm size. The entire column indicates the total number of patients with thoracic aortic aneurysms in each size range. The *black area* indicates the number of patients who incurred an acute dissection of the aneurysm.

the rate of dissection or rupture increases by 43.0 percentage points in descending aneurysms larger than 7 cm in diameter ($p = 0.006$).

**Operative mortality and perioperative morbidity.** A total of 136 patients underwent surgery for thoracic aortic aneurysms. The operative mortality by elective or emergency clinical status and aneurysm location are shown in Table V. The overall postoperative incidence of stroke was 2.94% (4/136). For ascending aorta and aortic arch repairs, the incidence was 2.3% (2/86); for descending aorta and thoracoabdominal repairs, the incidence was 4.0%

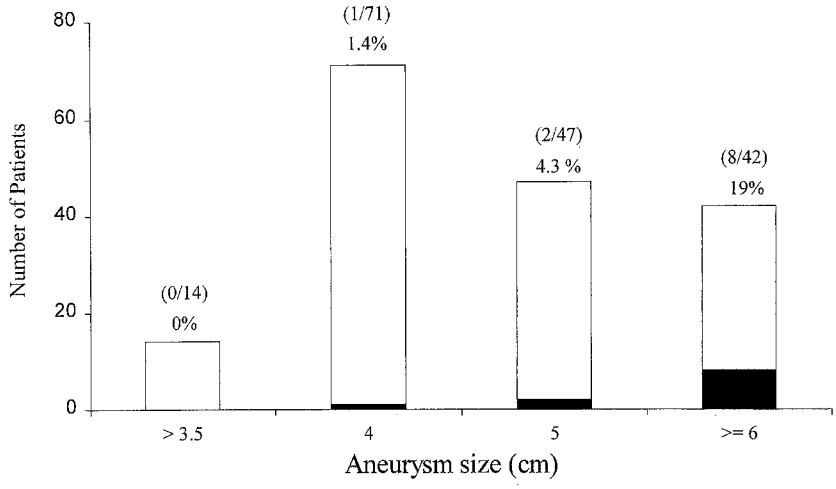


**Fig. 5.** Incidence of rupture as a function of initial aneurysm size. The entire column indicates the total number of patients with thoracic aortic aneurysms in each size range. The *black area* indicates the number of patients who incurred a rupture of the aneurysm.

(2/50). The paraplegia rate in our series was 4.0% (2/50) for patients who underwent resection of aneurysms of the descending thoracic aorta.

We used a multivariable regression analysis to isolate factors predicting operative mortality. As illustrated in Table VI, the presence of an acute dissection or rupture each independently increased the risk of operative death in this analysis. These increases were statistically significant at the 1% and 5% levels, respectively. When controlling for the presence of an acute dissection and rupture in this multivariable analysis, neither the location of the aneurysm nor the emergency nature of the procedure increased the operative mortality.

**Long-term survival.** Overall long-term survival rates at 1 and 5 years were 85% and 64%, respectively, as depicted in Fig. 8 and Table VII. Mortality in our series was predominately related to the aneurysmal disease process. Fig. 8 compares the survival in our patients with that of an age- and sex-matched cohort. There was a lower survival in patients having an aortic dissection (83% at 1 year; 46% at 5 years) than in the cohort not having aortic dissection (89% at 1 year; 71% at 5 years) (Fig. 9). Patients with descending thoracic aneurysms had lower long-term survivals (82% at 1 year; 39% at 5 years) than did patients with ascending aneurysms (87% at 1 year; 77% at 5 years) ($p = 0.031$) (Fig. 10). Neither surgical status nor the first imaged size significantly affected survival (Figs. 11 and 12).

**Table II.** *Aneurysm size at time of complication*

| *Patient category* | *Mean** | *Median* | *Range* |
|---|---|---|---|
| All ruptures or acute dissections ($n = 31$) | 6.2 cm (5.7-6.7) | 6.0 cm | 4.0-10.0 |
| All acute dissections ($n = 22$)† | 5.9 cm (5.4-6.4) | 6.0 cm | 4.0-8.3 |
| All ruptures ($n = 11$)† | 6.9 cm (5.8-7.0) | 7.0 cm | 4.6-10.0 |
| Ascending or arch aneurysm ($n = 23$) | 5.9 cm (5.4-6.4) | 6.0 cm | 4.0-8.3 |
| Descending or thoracoabdominal ($n = 8$) | 7.0 cm (5.7-8.3) | 7.2 cm | 5.0-10.0 |

*95% Confidence intervals for the mean are given in parentheses.

†The sum of all acute dissections and all ruptures is more than 31 because some patients incurred both acute dissections and ruptures.

## Discussion

### Natural history

*Survival.* Joyce and associates[4] reported the 5-year survivals for aneurysms of the ascending thoracic aorta with a diameter of 6 cm or less to be 61%; aneurysms larger than 6 cm had a 5-year survival of 38%. The overall 5-year survival in our series is 64%, as illustrated in Table VII. The mortality is believed to be related to the aneurysm itself in the vast majority of cases, although adequate details for this distinction were often unavailable. Survival is significantly lower for descending aortic aneurysms (39% at 5 years) ($p = 0.031$). Patients with a dissection had a lower survival (46% at 5 years). The long-term prognosis for patients

**Table III.** *Logistic regression analysis of factors predicting ruptures or acute dissections (dependent variables)* (n = 174)*

| | *Analysis of maximum likelihood estimates* | | | |
|---|---|---|---|---|
| *Variable* | *Parameter estimate†* | *Standard error* | *p Value* | *Odds ratio†* |
| Intercept team | −2.51‡ (−4.96-−0.10) | 1.23 | 0.042 | 0.08‡ (0.01-0.91) |
| Initial aneurysm size | | | | |
| 3.5-3.9 cm | 0.51 (−1.86-2.88) | 1.21 | 0.674 | 1.66 (0.16-17.78) |
| 5.0-5.9 cm | 0.50 (−1.16-2.16) | 0.85 | 0.559 | 1.64 (0.31-8.63) |
| 6.0-6.9 cm | 2.18‡ (0.67-3.68) | 0.77 | 0.005 | 8.84‡ (1.96-39.80) |
| ≥7.0 cm | 2.08‡ (0.45-3.71) | 0.83 | 0.012 | 8.00‡ (1.57-40.67) |
| Age | −0.01 (−0.05-0.03) | 0.02 | 0.687 | 0.99 (0.96-1.03) |
| Male | −0.38 (−1.44-0.68) | 0.54 | 0.482 | 0.68 (0.24-1.97) |

Criteria for assessing model fit: −2 Log L: intercept only: 115.743; intercept and covariates: 102. 090; $\chi^2$ for covariates: 13.652 with 6 df ($p = 0.0338$); c-statistic: 0.749

*This variable equals 1 if the patient incurred a rupture or acute dissection and 0 otherwise.

†95% Confidence intervals on parameter estimates and odds ratios are given in parentheses.

‡Statistically significant at the 1% level.

**Table IV.** *Estimated probability of rupture or acute dissection by initial aneurysm size**

| *Aneurysm size* | *All patients† (n = 174)* | *Ascending aneurysm† (n = 122)* | *Descending aneurysm† (n = 52)* |
|---|---|---|---|
| 3.5-3.9 cm | 6.7% (1.0-43.1) | 6.7% (1.0-43.1) | 6.7% (1.0-43.1) |
| 5.0-5.9 cm | 6.6% (1.3-27.0) | 6.6% (1.3-27.0) | 6.6% (1.3-27.0) |
| 6.0-6.9 cm | 27.4%‡ (7.8-62.5) | 36.2%‡ (5.1-85.6) | 12.2% (1.2-59.8) |
| ≥7.0 cm | 25.5%‡ (6.3-63.2) | 8.0% (1.0-50.6) | 47.1%‡ (12.6-84.8) |

*Statistical significance was assessed by comparing complication rates relative to the 4.0-4.9 cm cohort.

†95% Confidence intervals for estimated probability of dissection or rupture are given in parentheses.

‡Statistically significant at the 1% level.

treated surgically is similar to that of medically managed patients (Fig. 11). Because surgically treated patients tend to have more critical illness, these findings point to a beneficial survival effect from surgical intervention. In our series, as the first imaged aneurysm size increases, the survival decreases (59% 5-year survival at size ≥6 cm). This decrease in survival was not shown to be significant, however, when compared with that of the 4.0 to 4.9 cm cohort (Fig. 12, Table VII).

*Growth rates.* Our estimated annual growth for descending and thoracic aortic aneurysms is 0.29 cm/yr. This is in close agreement with results reported by Dapunt and associates[9] (0.32 cm/yr). In 1992, Masuda and colleagues[10] reported an overall growth rate for thoracic aortic aneurysms of 0.13 cm/yr. Again, this finding corresponds closely with our estimate of 0.12 cm/yr. Hirose and coworkers[11] reported a high annual growth rate of 0.42 cm/yr for thoracic aortic aneurysms. In a subsequent study, however, Hirose and colleagues[7] reported a substantially lower rate. The discrepancy in the two Hirose studies may well reflect the different growth rate estimation strategies used. The latter Hirose study[7] used regression approaches similar to those used by Dapunt and associates[9] and by us in the current study to estimate thoracic aortic aneurysm growth. The earlier study by Hirose's group simply calculated growth as the difference between last and first measured size divided by the duration between tests.

Size has traditionally been viewed as an important risk factor for complications (i.e., acute dissection or rupture) in patients with thoracic aneurysms, and it has been considered the most important independent factor in the decision to intervene surgically on a nonemergency basis.[9] The influence of size on the growth rate of aneurysms has been the subject of debate. Dapunt and coworkers[9] note that a higher

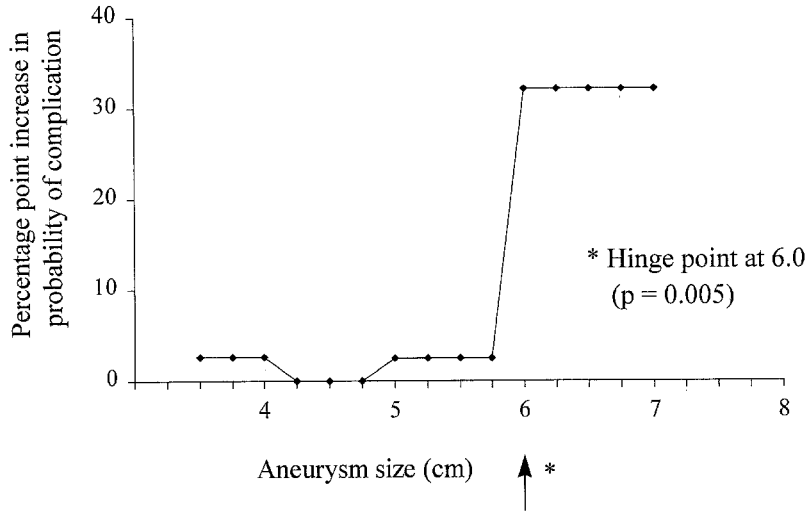


**Fig. 6.** Estimated effect of ascending aortic aneurysm size on risk of complication.

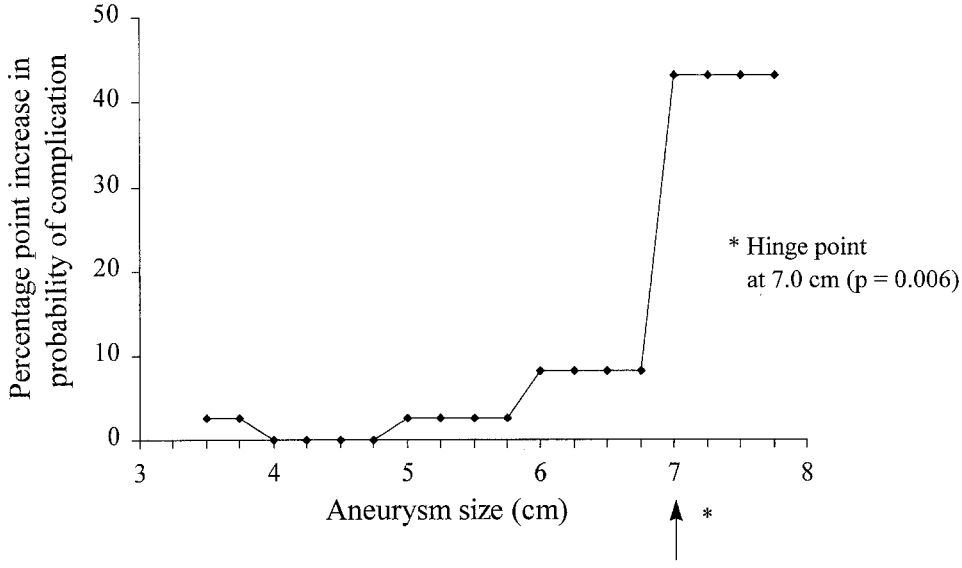


**Fig. 7.** Estimated effect of descending aortic aneurysm size on the risk of complication.

rate of expansion was found in those patients with a larger aortic diameter (>5 cm) at diagnosis. Hirose and associates,[11] on the other hand, found no significant effect of size on growth. Table I illustrates the annual growth rate in our series according to the patient's initial size, with a mean aneurysm expansion of 0.12 cm/yr. Size in our multivariable model was not shown independently to affect the overall aneurysm growth rate. The equation described in the statistical section for estimating the growth rate assumed a constant rate of change based on an exponential growth of thoracic aneurysms.

The influence of other risk factors examined for aneurysm growth is equivocal. Dapunt and associates[9] reported that a history of hypertension correlated with a greater aortic diameter at diagnosis but did not significantly affect the rate of aortic enlargement. Masuda and coworkers,[10] in contrast, reported a positive association between the diastolic blood pressure and the rate of aortic expansion. This was shown to be statistically significant in univariable but not multivariable analysis. In our multivariable analysis, the presence of chronic dissection was found to significantly increase the rate of aortic expansion.

**Table V.** *Operative mortality rates for patients with thoracic aortic aneurysms*

| *Patient category* | *Percent mortality** | *Death/cohort total* |
|---|---|---|
| All patients ($n$ = 136) | 15.4% (9.3%-21.5%) | 21/136 |
| All emergency operations ($n$ = 69) ($n$ = 69) | 21.7% (11.9%-31.5%) | 15/69 |
| All nonemergency operations ($n$ = 67) | 9.0% (3.1%-15.9%) | 6/67 |
| All ascending or arch aneurysms ($n$ = 86) | 11.6% (4.8%-18.4%) | 10/86 |
| Emergency ascending or arch ($n$ = 39) | 20.5% (7.4%-32.6%) | 8/39 |
| Nonemergency ascending or arch ($n$ = 47) | 4.3% (0.0%-10.3%) | 2/47 |
| All descending or thoracoabdominal aneurysms ($n$ = 50) | 22.0% (10.4%-33.6%) | 11/50 |
| Emergency descending or thoracoabdominal ($n$ = 29) | 24.1% (7.6%-40.6%) | 7/29 |
| Nonemergency descending or thoracoabdominal ($n$ = 21) | 19.0% (0.7%-37.3%) | 4/21 |

*95% Confidence interval for the mean are given in parentheses.

*Incidence of complications.* An important consideration in studying the natural history of patients with thoracic aneurysms is the incidence of acute dissection and rupture in this population. There is limited confirmation in the literature on aneurysm size at the time of acute dissection or rupture. McNamara and Pressler[12] reported that eight of nine ruptured descending thoracic aortic aneurysms in their series were larger than 10 cm. Subsequent studies report complications at much smaller sizes. A study by Gott and colleagues[13] on ascending aortic aneurysms in patients with Marfan's syndrome indicates a mean size of 7.8 cm at time of dissection. However, in seven of the 26 patients (26.9%), dissection occurred at aneurysm sizes measuring 6.5 cm or less. In addition, Crawford and coworkers[14] reported a median size at time of rupture of 8.0 cm among a cohort of 117 patients having descending thoracic and thoracoabdominal aneurysms. Dapunt and associates[9] related ruptures of descending thoracic aneurysms occurring at even smaller sizes, with a mean size at time of rupture of 6.1 cm.

Observational evidence from our series (Figs. 3 to 5) demonstrates a rising incidence of dissection or rupture with expanding aneurysm size. The median size at the time of rupture or dissection was 6.0 cm for ascending aneurysms and 7.2 for descending aneurysms. Multivariable regression analysis (see Table IV) to isolate risk factors for acute dissection or rupture revealed that a size greater than 6.0 cm increased the probability of these events 32.1 percentage points for ascending aneurysms ($p$ = 0.005). For descending aneurysms, this probability increased by 43.0 percentage points at a size greater than 7.0 cm ($p$ = 0.006). Figs. 6 and 7 depict these effects graphically for ascending and descending aneurysms, respectively. "Hinge points" in the risk of complication are strikingly apparent at 6 cm for the ascending aorta and at 7 cm for the descending aorta.

**Criteria for surgical intervention.** Three patterns of analysis in this series demonstrate the importance of thoracic aneurysm size on the incidence of the devastating complications of rupture and dissection. (1) Our observational data (Figs. 3 to 5) demonstrate clearly an increasing rate of complications with increasing aortic size. These observational data (Table II) show a median size at the time of rupture or dissection of 6.0 cm for ascending aneurysms and 7.2 cm for descending aneurysms. (2) The multivariable analysis for risk factors influencing acute dissection and rupture (Table III) finds size greater than 6.0 cm to be a significant risk factor ($p$ = 0.005). (3) Logistic regression analysis (Table IV; Figs. 6 and 7) indicates a 32.1 percentage point increase in likelihood of dissection or rupture for ascending aneurysms greater than 6.0 cm ($p$ = 0.005) and a 43.0 percentage point increase for descending aneurysms greater than 7.0 cm ($p$ = 0.006).

These data strongly support the application of a size criterion for preemptive surgical replacement of the aneurysmal aorta—to prevent the complications of rupture and dissection. Furthermore, these data argue strongly for application of a lower size criterion than those previously recommended in the literature.[15, 16]

If the median size at the time of complication—in our series 6.0 cm for the ascending and 7.2 cm for the descending aorta—were applied as the intervention criterion, half the patients would have had a devastating complication by the time of intervention. Accordingly, we propose intervention at a criterion somewhat below the median size at the time of complication. We propose that preemptive surgical therapy be applied at a size of 5.5 cm for ascending and 6.5 cm for descending aortic aneu-

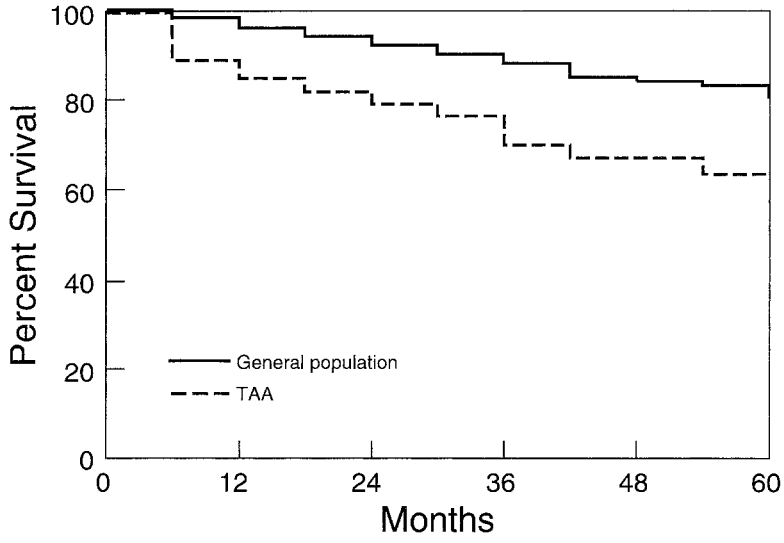


**Fig. 8.** Kaplan-Meier cumulative survival. Five-year survival estimates are illustrated for patients with thoracic aortic aneurysms *(TAA)* versus the general age- and sex-matched population.

**Table VI.** *Logistic regression analysis of factors predicting operative mortality of patients having thoracic aortic aneurysms (dependent variables)* (n = 136)*

| | *Analysis of maximum likelihood estimates* | | | |
|---|---|---|---|---|
| *Variable* | *Parameter estimate†* | *Standard error* | *p Value* | *Odds ratio†* |
| Intercept term | −2.96§ (−4.34 to −1.58) | 0.71 | 0.0001 | 0.05§ (0.01 to 0.21) |
| Emergency surgery | −0.16 (−1.39 to 1.07) | 0.63 | 0.8021 | 0.85 (0.25 to 2.93) |
| Ascending or arch | −0.94 (−2.00 to 0.11) | 0.54 | 0.0804 | 0.39 (0.14 to 1.12) |
| Acute dissection | 2.60§ (1.16 to 4.05) | 0.74 | 0.0004 | 13.52§ (3.19 to 57.29) |
| Rupture | 1.62‡ (0.0 to 3.23) | 0.82 | 0.0498 | 5.04‡ (1.00 to 25.36) |

Criteria for assessing model fit: −2 Log L: Intercept only: 117.083; intercept and covariates 92.683; $\chi^2$ for covariates: 24.355 with 4 df ($p = 0.0001$); c-statistic: 0.805.

*This variable = 1 if an operative death occurred and = 0 if the patient survived.

†95% Confidence intervals on parameter estimates are given in parentheses.

‡Statistically significant at the 5% level.

§Statistically significant at the 1% level.

rysms. These proposed criteria allow intervention before the "hinge points" of increased incidence of rupture and dissection depicted in Figs. 6 and 7.

These preemptive recommendations are further supported by the demonstration in this series (Table V) that elective surgery is much safer than emergency intervention. Especially for ascending and arch aneurysms, elective surgery was quite safe (mortality 4.3%), justifying elective preemptive intervention. These mortality results are broadly consistent with those reported by other centers.[17, 18] Although surgery on the descending aorta carried a higher risk (19.0%) in this series, the number of patients in this category is relatively small and quite subject to influence by a small number of events.

A number of developments, reflected only in the most recent portion of this series, have rendered descending aortic surgery safer. Left atrial–femoral artery bypass without heparin with the use of a

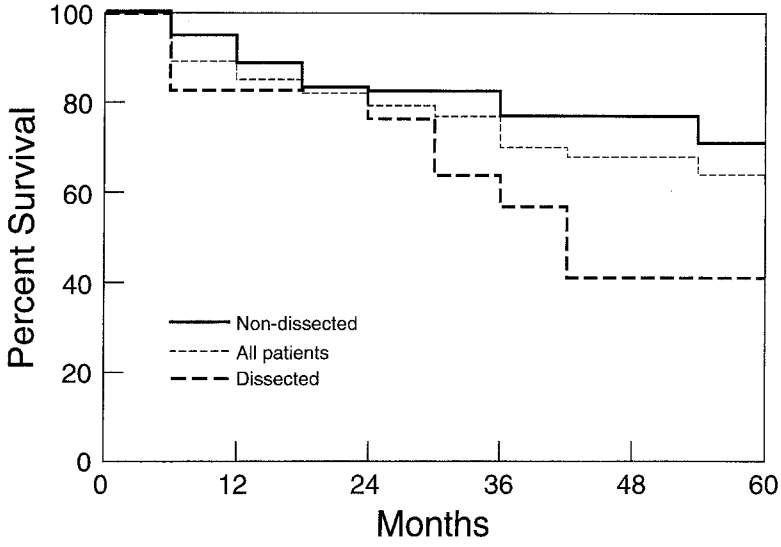


**Fig. 9.** Kaplan-Meier cumulative survival. Five-year survival estimates are illustrated for patients with dissected and nondissected thoracic aortic aneurysms compared with all patients with thoracic aortic aneurysms.

**Table VII.** *Long-term survivals for patients with thoracic aortic aneurysms**

| *Patient category* | *One year* | *Three years* | *Five years* |
|---|---|---|---|
| All ($n$ = 153) | 85% (±6.0) | 70% (±9.62) | 64% (±11.04) |
| Surgical status | | | |
| Received aortic graft | 80% (±18.28) | 66% (±28.68) | 66% (±28.68) |
| No graft | 88% (±6.42) | 72% (±10.56) | 67% (±11.70) |
| Location of aneurysm ($p < 0.4$) | | | |
| Ascending | 87% (±7.64) | 77% (±10.76) | 77% (±10.76) |
| Descending | 82% (±11.1) | 57% (±17.96) | 39% (±21.34) |
| Presence of dissection | | | |
| Yes | 83% (±12.64) | 57% (±23.4) | 46% (±27.74) |
| No | 89% (±6.90) | 77% (±10.32) | 71% (±12.38) |
| First imaged aneurysm size | | | |
| <4.0 cm | 96% (±8.50)† | 84% (±17.14)† | 84% (±17.14)† |
| 4.0-4.9 cm | 82% (±13.56) | 72% (±18.14) | 66% (±20.20) |
| 5.0-5.9 cm | 94% (±7.64)† | 72% (±11.20) | 60% (±28.02) |
| ≥6.0 cm | 83% (±13.12) | 69% (±18.26) | 59% (±24.06) |

*95% Confidence intervals are given in parentheses.

†In these cases, the upper limit confidence interval estimate exceeds 100%. The upper limit survival in these cases should be interpreted as being 100%.

centrifugal pump has been shown to be a safe and reliable method for supporting the distal circulation during aortic crossclamping, in addition to preventing ischemic complications such as renal failure and spinal cord injury.[19] Furthermore, the advent of the serine protease inhibitor, aprotinin, has led to a significant reduction in blood loss as a result of the protection of platelet adhesive receptors at the onset of bypass.[20] The recent market release of collagen-impregnated Dacron grafts (Hemashield, Meadox Medicals, Inc., Oakland, N.J.) has dramatically improved surgical hemostasis by virtually eliminating bleeding through the wall of the graft. These developments all mitigate in favor of preemptive elective intervention to avoid rupture and dissection in aneurysms that have attained criterion dimensions.

For descending aortic aneurysms, one must consider the risk of paraplegia as a significant perioperative complication. The risk of spinal cord paraplegia in the literature remains between 2% and 20%.[21] In our series, the incidence after resection of descending thoracic aneurysms was 4.0%.

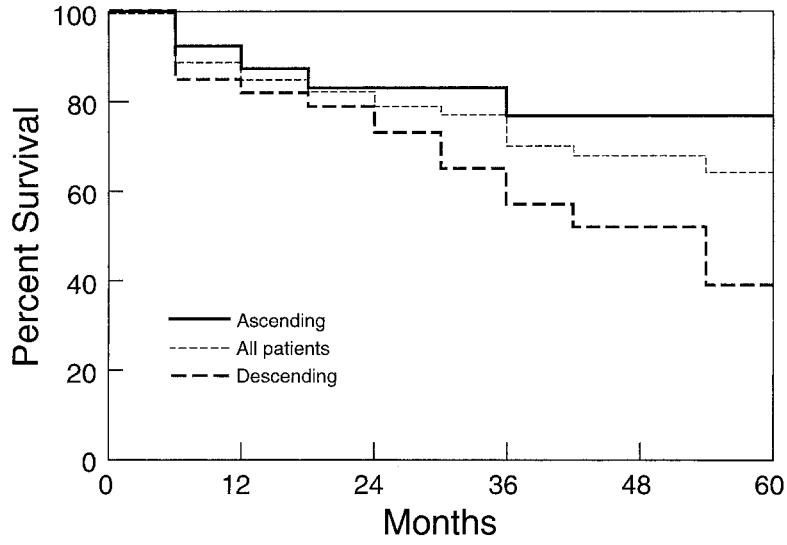


**Fig. 10.** Kaplan-Meier cumulative survival. Five-year survival estimates are illustrated for patients with ascending aneurysms and descending aneurysms compared with all patients with thoracic aortic aneurysms.

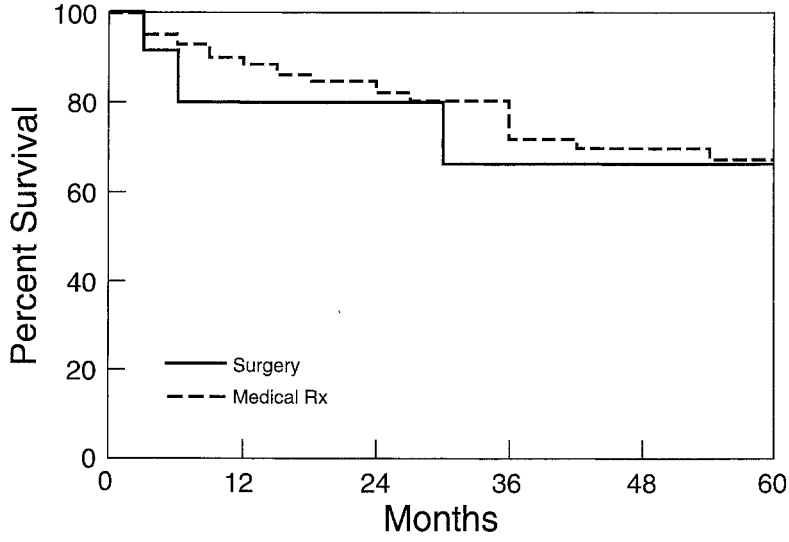


**Fig. 11.** Kaplan-Meier cumulative survival. Five-year survival estimates are illustrated for patients with thoracic aortic aneurysms managed medically and for those managed surgically.

It is self-evident that age and coexisting disease may well render aggressive surgical intervention inappropriate for some patients. Thus each patient must be evaluated independently, and anticipated risks of operation (and especially paraplegia with descending aortic aneurysms) must be weighed against the anticipated risks of rupture and dissection. Moreover, the level of experience at the treating medical center with these major surgical procedures must be taken into account. The size criteria presented herein are proposed for otherwise healthy patients cared for at experienced centers.

*Special considerations for the patient with Marfan's syndrome.* With more than 90% of the deaths from Marfan's syndrome related to complications of aneurysms of the ascending aorta, prophylactic repair is warranted.[22] Because most patients with Marfan's syndrome have some degree of aortic regurgitation by the time the aortic root is 6.0 cm,[23] and recognizing that the potential for dissection increases with

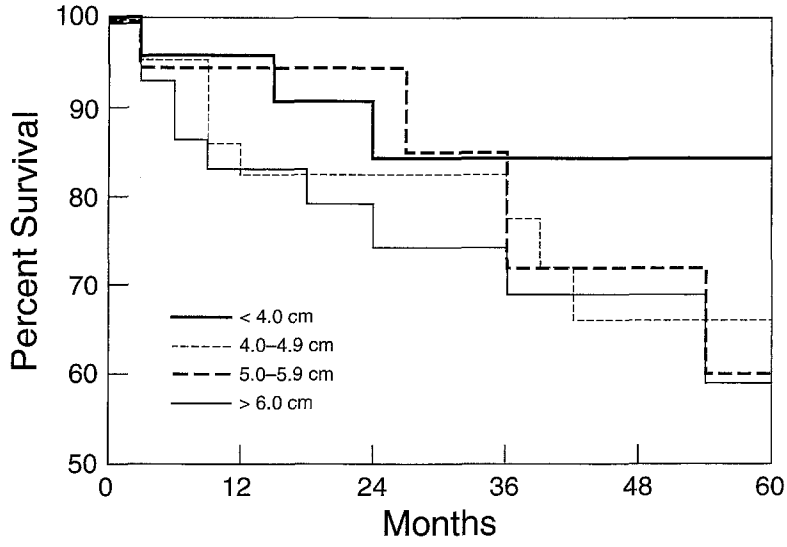


**Fig. 12.** Kaplan-Meier cumulative survival. Five-year survival estimates are illustrated for initial aneurysm sizes ranging from less than 4 cm to more than 6 cm.

**Table VIII.** *Recommended surgical intervention criteria for thoracic aortic aneurysms*

1. Rupture
2. Symptomatic states
   - A. Pain consistent with rupture and unexplained by other causes
   - B. Compression of adjacent organs, especially trachea, esophagus, and left main stem bronchus
   - C. Significant aortic insufficiency in conjunction with ascending aortic aneurysm
3. Absolute size
   - A. Ascending aorta
     5.0 cm in patients with Marfan's syndrome*
     5.5 cm in patients without Marfan's syndrome
   - B. Descending aorta
     6.0 cm in patients with Marfan's syndrome
     6.5 cm in patients without Marfan's syndrome
4. Documented enlargement
   - A. Growth ≥1 cm/yr or substantial growth, and aneurysm is rapidly approaching criteria in No. 3 above
5. Acute aortic dissection
   - A. Ascending aorta requires urgent operation
   - B. Descending aorta requires "complication-specific approach"[26]

*The Marfan intervention criteria should also apply if a family history of aortic disease other than Marfan's syndrome exists.

increasing aortic diameter, Gott,[22, 24] Lima,[23] and their associates recommend prophylactic repair when the aneurysm reaches 5.5 to 6.0 cm. We recommend an intervention criterion of 5.0 cm for individuals with Marfan's syndrome or other inherited collagen vascular disorders or familial patterns of aortic dissection. This size criterion is somewhat lower than our overall recommendations for intervention on arteriosclerotic aneurysms of the ascending aorta. It has been our experience that dissection or rupture has occurred at sizes less than 5.0 cm in several patients with Marfan's syndrome. These individuals are often young and otherwise healthy, and thus prophylactic intervention may confer substantial benefits.

In summary, the development of intervention criteria is a complex and challenging endeavor. Specific examination of this issue is crucial to the appropriate clinical care of patients. With these objectives in mind, we have drawn on our clinical experience to design, via statistical analysis, appropriate size criteria for intervention. These intervention criteria must be carefully weighed against the patient's age, overall physical condition, and anticipated life expectancy.[25] We have approached the criteria for intervention by using statistical methods from the standpoint of preventing complications (i.e., dissection and rupture). Symptomatic states, organ compression, concomitant aortic insufficiency, and acute ascending aortic dissection are widely accepted general indications for surgical intervention regardless of aortic size. Table VIII incorporates the size criteria developed in the current study as an integral component within a comprehensive strategy for treating patients with thoracic aortic aneurysms.

This study confirms that aneurysms of the thoracic aorta are potentially lethal, that attentive

follow-up is critical, and that adverse events can be anticipated on the basis of size criteria. Individualized decision-making regarding intervention in specific patients is recommended. This referral-based series includes patients whose aneurysmal disease is likely more advanced than would be found in a population-based study. Thus, although our findings may be representative of the experience at other referral centers, some caution should be exercised in extrapolating these results to the general population of patients with aneurysms.

As we continue to expand our database, we hope to refine further our statistically based recommendations for surgical intervention. Multiinstitutional enrollment with the concomitant statistical power of larger patient numbers and population-based studies would strengthen considerably the analyses applied in the current series.

We acknowledge the helpful statistical advice provided by Professor Heping Zhang of the Division of Biostatistics, Department of Epidemiology and Public Health, Yale University School of Medicine.

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## Discussion

**Dr. O. Wayne Isom** *(New York, N.Y.).* This thoughtful analysis of thoracic aneurysm size from one center significantly adds to our overall knowledge of the natural history of thoracic aneurysms, especially smaller aneurysms. The most important and compelling data are the serial imaging in 174 patients. Ideally this information will help guide us to the appropriate time of surgical intervention.

In abdominal aortic aneurysms the risk of spontaneous rupture becomes exponentially higher after a diameter of greater than 5.0 cm has been reached; therefore this figure is used as a criterion for surgical intervention. Such data

for thoracic aneurysms, however, have been lacking until recently.

Dr. Randall Griepp recently showed an exponential increase in growth rates of 0.17 cm to 0.79 cm/yr between the smallest and the largest thoracic aneurysms. Dr. Hirosi from Japan reported recently an average growth rate of 0.42 cm/yr, with a growth rate significantly higher in the aortic arch than in the ascending or descending thoracic aorta. My first question revolves around this: Your study reports a linear increase in growth rates of 0.1 to 0.19 cm/yr between the smallest and the largest thoracic aneurysms. Your growth rates seem to be much smaller than those of the previous two groups. Can you explain this discrepancy?

Your analysis demonstrated that the presence of chronic dissection increased the growth rate by four times for all sizes of thoracic aortic aneurysms, which is an absolute risk value that is reported for the first time, to my knowledge, in the literature. It is certainly consistent with the traditional surgical teaching.

You report that the growth rates of the descending and the thoracoabdominal aneurysms is about three times higher than those of aneurysms of the ascending aorta or arch. These observations are different from the previous studies. Can you explain the differential growth between the portions of the aorta?

You reported that 25 of the patients had Marfan's syndrome. What are the underlying causes of the aneurysms in the remaining patients? This certainly would play a role in the growth rates for the long-term risk of rupture or dissection. Your regression analysis nicely demonstrated that the incidence of dissection and rupture increases exponentially when the aorta is 6.0 cm in the ascending position and 7.0 cm in the descending. Your last conclusion of 5.5 cm and 6.5 cm for surgical intervention is certainly appropriate.

My final question is this: We noticed that in several of your patients with Marfan's syndrome the aneurysm ruptured or dissected at less than 5.0 cm. Do you have an absolute growth rate as an indication for surgical intervention in the smaller aneurysms?

**Dr. Randall B. Griepp** *(New York, N.Y.).* I think this is one area in which our medical colleagues have not a clue as to what proper operative indications are, and I think it is one to which we should direct our attention.

Dr. Isom asked a couple of the questions that I also had. We saw a relatively higher rate of expansion, and Dr. Elefteriades may want to comment on that. We have also seen that the growth rate was higher in a group of patients whose aneurysms ruptured than in those patients whose aneurysms did not rupture. For that reason we used the behavior of the aneurysm as an indication for operation; that is, if we observe a patient for several years and see a sudden increase in the rate of growth, we will then recommend operation to that patient. Dr. Elefteriades, did you notice any difference in the growth rate in the period immediately before the rupture in the aneurysms that ruptured?

One final point has to do with measuring sizes of aneurysms. The descending thoracic aorta frequently coils in the lower part of the chest. Using cross-sectional techniques, such as computed tomographic scanning, to look at the largest diameter will not offer a true diameter of the tube under observation. We try to avoid this distorting influence by taking the least diameter of each segment as the true diameter. Dr. Elefteriades, have you any thoughts on how we might standardize measurements of these aneurysms so that when we discuss them we are all talking about the same size?

**Dr. Francis Robicsek** *(Charlotte, N.C.).* To establish rigid criteria for indications for intervention in aneurysms is a dangerous thing; to try is certainly laudable. However, if you search for a mathematical formula, you should do it right. As you stated, an aneurysm ruptures or dissects when the stress on the aortic wall reaches a critical degree. This stress can be calculated by the Laplace equation. However, the aortic diameter is only part of the equation; the blood pressure and the wall thickness are also important components. I would suggest that if you establish a formula, those factors, which could also be readily measured, be part of the equation you derive at.

Furthermore, Marfan's disease is a different entity of atherosclerotic aneurysms because most Marfan aneurysms rupture, about 90% of them. I would suggest that you further divide your patients into these two subgroups.

Did you find any difference based on presence or absence of clots, which naturally radically changes the hemodynamics? Second, did you see any dissection in normal-sized aortas? Last, do you consider besides the measurement of absolute diameter of the radius, also the relative diameter, compared with the patient's aorta in other supposedly normal areas?

**Dr. Elefteriades.** I would like to thank all of the discussants for their kind comments. The impetus for carrying out this study was Dr. Griepp's call at the first aortic symposium 8 years ago when he pointed out the need for further fundamental information on the behavior of thoracic aortic aneurysm.

I will try to answer the questions one by one in a succinct fashion. The low overall growth rate in our review is found for one reason: very often serial measurements in a single patient show a negative growth rate. There is a variability in the aortic size that is reported, even by a good radiologist, and the size can vary in the negative direction. In the process of analysis, it is very common to truncate all of those negative values or set them at zero in the analysis; we did not do that with our method of statistical analysis. Hence the lower growth rates, which we believe are more accurately representative.

The next question concerned the differential growth between the ascending and descending portions of the aorta. I believe that finding is consistent with the fact that there are more lamellae, more layers in the ascending aorta, than there are in the descending aorta. Thus the ascending aorta might be expected to tolerate chronic blood pressure strain better. Similarly, for dissected aortas, fewer lamellae in the outer layers are consistent with a higher growth rate.

Regarding the different causes of aneurysm in our patients: Dr. Dave Tilson, who was at Yale previously, showed that many of these aneurysms, which are called "arteriosclerotic aneurysms," are really familial in incidence. We have observed a number of families in whom the pattern of disease is like Marfan's, although they don't

frankly have Marfan's disease. We have specific intervention criteria for Marfan's disease, which are lower than the general criteria, because we also have found that dissection is likely to occur in smaller aneurysms in these patients with Marfan's syndrome. We proposed a slightly lower criterion for the ascending and the descending aorta in patients with Marfan's disease because we have found as well that these aortas behave poorly. We did not have enough statistical information to analyze that issue formally.

Regarding the question from two discussants about whether we had a growth rate criterion, we tried to find such a criterion, to demonstrate that if the aorta is growing rapidly, it is more prone to complications, but we did not have the statistical power to do that analysis. I think as we recruit more patients, we will be able to do that shortly. As a matter of fact, in our overall clinical strategy we do use a criterion of rapid growth, which Dr. Griepp recommended in one of his publications.

As to how we measure size, Dr. Griepp, your points about the obliquity of the aorta giving a falsely high value on computed tomographic scan are very cogent. We try to mitigate that factor whenever possible by using magnetic resonance imaging, which is somewhat protected from those variables, as often as possible.

Dr. Robicsek, we did look at the influence of blood pressure, and we found that we could not demonstrate a correlation between the level of blood pressure and the rate of growth or the incidence of complications. We did not measure wall thickness. However, your point is very well taken. In a more complete iteration of Laplace's law,* the tension is mitigated by a thicker wall, and that factor deserves to be investigated. We did not look at the influence of clots inside the aorta. You asked if any of our patients with a normal aortic size had a dissection. The smallest aorta that dissected in our series was 3.5 cm. In terms of comparing the relative size of a patient's aorta with his body habitus, that has been done before, but we did not include that in our analysis.

*T = (P × r)/2t, where T is the wall tension, P is the distending pressure, r is the radius, and t is the wall thickness. From Schlent RC, Sunnenblick EH. Normal physiology of the cardiovascular system. In: Hurst JW, editor. The heart. New York: McGraw-Hill, 1990.

## Appendix: Estimation of aneurysm growth rates

The multivariable models for aneurysm growth rates are estimated as follows:

$$S_l = S_f \cdot e^{(\alpha \cdot \text{Time} + \beta^* \text{Dissection} \cdot \text{Time})}$$

where $S_l$ = last size measurement, $S_f$ = first size measurement, and Time = the duration between the last and first size measurement.

Taking the natural logarithm of each side of equation (1) yields:

$$\ln S_l = \ln S_f + \alpha \cdot \text{Time} + \beta \cdot \text{Dissection} \cdot \text{Time}.$$

Subtracting $\ln S_f$ from both sides of equation (2), we get:

$$\ln(S_l/S_f) = \alpha \cdot \text{Time} + \beta \cdot \text{Dissection} \cdot \text{Time}.$$

Equation (3) is the equation we estimate for the full sample of 79 patients. This equation is estimated without an intercept term because, when Time = 0, we must have $S_l = S_f$. The estimated regression was:

$$\ln(S_l/S_f) = 0.001395 \cdot \text{Time} + 0.004263 \cdot \text{Dissection} \cdot \text{Time}.$$

Separate regressions were estimated for ascending versus descending aneurysms. In these smaller regressions, the interaction between Dissection and Time was omitted because of sample size considerations. For the patients with aneurysms of the ascending aorta ($n$ = 54), the estimated equation was:

$$\ln(S_l/S_f) = 0.001571 \cdot \text{Time}.$$

For patients with aneurysms of the descending aorta ($n$ = 25), the estimated equation was:

$$\ln(S_l/S_f) = 0.004598 \cdot \text{Time}.$$

The estimated equation (2) is without an intercept term because when Time = 0, it must be true that $S_l = S_f$.