

# Natural History of Thoracic Aortic Aneurysms: Indications for Surgery, and Surgical Versus Nonsurgical Risks

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**Background.** The natural history of thoracic aortic aneurysm is incompletely understood. Over the last 10 years, at Yale University we have maintained a large computerized database of patients with thoracic aortic aneurysms and dissections. Analysis of this database has permitted insight into fundamental issues of natural behavior of the aorta and development of criteria for surgical intervention.

**Methods.** Specialized statistical methods were applied to the prospectively accumulated database of 1600 patients with thoracic aneurysm and dissection, which includes 3000 serial imaging studies and 3000 patient years of follow-up.

**Results.** Growth rate: the aneurysmal thoracic aorta grows at an average rate of 0.10 cm per year (0.07 for ascending and 0.19 for descending). Critical sizes: hinge points for natural complications of aortic aneurysm (rupture or dissection) were found at 6.0 cm for the ascending aorta and 7.0 cm for the descending. By the time a patient achieved these critical dimensions the likelihood of rupture or dissection was 31% for the ascending and 43% for the descending aorta. Yearly event rates: a patient with an aorta that has reached 6 cm maximal diameter faces the

following yearly rates of devastating adverse events: rupture (3.6%), dissection (3.7%), death (10.8%), rupture, dissection, or death (14.1%). Surgical risks: risk of death from aortic surgery for thoracic aortic aneurysm was 2.5% for the ascending and arch and 8% for the descending and thoracoabdominal aorta. Genetic analysis: family pedigrees confirm that 21% of probands with thoracic aortic aneurysm have first-order family members with arterial aneurysm.

**Conclusions.** In risk/benefit analysis the accumulated data strongly support a policy of preemptive surgical extirpation of the asymptomatic aneurysmal thoracic aorta to prevent rupture and dissection. We recommend intervention for the ascending aorta at 5.5 cm and for the descending aorta at 6.5 cm. For Marfan's disease or familial thoracic aortic aneurysm, we recommend earlier intervention at 5.0 cm for the ascending and 6.0 cm for the descending aorta. Symptomatic aneurysms must be resected regardless of size. Family members should be evaluated.

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At his first Aortic Surgery Symposium (New York, May 13-14, 1988) Dr Randall Griep emphasized the dearth of information on the natural history of thoracic aortic aneurysms. As late as 1995 our literature review disclosed more than 294 papers on how to do thoracic aortic operations but only seven papers on the natural history of aortic aneurysm or when to operate on the thoracic aorta. Our team at Yale University took up Dr Griep's challenge to define the behavior of these aneurysms. These investigations were done in conjunction with Dr John Rizzo of our School of Epidemiology and Public Health who developed specific statistical methodologies.

Our computerized database now includes more than 1,600 patients with thoracic aortic aneurysm with more than 3,000 serial imaging studies and more than 3,000 patient-years of follow-up. This database and these

methods of analysis have permitted information on the following topics and questions.

## How Fast Does the Thoracic Aorta Grow?

Calculation of growth rate of the aorta is more complicated than simply subtracting the original size of the aorta from the current size and dividing by the length of follow-up. Different modalities such as computed tomography (CT) scan, echocardiography, and magnetic resonance imaging (MRI) may give different values. There may be interobserver variability in size assessment. And most importantly some scans may show smaller size than original measurements. (This does not imply that the aorta gets smaller but rather that there is variability in size measurement especially in huge samples of data.) If these negative changes are truncated, falsely high growth rates result. By means of specifically designed statistical methods developed to account for these potential sources of error, our team has found that the aneurysmal thoracic aorta grows on average at 0.10 cm per year. The descending aorta grows faster than the ascending aorta at 0.19

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versus 0.07 cm per year. Also the larger the aorta the faster it grows.

One very important point is that in serial follow-up the current aortic scans should be compared not to the immediately prior scan but rather to the initial, original scan. Gradual growth can easily be missed when a current study is compared to a recent scan; although more work may be required, comparison to the patient's first scan may disclose significant cumulative growth.

**At What Size Does the Aorta Dissect or Rupture?**

Critical to decision-making in aortic surgery is an understanding of when complications occur in the natural history of unoperated thoracic aortic aneurysms. In the case of the thoracic aorta the two complications which are most important are rupture and dissection. To know when these complications occur would permit rational decision-making regarding elective, preemptive surgical intervention. It should be emphasized that these criteria apply to asymptomatic aneurysms.

**Symptomatic Aneurysms Should Be Resected Regardless of Size**

Our initial analysis revealed sharp "hinge points" in the aortic size at which rupture or dissection occurred. These are shown in Figure 1. For the thoracic aorta the hinge point is seen at 6.0 cm. By the time the aneurysm reaches this size 31% of patients have suffered rupture or dissection of the thoracic aorta. For the descending aorta the hinge point is located at 7.0 cm. By the time this size is reached 43% have suffered rupture or dissection (Fig 1).

It is important to emphasize that if a surgeon were to wait to intervene until the aorta achieved the median size at which complications occur it would mean rupture or dissection in half of the patients. Accordingly it is important to intervene before the median value. Our recommendations take this factor into account permitting preemptive surgical extirpation before rupture or dissection is expected in the majority of patients. Our current recommendations are indicated in Table 1.

The criteria for intervention in Marfan patients are lower than for non-Marfan patients because of the well-known propensity for patients with this disease to dissect at relatively small sizes. As we will see later we apply the lower criteria also to patients without Marfan's disease who have a positive family history for aortic disease.

**What Is the Yearly Rate of Rupture or Dissection for Thoracic Aortic Aneurysms?**

The data presented above indicate the cumulative lifetime rates of dissection or rupture by the time the aorta reaches a certain size. To determine the yearly risk of complications from the natural history of thoracic aortic aneurysm requires extremely robust data (so that enough hard end-points to permit analysis are reached within a year's time). Such data have not previously been avail-

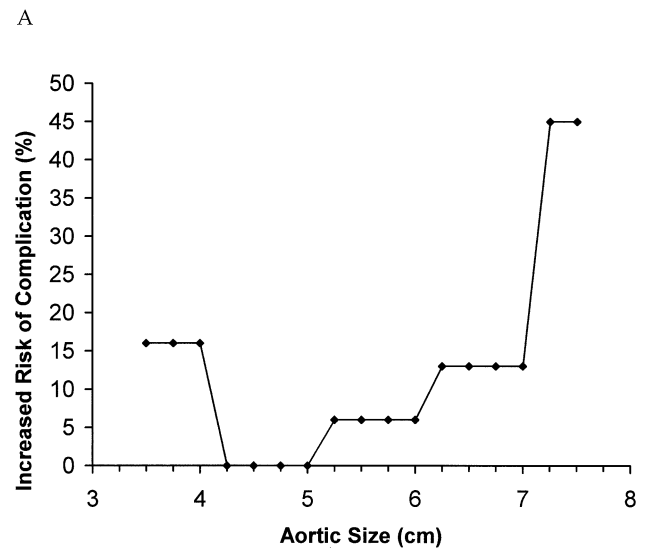
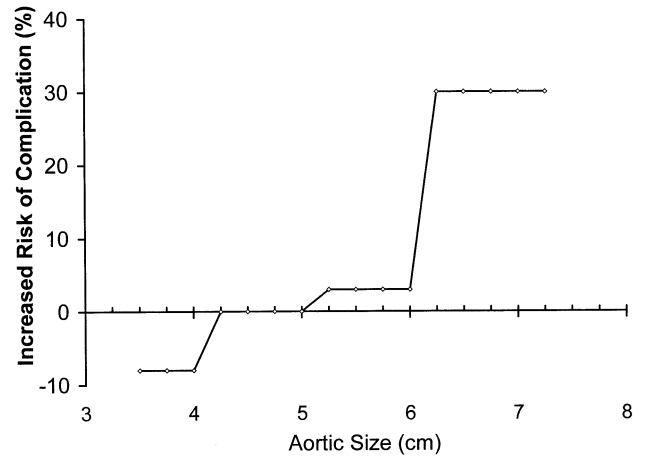


Fig 1. (A) Influence of aortic size on cumulative, lifetime incidence of natural complications of aortic aneurysm. On the y-axis is plotted the incidence of natural complications (rupture or dissection). On the x-axis is plotted the aortic size. This plot is for the ascending aorta. Note the hinge point at 6 cm. (B) The same plot, for the descending aorta. Note the hinge point at 7 cm.

able. Doctor Grieppe and his group were able to accomplish this goal producing an elegant equation which permits calculation of the yearly rate of rupture  $\lambda$ :  $\text{Ln } \lambda = -21.055 + 0.0093 (\text{age}) + 0.842 (\text{pain}) + 1.282 (\text{COPD}) + 0.643 (\text{desc dia.}) + 0.405 (\text{abd dia.})$ .

We have recently been able to produce calculations of yearly rates of rupture or other complications based

Table 1. Size Criteria for Surgical Intervention for Asymptomatic Thoracic Aortic Aneurysm

	Non-Marfan's	Marfan's (or familial)
Ascending	5.5 cm	5.0 cm
Descending	6.5 cm	6.0 cm

Table 2. Complications Based on Aortic Size

Yearly risk	Aortic Size			
	>3.5 cm	>4 cm	>5 cm	>6 cm
Rupture	0.0%	0.3%	1.7%	3.6%
Dissection	2.2%	1.5%	2.5%	3.7%
Death	5.9%	4.6%	4.8%	10.8%
Any of the above	7.2%	5.3%	6.5%	14.1%

solely upon the size of the aorta. These are presented in Table 2.

The intent of these analyses is to permit accurate decision-making for patients being seen in the office for consideration of preemptive surgical extirpation of thoracic aneurysms. These data allow the physician to form a reasonable estimate of the patient's risk of dissection, rupture, or death from his aorta for each future year of his life if the aorta is not resected. It should be noted that the risk of adverse events is extremely high—14.1%—for patients whose aneurysms have exceeded 6 cm in diameter. The risk of rupture, dissection, or death based on aortic size is presented graphically in Figure 2.

### What Causes Thoracic Aortic Aneurysm?

The genetics of Marfan's disease have been well delineated with more than 85 mutations identified at one locus on the fibrillin gene. It is being increasingly appreciated that non-Marfan's patients also manifest familial clustering of thoracic aortic aneurysms and dissections. Interviews often disclose known aneurysm in family members or suspicious sudden, unexpected cardiac-like death. In our database we have done detailed family trees on 300 of our 1,600 patients finding that 21% of our aneurysm probands have a first order relative with a known or likely aortic aneurysm. The true number is certainly much higher as these estimates are based only on family interviews and not on head-to-toe imaging of relatives. The most common pattern of inheritance appears to be autosomal dominant with incomplete penetrance.

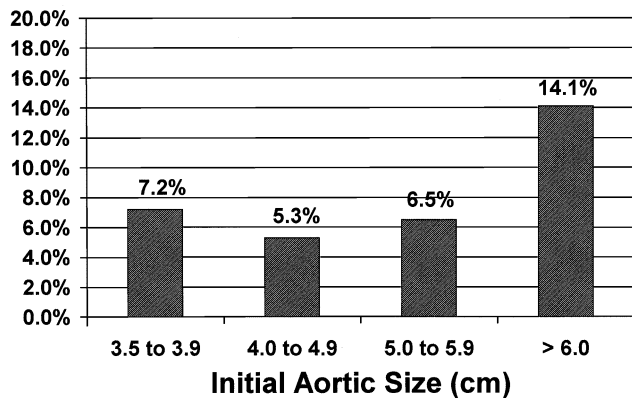


Fig 2. Graphic representation of cumulative natural risks of rupture, dissection, or death posed by aneurysms of various sizes.

### What About Aortic Ulcer and Intramural Hematoma of the Aorta?

Aortic ulcer resembles duodenal ulcer but affects the thoracic aorta with an outpouching of dye extending beyond the aortic lumen. Intramural hematoma presents as a crescentic collection of blood in the wall of the aorta. Both conditions are distinguished by their lack of a flap traversing the aortic lumen. In this respect they differ from typical dissection, which does have a flap.

As these variant pathologic conditions are largely diseases of the recent era of three-dimensional aortic imaging by CT scan, MRI, and echocardiography their behavior over time is just now being clarified. Our follow-up has recently been extended to the medium term (mean 47 months). We have noted three characteristics that render these lesions even more serious than typical dissection: (1) The rate of rupture on initial presentation is high (45%). (2) The rate of radiographic progression is high (>50%). (3) Late rupture does occur frequently and is lethal. Accordingly we are now recommending routine surgical correction for these variant lesions during the initial hospital admission providing that age, debility, or comorbidity do not render the patient an inappropriate surgical candidate. (While many centers report virulence similar to our observations some reports have found a more benign clinical course for these variant entities of ulcer and hematoma. The difference may reside in different presentations. All of our patients presented acutely with symptoms characteristic of acute aortic dissection. On occasion these abnormalities may be detected as incidental findings on aortic imaging; such lesions may have a more benign pattern of behavior.)

### What Is the Current Mortality Risk of Thoracic Aortic Surgery?

In order to decide whether to perform elective, preemptive aneurysmectomy one needs to estimate the balance of risk versus benefit from resection. The above data provide an estimate of the natural risks of unoperated thoracic aortic aneurysms. It is important to consider also the surgical risk. At our center in the hands of the most experienced operators the current risks of death for aortic surgery are 2.5% for the ascending and arch and 8% for the descending and thoracoabdominal aortas. The stroke risk is 8% for the ascending and 5% for the descending aorta. The risk of paraplegia is about 8% for descending operations only. These risks are representative of centers with a concentrated experience in aortic diseases.

### Conclusion: When to Intervene

The data presented above permit the conclusion that preemptive aortic surgery can be achieved with a mortality cost less than—or for ascending and arch, much less than—1 year's natural history of rupture, dissection, or aneurysm-related death.

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