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WHEN TO REPLACE THE ASCENDING AORTA?

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Abstract

Ascending aortic aneurysm, while usually detected incidentally, is a serious condition that requires close monitoring and timely surgical follow up. Management of patients with thoracic aortic aneurysms (TAA) is optimally performed in a multidisciplinary manner that prevents or delays the need for surgical intervention. Patients with aneurysmal degeneration should be followed in a medical aortic clinic that manages all risk factors in an effort to delay or prevent the need for replacement of the ascending aorta. Symptoms, aortic size, growth rate, and genetic/familial factors are taken into account to develop a treatment plan specific to each patient that is in line with the most recent national guidelines. This article provides an evidence-based overview and key recommendations for intervention on the ascending aorta.

Introduction

Aneurysm of the ascending aorta is a disease that is usually detected in patients between the fifth and seventh decade of life[1] and is the most common thoracic aortic pathology treated in the operating room.[2] Awareness of the clinical significance of TAA disease has increased in recent years. As diagnostic tools have improved our ability to identify aortic pathology, surgical outcomes have also improved, making intervention a life-saving option in the majority of cases. Elective surgical repair of aortic root and ascending aortic aneurysms is a relatively low-risk procedure with mortality risk less than 5% at experienced centers. Isolated ascending aortic aneurysm repair should have an even lower perioperative risk (2–3%).

The thoracic aorta is divided into four parts: the aortic root (which includes the aortic valve annulus, the aortic valve cusps, and the sinuses of Valsalva); the ascending aorta (beginning at the sinotubular junction and extending to the brachiocephalic artery origin); the aortic arch (which begins at the origin of the brachiocephalic artery and is the origin of the head and neck arteries); and the descending aorta (which begins at the isthmus between the origin of the left subclavian artery and extends through the diaphragm into the abdomen). It has been recognized that the "normal aortic diameter" is influenced by a number of factors, including patient age, sex, body size, location of aortic measurement, method of measurement and the robustness and type of imaging methods used.

Aortic aneurysm histology is characterized by medial degeneration with disruption and loss of elastic fibers. These changes differ depending on the etiology of the aneurysm and are particularly pronounced in patients with connective tissue disorders.

Figure 1. MRI of ascending aortic aneurysm.

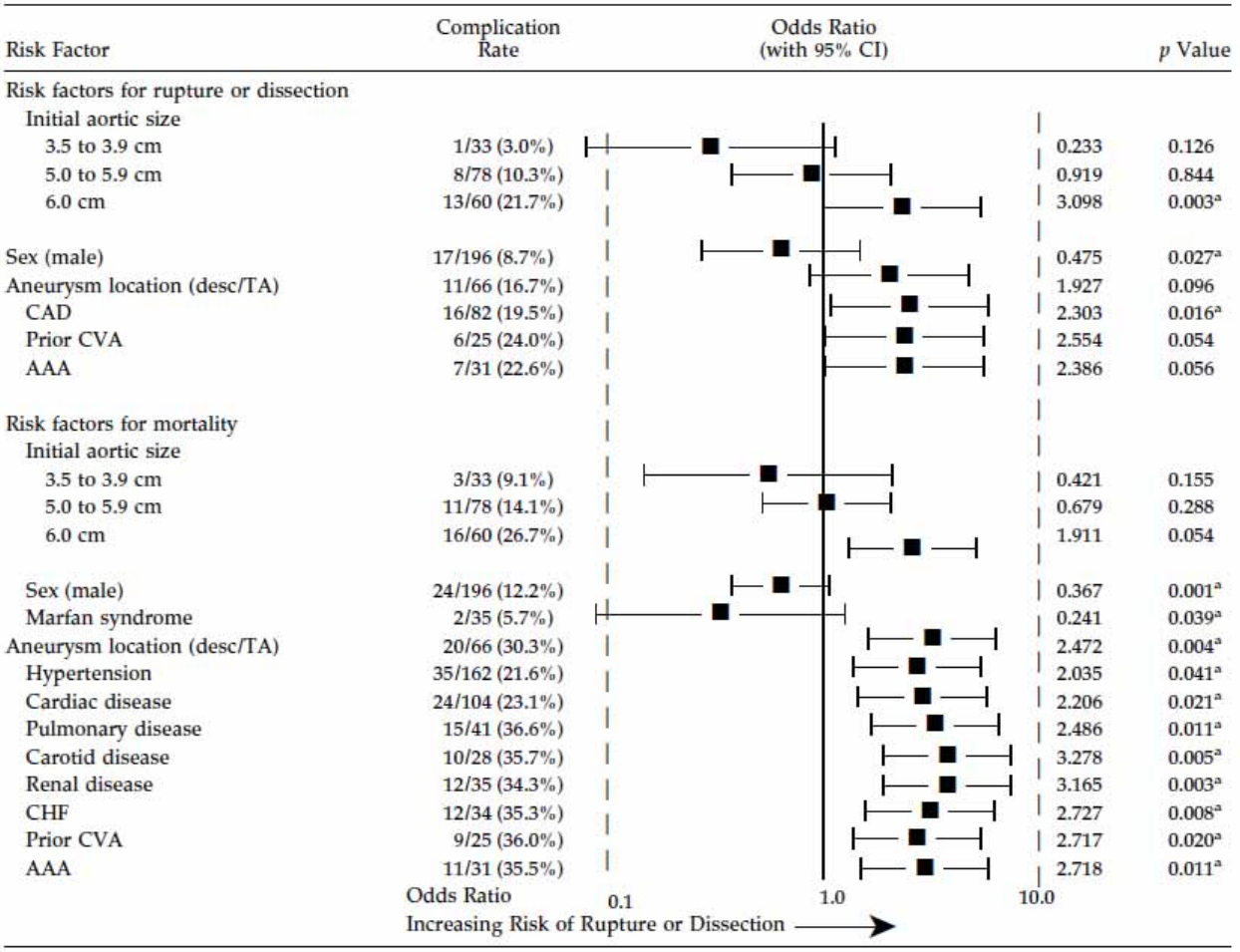
Ascending Aortic Aneurysms

Patients presenting with TAA are most commonly asymptomatic. Aneurysmal aorta is usually detected by an astute primary care physician or cardiologist during routine chest X-ray, computed tomography (CT) scan, or echocardiography (Figure 1).[3] Symptomatic patients often will complain of a sudden chest pain with no prior manifestation. In an ascending aortic aneurysm, the cusps of the aortic valve remain normal until dilatation of the sinotubular junction leads to poor coaptation of the aortic cusps, with a central jet of aortic valve insufficiency.[1]

Prophylactic intervention is the best treatment for patients with aortic aneurysms who meet guideline criteria for intervention. In an aortic emergency situation, surgery is mandatory but carries a significantly increased risk.[4] A supracoronary graft is a viable and simple option when the aneurysm is located just in the ascending aorta without involvement of the aortic root.

Thoracic Aorta	Range of Reported Mean (cm)	Reported SD (cm)	Assessment Method
Root (female)	3.50–3.72	0.38	CT
Root (male)	3.63–3.91	0.38	CT
Ascending (female, male)	2.86	NA	CXR
Mid-descending (female)	2.45–2.64	0.31	CT
Mid-descending (male)	2.39–2.98	0.31	CT
Diaphragmatic (female)	2.40–2.44	0.32	CT
Diaphragmatic (male)	2.43–2.69	0.27– 0.40	CT, arteriography

Table 1. Normal adult thoracic aortic diameters. CT: Computed Tomographic imaging; CXR: Chest X-ray; NA: Not Applicable.



[a] Statistically significant result. All of the following variables were analyzed: initial aortic size, sex, Marfan syndrome, aneurysm location, hypertension, cardiac disease, tobacco history, pulmonary disease, carotid disease, renal disease, coronary artery disease (CAD) congestive heart failure (CHE), prior cerebrovascular accident (CVA), and history of abdominal aortic aneurysm (AAA). Only results for initial aortic size and those where $p < 0.10$ are shown. Bars on graph indicate 95% confidence intervals (CI), odds ratios cannot be calculated when the incidence of disease is zero. desc/TA = descending or thoracoabdominal aorta.

Table 2. Univariate analysis of risk factor predictive of dissection rupture or of mortality. Reprinted with permission from Elsevier.[10]

Aortic Size and Growth Rate

Population studies have provided us with a reliable measure of normal adult thoracic aortic diameters (Table 1).[5] Studies of the natural history of ascending aortic aneurysms indicate that aneurysms exceeding 6 cm in maximum diameter are associated with a particularly high risk of complications. The yearly risk of rupture increased 11-fold for aneurysms 5.0–5.9 cm in diameter compared with those less than 4.0 cm in maximum size, and it increased 27-fold for those over 6.0 cm. The annual risk of the composite endpoint of dissection or death was 15.6% for aneurysms greater than 6.0 cm (Table 2). By the time a patient's ascending aortic size reaches 6 cm, that patient has incurred a cumulative 34% risk of rupture or dissection. An even stronger correlation with risk of rupture is seen when diameter is indexed to body surface area, with less than 2.75 cm/m^2 associated with low risk (4% per year), 2.75–4.25 cm/m^2 associated with intermediate risk (8% per year), and greater than 4.25 cm/m^2 associated with high risk (approximately 20% per year).[6] In a study by Clouse et al., the annual rupture risk was nil for aneurysms less than 4.0 cm in diameter, 16% for 4.0–5.9 cm, and 31% for 6.0 cm or larger.[7]

Intervention on an ascending aortic aneurysm is usually considered when the aortic diameter is ≥5.5 cm since size is the most powerful predictor of complications (Figure 2). Coady et al. suggested that the growth rate is 0.08 cm per year in a small aneurysm and 0.16 cm annually in larger aneurysms.[8] A faster growth rate was found in patients with bicuspid aortic valve (0.19 cm per year) when compared to tricuspid aortic valves (0.13 cm per year).[9]

In the interest of providing some margin of safety, most aortic surgeons would agree that intervention is indicated with an aortic diameter of 5.5 cm. However, for some patients at low surgical risk or for those with known connective tissue disorders, bicuspid aortic valve, or family history of aortic emergency, surgical intervention at an earlier stage (4.5–5.0 cm diameter) may be appropriate. These recommendations for surgical intervention were comprehensively addressed in the *2010 Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease*.[5]

Other Criteria for Intervention

Emergency and Mandatory Intervention

There are well-established situations where surgical intervention is mandatory without symptoms, increased aortic size, or any other criteria. These are urgent situations related to pathology of the ascending aorta: dissection, spontaneous rupture, intramural hematoma, and symptoms related to the aneurysm.[10] While some authors have advocated serial imaging and conservative management of intramural hematoma, these are largely considered a precursor to aortic dissection and should be treated aggressively.

Symptoms

A symptomatic TAA must be resected regardless of size. When a patient presents with symptoms related to a TAA rupture or dissection such as chest pain, the size of the aneurysm has no relevance in the decision to proceed with surgical intervention.[11] Substernal or interscapular pain may be a precursor or a sign of insidious rupture or dissection and should be taken seriously despite benign aortic imaging studies.[12] Patients can be harmed by not being offered surgery despite symptoms because aortic dimensions do not satisfy a particular size criterion. The size criteria are only for asymptomatic patients.

Genetic Factors

There is a strong link between certain genetic factors that predispose patients to aortic pathology — including aneurysmal degeneration, rupture, and/or dissection. There are several syndromic and nonsyndromic genetic conditions that are associated with the development of TAA and present with dissections at smaller diameters than usual. These conditions include Marfan syndrome, Loeys-Dietz syndrome, Turner syndrome, bicuspid aortic valve, and other genetic mutations (TGFBR1, TGFBR2, FBN1, ACTA2, COL3A1, MYH11). If such syndromes are suspected, referring the patient to a center for genetic sequencing and counseling is warranted and may influence therapy.

Some patients who do not meet the phenotypic criteria for Marfan syndrome but present with a characteristic degenerative aneurysm are termed forma frusta of Marfan syndrome. Patients with Marfan syndrome present with aneurysmal disease at an earlier age,[13] with unpredictable manifestations and a faster aneurysmal growth rate compared with the rest of the population.[10] In addition, the rate of aneurysm growth and the risk of dissection are markedly increased in this patient group,[10] as is the degree of elastin fiber disarray seen histologically. Such characteristics have required the aortic size recommendation for surgical intervention be lowered to 4.0–4.5 cm. Intervention should be lowered further to 4.0 cm when there is a rapid increase in aortic size. Similarly, when a patient with Marfan syndrome has a family history of dissection or presents with aortic regurgitation, intervention is warranted at 4.0 cm. Early referral for aortic root and ascending aortic replacement has the added potential benefit of increasing the likelihood that the aortic valve will be spared.

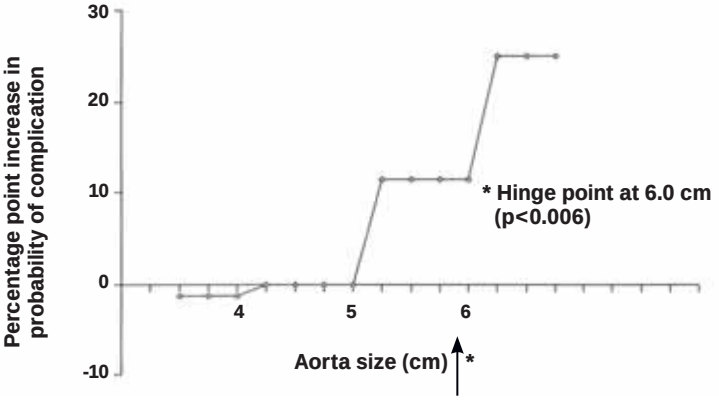


Figure 2. Regression analysis for the ascending aorta.
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Bicuspid Aortic Valve

Bicuspid aortic valve (BAV) is a relatively common heritable condition. Contrasting to Marfan syndrome where there is a genetic link, the genetics of BAV has not been clearly identified.[14] BAV is seen in 1–2% of the population[15] and is associated with aneurysmal aortic dilatation in 30–50%, even in patients with a normal functioning aortic valve.[16] BAV has been associated with genetic mutations involving NOTCH1 — a gene encoding a transmembrane signaling protein involved in the development and maintenance of the aorta. Another genetic mutation involving UFD1L has also been linked to BAV. The most common aortic aneurysm associated with BAV is located just above the sinotubular junction, ends below the innominate artery, and is often associated with aortic stenosis.

Patients with BAV are particularly susceptible to aortic dissection, and their risk of aortic emergencies is increased compared to other patients with degenerative aneurysmal disease. Similar to Marfan syndrome, BAV patients display advanced elastin fragmentation and increased matrix metalloproteinases (MMP) that may weaken the aortic wall and lead to a more unpredictable complication rate. In addition, increased rates of aortic dilatation following aortic valve replacement have been described in BAV patients compared to controls with trileaflet aortic valves.[17] For these reasons, many have advocated earlier aortic intervention for smaller-diameter aortic aneurysms (4.0–5.0 cm).[5, 9, 18]

Family History

If a patient has a family history of aortic dissections, aneurysms, or ruptures, they should be considered for surgery when the aortic size is in the range of 4.5–5.0 cm. Aortic imaging is recommended for first-degree relatives of patients with TAA and/or dissection to identify those with asymptomatic disease. If one or more first-degree relatives of a patient with known TAA and/or dissection are found to have thoracic aortic dilatation, aneurysm, or dissection, then imaging of second-degree relatives is advised.[5]

Medical Therapy for Aneurysms

While surgical resection remains the primary method for treating ascending aortic aneurysms, appropriate medical therapy has an important role in decreasing the rate of enlargement and possibly preventing emergency situations. Studies on Marfan syndrome patients proved that β-blockade will help to decrease the rate of extension.[19] Also, it has been recently shown that a fibrillin 1 (FBN1) gene mutation is associated with Marfan syndrome and leads to dysregulation of TGF-β signaling, which may explain the connective tissue abnormalities seen in these patients. These important findings have prompted investigations of the ability of Losartan, an angiotensin II receptor blocker with TGF-β antagonist properties, to reduce aortic complications in an animal model of Marfan syndrome. These studies may offer an important therapeutic option to improve the connective tissue abnormalities seen in patients.[20]

In general, a reduction in the rate of rise of left ventricular pressure (dP/dt) would reduce wall tension, degeneration, and possibly the risk of acute rupture. Aggressive blood pressure control with beta blockade and risk factor modification (smoking cessation, cholesterol lowering, etc.) are necessary treatment adjuncts to improve short- and long-term outcomes in patients with ascending aortic aneurysms. Such management protocols are optimally done in a multidisciplinary aortic clinic where aortic specialists follow patients in a regular fashion along with their primary care physician.

Summary

Optimal management of ascending aortic aneurysms is performed in an elective manner, usually in asymptomatic patients. Aggressive screening and comprehensive follow-up protocols will reduce the frequency of aortic emergency situations. The risk associated with elective open surgical repair in the current era is low (usually less than 5%), and long-term results are excellent. In summary, the following size criteria should be used for early surgical referral:

- Symptomatic TAA must be resected regardless of size. Symptoms may be due to pain, compression of adjacent organs, or significant aortic insufficiency.
- Asymptomatic patients with degenerative thoracic aneurysm, chronic aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer, mycotic aneurysm, or pseudoaneurysm who are otherwise suitable candidates and for whom the ascending aorta or aortic sinus diameter is 5.5 cm or greater should be evaluated for surgical repair.
- Patients with BAV, genetically mediated disorders, or familial history of thoracic aortic disease should undergo elective operation at smaller diameters (4.0–5.0 cm depending on the condition) to avoid acute dissection or rupture.
- Patients with an aneurysm growth rate of more than 0.5 cm/year in an aorta that is less than 5.5 cm in diameter should be considered for operation.
- Patients undergoing cardiac surgery and who have an ascending aorta or aortic root of greater than 4.5 cm should be considered for concomitant repair of the aortic root or replacement of the ascending aorta.
- Aortic imaging is recommended for first-degree relatives of patients with TAA and/or dissection. If one or more first-degree relatives of a patient with known TAA and/or dissection are found to have TAA, then imaging of second-degree relatives is advised.

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