Thoracic Aortic Aneurysms: At What Size Should We Intervene?

Key factors to consider when selecting patients for TAA repair.

BY ROBERT J. HINCHLIFFE, MD, FRCS, AND PAUL HOLLERING

Thoracic aortic aneurysm (TAA) is a potentially life-threatening disorder that without intervention carries a poor prognosis. Once diagnosed, the 3-year survival for large degenerative TAAs (> 60 mm in diameter) is approximately 20%.[1] Hospital admissions in the United Kingdom for TAAs have doubled in the last decade, and von Allmen and colleagues reported a TAA hospital admission rate of nine per 100,000 population.[2] The causes and treatment of TAAs vary depending on their location. Approximately 60% of TAAs occur in the root or ascending aorta, 10% in the arch, 40% in the descending aorta, and 10% in the thoracoabdominal aorta, with some aneurysms involving multiple aortic segments.[3]

Multiple factors, rather than a single process, are implicated in the pathogenesis of TAA. Whereas abdominal aneurysms are characterized by severe intimal atherosclerosis, chronic transmural inflammation, and destructive remodeling of the elastic media, the microscopic findings in TAAs are frequently associated with cystic medial degeneration, reflecting a noninflammatory loss of smooth muscle cells, causing degeneration of elastic fibers within the media of the aortic wall.[4] This degenerative process, which can be genetically determined, is typically seen in connective tissue diseases such as Marfan, Loeys-Dietz, and Ehlers-Danlos syndromes. However, varying degrees of degeneration can be seen in patients without these disorders, occurring as an idiopathic variant in familial syndromes or as an acquired form. Other TAAs are those that result from aortic dissection or acute aortic syndrome or are associated with anatomic variants such as an aberrant left subclavian artery (Kommerell diverticulum). False aneurysms are different but are nevertheless not an uncommon presentation of thoracic aortic disease. These include pseudoaneurysms after trauma (aortic transection) and aortic cannulation (cardiac surgery and cardiopulmonary bypass).

Open surgery for thoracic aneurysmal disease is a complex procedure with a high perioperative risk. The overall surgical mortality for an elective open TAA repair is 5% to 9%.[5,6] In the last decade, we have seen a significant decrease in open procedures for TAAs. Before 2003, fewer than 10% of all intact TAAs were repaired using thoracic endovascular aortic repair (TEVAR). After 2003, more than 10% of all intact TAAs were repaired with TEVAR, and this rate grew to 27% by 2007.[7] The first endovascular solutions for TAA repair were minor modifications of the stents used in the treatment of abdominal aortic aneurysms (AAAs).[8] Since then, existing stent grafts have undergone several modifications to meet the specific challenges for TAA repair. These include longer delivery systems and more accurate deployment systems (necessary in tortuous anatomy with very high blood flow and exceptionally large forces and motion).

TEVAR has been proven to be a relatively safe procedure with acceptable morbidity and mortality rates. There have been device-specific trials and registries that demonstrated the perioperative safety of this procedure, with 30-day mortality rates of 2.1% in the phase 2 multicenter trial of the TAG thoracic endoprosthesis (Gore & Associates) and 2% in the VALOR trial of the Talent thoracic stent graft system (Medtronic).[9,10] Despite the protection that TEVAR confers against aortic rupture, patients treated with

TEVAR appear to be at high risk of premature death from all causes (malignancy, cardiovascular, or other nonaortic-related causes) compared with age- and sex-matched populations of nonthoracic aneurysm patients.[11]

Because of the increase in hospital admissions for TAAs over the last decade,[2] the decision regarding who will benefit from surgical repair became even more important. Aortic aneurysms account for 40,000 deaths annually in the United States.[12] Maximum aortic diameter is the key parameter used to predict rupture risk and is therefore central in directing clinicians whether to offer surveillance or surgical repair.[13] However, despite the increase in patients undergoing operations, natural history data concerning the risk of aneurysm rupture and the evidence base for threshold diameters at which TAA repair becomes beneficial are limited.

ANEURYSM SIZE

Data from Yale have described the incidence of rupture and dissection as a function of initial aneurysm size and that the risks of these events increase with greater aneurysm diameter.[14] Further analyses revealed that baseline aortic diameter was the only significant risk factor for adverse aortic events, with a hinge point of aortic diameter around 60 mm, while the yearly rate of serious aortic complications increased exponentially from 10% at 6 cm to 43% at 7 cm.[14] Based on these findings, the authors suggested the threshold of 5.5 to 6 cm for prophylactic surgical aortic repair.

The 2017 European Society for Vascular and Endovascular Surgery (ESVS) guidelines on descending thoracic aortic disease suggested that endovascular repair should be considered for descending TAAs > 60 mm diameter, as this is the diameter where risk of rupture sharply escalates (classification IIa, level B evidence).[15] To evaluate the possible benefit of repair in a population with smaller aneurysms (< 55 mm), a randomized controlled trial would be necessary.

Other groups have demonstrated similar results. Perko et al[1] report a fivefold increase in cumulative hazard of rupture in aneurysms > 6 cm compared to those smaller than this threshold, as well as a 66% probability of rupture within 5 years. Elefteriades showed that patients with aneurysms > 6 cm have a 14.1% annual risk of rupture, dissection, or death, compared with 6.5% for patients with aneurysms between 5 and 6 cm.[16]

Instead of looking only at the aortic diameter, some data suggest that aortic aneurysm size relative to body surface area is more important than absolute diameter.[17] Davies and colleagues used an aortic size index (ASI) of aortic diameter (cm) divided by body surface area (m^2). Based on this, they stratified patients into three groups: those with an ASI < 2.75 cm/m^2 who were at low risk for rupture (4% per year), an ASI of 2.75 to 4.25 cm/m^2 was considered moderate risk (8% per year), and those with an ASI > 4.25 cm/m^2 were at high risk (20%–25% per year).

In regard to TAA outcomes, the growth rate of the aneurysm is a relevant parameter for risk assessment and monitoring. In a recent study, Patterson et al aimed to determine the rate of TAA expansion.[18] After analyzing CT scans from nearly 1,000 TAA patients, an aortic expansion rate of 2.76 mm per year was reported for all patients. Only 5.3% of those with a diameter of 40 to 44 mm achieved the theoretical threshold size (55 mm) within 2 years. Patients with a maximum aortic diameter of 50 to 54 mm had a 74.5% risk of expanding to > 55 mm in the subsequent 2 years. The results of this study were important in terms of the frequency of surveillance imaging, as it would appear that patients with an aortic diameter < 40 mm could safely undergo surveillance at 2-year intervals, instead of the annual follow-up required for patients with aortic diameters > 45 mm.

Because the wall stress for saccular aneurysms is believed to be greater than that for fusiform aneurysms, saccular aneurysms are considered to be at greater risk of rupture. Therefore, guidelines have suggested that repair is appropriate for saccular aneurysms > 2 cm or saccular aneurysms associated with a total aortic diameter > 5 cm.[16]

The latest ESVS guidelines suggest that based on the size differential between men and women at baseline, the threshold can be reduced to 50 to 55 mm for women. For patients with aneurysms secondary to connective tissue disorders, the recommended threshold for repair is an aneurysm diameter exceeding 50 mm. Symptomatic aneurysms and aneurysms associated with a rapid growth rate of > 1 cm per year should also be repaired because of an increased risk for rupture. Because of the unique morphology of aneurysm following coarctation repair, there is little evidence about the threshold diameter, although a small series suggests that surgery is justified, even if the size does not exceed 6 cm.[19]

NOVEL MOLECULAR IMAGING

In a recent study, Forsythe et al have examined the pathobiologic processes of AAA progression and rupture including neovascularization, necrotic inflammation, microcalcification, and proteolytic degradation of the extracellular matrix.[20] With emerging cellular and molecular imaging techniques, there remains the potential to allow improved prediction of expansion or rupture and better guide elective surgical intervention for AAAs. Nevertheless, thoracic aneurysms feature a distinct pathobiology, as they are characterized by medial necrosis and mucoid infiltration, as well as elastin degradation and vascular smooth muscle cell apoptosis. Therefore, it is still unclear if these new molecu-

lar imaging technologies can be helpful in the management of patients with TAAs.

RISKS

Open surgical repair of TAAs is associated with high mortality and morbidity rates. Thoracotomy, aortic cross-clamping, and partial cardiopulmonary bypass are associated with long operating times and major blood loss and are responsible for a considerable number of surviving patients who suffer from disabling complications such as permanent paraplegia or stroke.[21,22] There is evidence that TEVAR offers a less invasive alternative for the management of descending thoracic aortic pathologies. In the VALOR trial, the rate of serious morbidity among patients undergoing open surgical repair of the descending aorta was double that of the TEVAR patients (84% vs 41%, respectively). In the trial of the Zenith TX2 graft (Cook Medical), this rate was 44.3% versus 15.6%. Patients undergoing open repair also had a more than twofold risk of developing spinal cord ischemia across these studies. These findings were borne out in the national data sets, which concluded that TEVAR can be performed in older, sicker patients with less perioperative morbidity and shorter length of hospital stay.[23,24]

The mortality risks from TEVAR are strongly related to timing of intervention and age. In the MOTHER database of 1,010 patients undergoing TEVAR (an amalgamation of device-specific Medtronic registries, which include TEVARs performed for a range of pathologies), increasing age was an independent predictor of 30-day mortality, with an odds ratio of 1.05 per additional year of age.[25]

It would be useful to determine who is not likely to achieve an overall benefit from having their aneurysm repaired. The EVAR 2 trial compared endovascular AAA repair with no intervention in patients unsuitable for an open procedure.[26] With regard to all-cause mortality, there were no significant differences between the two groups at any time point following the repair. Bahia et al revealed that AAA patients with appropriate risk factor modification can significantly reduce their long-term mortality.[27]

Unfortunately, there are no trials that comprehensively analyze the natural history of TAA (like the EVAR 2 trial for AAA). A recent systematic review revealed that smoking, peripheral artery disease, cerebrovascular disease, male sex, renal failure, high diastolic blood pressure, and history of AAAs were reported to accelerate TAA growth rates. Likely secondary to the destructive effects of tobacco use on connective tissue, a history of smoking is also strongly associated with the development of TAAs and is a predictor for aneurysm rupture.[28]

There is little evidence that long-term statin therapy reduces TAA growth or rupture rates. They are, however, very useful in preventing cardiovascular events.[29] Angiotensin II receptor blockers are currently a major source of optimism in the treatment and prevention of TAAs in patients with Marfan syndrome. On the basis of existing evidence, angiotensin II receptor blockers may have more beneficial effects than β-blockers on the progression of aortic dilation.[30] However, large-scale controlled studies are required to confirm this beneficial effect for patients who do not have connective tissue disease–related aneurysms.

SHOULD WE CHANGE THE AORTIC SIZE THRESHOLD FOR ELECTIVE REPAIR?

Considering the available trials and registries that have demonstrated the high all-cause mortality in TAA patients, it would appear justified to increase the threshold in high-risk (complex comorbidities) patients or where the procedure is predicted to be technically difficult (ie, off label or outside the instructions for use). Dividing patients into high- or low-risk groups would be very helpful to identify who may or may not benefit from early intervention. Unfortunately, there is no consensus or evidence that one criterion or composite of features precisely define such a group or predict within what time frame after diagnosis they are most susceptible to all-cause mortality.

CONCLUSION

Current guidelines for repair suggest the threshold for prophylactic surgical aortic repair to be within the range of 5.5 to 6 cm, but the decision regarding which individual will benefit from repair remains challenging. Aside from morbidity and mortality rates, which have widely been published, few available data exist on the quality of life of patients who have undergone TAA repair. Complications in frail and elderly patients can be the reason for loss of independence, and thus, quality of life should be an important consideration, especially in patients whose aneurysms were not symptomatic before surgery.

At present, it seems that there is no "one-size-fits-all" treatment, and therefore, patient selection should be performed on an individual basis according to morphological complexities, comorbidities, and anticipated overall survival and durability of any repair. Because patients with high rates of growth and large aneurysm size are selected out for surgery, following the natural history of the disease in an unbiased manner is difficult. There are some promising developments, such as molecular imaging and new insights in medical therapy, that may also help in this process when they become available for clinical use. ■

1. Perko MJ, Norgaard M, Herzog TM, et al. Unoperated aortic aneurysm: a survey of 170 patients. Ann Thorac Surg. 1995;59:1204–1209.
2. von Allmen RS, Anjum A, Powell JT. Incidence of descending aortic pathology and evaluation of the impact of thoracic endovascular aortic repair: a population-based study in England and Wales from 1999 to 2010. Eur J Vasc Endovasc Surg. 2013;45:154–159.

3. Isselbacher EM. Thoracic and abdominal aortic aneurysms. Circulation. 2005;111:816-828.
4. Diehm N, Dick F, Schaffner T, et al. Novel insight into the pathobiology of abdominal aortic aneurysm and potential future treatment concepts. Prog Cardiovasc Dis. 2007;50:209-217.
5. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. Ann Thorac Surg. 2007;83:S862-S864; discussion S890-S892.
6. Svensson LG, Crawford ES, Hess KR, et al. Experience with 1509 patients undergoing thoracoabdominal aortic operations. J Vasc Surg. 1993;17:357-368.
7. Scali ST, Goodney PP, Walsh DB, et al. National trends and regional variation of open and endovascular repair of thoracic and thoracoabdominal aneurysms in contemporary practice. J Vasc Surg. 2011;53:1499-1505.
8. Dake MD, Miller DC, Semba CP, et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med. 1994;331:1729-1734.
9. Makaroun MS, Dillavou ED, Kee ST, et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the Gore TAG thoracic endoprosthesis. J Vasc Surg. 2005;41:1-9.
10. Fairman RM, Criado FJ, Farber M, et al. Pivotal results of the Medtronic vascular Talent thoracic stent graft system: the VALOR trial. J Vasc Surg. 2008;48:546-554.
11. Karthikesalingam A, Bahia SS, Patterson BO, et al. The shortfall in long-term survival of patients with repaired thoracic or abdominal aortic aneurysms: retrospective case-control analysis of hospital episode statistics. Eur J Vasc Endovasc Surg. 2013;46:533-541.
12. Svensson LG, Rodriguez ER. Aortic organ disease epidemic, and why do balloons pop? Circulation. 2005;112:1082-1084.
13. Conrad MF, Ergul EA, Patel VI, et al. Management of diseases of the descending thoracic aorta in the endovascular era: a Medicare population study. Ann Surg. 2010;252:603-610.
14. Davies RR, Goldstein LJ, Coady MA, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg. 2002;73:17-27.
15. Writing Committee, Riambau V, Böckler D, et al. Editor's choice--management of descending thoracic aorta diseases. Eur J Vasc Endovasc Surg. 2017;53:4-52.
16. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. Ann Thorac Surg. 2002;74:S1877-S1880.
17. Davies RR, Gallo A, Coady MA, et al. Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. Ann Thorac Surg. 2006;81:169-177.
18. Patterson BO, Sobocinski J, Karthikesalingam A, et al. Expansion rate of descending thoracic aortic aneurysms. 2016;103:1823-1827.
19. Knyshov GV, Sitar LL, Glagola MD, Atamanyuk MY. Aortic aneurysms at the site of the repair of coarctation of the aorta: a review of 48 patients. Ann Thorac Surg. 1996;61:935-939.
20. Forsythe RO, Newby DE, Robson JM. Monitoring the biological activity of abdominal aortic aneurysms beyond ultrasound. Heart. 2016;102:817-824.
21. Schermerhorn ML, Giles KA, Hamdan AD, et al. Population-based outcomes of open descending thoracic aortic aneurysm repair. J Vasc Surg. 2008;48:821-827.
22. Achneck HE, Rizzo JA, Tranquilli M, Elefteriades JA. Safety of thoracic aortic surgery in the present era. Ann Thorac Surg. 2007;84:1180-1185.
23. Gopaldas RR, Huh J, Dao TK, et al. Superior nationwide outcomes of endovascular versus open repair for isolated descending thoracic aortic aneurysm in 11,669 patients. J Thorac Cardiovasc Surg. 2010;140:1001-1010.
24. Goodney PP, Travis L, Lucas FL, et al. Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the Medicare population. Circulation. 2011;124:2661-2669.
25. Patterson B, Holt P, Nienaber C, et al. Aortic pathology determines midterm outcome after endovascular repair of the thoracic aorta: report from the Medtronic Thoracic Endovascular Registry (MOTHER) database. Circulation. 2013;127:24-32.
26. EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. Lancet. 2005;365:2187-2192.
27. Bahia SS, Vidal-Diez A, Seshasai SR, et al. Cardiovascular risk prevention and all-cause mortality in primary care patients with an abdominal aneurysm. Br J Surg. 2016;103:1626-1633.
28. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. UK small aneurysm trial participants. Ann Surg. 1999;230:289-296.
29. Jovin IS, Duggal M, Ebisu K, et al. Comparison of the effect on long-term outcomes in patients with thoracic aortic aneurysms taking versus not taking a statin drug. Am J Cardiol. 2012;109:1050-1054.
30. Thakur V, Rankin KN, Hartling L, Mackie AS. A systematic review of the pharmacological management of aortic root dilation in Marfan syndrome. Cardiol Young. 2013;23:568-581.

Robert J. Hinchliffe, MD, FRCS
Professor of Vascular Surgery
University of Bristol
Bristol, United Kingdom
robhinchliffe@gmail.com
Disclosures: None.

Paul Hollering
Vascular Surgery Fellow
Weston Vascular Network
Bristol, Bath, United Kingdom
Disclosures: None.