Is TEVAR Safe Enough?

Weighing the risk of rupture and the benefits of treating thoracic aortic aneurysms < 6 cm.

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Thoracic endovascular aortic repair (TEVAR) of aneurysms of the distal arch and descending thoracic aorta is relatively safe and has been demonstrated to be effective in preventing aortic rupture. As a result, many surgeons have adopted TEVAR as their primary method of repair, and this is reflected in the increasing number of TEVAR procedures reported in the United Kingdom and the United States in recent years.[1,2] The observed increased incidence of thoracic aortic aneurysms (TAAs) is likely related to the widespread use of cross-sectional imaging techniques to investigate unrelated conditions, resulting in incidental diagnosis. Consequently, there has been a corresponding increase in the number of hospital admissions related to thoracic aortic pathology; therefore, clinicians are increasingly required to make informed decisions regarding which patients will benefit from endovascular repair.[2,3] The decision to repair a descending TAA relies on balancing the risk of rupture with that of serious perioperative complications, which is still significant despite the proliferation of minimally invasive endovascular techniques.[4] Unfortunately, the natural history of the condition remains relatively poorly studied compared with abdominal aortic aneurysms, and the existing literature is considerably heterogeneous in terms of methodology and outcomes.

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NATURAL HISTORY OF TAAS

The seminal natural history study from Yale University noted a "hinge point" in descending thoracic aortic diameter of approximately 6.5 cm, in which the yearly rate of serious aortic complications increased exponentially from 10% at 6 cm to 43% at 7 cm.[5] The tendency toward deteriorating mechanical function and rupture at this diameter has been observed by in vivo measurements taken from the thoracic aorta intra-operatively.[6,7] Based on this evidence, the threshold for repair of the descending thoracic aorta is often considered to be 5.5 to 6 cm, and this has been reflected in the recommendations of published consensus guidelines.[8] This is broadly similar to the diameter at which abdominal aortic aneurysms are repaired, which is surprising given they are different-sized arteries in healthy patients.[3] There are several studies of the growth rates of TAAs of varying quality, which concluded that the maximum aortic diameter increases by a mean of 1.3 to 4.6 mm per year, and these rates depend on a number of other factors. The rate of growth is influenced by the presence of connective tissue disease, a bicuspid aortic valve, chronic obstructive pulmonary disease, and the current maximum diameter of the aorta (growth rate is greater in larger aneurysms). At present, there is little to no evidence that any form of medical management prevents expansion or subsequent rupture or that rupture occurs in female patients at a smaller diameter as has been suggested for infrarenal aneurysms. Due to the paucity of robust evidence to determine the risk of rupture posed by a particular aneurysm, an assessment of the risk of surgery for each patient is vital.

PERIOPERATIVE SAFETY OF TEVAR FOR TAAS

The evidence for the perioperative safety of TEVAR for descending TAAs can be best considered by examining

prospective, device-specific trials, registries, and routine hospital data.

The Gore TAG trial recruited 140 patients to undergo implantation of the Gore TAG (Gore & Associates) device to treat descending TAAs and found a 30-day mortality rate of 1.5%.[9] The VALOR trial evaluated 195 patients who underwent implantation of the Talent thoracic endograft (Medtronic Inc.). An open surgical repair (OSR) control group of 189 patients was matched retrospectively.[10] A lower 30-day mortality was noted in the TEVAR group as compared with the OSR group (2% vs 8%), and there were approximately half the number of major adverse events. The Zenith TX2 pivotal trial compared 160 patients who underwent treatment with the Zenith TX2 thoracic endograft (Cook Medical) with 70 historical open surgical controls.[6] The rate of perioperative adverse events was low in both groups, but morbidity was significantly less severe in the TEVAR group. The MOTHER registry included data from five Medtronic device–specific trials (including VALOR I) and a single institutional series. Of 670 patients who underwent TEVAR for aneurysmal disease, the mortality rate was 5%.[4]

Data from the US Nationwide Inpatient Sample showed that the mortality rate was 2.3% among those who underwent TEVAR for aneurysm.[11] Analysis of US Medicare data from 1998 to 2007 showed a 30-day survival rate of 6.1%,[11] and data from the UK Hospital Episode Statistics database showed similar early mortality rates of 6.5%.[12] The discrepancy between the nationally collected data and the trials may be explained by the fact that trial patients had to be healthy enough to have undergone open surgical repair if required, whereas administrative databases included patients undergoing TEVAR who were generally more physically frail.

The rate of serious morbidity among OSR patients in comparative studies was double that of patients who underwent TEVAR. In the VALOR trial, the rate of serious morbidity was 41% versus 84%, and was 15.6% versus 44.3% in the Zenith TX2 trial. Patients who underwent OSR also had a more than twofold risk of developing spinal cord ischemia across the three studies. These findings were borne out in the national datasets, which concluded that TEVAR can be performed in older, sicker patients with less perioperative morbidity and results in a shorter length of stay.[11,13]

DURABILITY OF TEVAR FOR TAAs

The long-term durability of TEVAR can be considered in terms of protection from aortic-related death, all-cause mortality, and freedom from aortic-related events such as reintervention. The "catch-up effect" of late aortic-related death that negated the early mortality benefits observed in the EVAR-1 randomized trial have not yet been seen in the major trials of TEVAR, although there are limited data describing follow-up beyond 5 years.[14] Freedom from aortic-related death in the pivotal trials evaluating TEVAR was 94% to 97% at 5-year follow-up, which is similar to other recent studies.

Despite the protection that TEVAR confers against aortic rupture, patients appear to be at high risk of premature death from all causes compared with age- and sex-matched populations without aneurysms.[15] The MOTHER registry reported a 5-year survival rate of 56%, with most patients (66%) dying of malignancy, cardiovascular causes, or other non–aortic-related causes when they could be established.[2,4] The UK (Hospital Episode Statistics) and US (Medicare) population–based studies showed similarly poor long-term survival rates, with many patients dying of "cardiorespiratory" causes.[4,12,13] These data underscore the importance of secondary cardiovascular risk modification with appropriate pharmacotherapy and lifestyle advice in patients with TAAs.

BALANCING THE RISK OF RUPTURE WITH THE RISK OF INTERVENTION

The key determinants that must be satisfied before proceeding with repair of a TAA include that the TAA is at significant risk of rupturing, the patient is fit enough to survive an operation, there is a reasonable life expectancy after the procedure, and, of course, that TEVAR will offer a durable repair, protecting the patient from aortic-related events and death.

Approximately 50% of patients in the endovascular arm of the VALOR trial had an aortic diameter < 6 cm, and in the Gore TAG and Zenith TX2 trials, the mean diameter was 6.4 and 6.1 cm, respectively. This could imply that the majority of patients in routine clinical practice are being treated in the range of 5.5 to 6.5 cm.

It is difficult to quantify the level of individual risk posed by a particular aneurysm, given the lack of strong natural history data. There is no equivalent small thoracic aneurysm trial for thoracic aneurysms, and it would appear that practice has been partially extrapolated from the UK Small Aneurysm Trial (using an arbitrary threshold diameter of 5.5 cm). Due to the sudden increase in complications seen as aneurysms reached 6 to 7 cm in the Yale study, a threshold of 5.5 cm for descending aortic repair has been suggested by expert consensus, with lower thresholds for patients with connective tissue disease.[5,8] There are several potential disadvantages to continuing to monitor patients with aneurysms < 6 cm as opposed to offering repair. Considering that the growth rate increases proportionately in relation to aortic diameter, aortic expansion may continue to accelerate and will reach 7 cm

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within the next few years, and in some patients, the aneurysm will have ruptured. If TEVAR is performed later, the patient will be older and unlikely to be as fit as they were previously. Furthermore, the aneurysm could have become morphologically more complex, for example, requiring debranching procedures to secure adequate landing zones.

Combined data from the Gore TAG, VALOR, and Zenith TX2 trials suggest that TEVAR for TAA has an early mortality rate of only 2%. Two large registries from the United Kingdom and United States suggest that the mortality rate is approximately 6% to 7%, which probably more accurately reflects everyday practice. It is important that institutions are aware of their own mortality rates and are able to discuss this with patients during informed consent.

Midterm survival is poor in some individuals after repair of descending TAAs, so the final consideration should be the patient's life expectancy. Efforts to stratify patients may identify those that are likely to die from unrelated causes within the next 5 years, which would be useful in determining which patients would have no overall benefit from undergoing aneurysm repair. These are probably the same individuals who will have high perioperative mortality due to the presence of significant comorbidities.

CONCLUSION

A patient at low operative risk with a descending TAA of 5.5 to 6 cm in diameter and a reasonable predicted life expectancy should probably be offered TEVAR. This threshold may be lower in the presence of high-risk features for aortic events, such as a bicuspid aortic valve or connective tissue disorder. In those with poor physiologic reserve, hostile aortic morphology, or a poor life expectancy, a judgment must be made weighing the risk that the aneurysm poses in the immediate future and whether the patient will benefit from repair. It may be appropriate to set higher thresholds for repair in these cases. Further studies of the natural history of thoracic aortic expansion would improve objective decision making. ■

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1. 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.
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. Wolak A, Gransar H, Thomson LE, et al. Aortic size assessment by noncontrast cardiac computed tomography: normal limits by age, gender, and body surface area. JACC Cardiovasc Imaging. 2008;1:200-209.
4. 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.
5. 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;73:17-28.
6. Matsumura JS, Cambria RP, Dake MD, et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg. 2008;47:247-257.
7. Koullias G, Modak R, Tranquilli M, et al. Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta. J Thorac Cardiovasc Surg. 2005;130:677-683.
8. Svensson LG, Kouchoukos NT, Miller DC, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. Ann Thorac Surg. 2008;85:S1-S41.
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 MA, et al. Pivotal results of the Medtronic Vascular Talent Thoracic Stent Graft System: the VALOR trial. J Vasc Surg. 2008;48:546-554.
11. 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.
12. von Allmen RS, Anjum A, Powell JT. Outcomes after endovascular or open repair for degenerative descending thoracic aortic aneurysm using linked hospital data. Br J Surg. 2014;101:1244-1251.
13. 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.
14. United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, et al. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med. 2010;362:1863-1871.
15. 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.