

EDUCATIONAL REVIEW ARTICLE

Thoracoabdominal Aneurysm Disease

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Introduction

Aneurysmal degeneration is the most common condition affecting the thoracic aorta which requires surgery. Throughout the ages the challenge of managing aneurysmal disease has attracted many great surgeons from the ancient Egyptians to the mediæval barber surgeon Ambrose Paré, the father of modern surgery John Hunter, famous 20th century surgeons DeBakey and Cooley and a number of contemporary surgeons. Recent advances in the understanding of the pathophysiology of aneurysm disease, imaging techniques and evolving open and endovascular surgical strategies have resulted in significant progress in the management of this condition. This article aims to review current thinking on the biology of aneurysm disease as well as highlighting the challenges it poses to the vascular surgeon in terms of evaluation of the clinical course and subsequent management options.

Epidemiology

Aortic aneurysm has a prevalence of around 5% in men over the age of 65 years, of which it is thought, around 25% will have a thoracic or suprarenal component to their aneurysm. Study of the exact prevalence of thoraco-abdominal aneurysm (TAAA) in the United Kingdom (UK) has been hampered by the low numbers of post-mortem examinations performed, and the unreliability of death certificate data. Ruptured aortic aneurysm is the thirteenth leading cause of death in the United States, and in the UK accounts for approximately 8000 deaths per year. Aneurysmal disease of the aorta demonstrates a male preponderance but this is less marked for thoraco-abdominal (1.1:1 – 2.1:1) than for infra-renal aneurysms (3:1 – 7:1).

Aetiology and Pathophysiology

Historically the most common cause of aneurysmal disease was syphilis but, since the identification of *Treponaema pallidum* and advances in its treatment, the incidence of aneurysm has declined. Today degenerative disease is the leading cause of aneurysm formation. The exact relationship between aneurysmal disease and atherosclerosis has yet to be fully elucidated. It may be that aneurysmal disease is part of the spectrum of atherosclerotic disease or that, sharing similar risk factors, they simply co-exist. Other important causes include chronic aortic dissection, connective tissue disorders (eg Marfan's syndrome), trauma, arteritis (eg Takayasu's) and bacterial infection.

It is also evident that family history is important in aneurysmal disease of the thoracoabdominal aorta. One study found that 21% of probands with a TAAA had at least one first-degree relative with an aneurysm.¹

Pathophysiology

The extracellular matrix (ECM) of a blood vessel wall is made up of elastin and collagen fibres. In health, the wall of the thoracic aorta has a high elastin content to cope with wide fluctuations in pressure during the cardiac cycle. The elastin content declines distally with collagen being more prominent in the infrarenal aorta. Neovascularisation, a ubiquitous finding in aneurysmal disease, facilitates the infiltration of inflammatory cells, particularly macrophages and B lymphocytes, into the wall of the aorta.^{2,3,4} Inflammatory cells both secrete matrix metalloproteinases (MMPs) and induce vascular smooth muscle cells to secrete further MMPs. MMPs are a family of zinc-dependent endopeptidases the principal substrates of which are elastin and collagen. Dysregulation of the ratio between MMPs and their endogenous inhibitors, the tissue inhibitors of metalloproteinases (TIMPs), is thought to be central to the pathogenesis of aneurysmal disease.^{5,6,7} ECM degradation products promote inflammatory infiltration, which in turn amplifies the proteolytic process.

In contrast to atherosclerosis, which is a disease of the tunica intima, aneurysmal disease principally affects the tunica media. The irreversible remodelling of the aortic wall that results in aneurysm formation, expansion and rupture involves an imbalance between the synthesis and breakdown of elastin and collagen, the principal proteins of the ECM. Elastolysis results in initial dilatation of the vessel, transfer of load bearing to collagen fibres and increased wall stiffness. Early on, this is accompanied by an increase in the collagen content but later in the process, localised loss of collagen fibres and impairment of tensile strength precede rupture.

There is also a great deal of interest in the complex biomechanical factors involved in aneurysmal disease. Radial forces (perpendicular to the vessel wall) exerted on the vessel wall tend to promote rupture according to the Law of Laplace (wall stress \propto radius of vessel). More interestingly, shear wall stress (parallel to vessel wall) promotes the biological processes of atherosclerosis and aneurysmal change.⁸

Natural History

There is a paucity of reliable data on the natural history of TAAA. Elefteriades¹ published a series of 1,600 patients and showed that, for a six cm aneurysm of the descending aorta, the annual risk of rupture was 3.6% and the risk of the combined endpoint rupture/dissection/death was 14.1% per year. In addition to diameter, other factors observed to increase the risk of rupture include smoking, chronic obstructive pulmonary disease (COPD), increasing age, renal failure, connective tissue disorders and dissection.⁹ These studies have helped to inform the threshold at which intervention is considered (see below).

Classification

Descending thoracic aneurysms begin just beyond the left subclavian artery and are confined to the aorta above the coeliac trunk. Thoraco-abdominal aneurysms involve both the descending thoracic and abdominal components of the aorta and may be described by the Crawford classification (see Table I) which is based on the anatomical extent of the aneurysm. This is of practical use when considering intervention, for example, in choosing the extent of the incision and planning the graft to be implanted. A laparotomy will suffice for a type IV TAAA whilst a thoraco-laparotomy is required for a type II TAAA. This classification also stratifies the risk of complications. For example there is a lower risk of neurological complications for lesions starting below T6 (types III and IV) than for repair of more extensive aneurysms (types I and II) which puts the intercostal vessels supplying the spinal cord at risk.

Table I: Crawford Classification of Thoracoabdominal Aneurysms

Type	Proximal Extent	Distal Extent
I	Left subclavian artery	Visceral aorta (usually suprarenal)
II	Left subclavian artery	Infrarenal aorta
III	Mid-thoracic aorta	Infrarenal aorta
IV	Diaphragm	Infrarenal aorta
V	Mid-thoracic aorta	Visceral aorta (usually suprarenal)

Clinical Presentation

The majority of patients are asymptomatic and the aneurysm is detected as an incidental finding on routine clinical examination or during an imaging investigation undertaken for another reason. Symptomatic patients may complain of abdominal or back pain if the aneurysm is abdominal and chest or interscapular pain if the descending aorta is affected. Blue toe syndrome in the presence of an aneurysm suggests distal embolisation of intra-luminal thrombus. An inflammatory aneurysm is a variant characterised by an inflammatory response that results in a thickened wall and may extend beyond the vascular plane into the surrounding tissues. The classic triad of symptoms (abdominal pain, obstructive uropathy and low grade fever with elevated inflammatory markers) associated with inflammatory aneurysms is only seen in around 20% of such patients. Occasionally aneurysms may result in extrinsic compression of surrounding structures. In the abdomen these include the ureters, the duodenum, the vertebral column and the major veins. In the chest a thoracic aneurysm may occasionally cause obstruction of the oesophagus, resulting in dysphagia aortica, or the left bronchus resulting in stridor. On examination, if the aneurysm has an abdominal component, an expansile mass is felt which should be differentiated from a transmitted pulsation. It is important to remember that 20% of patients with an aortic aneurysm also

have a popliteal artery aneurysm. The converse is also true and 50% of patients with a popliteal aneurysm also have an aortic aneurysm.

The most common emergency presentation of an aortic aneurysm is rupture. Anterior rupture into the peritoneal/pleural cavity results in sudden death in the majority of cases. Posterior ruptures in the retroperitoneum may be tamponaded by surrounding tissues. In these patients, severe chest/back/abdominal pain often radiates to the left iliac fossa or into the left groin/testicle. This is associated with a syncopal episode or profound cardiovascular collapse rendering the peripheries, particularly the lower limbs, cool and mottled. On examination the resulting haematoma is evident as a tender mass usually extending to the left side of the abdomen which may or may not be pulsatile. If the rupture point is in the chest the haematoma will not be evident on examination.

Imaging and Aneurysm Screening

Ultrasonographic measurement of the antero-posterior diameter of the aneurysm is the method used for detection and surveillance of asymptomatic aneurysms of the abdominal aorta. Computed tomography (CT) yields more information on the proximal/distal extent of the aneurysm. It is also useful in patients thought to require intervention and to assess the thoracic aorta which is inaccessible using an ultrasound probe.

In cardiovascularly stable patients with a symptomatic or ruptured aorta CT scanning is also indicated. Imaging should not delay intervention in those patients in whom it is possible to make the diagnosis on clinical grounds.

Following the MASS (Multi-centre Aneurysm Screening Study) trial, which showed a 53% reduction in aneurysm-related death in the screened population, the Department of Health in the United Kingdom has recommended nationwide screening for infrarenal AAA.¹⁰ This would take the form of a single ultrasound scan of the abdominal aorta in men at the age of 65 years. It is not cost-effective in any other sector of the population.

Surveillance

Patients with a small aneurysm enter a surveillance programme involving serial imaging usually at six-monthly intervals. For AAA duplex ultrasound is used and for TAAA CT scanning is undertaken. The majority of patients never require intervention and remain under surveillance. There is currently no evidence-based medical treatment for this large number of patients to slow the progression of their disease. Animal studies and observational studies have shown promising results for the use of statins and angiotensin converting enzyme inhibitors in reducing the risk of rupture.^{11,12,13}

Intervention is considered when the risk of rupture exceeds the risk of the proposed procedure and patients remain under surveillance until that time. The United Kingdom Small Aneurysm Trial (UKSAT)¹⁴ and the United States Aneurysm Detection and Management (ADAM) trial¹⁵ demonstrated that there was no survival advantage for surgical intervention over surveillance for patients with infrarenal AAA <5.5cm. No large trials have compared intervention with surveillance for aneurysms greater than 5.5cm. This is largely because of the ethical issues of patients being randomised to no treatment when there is thought to be an appreciable risk of rupture. The only data available for TAAA and for AAA >5.5cm are derived from natural history studies.¹

The consensus for infrarenal aneurysms is that elective intervention should be considered once a diameter of 5.5cm is reached. For thoracic aneurysms the evidence is less solid and practice is more variable as a result. In addition for TAAA there is more heterogeneity in the magnitude of the operation required and the risks associated with it than for infrarenal AAA for which the procedure is reasonably standardised. Most surgeons would agree that intervention should be considered if the thoracic component of the aneurysm is greater than 6.0 - 6.5cm and some would have a lower threshold if the patient has Marfan's syndrome or a familial TAAA as the risk of rupture is thought to be higher in these groups. Intervention is expedited if there is evidence of rapid growth (>1cm/yr) or if the patient develops symptoms.

Whilst diameter is the most accurate and best validated predictor of rupture that we have available at present¹⁶ further improvement on this somewhat crude method is necessary. Supporting this, it is known that diameter is not the sole determinant of the risk of rupture,¹⁷ that the tensile strength of the aneurysm sac is not directly related to the diameter and that approximately one in five ruptured infrarenal aneurysms is less than 5.5cm.^{18,19}

Management

It is clear that the outcome for elective open surgery for AAA is better for high volume surgeons (>13 cases per year),²⁰ in high volume centres (>43/yr)²¹ with dedicated vascular anaesthetists. For TAAA it is easy to see why centralisation of services is required as the caseload is relatively small, the complexity of management is great, and it has been shown that regionalisation of cases to high-volume providers results in better outcomes.²² In Scotland, the Royal Infirmary in Edinburgh provides a National Service for the assessment and management of patients with TAAA. Centralisation allows a highly specialised, experienced, multi-disciplinary team to evaluate each case and individualise treatment.

Pre-Operative Assessment

A comprehensive assessment of both the aneurysm, determining the extent of surgery, and the patient's general health is used to gauge the risk-to-benefit ratio and decide whether intervention is in the best interests of the patient. Multi-slice CT with 3D reconstruction is used to obtain detailed images of the aorta, plan the surgical approach and anticipate its challenges. Duplex ultrasound of the carotid arteries is performed when it is envisaged that the aortic arch will be clamped. Similarly the femoral vessels may be imaged in selected patients in whom the aneurysm extends distal to the aortic bifurcation.

All TAAA patients have a chest radiograph, pulmonary function tests, resting echocardiogram and routine blood tests including estimated glomerular filtration rate. A consultant cardiologist sees every patient and performs an exercise test, dobutamine stress echo and/or coronary angiography where indicated. With all this information available, the patient is assessed by a consultant vascular anaesthetist and can then be given a realistic idea of the risks involved if intervention is undertaken.

Surgery

In an open surgical procedure the affected segment of the aorta is replaced with a synthetic graft. The native aorta is not removed as this risks damaging neighbouring structures.

Instead the vessel is clamped and opened, the graft is sutured in place and the redundant sac is left in situ. The surgical approach varies depending on the extent of the aneurysm. The necessary incision is planned based on the Crawford classification (Table I). It is our practice to approach type IV aneurysms through a laparotomy incision without entering the chest. Once in the abdomen a type IV aneurysm is best accessed from the retroperitoneal space. This involves division of the peritoneum in the left paracolic gutter with further retroperitoneal dissection enabling the viscera (left kidney, spleen and colon) to be rotated medially allowing access to the aorta. Aneurysms affecting the arch or descending aorta require a thoracolaparotomy (left sixth interspace to right iliac fossa).

For extensive aneurysms care must be taken to preserve the blood supply to all major branches. During the procedure left heart bypass is employed to enable retrograde perfusion of the viscera whilst the thoracic aortic is clamped, and serial clamping allows reperfusion of the intercostals and visceral branches as the anastomoses are completed. Branches to the abdominal viscera (renal, coeliac and superior mesenteric arteries) are taken on a patch of native aorta which is sewn into the graft. Intercostal vessels are attached using a patch or a jump graft, and ensure perfusion of the spinal cord. Other branches, such as lumbar arteries and the inferior mesenteric artery, are often chronically occluded as a result of the disease process and may be sacrificed. If the aortic arch is involved pre-emptive procedures such as carotid-carotid bypass may be performed in advance.

Interventional Radiology

Endovascular repair is an established treatment option for aneurysmal disease of the aorta. Certain segments such as the descending thoracic aorta and the infrarenal aorta are particularly amenable to endovascular strategies, being relatively straight and not requiring the revascularisation of any key branches. The technology is constantly advancing however, and options such as fenestrations and branched grafts may be used to treat the aortic arch or the visceral part of the abdominal aorta. Such devices must be tailor-made for each patient and are technically challenging to deploy. Alternatively a hybrid procedure combining surgical and endovascular strategies may be used. For example the infrarenal aorta may be treated in with a straight-forward surgical procedure, whilst the less accessible thoracic/visceral aorta is treated using a stent graft. This avoids the need for a thoracolaparotomy which significantly increases the morbidity of the procedure and also avoids potentially challenging placement of a branched stent graft. Retrograde revascularisation of the visceral vessels occluded by the bottom of the endovascular thoracic stent graft is performed by taking a jump graft from the infrarenal graft to the native renal, coeliac and superior mesenteric vessels.

The choice of strategy can be made based on the anatomy of the aneurysm and the fitness of the patient. Whilst short term survival seems to be better for endovascular repair, late survival (48 months) is similar for open and endovascular repair.²³ Re-intervention rates are also higher for endovascular (up to 40%) compared to open surgery and endovascular repair is associated with specific complications including endoleaks, stent migration, stent fracture and rupture/dissection of the access vessel.²³ Endovascular stent grafts are expensive and also require long-term follow up in the form of annual CT scanning which could mean a significant cumulative radiation dose for young patients with a long life expectancy.

Complications and Peri-operative Management

Both open and endovascular repair of thoracoabdominal aneurysms are associated with a number of potentially catastrophic complications. The duration of the operation can be long, often in excess of 12 hours for open repair of type II aneurysms. The incision is extensive, a large volume of blood products is transfused and both ischaemic and ischaemia-reperfusion damage results from serial clamping of the aorta. The mortality for extensive TAAA repair was reported as being as high as 40%²⁴ but has been reduced to 3.3%²⁵ with the addition of a number of peri-operative adjuncts. Vascular patients constitute a high-risk population vulnerable to peri-operative cardiac complications, stroke, respiratory failure and renal dysfunction. In addition TAAA repair is associated with some specific risks.

Paraplegia is perhaps the most feared complication resulting from interruption of spinal cord perfusion. Factors such as previous aortic surgery and aortic dissection multiply the risk. The blood supply to the spinal cord is principally from the anterior spinal artery into which the vertebral, intercostal, lumbar and internal iliac arteries feed. The risk of paraplegia is highest in the most extensive aneurysms and it is important that two or three large intercostals vessels are anastomosed to the graft to restore perfusion. Other evidence-based measures include moderate hypothermia to reduce the metabolic demands of the cord, left heart bypass enabling retrograde perfusion and motor-evoked potentials to monitor spinal cord function intraoperatively.^{25,26,27} Despite these measures a degree of spinal cord ischaemia is inevitable. The ischaemic cord becomes oedematous and swollen, and since it is contained in a rigid bony canal, the pressure rises limiting perfusion pressure. A CSF drain is placed pre-emptively in the anaesthetic room in all patients allowing CSF pressure monitoring. The mean arterial pressure (MAP) is maintained above 80mmHg and CSF can be drained if the pressure rises to optimise the perfusion pressure to the spinal cord.

End-organ dysfunction results from clamping of the aortic segment supplying the abdominal viscera. There is a risk of patients requiring temporary or permanent renal replacement therapy, particularly in patients known to have renal dysfunction pre-operatively. The intestine, liver and spleen are also susceptible to ischaemic damage. The risk is reduced by serial clamping, mannitol infusion and left-heart bypass.

Coagulopathy and transfusion related complications may be problematic both in theatre and in the intensive care unit. Blood loss can be copious and massive transfusion is associated with a number of complications. Amongst them is coagulopathy which is exacerbated by hypothermia, heparinisation, bypass and a host of other factors. Thromboelastography offers real-time measures of coagulation in theatre and guides transfusion of coagulation products helping to minimise further blood loss.

Conclusion

Despite significant advances in the management of thoracoabdominal aneurysm disease, this complex condition still presents us with many challenges. The majority of patients remain under surveillance and never require intervention. Future attention should focus on pharmacological treatment to attenuate the progression of the disease and novel imaging strategies to predict patients requiring intervention. Evolving endovascular technology and the accumulation of evidence regarding long term outcome is likely to mean that minimally invasive procedures gradually replace open surgery.

References

1. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg* 2002; 74: S1877-80: discussion S1892-8.
2. Choke E, Thompson MM, Dawson J et al. Abdominal aortic aneurysm rupture is associated with increased medial neovascularization and overexpression of proangiogenic cytokines. *Arterioscler Thromb Vasc Biol* 2006; 26: 2077-82.
3. Choke E, Cockerill GW, Dawson J et al. Increased angiogenesis at the site of abdominal aortic aneurysm rupture. *Ann N Y Acad Sci* 2006; 1085: 315-9
4. Thompson MM, Jones L, Nasim A, et al. Angiogenesis in abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 1996; 11: 464-9.
5. Wilson WR, Anderton M, Schwalbe EC et al. Matrix metalloproteinase-8 and -9 are increased at the site of abdominal aortic aneurysm rupture. *Circulation* 2006; 113: 438-45.
6. Vine N, Powell, JT. Metalloproteinases in degenerative aortic disease. *Clin Sci (Lond)* 1991; 81: 233-9.
7. Freestone T, Turner RJ, Higman DJ et al. Inflammation and matrix metalloproteinases in the enlarging abdominal aortic aneurysm. *Arterioscler Thromb Vasc Biol* 1995; 15: 1145-51.
8. Spring S, vander Loo B, Krieger E et al. Decreased wall shear stress in the common carotid artery of patients with peripheral arterial disease or abdominal aortic aneurysm: relation to blood rheology, vascular risk factors, and intima-media thickness. *J Vasc Surg* 2006; 43: 56-63. Discussion 63.
9. Juvonen T, Ergin MA, Galla T et al. Prospective study of the natural history of thoracic aortic aneurysms. *Ann Thorac Surg* 1997; 63: 1533-45.
10. Ashton HA, Buxton MJ, Day NE et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet* 2002; 360: 1531-9.
11. Diehm N, Baumgartner I. ACE inhibitors and abdominal aortic aneurysm. *Lancet* 2006; 368: 622-3.
12. Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and aortic rupture: a population-based case-control study. *Lancet* 2006; 368: 659-65.
13. Wilson WR, Evans J, Bell PR et al. HMG-CoA reductase inhibitors (statins) decrease MMP-3 and MMP-9 concentrations in abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2005; 30: 259-62.

14. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *Lancet* 1998; 352: 1649-55.
15. Lederle FA, Wilson SE, Johnson GR et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002; 346: 1437-44.
16. Mofidi R, Goldie VJ, Kennan J et al. Influence of sex on expansion rate of abdominal aortic aneurysms. *Br J Surg* 2007; 94: 310-4.
17. Di Martino ES, Bohra A, Vande Geest JP et al. Biomechanical properties of ruptured versus electively repaired abdominal aortic aneurysm wall tissue. *J Vasc Surg* 2006; 43: 570-6. Discussion 576.
18. Darling RC, Messina CR, Brewster DC et al. Autopsy study of unoperated abdominal aortic aneurysms. The case for early resection. *Circulation* 1977; 56: 1161-4.
19. Nicholls SC, Gardner JB, Meissner MH et al. Rupture in small abdominal aortic aneurysms. *J Vasc Surg* 1998; 28: 884-8.
20. Young EL, Holt PJ, Poloniecki JD, et al. Meta-analysis and systematic review of the relationship between surgeon annual caseload and mortality for elective open abdominal aortic aneurysm repairs. *J Vasc Surg* 2007; 46: 1287-94.
21. Holt PJ, Poloniecki JD, Gerrard D, et al. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *Br J Surg* 2007; 94: 395-403.
22. Cowan JA Jr, Dimick JB, Henke PK et al. Surgical treatment of intact thoracoabdominal aortic aneurysms in the United States: hospital and surgeon volume-related outcomes. *J Vasc Surg* 2003; 37: 1169-74.
23. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005; 365: 2179-86.
24. Cunningham JN Jr. Spinal cord ischemia. Introduction. *Semin Thorac Cardiovasc Surg* 1998; 10: 3-5.
25. Safi HJ, Estrera AL, Miller CC et al. Evolution of risk for neurologic deficit after descending and thoracoabdominal aortic repair. *Ann Thorac Surg* 2005; 80: 2173-9. Discussion 2179.
26. Jacobs MJ, Mess W, Mochtar B et al. The value of motor evoked potentials in reducing paraplegia during thoracoabdominal aneurysm repair. *J Vasc Surg* 2006; 43: 239-46.
27. Svensson LG, Hess KR, Coselli JS et al. Influence of segmental arteries, extent, and atriofemoral bypass on postoperative paraplegia after thoracoabdominal aortic operations. *J Vasc Surg* 1994; 20: 255-62.