Complex aortic disease: Changes in perception, evaluation and management

Tara M. Mastracci, MD, and Roy K. Greenberg, MD, Cleveland, Ohio

Complex aortic disease continues to have a high mortality and morbidity despite advances in medical and surgical treatment. Repair of thoracoabdominal aneurysms, treatment of patients with connective tissue disorders, and the approach to dissections of the ascending and descending aorta have evolved over time; however, the results of intervention in all but highly specialized centers remain poor. As vascular surgeons, our role must extend beyond that of the pure technician; we have been vested with the life-long care of these patients and, therefore, have a responsibility to the patient in addition the scientific community and society at large to create a strategy for management that serves all three interests justly. We will outline some of the changes in the conceptual approach that we consider important to the treatment of complex aortic disease. (J Vasc Surg 2008;48:17S-23S.)

THORACOABDOMINAL ANEURYSM

Open thoracoabdominal aortic aneurysm (TAAA) repair was first reported by Etheredge in 1955.1 He described the use of a polylethylene shunt to assist with the placement of an aortic homograft, anastomosed systematically using 4-0 cardiovascular silk to the celiac and superior mesenteric arteries, as well as proximal and distal aorta, with resection of the left kidney and intervening aneurysmal aorta. DeBakey subsequently presented the first series of cases in 1956,2 where he emphasized the use of a shunt to prevent prolonged end-organ ischemia. By 1965 DeBakey’s group had amassed 42 cases and reported an operative mortality of 26%.3 Modifications on the original technique, specifically the use of a Carrell patch4 to expedite revascularization of the mesenteric vessels and minimize ischemia time, were proposed by Crawford and heralded the onset of a series of incremental improvements in the operative management of complex aortic repair.5

Now, modern series of elective TAAA repair from single-center, high-volume institutions report comparatively low mortality rates (Table).6-15 but these results are not likely to reflect the true efficacy of the operation. Aggregate data that include outcomes from institutions with lower volume or limited expertise, such as reported by Rigberg et al,16 do not reflect the same perioperative success. In the Rigberg report, the elective operative mortality was 19% at 30 days and 31% at 1 year.16

A disappointing finding was that the highest volume centers in this series performed only seven to 14 TAAA cases per year, suggesting that volume is likely associated with outcomes. Unfortunately, there are no multicenter trials or even prospective studies that have evaluated open TAAA surgery outcomes that may be used to help with the decision making regarding the risks and benefits of treatment.

Mortality alone is not a sufficient metric on which to base conclusions about TAAA repair. Serious morbidities have also been associated with the open approach, including spinal cord injury, stroke, and renal dysfunction. When combined with mortality, complications of open surgery have been frequent even in high-volume institutions. At institutions with reported perioperative mortality rates (6% to 9%), spinal cord ischemia has been reported in up to 15.5% of patients (range, 1.4%-15.5%), and renal complications occur in as many as 21% (range, 5.6-21). The reported outcomes challenge the role for open surgical treatment of extensive TAAA in institutions other than highly specialized open vascular surgery centers and call for an innovative new approach.

ACUTE AORTIC DISSECTION

Acute aortic dissection was found in 3.5 per 100,000 population (95% confidence interval [CI], 2.4-4.6) in a population-based study from Olmsted County, Minnesota.17 In that review, 85% of dissections occurred in the ascending aorta and 15% in the descending. The survival rate was dismal in the mid-20th century, with a 5-year survival of 5% between 1951 and 1980, and demonstrated a moderate improvement to 32% between 1980 and 1994 as a result of improved early diagnosis, surgical techniques, and nonoperative medical management.18

The treatment for acute dissection is tailored to the anatomic regions involved. When the ascending aorta is affected, the risk of deterioration as a result of dissection progression to involve the aortic valves, coronary vasculature, or rupture into the pericardium is significant. The treatment for this condition is ascending aortic replacement.

The Stanford experience of acute proximal dissections from 1963 to 1982 was associated with a perioperative mortality of 42% ± 10%, which dropped to 27% ± 7% between
Groups. Likewise, review of the Nationwide Inpatient Sampling perioperative mortality rates averaged 25% at 30 days for both types of mortality of 56% at 6 years. Results from a single-center study do not provide any further encouragement. The data from high-volume centers, have estimated more significant improvements in contemporary series.

Detailed study of aortic dissection has evolved an appreciation of the continuum of disease that can be found when a patient presents with what is now termed "acute aortic syndrome." The treatment for penetrating ulcer and the management of intramural hematoma has evolved during the last decade, and an understanding of the common pathologies has had an effect on management.

Several factors have been noted to drive patient management decisions. The location of the primary fenestration during the last 4 decades, from primary operative management to a nonoperative strategy involving an aggressive medical therapy in the absence of complications such as rupture or malperfusion. The reasoning for this approach relates to the dismal surgical outcomes when early operative treatment is attempted in conjunction with the reasonable results associated with pure medical management.

The Stanford group reported acute type B dissection perioperative outcomes and found that they decreased from 43% ± 13% to 20% ± 19% from the time intervals of 1963 to 1976 and 1988 to 1992, respectively. Similarly, the IRAD database reports a contemporary mortality of 31% for acute type B dissections treated surgically. It is important to take note of this history in the era of endovascular repair, where some authors advocate early intervention in type B dissection even in the absence of conventional surgical indications.

Further evidence lies in the medical arm of the single randomized trial for acute type B dissection, had notably few complications through two years of follow-up (personal communication from C. Nienaber).

### ROLE OF THE ENDOVASCULAR APPROACH

In the context of the sustained poor outcomes outside of centers of excellence reported in the literature for both TAAA and acute aortic dissection, it follows that a minimally invasive approach would be welcome and may be beneficial. However, much like the trend demonstrated above, the same may be echoed in the endovascular treatment of the above diseases: Except for a small sample of reported good outcomes from high-volume, expertise-dense centers, the outcomes for endovascular intervention of complex aortic disease have been guarded. As reporting standards become more stringent, challenges will arise in the ability to interpret the applicability of outcomes reported heterogeneous populations that may be used to imply efficacy and safety of the interventions themselves.

Few series have studied the role of endovascular repair for TAAA. Early-generation techniques such as mesenteric bypass procedures coupled with endovascular aortic relining confer high-risk solutions where the perioperative results are still associated with a mortality as high as 23% (range, 12%-23%). A few groups have reported series of branched endografts (Fig 1) in patients considered to be high operative risk, with mortality ranging from 0% to 9%. Because of the technical challenges associated with the technique, widespread utilization has not been reported, thus its adoption as a replacement for open repair remains untested.

The endovascular approach to type B dissection is the subject of much debate, with variable agreement on the timing and indications for repair and a great deal of heterogeneity in the patients included in reports of acute or chronic outcomes. Endovascular intervention for patients with acute, symptomatic, or complicated type B dissection is accepted as an option by most; however, the procedure performed varies, with some groups suggesting septal fenestration, simple branch stenting, or thoracic endografting, depending on the clinical scenario.

### Table

<table>
<thead>
<tr>
<th>Trial, year</th>
<th>No.</th>
<th>Mortality, No. (%)</th>
<th>Spinal cord injury, No.</th>
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<tr>
<td>Coselli, 6 2007</td>
<td>2286</td>
<td>150 (6.56)</td>
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<td>500</td>
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<td>455</td>
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<td>43 (9.66)</td>
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<td>4 (1.43)</td>
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<td>162 (14.65)</td>
<td>36 (3.25)</td>
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<td>Grabitz, 14 1996</td>
<td>260</td>
<td>37 (14.23)</td>
<td>6 (2.31)</td>
</tr>
<tr>
<td>Svenson, 15 1993</td>
<td>1509</td>
<td>123 (8.15)</td>
<td>234 (15.51)</td>
</tr>
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</table>

1988 and 1992. This is consistent with other publications reporting a 19.6% perioperative mortality for type A dissection and the International Registry of Acute Aortic Dissection (IRAD), which reported an in-hospital mortality of 26% for type A. A review of the national database in Taiwan (1996 to 2001) stratified outcomes for acute type A dissection by age >70 or ≤70 years. They found that contemporary perioperative mortality rates averaged 25% at 30 days for both groups. Likewise, review of the Nationwide Inpatient Sample in the United States revealed an in-hospital mortality rate of 26% for the study period of 1995 to 2003. However in keeping with the trend in TAAA, other authors, notably at high-volume centers, have estimated more significant improvements in contemporary series.
A recent review of penetrating aortic ulcer described the risk of death, endoleak, and spinal ischemia in the available published series and found that perioperative mortality ranges from 0% to 12%.47 One high-volume center that uses central aortic fenestration and renal artery stenting as a treatment for malperfusion complicating acute dissection reports a perioperative mortality of 21%.44 Other groups, reporting on their experience in both the acute and chronic thoracic aortic population, found a perioperative mortality of 5% to 16%, but these results are difficult to interpret because of the heterogeneity of the patients undergoing intervention.45,48-51

THE SURGEON’S RESPONSIBILITY

Balancing accountability to patients, the scientific community, and the society in which we live provides the parameters within which further progress in the treatment of complex aortic disease will be made.

From a patient-care perspective, finding a treatment approach that confers the maximum benefit with minimal invasiveness and expedites rapid and complete recovery is the aim. This mandates an outcomes-driven approach, where clinicians with greatest expertise are vested with the dual responsibilities of providing both excellent patient care and detailed outcome-driven training to emerging professionals. An environment that best serves the needs of clinicians dedicated to innovative and effective treatment should be developed.

Our accountability to society lies in creating an approach to complex aortic disease that emphasizes distributive justice. Our understanding of mortality can be expressed as a sum of two factors: one age-dependent and one age-independent (the Gompertz-Makeham Law).52,53 Basic improvements in health care through the early 19th century, such as effective treatments for infection and traumatic injury, have decreased the age-independent factors and contributed to the rectangularization of the survival curve.54 Pursuit of more effective treatments for conditions known to shorten survival will mean that a greater fraction of society will continue to thrive and contribute at older ages, using fewer health care resources for chronic or debilitating conditions.

Applying this theory to aortic disease requires two fundamentals: first, a treatment that eliminates the risk of aortic mortality but returns the patient back to a normal level of functioning; and second, the ability to identify, among a group of patients with multiple life-threatening comorbidities, those who are most likely to die from aortic causes. Investing in an approach that fulfills these criteria is the most just method of distributing limited health care resources.

Surgeons’ accountability to the scientific community implies that effective and innovative treatments, distributed justly, should be developed and tested using rigorous scientific methods in a timely fashion. Providing care that meets the highest standards of clinical excellence requires that the rate of investigation and testing of new treatments keeps pace with the rate of emerging technology. Thus, it follows that innovation in basic science, methodologic, and statistical techniques will have to be as rich and creative as that which is applied to aortic disease itself. Authors who question the role of evidence-based surgery and, specifically, randomized controlled trials, cite an intrinsic lack of individual equipoise, challenges with blinding or inherent bias.55 However, alternate methods have been proposed, such as expertise-based randomized controlled trials56 that address these concerns and provide a framework for the testing of new devices. The recent upsurge in the use of propensity score analysis for observational data is another example of how creative statistical innovation can increase the strength of evidence for emerging treatments.57,58

CHANGING THE APPROACH: PERCEPTION AND MANAGEMENT

Changes in the conventional approach to aortic disease are necessary because the diseases themselves have taken on a Hausdorff dimension. The new paradigm for care of the aorta involves clinicians from multiple disciplines with diverse skills sets and training programs that cross traditional boundaries. Evaluating the patient with aortic disease has, in many circumstances, evolved into a multidisciplinary pursuit. Acute aortic syndrome is one example of how improved ability to differentiate among aortic dissection, intramural hematoma, and penetrating ulcers has affected management strategies.

Another important paradigm shift has come with a deepening appreciation of the hereditary nature of many forms of aortic disease. Connective tissue disorders such as Marfan syndrome59 have been described for years, and the quest for other uncharacterized genetic links has intensi-
fied and resulted in newer recognition for familial patterns, such as Loeys-Dietz syndrome. It is estimated that 21% of non-Marfan patients presenting with aneurysm have some family member with aneurysmal disease, and TAAs have a predominant autosomal dominant mode of inheritance with variable penetrance and expressivity. Monitoring this group reveals that familial TAAs grow at a higher rate relative to aneurysms that occur sporadically and even aneurysms associated with Marfan syndrome.

Furthermore, the differentiation of ascending, descending, and abdominal aortic disease is also likely genetically linked. Pathologic comparison of specimens taken from Marfan and non-Marfan aneurysmal aortas have very similar features, with the Marfan tissue merely demonstrating a greater quantity of tissue degeneration.

Certainly, in our practice, the role of transforming growth factor \(\text{TGF-}\beta\) in the diagnosis and investigation of such disorders is becoming more important as we routinely involve the medical geneticist in the plan of care to coordinate genetic testing and provide genetic counseling to younger patients (<60 years old) presenting with aortic disease.

**CHANGING THE APPROACH: EVALUATION**

Imaging for the aorta is also rapidly evolving. The endovascular era has ushered in an expansion in the noninvasive imaging technology necessary for planning and evaluation, so that diagnostic angiography is becoming extinct. Isotropic voxel resolution from 64 slice computed tomography (CT) scans has enhanced postprocessing algorithms and enabled more accurate multiplanar reconstructions. Thus in the absence of a contraindication, CT scanning has become the standard of care for cardiovascular imaging, given that a broad range of conditions can be assessed, making it both versatile and more economically feasible. Center lumen of flow analysis is essential to the planning of the repair of most complex endovascular approached to aortic disease, such as branched and fenestrated endografts (Fig 2) and now vascular surgeons are often trained in postprocessing software and image interrogation.

**THE FUTURE: AUTOMATION, ENGINEERING AND ETIOLOGY**

The future of treatment for complex aortic disease lies in use of minimally invasive technology and growing an expertise base. The challenge will be at the convergence of innovation that simplifies and standardizes procedures with the development of training programs and implementation of techniques to maintain benchmark outcomes. The Cleveland Clinic is changing its approach to aortic disease by creating an Aortic Institute that will combine expertise in multiple disciplines to strengthen treatment options.

The current process to design and plan an endovascular TAAA repair requires knowledge of graft engineering, and the experience that has been accrued by a few individuals in the field is very difficult to replicate and limits its widespread use. However, because most errors arise during the planning stages of the procedure, creation of a semiautomated process to measure and design the grafts may expand the feasibility of the technique and decrease the time-intensive process of measurement and graft design. The goal of automation of this process is to find the balance that will increase precision of assessing the geometric relationships while allowing the physician user to determine the critical aspects of treatment that require clinical judgment.
To that end, our group has developed a patient-specific mathematic model based on Digital Imaging and Communications in Medicine (DICOM; NEMA, Rosslyn, Va) CT data to create geometric analysis of aortic dimensions in an efficient and reproducible way and has evaluated this against traditional measurement techniques (Fig 3). This work demonstrates that a mathematic algorithm can be developed to measure critical aortic dimensions of TAAA for the purpose of automated graft design with an acceptable degree of error compared with individual expert measurements, although more work needs to be done. Models that are created for planning and sizing of endografts can then be used in concert with the procedures using registration processes, allowing physicians to visualize the procedure in three, rather than two, dimensions.

Devices and delivery systems have undergone iterative improvements for conventional applications in infrarenal aneurysms and descending thoracic aneurysms. Systems have been developed and used clinically that readily navigate the entire aorta, allowing endovascular treatment of the ascending aorta. The curvature of the arch, variability of the rotational alignment of the supra-aortic trunks, and the anatomic limitations of the proximal ascending aorta have posed a hurdle for graft design at present, but the experience being gained with visceral devices will certainly inform the evolution of devices that are steerable, even within the inherent tortuosity of the aortic arch. Implants also have undergone improvements. It is unusual to find tears within the fabric of endografts, and stent fractures have become increasingly less common.

Yet late failures are reported at an alarming rate, many likely because of an under-appreciation of the extent of the aneurysmal disease, resulting in device fixation or sealing in unhealthy aorta. Although this may be due to an inability to assess the true extent of the disease, often it relates to the limits imposed by adding complexity to the repair (open or endovascular) such as the visceral or internal iliac arterial branches. Early devices capable of maintaining flow to critical aortic branches have been used clinically in thousands of patients already. New devices that require less customization have more simplified implantation paradigms and may combat some of the recognized late complications are under investigation.

The implementation of individualized methods of predicting the long-term survival of patients juxtaposed with their risk of an aortic-related death is underway. Improved methods for determining rupture risk, coupled with validated scoring systems capable of assessing perioperative and long-term risk, must be used to appropriately recommend intervention. Current treatment paradigms result in the lumping of patients into surgically fit or unfit groups, yet the means and validation of the discrimination process is subject to skepticism.

Finally, even more research and understanding will need to be gained with respect to the etiology and natural history of the diseases of the aorta. Understanding the role of intervention in complex aortic diseases, such as aortic dissection or TAAA, will only be achieved if the mechanisms of disease are understood. That knowledge will afford us the ability to determine who requires treatment, the ability to properly treat patients, provide counseling to relatives, and limit the debilitating and often fatal aspects of this complex disease.

In conclusion, the next generation of discovery in aortic disease will focus less on the characterization of new disease entities and more on the exploration of the complexities that lurk below the surface of the conditions we already know. Creating an environment to house innovation in all aspects of training, treatment, and investigation will be the challenge for the future.
REFERENCES


How can we put it in the hands of everyone to say, okay, you want a branch device, here is how you design it. This is in the form of a computer program involving mathematical modeling. This was recently published in JVS (Journal of Vascular Surgery) and by IEEE (Institute of Electrical and Electronics Engineers) and it allows the physician to determine the proximal extent of the repair and then determines the geometric configuration of the specified branches. This allows for a semi-automated design.

Critically, it is the treating physician that is still making the decisions. This is a really important thing. It allows clinicians to develop judgment based on who does well with different designs, and the amount of the aorta that can be repaired safely in a given patient and the extent of the repair. You can’t send your films off to someone else and say design me a device, without any context of anatomy? J Theor Biol 2001;213:527-45.