

» **Special Contribution** «

Evolution of Endovascular Treatment for Complex Thoracic Aortic Disease

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In a relatively short period of time, transcatheter and endovascular approaches to treat thoracic aortic and structural heart disease have exploded onto the scene. New device frontiers already being forged in the experimental stages include expanded indications and variations of fenestrated and branch stentgrafting to treat thoracoabdominal and arch disease, endovascular ascending and aortic root repair, and all of the cardiac valves. A fundamental concept to optimize durability of endovascular repair is the need for fixation and seal in healthy tissue. Before long, the entire vascular and cardiovascular system will be within the reach of endovascular interventions. Ultimately, achieving success in this endeavor will require a combination of skill sets including familiarity with high definition imaging, surgical access, and the mastery of interventional techniques, as well as the development of better anatomy-specific and disease-specific devices.

Key words: endovascular, transcatheter, thoracic aorta, thoracoabdominal, aortic valve

INTRODUCTION

The leading causes of death in the United States are heart disease, cancer and stroke and as such they have received the greatest amount of attention and research money. However, an analysis of the database from the Centers for Disease Control and ICD9 codes database show that a minimum of forty thousand people a year die from aortic disease – a number greater than the annual deaths from breast cancer, prostate cancer or motor vehicle accidents.¹⁾ Despite these alarming statistics, this disease receives relatively little attention.

Improvements in the treatment of cardiovascular disease means more people with more comorbidities are living longer. As a consequence, we are seeing more aortic aneurysms and valve disease in older and sicker patients. Nonetheless, mortality rates for great vessel and valve surgery are decreasing. Particular subsets of patients such as those with involvement of the descending and

thoracoabdominal aorta, however, continue to fair worse than those with disease involving the ascending or arch segments. This disparity in outcomes demands a change.

Minimally invasive advances were initially directed at making smaller incisions to do the same operations, and percutaneous approaches were directed solely at coronary artery disease. What we are seeing now is a huge investment from both academia and industry to shift towards more intraluminal approaches for all aspects of structural heart disease.²⁾ Such a change has occurred in the field of vascular surgery where there has been a dramatic shift towards endovascular surgery since it was first introduced for abdominal aneurysm repair in 1991. At institutions where close working relationships exist between the disciplines of cardiothoracic surgery, vascular surgery, cardiology, and interventional radiology, a new paradigm shift towards endoluminal repair of complex cardiovascular and thoracic aortic disease is occurring through the collaborative efforts to innovate.

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LESSONS LEARNED

Percutaneous procedures can still be dangerous. Short term advantages of the less invasive approach must be weighed against potential compromises in long-term du-

rability and the cumulative risk of reintervention.

Patient Selection: Comorbidities

A review of the endovascular experience to treat infrarenal aneurysms may shed light on prospective issues for transcatheter treatment of structural cardiovascular disease. A recent report of a random sample of Medicare patients from multiple centers demonstrated a mortality benefit for endovascular aneurysm repair (EVAR) for all age groups.³⁾ This univariate analysis did not take into account other confounding factors, but it does represent a real life experience which included both academic and private practices. We know from the EVAR 1 and DREAM trials, however, that in a randomized comparison of select groups of low risk patients there was only a trend towards benefit from EVAR over open surgery during the acute phase, and no significant difference in all cause mortality at later follow up.^{4,5)} A more focused look at aneurysm-related death demonstrated a slight benefit for endovascular repair.

In EVAR 2, which randomized patients who were unfit for open surgery to endovascular versus medical therapy alone, no benefit was seen.⁶⁾ Problems with this study are related to the selection criteria (“unfit for surgery”), quality of the early generation of devices used, and the small number of patients at risk during late follow up.

What we have learned from these experiences is that defining high risk patients with large aneurysms is a difficult task. In fact, defining high risk patients for most cardiac or vascular operations is an imprecise science. The answer lies in our ability to more precisely differentiate between those at high risk and those who are unfit for surgery. When we looked at our own recent experience with high risk patients at the Cleveland Clinic that were enrolled in investigational device exemption trials for the Zenith (Cook, Inc., Bloomington, Indiana, USA) infrarenal and fenestrated devices, we found a very similar profile of patients to those in EVAR 2 with regard to aneurysm size, and cardiac and pulmonary disease. Yet our one, two and three year survivals were greater than 90%, 80% and 70% respectively compared to approximately 80%, 60% and 50%, respectively for EVAR 2. Patients in our studies who were determined to be “unfit” for surgery due to comorbidities such as poorly controlled congestive heart failure, were not treated endovascularly until they were deemed fit (i.e. their heart failure was controlled) or they were not intervened upon at all.

Similarly, we can look to the pivotal experience with

the now commercially available devices used to treat descending thoracic aortic aneurysms.⁷⁾ These patients were not randomized, but enrolled at a ratio of approximately 1.5:1 for endovascular versus open repair. The differences in outcome between these two approaches manifests during the acute phase as demonstrated by an early separation in survival curves (**Fig. 1A**). The perioperative mortality rate of 12% seen for open surgery in the open control group, however, seems quite high for the patients included in this trial. Most centers with a large experience in the open therapy of descending aneurysms report an operative mortality in the single digits. Although the survival advantage is debatable, the reduction in adverse events attributable to the avoidance of a thoracotomy clearly favors the endovascular approach (**Fig. 1B**).

The downside of endovascular repair is the potential for late complications due to device durability issues and the need for late reinterventions. Data from EVAR 1 reports the rate of reintervention at 20% at four years.⁴⁾ Late complications are due to endoleaks and continued sac growth due to endotension. Continued sac growth without endoleaks (endotension) is less common with later generation devices which are less porous. Only occasionally do type II endoleaks require additional intervention. Type I and III endoleaks demand intervention, but can usually be avoided by good judgment based on pre-operative planning and sound interventional techniques. The occurrence of migration is related to both the device and the operator such that the potential for changes in morphology of the patient’s aorta must be accounted for.

Avoiding Complications: Anatomic Considerations

Important judgments relate not only to whom we should treat, based on comorbidities and aneurysm size, but on the specifics of their anatomy and the morphology of their disease. Important decisions revolve around the questions – where should we achieve fixation and sealing? And – which other factors in planning the procedure are important to optimize this fixation? What we have learned from the initial experience with infrarenal aneurysms is that a conical or irregular neck is really just a more proximal aneurysm in evolution, and therefore not a good substrate for long term durability.

JUXTARENAL ANEURYSMS

A fundamental concept to achieve durable endovascular repairs is that the sealing segment must be placed in healthy aorta. In 2000, a patient with a short necked

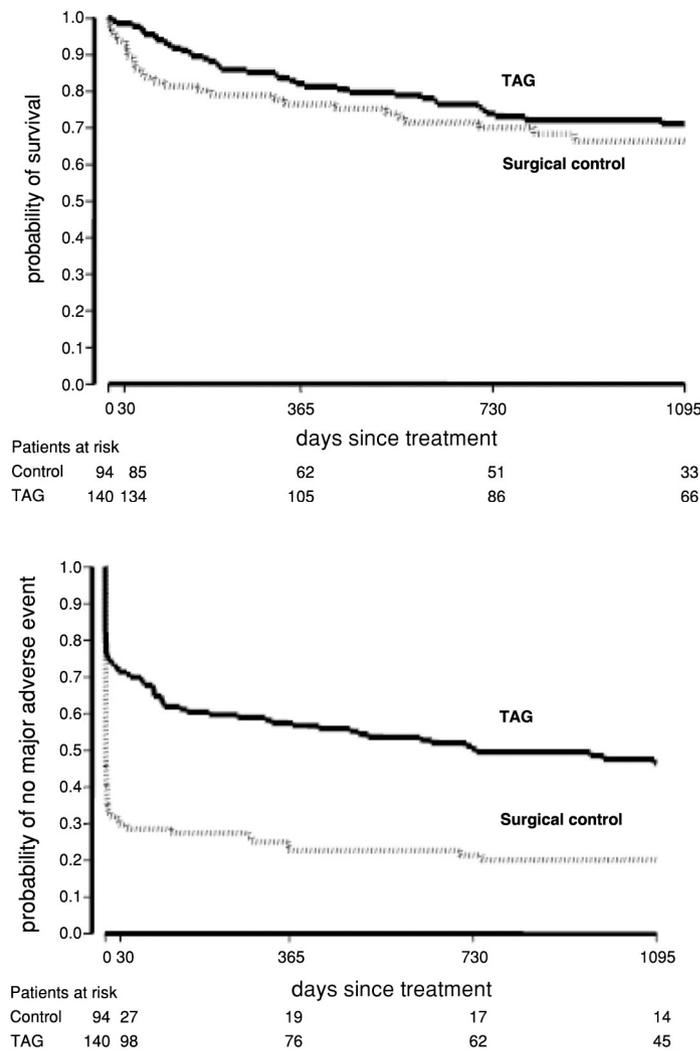


Fig. 1 Results of initial Gore TAG U.S. clinical study.
A: Probability of survival
B: Probability of no major adverse event

infrarenal aneurysm may have been treated by placing the fabric edge right up to the renal arteries then stenting them open through the uncovered suprarenal stent. The same patient would now be treated with a fenestrated device to achieve seal and fixation in the normal, visceral segment of the aorta (**Fig. 2**).

The key to success with such devices starts with detailed preoperative planning which is best performed using three dimensional imaging techniques. The planning steps include 1) determine the location of the proximal and distal sealing zones, 2) formulate the device design based on the anatomic relationships of the visceral vessels, 3) evaluate the access vessels and their ability to accommodate a large bore device, and 4) accurately size the device to maintain durability.

Precise sizing and planning the location of fenestrations requires the use of a center line of flow analysis. First a center line of flow is chosen through the aorta – then the computer generates a stretched view of the tortuous aorta allowing for precise measurements between vessels. Such an analysis is critical because the successful deployment of these custom made devices depends upon accurate placement of fenestrations and branches to accommodate the target vessels. **Fig. 3** demonstrates a stretched view of the entire aorta based on the center line of flow CPR and stretched MPR images, and the multiple measurements that are made along the aorta to allow for the precise design of a device that incorporates the visceral segment.

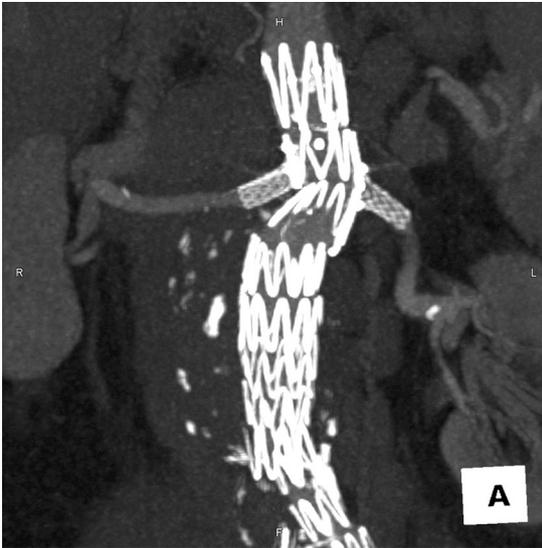


Fig. 2 MIP image of postoperative CT of juxtarenal aneurysm status post fenestrated stentgraft repair.

Device Design Considerations

Another fundamental concept when designing the device is the need to maximize overlap. The modular design of these devices allows for the beneficial conversion of migration forces into component separation forces. Devices will change their contour to lie along the anterior wall of an infrarenal aneurysm sac and the greater curve of a thoracic aneurysm. We have learned to take this factor into account at the time of preoperative planning to maximize overlap between components. Such planning allows for a “tromboning effect” to take place between modular components as they shift within the aneurysm sac and thus converts the forces of migration from the sealing zones into component separation forces felt within the overlap segment of devices.

Results of Fenestrated Stentgraft Repair of Juxtarenal Aneurysms

Survival for the first 137 patients receiving fenestrated devices to treat juxtarenal aneurysms at one, two and three years exceeds 90%, 80% and 70%, respectively. We have also been able to document a decrease in aneurysm size in most of these patients.⁸⁾

Fenestrated repair for juxtarenal aneurysms is safe and effective. Prospective long term follow up is ongoing and dissemination of the techniques to perform these procedures is yet to be proven, but currently there have been over 1000 implants worldwide by over 100 physicians.



Fig. 3 Stretched view of curved planar CT reconstruction of thoracoabdominal aorta depicting linear measurements across seal zones, graft lengths, and relationships between visceral branches. Notice the left common carotid and left subclavian arteries proximally and the celiac artery distally.

THORACOABDOMINAL ANEURYSMS

We know from the open surgical experience that as we move more proximal across the visceral segment of the aorta, the mortality increases. Even in single centers with demonstrated excellence, the mortality of thoracoabdominal aortic aneurysm repair is relatively high.^{9, 10)} A recently published population based study reported 19% perioperative mortality and only 69% survival at 12 months. This included all patients in the state of California during a one year period.¹¹⁾ And the greater the mortality, the better the potential benefit from a minimally invasive approach.

Toward Endovascular Repair of Thoracoabdominal Aneurysms

Hybrid Repairs

Initial attempts to improve outcomes in high risk patients first focused on the mesenteric “debranching” procedures where repair is staged by first performing a bypass to the visceral vessels based off of a more normal arterial inflow, commonly the iliac vessels. After performing the visceral bypass, the diseased segments

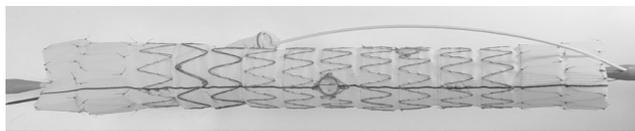


Fig. 4 Main body of loaded and deployed thoracoabdominal branched stentgraft.

Notice the combination of both a direction limb (for the celiac) and the two visible fenestrations (for the superior mesenteric and left renal arteries).

of aorta are lined with tubular stentgrafts. We reported our results in the first 13 of these patients – all of whom were too high risk for conventional thoracoabdominal aortic repair.¹²⁾ The results were not promising for this procedure with mortality over 20%, survival of only 62% at two years and several patients requiring additional aortic surgery. Ironically, others have also reported mortality rates of ~20% but concluded that this is a feasible approach. Mortality of 23% and paraplegia rate of 15% is too high for even high risk patients.

Branched Stentgrafts

The results with fenestrated devices, as described earlier, were so promising that this technology has evolved into branched devices for the treatment of aneurysms that involve the visceral segment. The fenestrations for these devices are modified by the addition of a nitinol ring for support. Directional branches have also been developed and first used to treat patients with iliac aneurysms to maintain patency in the hypogastric arteries. These hypogastric branch devices are a modified limb extension of the Zenith system and are quite easily and readily deployed.¹³⁾

Patients with thoracoabdominal aneurysms are often older and commonly have comorbid conditions like COPD, left ventricular dysfunction, and renal dysfunction. Comorbidities limit the number of patients eligible for safe surgical repair and encouraged the development of totally endovascular thoracoabdominal aortic aneurysm repair techniques. Data for the first seventy-three patients have been prospectively collected and were presented in Philadelphia at the American Association for Thoracic Surgery meeting in the spring of 2006. The manuscript will be published soon. These were all high-risk patients and excellent outcomes were reported.¹⁴⁾

The devices are modular and the main body portion is custom designed to the visceral segment for each patient. A representative device is shown in **Fig. 4**. These can feature fenestrations, directional branches or a combination of both.

Deployment

Once the main body device is aligned within the visceral segment, it is partially deployed and access is gained into each of the branch vessels via the fenestrations or branches. Once this is accomplished the main body is completely deployed by releasing the constraining sutures and allowing for full expansion of the device. Each individual target branch vessel is then grafted with smaller covered stents deployed across the aneurysm from the main body to the target vessel. The proximal end of the branch graft components is flaired with a larger balloon to create a rivet effect between devices (**Fig. 5**). For directional branches, self expanding stentgrafts are used to complete the repair.

These are complex procedures which require lengthy fluoroscopy times and significant contrast doses. Furthermore, many patients required the placement of an iliac conduit to allow for large bore access. Nonetheless, more than half of the patients had the procedure performed under regional anesthesia due to severe lung disease. In patients without complications, intensive care and hospital stays were short. All patients are regularly imaged in follow-up and these results have also been promising (**Fig. 6**). Since the initial report of those 73 patients, over seventy-five more patients have been treated successfully with these devices. Usual complications of thoracoabdominal repair are not eliminated but the early outcomes are excellent. Once the device design and delivery techniques become stable, we may look to evaluate this approach in healthier patients with thoracoabdominal aneurysms.

ADDITIONAL ADVANCES

Fenestrated Arch and Descending Thoracic Stentgrafts

In addition to the thoracoabdominal patients described, we have begun using modified branch devices to treat patients with distal arch and descending aneurysms including patients with post coarctation repair aneurysms (**Fig. 7**).

Extensive Thoracic Aneurysmal Disease

Hybrid Approaches

Several high-risk patients with more extensive aneurysmal disease have been treated using hybrid procedures – either open total arch elephant trunk with endovascular completion, or the so-called arch transposition procedures.

First stage total arch and elephant trunk repair has

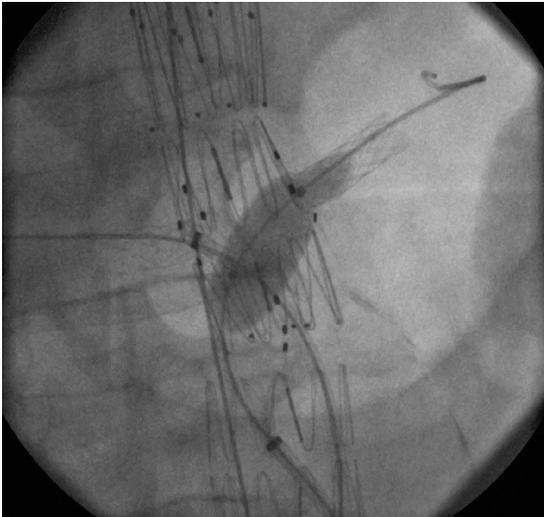


Fig. 5 Fluoroscopic image depicting proximal flairing of the left renal branch graft.

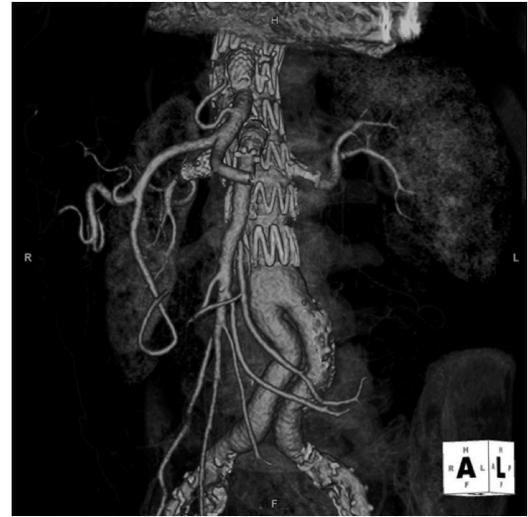


Fig. 6 Volume rendered CT reconstruction of completed endovascular thoracoabdominal repair with a 4-vessel branched device.

been slightly modified by the inclusion of two clips and a pacing wire loop at the end of the graft which serve as both radiographic markers and a point of fixation should the need arise to snare the edge of the elephant trunk at the time of endovascular completion.¹⁵⁾

Another option for patients with total arch or arch and descending disease is off pump brachiocephalic transposition followed by endovascular exclusion (**Fig. 8**).¹⁶⁾ So far we have reserved this approach for very high risk patients who we believe cannot tolerate deep hypothermic circulatory arrest, but further clarification of the indications, safety, and efficacy of this approach is needed.

Ascending Aortic Disease

As we have continued to move proximally, we have also treated several high risk patients with ascending aortic aneurysms or pseudoaneurysms with custom-designed short stentgrafts which seal between the sinotubular junction and the innominate artery.

Challenges presented by endovascular interventions in the ascending aorta include navigating the various areas of tortuosity encountered between the femoral and more proximal aorta; the proximity of the aortic valve and the risk associated with instrumenting the left ventricle; accurate deployment within the harsh hemodynamic environment; and avoidance of coronary artery impingement.

The techniques we have used to deal with this include the use of through and through wire access; specially designed delivery systems that are highly flexible, kink-resistant, hydrophilic-coated and have a short-tipped taper

at the end of the catheter; decreasing cardiac output by the use of femoral to femoral bypass, or rapid ventricular pacing; and obtaining coronary artery wire access prior to device positioning as well as reassessing coronary vasculature after device deployment.

High Risk Transcatheter Aortic Valve Surgery

With an aging population we are also seeing increasing numbers of patients with valve disease. They are increasingly sicker and over 25% of patients undergoing operations in our institution requires redo sternotomy.

Based on the same technology used to treat aortic aneurysms, valves mounted on stents are now being used for high risk surgical patients. We are one of three centers in the United States involved with the initial pilot studies for using one such device in prohibitively high risk patients with critical aortic stenosis –the results so far have been promising.¹⁷⁾

The procedure first entails balloon valvuloplasty, followed by delivery and deployment of the valve. The valve prosthesis consists of heterograft pericardial cusps mounted on a balloon expandable stent (Edwards Lifesciences Inc., Santa Rosa, California) which can either be delivered in a retrograde fashion via the femoral or iliac artery, or from an ante-grade approach through the left ventricular apex¹⁸⁾ (**Fig. 9**).

Literally, dozens of transcatheter valves or valve repair devices are on the horizon for the treatment of aortic, mitral and tricuspid disease. Other catheter based devices already in use to treat a variety of structural heart



Fig. 7 Volume rendered CT reconstruction of post-coarctation repair aneurysm after endovascular repair with a fenestrated stentgraft to accommodate the left common carotid artery.

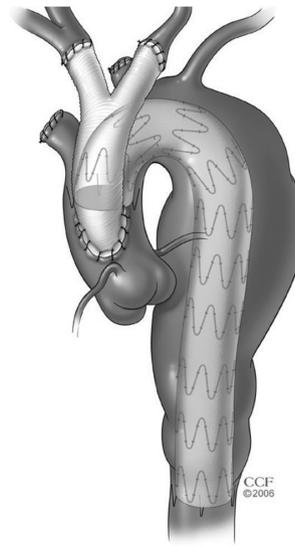


Fig. 8 Arch transposition with endovascular completion.

disease include atrial septal defect closure devices, percutaneous ventricular assist devices, pulmonic valves, and left atrial appendage occluders.

Additional Considerations

Additional challenges include concerns about the graft-patient interface. Patients with connective tissue disease may be prone to retrograde dissections or further aneurysmal degeneration of the seal segment.

Migration continues to be an issue with any endovascular device, so the need for regularly scheduled radiographic evaluation is critical. Determining if a patient has really had migration of the device, however, isn't always so easy and may require the use of three-dimensional analysis techniques to differentiate migration from longitudinal aortic growth.¹⁹⁾

CONCLUSION

In a relatively short period of time, transcatheter and endovascular approaches to treat thoracic aortic and structural heart disease have exploded onto the scene. New device frontiers already being forged in the experimental stages include expanded indications and variations of fenestrated and branch stentgrafting to treat thoracoabdominal and arch disease, endovascular ascending and aortic root repair, and all of the cardiac valves.

A fundamental concept to optimize durability of endovascular repair is the need for fixation and seal



Fig. 9 Transcatheter aortic valve.

in healthy tissue. Before long, the entire vascular and cardiovascular system will be within the reach of endovascular interventions. Ultimately, achieving success in this endeavor will require a combination of skill sets including familiarity with high definition imaging, surgical access, and the mastery of interventional techniques, as well as the development of better anatomy-specific and disease-specific devices.

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