Current State and Future of Fenestrated Technology

The appropriate patient selection, imaging, device design, and technical expertise needed for this technology to continue evolving.

BY MARK FARBER, MD

Pararenal, paravisceral, and thoracoabdominal aortic aneurysms pose complex problems for the vascular surgeons who manage them. Endovascular repair of aortic aneurysms (EVAR) has been associated with low perioperative morbidity and mortality, even in high-risk patients. Recent publications reveal that almost half of these aneurysms are not amenable to treatment with endovascular techniques based on the instructions for use for infrarenal aortic devices.[1] Until recently, EVAR has not been available for these patients in the United States, unless they were participating in investigational device exemption studies.

In general, exclusion from EVAR is due to adverse proximal neck anatomy including short, nonexistent, or angulated necks, which preclude an adequate, durable proximal seal. Good surgical candidates may tolerate the complex open procedures necessary to exclude these aneurysms, but many patients possess serious cardiac, pulmonary, or renal comorbidities, predisposing them to the significant risk for perioperative morbidity and mortality that is associated with an extensive open procedure. These patients may be best served by a minimally invasive approach to aneurysm exclusion, with the most appropriate treatment determined by an experienced surgeon after consideration of each patient's risk profile.

AN APPROVED FENESTRATED DEVICE

In April 2012, the Cook Zenith Fenestrated device (Cook Medical, Bloomington, IN) received approval from the US Food and Drug Administration (FDA) for implantation in patients with short infrarenal necks (4–14 mm in length). During this past year, numerous physicians have undertaken extensive training so that these procedures can be conducted safely at more centers across the United States. To date, more than 100 procedures have been performed since FDA approval in the US. Currently, physicians without experience with the fenestrated technology are required to submit data on their first few cases to a registry so that the FDA can confirm the safety of this device outside the centers of excellence that helped advance the technology over the past decade.

It should be noted that there are limitations to the current device. At most, three fenestrations/scallops can be utilized, each with their own restrictions with respect to location and positioning in the proximal aspect of the graft. Furthermore, the instructions for use restricts implantation to suprarenal neck and aortic neck angulations within 45° each. Neck angulation poses a particularly difficult problem, as device orientation and positioning of the fenestration can become extremely difficult in these situations, resulting in either severe stenosis or occlusion of the target vessels due to malalignment with the fenestrations.

CLINICAL RESULTS IN THE LITERATURE

Clinical results supporting the use of fenestrated endovascular aortic repair (FEVAR) in complex cases are mainly derived from approval in 2005. Since that time, there have been three reviews published regarding its use.

In 2009, Nordon et al[2] analyzed eight reports involving 368 patients who underwent FEVAR and compared them to 12 open surgical cohort studies involving 1,164 patients. They determined that there was an increased risk of 30-day mortality associated with open repair between the homogenous groups (increased absolute risk, 2%; relative risk, 1.03). Although there was no increase in the incidence of permanent dialysis, transient renal failure occurred more commonly after open repair. As with most comparative studies involving endovascular techniques, reinterventions occurred more commonly with endovascular repair.

Two additional reviews[3,4] have also been published, each involving more than 600 patients in the FEVAR cohort and containing many of the same patients in their analysis. In an article by Linsen et al,[3] nine studies were evaluated, with a total of 629 patients and 1,622 target vessels. The combined estimate of technical success and 30-day mortality was 90.4% and 2.1%, respectively. Branch vessel patency was 93.2% during follow-up.

Renal impairment was reported in 22.2% of patients, with only 2.1% requiring dialysis. They concluded that the immediate and midterm outcomes were very promising, but the long-term durability is yet to be determined.

Recently, there has been a GLOBALSTAR publication[5] involving 314 patients who were treated by FEVAR at experienced institutions (> 10 procedures) between January 2007 and December 2010 in the United Kingdom. Technical success was 99%, with a 30-day mortality rate of 4.1%. Kaplan-Meier survival at 1, 2, and 3 years was 94%, 91%, and 89%, respectively. Target vessel patency was 85% at 3 years, with a reintervention rate of 30% at 3 years. These outcomes demonstrated high technical and clinical success in regard to satisfactory target vessel patency and reintervention rates.

The final results of the US multicenter fenestrated trial have not been published yet, but the intermediate results from the first 30 patients have been reported.[6] In an article by Greenberg et al,[6] there was no loss of visceral target vessels during the initial procedure and no aneurysm-related deaths, ruptures, or conversions to open repair through 2 years. No type I or III endoleaks were detected; however, there were eight renal events that occurred during follow-up. Five of the eight renal events required secondary interventions, but no patient progressed to dialysis.

Because all of these reports are based upon the Cook Zenith Fenestrated graft, the conclusion can be made that fenestrated repair with this device provides a viable alternative to open repair with favorable midterm results supporting its use.

CHALLENGES OF THIS TECHNIQUE

Fenestrated device development is still in its early phases. The current FDA-approved device does not treat all patients due to limitations in location, number, and type of fenestrations that can be manufactured. Combined with the anatomic applicability criteria, many patients still cannot be treated at this time. Implantation of the fenestrated device in specific patient populations, as described later, can also pose a significant problem as target vessel patency and durability will most likely be compromised.

Patient selection has always been critically important in achieving excellent results with vascular procedures. Recognition of these limitations and their impact on outcomes is important in counseling patients appropriately and achieving outcomes that are comparable to published clinical trial results.

Target Vessel Stenosis

The presence of target vessel stenosis > 50% creates potential problems for FEVAR. Its presence can increase the difficulty and duration of the procedure, resulting in increased perioperative morbidity. Lower extremity ischemic complications have been noted when the total procedure time exceeds 3 to 4 hours. Successful target vessel cannulation and revascularization may also be affected, resulting in a higher incidence of renal and mesenteric complications.

Angulation

Aortic angulation in the visceral and iliac regions is often overlooked as a contraindication for FEVAR. Severe vessel tortuosity creates alignment issues with respect to the position of the endoprosthesis to the native target vessel origins. Failure to correct for even mild neck tortuosity by manually adjusting the centerline analysis tools can result in misalignment of the fenestrations and target vessel occlusion. Even when appropriate accommodation for tortuosity is undertaken, severe angulation can result in difficult target vessel cannulation strategies that increase the risks of complications associated with the procedure.

Aortic Neck Diameter/Contour

Special attention should be focused on the aortic neck contour when performing all EVAR procedures in order to detect early aneurysmal disease. Although large devices may create a seal in a region based on size measurements, aortic diameters that are larger than their more proximal segment indicate early aneurysmal disease and should not be used as a sealing region. Placing infrarenal EVAR devices in dilated necks can result in early device failures, which often require secondary procedures for aneurysm exclusion that are difficult but feasible. Placing fenestrated devices in regions that are prone to failure is extremely dangerous, as techniques for repair other than device removal do not currently exist.

Renal Issues

Attention must also be given to renal artery diameters and orientation relative to the aorta. Small renal arteries (< 5 mm) have a higher incidence of failure with renal artery stenting as compared to larger renal arteries. The orientation of the artery must also be inspected. Severely ptotic renal arteries may be difficult to cannulate, and in some cases, early bifurcations or severe renal artery tortuosity precludes successful FEVAR. Important determinates of success after FEVAR are not only aneurysmal exclusion but also renal function. Deterioration of renal function during complex aortic repair may depend on numerous factors (nephrotoxic contrast, wire manipulation, microembolization, etc.). After FEVAR, as many as one-third of patients may experience deterioration in their renal function.[7] This is especially true if they possess preexisting renal insufficiency. Nordon et al[2] reported that 14.9% of patients experienced an increase of their serum creatinine of > 30%. This was significantly lower
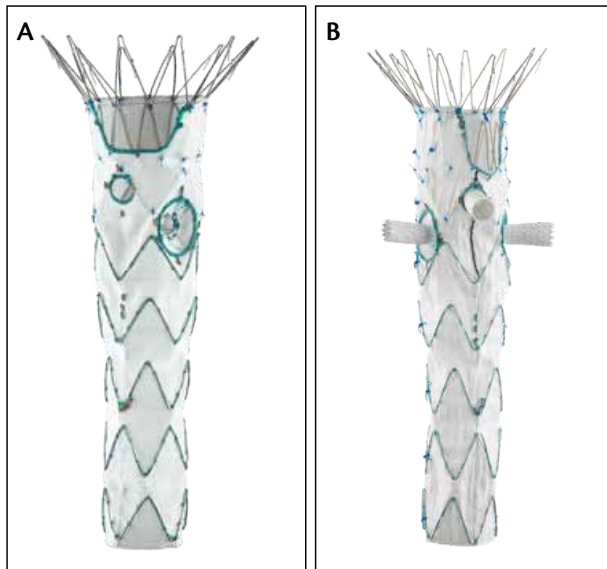
Figure 1. The Zenith p-Branch device with pivot fenestrations (A). The Zenith p-Branch device with stent inserted (B).

than the 20% incidence in the surgical cohort (relative risk, 1.06). Haddad et al from the Cleveland Clinic reported[8] a 16% incidence of perioperative renal insufficiency in patients with a normal glomerular filtration rate (> 60 mL/min/1.73 m^2) and 39% in those with preoperative chronic renal insufficiency. Baseline renal insufficiency was also a good predictor of mortality (P = .02) with a relative risk of 8.52. The majority of the changes observed in the Cleveland Clinic cohort[8] occurred during the first month after repair, with a return to their mean estimated glomerular filtration rate within 6 months.

Long-term patency of renal artery fenestrated vessels has also been a concern. Early experience with bare stents revealed a low incidence of in-stent stenosis. This complication appears to have been rectified with the routine use of covered stents. Currently, renal artery complications are most likely related to the native renal artery kinking as a result of compliance mismatch induced by the balloon-expandable renal artery stent. Careful attention must be paid to the native vessel contour, and often, a self-expanding stent is implanted distally in order to provide a transition region and avoid renal artery occlusion due to kinking.

Production Time

The current production time involved in creating these devices can pose a problem for patients requiring urgent or emergent repair. Device manufacturing, including sterilization, takes approximately 3 weeks, with an additional week required for shipping, as devices are not currently manufactured in Europe or the United States. As a result, efforts are underway to develop an "off-the-shelf" alternative to enable treatment with minimum delay.

DEVICES IN DEVELOPMENT

Two devices are currently undergoing investigation as off-the-shelf designs in order to help reduce treatment delay in patients. The first is the Cook Zenith p-Branch device (Cook Medical) (Figure 1). This device design is centered around a fixed fenestration for the superior mesenteric artery (SMA). A double- or triple-wide scallop is used to incorporate the celiac artery, and two pivot fenestrations provide flexibility in the treatment locations of the renal arteries. There are currently two different configurations of the device to accommodate a larger proportion of patients. The extent of aneurysmal disease can extend up to the level of the base of the SMA. The renal fenestrations are also precannulated, making it easier to catheterize the target vessels. There are several centers with early access to this device, and the US trial has started patient enrollment. The only published report of its use is from Resch et al,[9] which details the initial seven patients with 100% target vessel catheterization and 0% 30-day mortality. During follow-up, there was one renal artery stent occlusion. The only other report was presented in an abstract format during the recent Society of Clinical Vascular Surgery, detailing successful implantation in seven additional patients. All procedures were technically successful (no type I or III endoleaks) with 0% 30-day mortality. One patient experienced renal insufficiency, which resolved within 30 days.

The other device undergoing evaluation is the Ventana fenestrated device (Endologix, Inc., Irvine, CA). It incorporates a large scallop for the SMA and celiac artery, with two fenestrations for the renal arteries. Flexibility in the location of the renal artery fenestration is accomplished by having fabric redundancy in the mid-section without attaching it to the stent frame. A nonaneurysmal neck length of 15 mm must exist below the SMA in order to achieve aneurysmal exclusion. The report of the first 15 implants was recently published.[10] Among these patients, there was no perioperative mortality, and all vessels were successfully treated. With 11 of the 15 patients having reached their 6-month follow-up visit, there have been no type I or III endoleaks and only one patient experiencing bilateral renal artery stenosis. Early reports of these devices are encouraging; however, approval will require more extensive clinical trial enrollment and follow-up.

Applicability of New Designs

As future designs are developed, mesenteric and renal vessel variability must be taken into account so that a larger proportion of patients can be treated without individual customization. Sobocinski et al[11] evaluated a total of 100 patients with juxtarenal and/or pararenal aortic aneurysms who had undergone treatment with custom-manufactured fenestrated designs to determine their applicability for off-the-shelf options. Surprisingly, 72% of patients had anatomy amenable to a standard

fenestrated approach, with the right renal artery location causing exclusion in most cases. This percentage seems slightly high and may be the result of prior exclusion of some patients based upon their initial CT scan results. Other limitations may also exist, such as the relative location of each branched vessel and early bifurcation vessels. As previously mentioned, neck characteristics including angulation, shape, and quality play a critical role in treatment success. In some cases, aortic narrowing in the visceral region can create challenging anatomy for standardized treatment designs.

Alternative device designs also merit mention. Most renal arteries are transversely or cranially oriented with respect to the aorta and lend themselves to fenestrated repair. The mesenteric vessels are often longitudinally oriented, and thus may be better treated with branched graft designs. Chuter[12] has advocated branched designs for treatment of most complex aortic aneurysms, with good results. However, difficulties exist when the renal arteries are cranially oriented and severe angulation exists. Combining these two approaches may also allow for a larger portion of patients to be treated with off-the-shelf designs.

CONCLUSION

Endovascular repair of aneurysms involving the visceral aorta has become a reality with the approval of the Zenith Fenestrated device. It is estimated that more than 5,000 cases have been performed worldwide, with promising midterm results with respect to safety and success. Appropriate patient selection, high-resolution imaging, proper device design, and technical expertise will be required for this therapy to continue. As technology and techniques evolve, the endovascular treatment of thoracoabdominal aortic aneurysms and juxtarenal aneurysms is certain to become more commonplace. The continued efforts to make safe, prefabricated devices available to more patients will certainly allow the dissemination of the technology. In the future, the number of devices and the percentage of patients amenable to this therapy will gradually increase until it becomes the procedure of choice in appropriately selected patients. ■

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