

FEVAR: Long-term Data From the Cleveland Clinic

Continued development and application of fenestrated endovascular technology to treat complex aortic disease and directions for the future.

BY MATTHEW J. EAGLETON, MD

On the 5-year anniversary of commercial approval of the Zenith Fenestrated (ZFEN) system (Cook Medical) in the United States, it is remarkable to note that the first descriptions of use of fenestrated and branched endografts to treat complex aortic aneurysms date back to the mid and late 1990s.¹⁻⁴ These early device designs share many similarities with the more sophisticated endografts in use today. The devices were custom made and modular, allowing for the endoluminal assembly of components specifically designed to interact with different sections of the aorta while preserving perfusion to the renal and visceral arteries.

In 2001, the first series of patients from Australia who underwent endovascular aneurysm repair (EVAR) incorporating the renal and superior mesenteric arteries with graft fenestrations was reported.⁵ This series included 13 patients treated with devices based on the Zenith EVAR platform (Cook Medical). Similar to current systems, the fenestrated stent graft was placed using a modified delivery system that provided staged deployment of the components that allowed for exact alignment of the fenestrations with their target vessels. Fenestrations were held in alignment with their target vessels using flared bare-metal stents.

However, early experience in the United States was limited primarily to physician-sponsored investigational device exemption (PS-IDE) trials. Despite this, much of our procedural protocols, device enhancements, and understanding of device and repair durability have arisen from these assessments. One of the most prolific contributors to this body of literature was the late Dr. Roy Greenberg, who established an early PS-IDE at the Cleveland Clinic. During and following his tenure, significant contributions based on these studies have helped guide the endovascular care of patients with complex aortic disease. Although the work at the Cleveland Clinic has evolved to primarily focus on the treatment of thoracoabdominal aortic aneurysms (TAAAs), the focus of this article will be on the major contributions and long-term follow-up of patients treated with fenestrated endovascular aneurysm repair (FEVAR).

EARLY EXPERIENCE WITH FEVAR

The first fenestrated endograft placement at the Cleveland Clinic was performed in 2001, and a report in 2004 outlined the outcomes of 22 patients treated in this fashion.⁶ This was followed shortly by an update that reported outcomes for a total of 32 patients.⁷ These early grafts were more rudimentary than those employed in the United States Zenith Fenestrated AAA Endovascular Graft clinical trial, as they lacked reinforced fenestrations. By 2006, 119 patients had been treated within Dr. Greenberg's program with incorporation of 302 renal and visceral vessels.⁸ Outcomes appeared to be excellent with a 30-day endoleak rate of 10% (all type II), aneurysm regression (> 5 mm) occurring in nearly 80% of patients by 2 years, and renal stenosis/occlusion occurring in only 4% of patients. These initial results raised several questions for study.

With excellent early results, it became apparent that more information was needed on long-term follow-up, particularly with regard to aortic stent and branch vessel durability and renal function. In addition, it was clear that device improvements would be necessary to allow for incorporation of more visceral vessels and treatment of more complex aneurysms. Since then, the Cleveland Clinic group has reported outcomes of 607 patients undergoing FEVAR for juxtarenal and type IV TAAA repair with a mean follow-up of 8 years.⁹

RENAL FUNCTION

Given the manipulation and stenting of the renal arteries, as well as the use of iodinated contrast during the procedure and in the repeated follow-up imaging, renal failure following FEVAR has remained one of the greatest concerns. The need for hemodialysis after FEVAR has ranged from 0% to 6% and varies based on the extent and complexity of the aneurysm repaired.⁹⁻¹² In fact, the United States Zenith Fenestrated trial boasted a 30-day freedom from acute renal injury rate of 100%, despite nearly 10% of patients having radiographic evidence of renal embolization.¹³ Early experience with FEVAR at the Cleveland Clinic demonstrated that acute kidney injury developed in 16% of patients without preoperative renal

insufficiency and in 39% of those with chronic renal disease.¹⁴ The incidence of permanent dialysis was higher in the group with preoperative renal dysfunction, and these patients similarly had a higher mortality. Estimated glomerular filtration rates (eGFRs) stabilized in this population within 6 months of the index surgery. Since then, others have reported that post-FEVAR acute renal failure (assessed with the RIFLE criteria) is as high as 29%, with a 14% decrease in eGFR and renal volume noted at 3 years postoperatively.¹⁵ However, these findings are not unique to FEVAR, as similar rates of acute kidney injury have been observed after open surgery and EVAR, with similar rates of long-term renal decline.

DEVICE DURABILITY

With the evolution of more complex devices, the durability of the repair comes into question, as there are potentially increased modes and locations of failure. In 2008, the Greenberg group reported on the risk of component separation in FEVAR performed at the Cleveland Clinic.¹⁶ Data from 106 patients who underwent cross-sectional imaging follow-up beyond 1 year were analyzed. A total of 14 patients (13%) were identified as having component movement of 10 mm or more, with the range of movement between 11 and 42 mm. This component movement occurred between 2 and 4 years of follow-up. Eight of these patients were noted to have less than two-stent overlap, with one patient presenting with a ruptured aneurysm that resulted in open conversion. The remaining patients had additional stents placed.

An algorithm was developed to assess the risk of potential component separation. It used numerical computing software and predicted the maximum amount of possible intercomponent movement, thereby deriving the minimum overlap required to prevent the risk of complete component separation. This algorithm was based on the distance from the renal artery to the aortic bifurcation (straight line and center line) and maximum aortic diameter. When applying these calculations to the entire cohort of FEVAR patients, it was determined that 38% were at risk for component separation. This meant that if the components had maximum morphologic device changes, they did not have enough component overlap to accommodate the shift. It was determined that a new baseline at attempting to achieve three- to four-stent overlap for components was both possible and would mitigate nearly every risk of aortic component separation. These findings changed device planning parameters for FEVAR!

BRANCH VESSEL DURABILITY

One of the keys to long-term FEVAR success is maintaining branch vessel patency. Midterm branch vessel patency rates have recently been reported by most large series and range

from 93% to 98% (at 3–5 years) overall.^{10,11,17-19} As with most endovascular procedures, FEVAR requires reintervention to maintain graft and branch vessel patency and ameliorate endoleak development. This requires an active surveillance program in order to identify stented branch vessels at risk for failure. Historically, the Cleveland Clinic program has mandated patient follow-up on an annual basis with contrast-enhanced imaging (provided renal function will allow it) combined with duplex ultrasonography. Early assessment identified that some unique findings have altered both treatment and follow-up protocols.²⁰ It was determined that revised duplex criteria were necessary in FEVAR given the hemodynamic alterations induced by adding stiff stent systems to both the aorta and the target vessels. Changing a peak systolic velocity criteria to > 280 cm/sec in order to identify 60% to 99% renal artery stenosis improved the sensitivity (93%), specificity (100%), and positive and negative predictive values (99% for both). In addition, it was noted that covered bridging stent use was associated with a lower rate of renal artery stenosis compared to treatment with bare-metal stents. However, there was no difference in branch vessel occlusion rates. This has led to the primary use of covered stents when performing FEVAR, regardless of the need to obtain a seal with the fenestration at that location.

Mastracci et al provided the largest series evaluating the durability of branch vessels after FEVAR.²¹ This analysis includes not only patients who underwent FEVAR for short-necked and juxtarenal abdominal aortic aneurysms (AAAs), but also more extensive TAAAs. Given the excellent outcomes in this more complex cohort, extrapolation to standard FEVAR is obvious. Secondary procedures were performed in only 0.6% of celiac arteries, 4% of superior mesenteric arteries, 6% of right renal arteries, and 5% of left renal arteries. Reinterventions are divided equally between restenosis/occlusion and endoleak development. The 5-year freedom from branch vessel reintervention rate was 89%. Unfortunately, there did not appear to be a specific time frame in which the majority of the reinterventions occurred, which again highlights the necessity for lifelong surveillance. As aneurysms become more complex (ie, extensive TAAAs), the rates of reintervention appear to increase over time.^{9,10}

AORTIC DURABILITY AND FUTURE NEEDS

Complex aortic endografting is an investment made by the physician and the patient. Proximal endograft failure (ie, type Ia endoleak) is a devastating complication of FEVAR, as further repair becomes even more complicated. This is likely related to either poor judgment of candidates in whom to place an endograft or a failure to recognize the potential for disease progression. This becomes equally important in those who undergo FEVAR. One of the reasons that repairs fail is due to disease progression. The best-designed stent graft in

the world will not survive the continued dilation of the aorta that it relies on for its foundation. FEVAR is not immune to this. Despite the increased ability to land the stent graft in nearly any segment of the aorta, approximately 2% to 3% of FEVAR patients will develop a proximal type I endoleak if given enough time.²² Some of this may be related to poor patient selection, but the majority is due to disease progression.

In the Cleveland Clinic experience, some of the early failures were due to our lack of appreciation of disease progression, as represented by the higher failure rates observed early in our application of this technology. In those series, we attempted to treat patients with the shortest amount of coverage possible, utilizing only a 15-mm landing zone in the paravisceral segment. Since then, we recognized several aspects particular to FEVAR. Shorter necks are not better, especially in those with potentially other unattractive neck attributes such as the presence of thrombus, a large diameter, or atherosclerosis—all harbingers of potential future degeneration. Currently, we routinely attempt to achieve a 2- to 3-cm landing zone when extending a repair into the visceral aortic segment while balancing the risks of developing other complications such as spinal cord ischemia.

However, commercial FEVAR does not accommodate for this and represents the need for more advanced devices that allow for the incorporation of more visceral vessels and more cephalad extension of these devices for improved durability. Most surgeons with access to devices that can incorporate more fenestrations than the currently approved ZFEN choose to increase the extent of coverage and make the treatment of later disease progression easier. Evolution toward more widespread application of these types of devices has been supported again through the initial evaluations of PS-IDEs (at least in the United States). In the Cleveland Clinic experience, long-term outcomes on 610 patients treated with FEVAR for juxtarenal and type IV TAAAs has been reported.⁹ Mean follow-up duration for the cohort was 8 years. The results of this analysis clearly demonstrate successful utilization of this complex treatment option, but more complex device configurations result in higher rates of reintervention. However, these complex designs can be utilized with similar rates of perioperative morbidity and mortality, have lower rates of type I endoleak development, and are associated with nearly 98% freedom from aneurysm-related mortality.

CONCLUSION

As we celebrate the 5-year anniversary of the ZFEN commercialization in the United States, it is still an exciting time to be involved with the development and application of endovascular technology to treat complex aortic disease. Over the next decade, we will certainly attain

commercialization of devices that can treat more complex AAA pathology, TAAA disease, and aortic arch aneurysms. Devices will become easier to use, and we will observe lower perioperative morbidity and mortality rates. Failure modes will be better understood, as will the best application of these technologies. All of this, which will be the result of a collaboration between physician- and industry-driven evaluations, will ultimately result in better care for patients with aneurysmal disease. ■

1. Park JH, Chung JW, Choo IW, et al. Fenestrated stent-grafts for preserving visceral arterial branches in the treatment of abdominal aortic aneurysm: preliminary experience. *J Vasc Interv Radiol*. 1996;7:819-823.
2. Faruqi RM, Chuter TAM, Reilly LM, et al. Endovascular repair of abdominal aortic aneurysm using a pararenal fenestrated stent-graft. *J Endovasc Surg*. 1999;6:354-358.
3. Kinney EV, Kaebnick HW, Mitchell RA, Jung MT. Repair of mycotic paravisceral aneurysm with a fenestrated stent-graft. *J Endovasc Ther*. 2000;7:192-197.
4. Browne TF, Hartley D, Purchas S, et al. A fenestrated covered suprarenal aortic stent. *Eur J Vasc Endovasc Surg*. 1999;18:445-449.
5. Anderson JL, Berce M, Hartley DE. Endoluminal aortic grafting with renal and superior mesenteric artery incorporation by graft fenestrations. *J Endovasc Ther*. 2001;8:3-15.
6. Greenberg RK, Haulon S, Lyden SP, et al. Endovascular management of juxtarenal aneurysms with fenestrated endovascular grafting. *J Vasc Surg*. 2004;39:279-287.
7. Greenberg RK, Haulon S, O'Neill S, et al. Primary endovascular repair of juxtarenal aneurysms with fenestrated endovascular grafting. *Eur J Vasc Endovasc Surg*. 2004;27:484-491.
8. O'Neill S, Greenberg RK, Haddad F, et al. A prospective analysis of fenestrated endovascular grafting: intermediate-term outcomes. *Eur J Vasc Endovasc Surg*. 2006;32:115-123.
9. Mastracci TM, Eagleton MJ, Kuramochi Y, et al. Twelve-year results of fenestrated endografts for juxtarenal and group IV thoracoabdominal aneurysms. *J Vasc Surg*. 2015;61:355-364.
10. Eagleton MJ, Follansbee M, Wolski K, et al. Fenestrated and branched endovascular aneurysm repair for type II and III thoracoabdominal aortic aneurysms. *J Vasc Surg*. 2016;63:930-942.
11. Reilly LM, Rapp JH, Grenon SM, et al. Efficacy and durability of endovascular thoracoabdominal aortic aneurysm repair using the caudally directed cuff technique. *J Vasc Surg*. 2012;56:53-63.
12. Amiot S, Haulon S, Becquemin JP, et al. Fenestrated endovascular grafting: the French multicentre experience. *Eur J Vasc Endovasc Surg*. 2010;39:537-544.
13. Oderich GS, Greenberg RK, Farber M, et al. Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *J Vasc Surg*. 2014;60:1420-1428.
14. Haddad F, Greenberg RK, Walker E, et al. Fenestrated endovascular grafting: the renal side of the story. *J Vasc Surg*. 2005;41:181-190.
15. Martin-Gonzalez T, Pincon C, Hertault A, et al. Renal outcomes analysis after endovascular and open aortic aneurysm repair. *J Vasc Surg*. 2015;62:569-577.
16. Dowdall JF, Greenberg RK, West K, et al. Separation of components in fenestrated and branched endovascular grafting—branch protection or a potentially new mode of failure? *Eur J Vasc Endovasc Surg*. 2008;36:2-9.
17. Verhoeven EL, Katsargyris A, Bekkema F, et al. Editor's Choice—ten-year experience with endovascular repair of thoracoabdominal aortic aneurysms: results from 166 consecutive patients. *Eur J Endovasc Surg*. 2015;49:524-531.
18. Verhoeven EL, Vourliotakis G, Bos WT, et al. Fenestrated stent grafting for short-necked and juxtarenal abdominal aortic aneurysm: an 8-year single-centre experience. *Eur J Vasc Endovasc Surg*. 2010;39:529-536.
19. GLOBALSTAR Collaborators. Early results of fenestrated endovascular repair of juxtarenal aortic aneurysms in the United Kingdom. *Circulation*. 2012;125:2707-2715.
20. Mohabbat W, Greenberg RK, Mastracci TM, et al. Revised duplex criteria and outcomes for renal stents and stent grafts following endovascular repair of juxtarenal and thoracoabdominal aneurysms. *J Vasc Surg*. 2009;49:827-837.
21. Mastracci TM, Greenberg RK, Eagleton MJ, Hernandez AV. Durability of branches in branched and fenestrated endografts. *J Vasc Surg*. 2013;57:926-933.
22. O'Callaghan A, Greenberg RK, Eagleton MJ, et al. Type Ia endoleaks after fenestrated and branched endografts may lead to component instability and increased aortic mortality. *J Vasc Surg*. 2015;61:908-914.

Matthew J. Eagleton, MD

Professor of Surgery

Cleveland Clinic Lerner College of Medicine-CWRU

Cleveland, Ohio

(216) 445-1168; eagletm@ccf.org

Disclosures: None.