Exploring EVAR Instructions for Use in 2016

A discussion of how practice patterns may affect patient outcomes and a look at newer-generation devices.

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Our group has had a long-standing interest in better understanding practice patterns associated with endovascular aneurysm repair (EVAR) throughout the United States. Specifically, we have evaluated how often patients are treated within or outside of EVAR device instructions for use (IFU) and what effects these practice patterns may have on patient outcome. With the rapid evolution in the approach to managing abdominal aortic aneurysms (AAAs) that has occurred over the last 2 decades, and with many new devices available on the market, it is critically important to understand the role of IFU in contemporary EVAR practice.

THE EVOLUTION OF AAA REPAIR

The most dramatic shift in the surgical management of AAAs occurred in 1991 when Juan Parodi reported the first EVAR.[1] This transformative moment paved the way for minimally invasive AAA repair to surpass open surgical repair as the leading therapy for the treatment of AAA. In 2006, only 15 years after the initial publication describing EVAR, 21,725 EVAR procedures had been performed in the United States, exceeding the number of open surgical AAA repairs for the first time.[2] Currently, over 80% of elective AAA repairs in the United States are performed with EVAR.[3]

The results from the three largest prospective randomized trials (EVAR, DREAM, and OVER) that compared early and late outcomes after open and endovascular repair of AAAs were remarkably consistent in all major respects.[4-6] In aggregate, the findings can be summarized as follows: (1) perioperative morbidity and mortality rates are significantly lower after EVAR repair than after open repair of AAAs; (2) the short-term survival advantage associated with EVAR diminishes during long-term follow-up, such that if patients survive beyond approximately 2 years, the long-term survival of patients is similar for both groups; and (3) although the reintervention rate after EVAR is higher than after open repair, most reinterventions are performed with catheter-based techniques, albeit at overall higher costs.

However, the rate of AAA sac enlargement after EVAR is not negligible. In an initial report on this topic, the rate of aortic sac enlargement after EVAR was 21% at 5 years.[7] A more recent study involving 478 patients who underwent EVAR demonstrated a 42% rate of aneurysm sac enlargement at 5 years.[8] In another study, even in patients who were treated for a type II endoleak when surveillance detected AAA sac enlargement, 55% continued to show sac expansion > 5 mm by 5 years after EVAR.[9]

IFU GUIDELINES FOR EVAR

To better understand AAA sac enlargement after EVAR, we conducted a study using data from a large multicenter cohort to evaluate the degree of compliance with IFU anatomic guidelines for EVAR, examine changes in compliance with the IFU over the last decade, and determine the relationship between baseline aortic and iliac artery anatomic characteristics and incidence of AAA sac enlargement after EVAR.[10] Patients who had an AAA with an aortic diameter > 30 mm; underwent EVAR between January 1, 1999, and December 31, 2008; and had a pre-EVAR CT scan and at least one post-EVAR CT scan were identified from a medical imaging database at M2S, Inc. For the

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purposes of this study, M2S, Inc. provided deidentified data on all patients in their prospectively acquired database but had no other role in the study. Based on the aforementioned criteria, 10,228 patients were eligible for analysis. The primary limitations of this study were that although a large number of patients were studied, no clinical characteristics were available, and the generalizability of this population to patients undergoing EVAR in the United States could not be established.[11]

This study found a 41% incidence of AAA sac enlargement after EVAR in this cohort of patients at 5 years, a rate that increased over the time of the study. When all EVAR-treated patients were classified according to compliance with IFU criteria, 5,983 (58.5%) treated patients had anatomy outside the most conservative device IFU, and 3,178 (31.1%) treated patients had anatomy outside of the most liberal IFU available on the United States market. These findings demonstrate unequivocally that physicians often choose to utilize a liberal interpretation of the anatomic characteristics deemed suitable for EVAR when offering this therapy to patients. Our analysis has shown that several of these anatomic factors, including aortic neck diameter, aortic neck angle, and common iliac artery diameter, were independently associated with aortic aneurysm sac enlargement. These observations raise the question as to whether such liberal choice of anatomic criteria is justified using current endovascular device designs.

In contrast to our study's findings and those published by several other groups,[8,12-17] a recent study by Walker and colleagues found no association between nonadherence to IFU and either all-cause or aneurysm-related mortality.[18] However, several important limitations should be considered, most notably the relatively short overall follow-up of 3.1 years and the significant number of patients who were excluded due to a lack of follow-up. Similarly, a retrospective analysis of a single institution's experience with EVAR outside of IFU found no significant difference in reintervention rates, sac enlargement, or aneurysm-related mortality at a mean follow-up of 35 months.[19] Torsello and colleagues also reported satisfactory results for patients treated with the Endurant device (Medtronic, Inc.) outside of IFU, but the outcomes were only at early and intermediate follow-up.[20,21] Results of these reports are in contrast to the aforementioned studies that consistently described the risks of EVAR outside of IFU as late complications (specifically, 5 years and beyond), as would be expected given the hypothesized failure modes. The lack of association described in these studies deserves careful interpretation when considered in context with the large body of evidence established from previously published reports.

Our analysis of M2S, Inc. data was meant to be a starting point for a critical conversation in the evolving field of EVAR rather than a conclusion. It has now been established that the risk of late rupture after EVAR is higher than initially believed.[22] A consensus exists that the primary anatomic determinant of late AAA rupture after EVAR is aortic sac enlargement.[22,23] It is likely that the rate of aortic sac enlargement after EVAR is dependent on the specific patient population and endovascular device studied. Based on our analysis of M2S, Inc. data, EVAR is frequently performed in patients outside of industry-recommended anatomic guidelines, and this practice increases the risk of late aortic sac enlargement.

SURVEILLANCE AFTER EVAR

The frequent treatment of patients outside of IFU and the higher-than-expected rates of aneurysm sac enlargement after EVAR underscore the critical importance of lifelong surveillance after EVAR. The Society for Vascular Surgery practice guidelines call for contrast-enhanced CT scans at 1, 6, and 12 months, with annual surveillance with either contrast-enhanced CT or duplex ultrasound indefinitely thereafter.[24] Despite this, studies conducted in the United States Medicare beneficiary population suggest that rates of long-term imaging follow-up after EVAR are low. Using a liberal definition of adequate surveillance (either CT scan or ultrasound every 15 months after EVAR), Garg and colleagues reported compliance in 43% of beneficiaries; nonadherence was independently associated with late AAA rupture (hazard ratio, 1.51; 95% confidence interval, 1.24–1.84; $P < .001$).[25] Using a liberal definition of adequate surveillance imaging, our group also performed a study of Medicare beneficiaries and found that 50% of patients were lost to imaging follow-up at 5 years after EVAR. For a subset of patients with 8 years of follow-up data after EVAR, the substantive declines in imaging follow-up continued, with only 37% undergoing an imaging study between 6 and 8 years.[26]

TABLE 1. IFU FOR NEWER-GENERATION DEVICES

	Nellix Endovascular Aneurysm Sealing System*	Ovation iX Abdominal Stent Graft System†	Zenith Fenestrated AAA Endovascular Graft†	Zenith p-Branch Standard Fenestrated Endovascular Graft‡	Aorfix AAA Endovascular Stent Graft†
Proximal neck diameter	18–32 mm	16–30 mm	19–31 mm	18–32 mm	19–29 mm
Proximal neck length	Infrarenal ≥ 10 mm	Not specified; seal ring is 13 mm below lowest renal	Infrarenal ≥ 4 mm	Infra-SMA sealing zone length ≥ 4 mm	Infrarenal ≥ 15 mm
Proximal neck angulation	≤ 60°	≤ 60° if neck length ≥ 10 mm; ≤ 45° if neck length < 10 mm	≤ 45°	≤ 45°	≤ 90°

Abbreviations: AAA, abdominal aortic aneurysm; SMA, superior mesenteric artery.
*CE Mark approved.
†CE Mark and US Food and Drug Administration (FDA) approved.
‡Not yet CE Mark or FDA approved; currently in an active US pivotal study.

Undoubtedly, EVAR represents a tremendous advance in the treatment of AAAs and has provided significant benefit to many patients. However, if the widespread application of this technique continues to grow in patients with unfavorable anatomy, the benefits of EVAR may be offset by increased rates of treatment failure, costly reinterventions, and the potential for late aneurysm rupture. Endovascular technologies must continue to evolve so that patients with anatomy that is disadvantageous for currently available devices can be treated more effectively.

NEXT-GENERATION DEVICES

Next-generation fenestrated and branched EVAR devices appear to offer a more durable repair option for patients with compromised sealing zones for standard EVAR devices. The Zenith fenestrated AAA endovascular graft (Cook Medical) received US Food and Drug Administration approval in April 2012 for the treatment of short-neck infrarenal and juxtarenal AAAs. Results of a prospective multicenter trial demonstrated the safety and efficacy of the device, with a 100% technical success rate and mean follow-up of 37 months.[27] Five-year survival was 95% ± 4%, with targeted renal artery primary and secondary patency rates of 81% ± 5% and 97% ± 2%, respectively. The authors note that these results require a carefully selected patient population and experienced centers. For juxtarenal AAAs, the Zenith p-branch standard fenestrated device (Cook Medical) has been shown to have excellent technical success and outcomes in the perioperative period, with the added advantage of application to ruptured AAAs, given its standardized configurations and off-the-shelf availability.[28]

The PYTHAGORAS trial evaluated the Aorfix device (Lombard Medical, Inc.), which extended traditional IFU to include aneurysms with severe neck angulation.[29] Mortality rates up to 2 years postoperatively were comparable between the open repair control group and all of the EVAR groups (standard angle, high angle, and severe angle); however, there was a fourfold increased relative risk of graft migration for necks that demonstrated > 10% increase in diameter at follow-up.

Newer-generation EVAR devices have been developed that seal in novel manners rather than extend the seal zone proximally (Table 1). The Nellix endovascular aneurysm sealing system (Endologix, Inc.) uses a biocompatible copolymer injected into an endobag that surrounds the endograft limbs, which is intended to seal the device into position and reduce the incidence of type II endoleaks.[30] Initial results demonstrated a 100% technical success rate with low morbidity and mortality; type II endoleaks were noted in 5.4% of patients on 30-day follow-up, but long-term rates were not reported.[30] Another early report showed similar technical success and an 8% incidence of limb

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thrombosis.[31] The Ovation iX abdominal stent graft system (TriVascular, Inc.) addresses challenging aortic anatomy by using a network of channels and inflatable sealing rings at the proximal seal that are inflated at deployment to conform to the neck.[32] The 1-year treatment success rate was 97%, with a 34% incidence of type II endoleak on imaging.[32] These novel devices may play a role in expanding amenable anatomy with different, more liberal IFU requirements. More time and data are necessary to make definitive conclusions.

CONCLUSION

Over the last 2 decades, countless patients have benefitted from a minimally invasive approach to the treatment of AAAs. In an exceptionally brief span of time, vascular surgeons have developed and implemented the necessary skill set required to provide EVAR to patients safely, with extremely low perioperative mortality. In order to treat patients with more complex anatomy and to prevent late AAA sac enlargement and rupture, continued device development with a focus on durability is imperative. Next-generation EVAR devices, such as the highly promising branched and fenestrated solutions, will expand the anatomic criteria suitable for successful EVAR. However, with standard EVAR technology, careful patient selection, informed by an awareness of the risks of deviation from device IFU, is critical for successful long-term patient outcomes. ■

Adapted from Schanzer A, Messina LM. Two decades of endovascular abdominal aortic aneurysm repair: enormous progress with serious lessons learned. J Am Heart Assoc. *2012;1:e000075.*

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