From the Society for Vascular Surgery

Characterization and outcomes of reinterventions in Food and Drug Administration-approved versus trial endovascular aneurysm repair devices

Alexander S. Fairman, MD, Grace J. Wang, MD, Benjamin M. Jackson, MD, Paul J. Foley, MD, Scott M. Damrauer, MD, Venkat Kalapatapu, MD, Michael A. Golden, MD, *and* Ronald M. Fairman, MD, *Philadelphia, Pa*

ABSTRACT

Objective: Published rates of reintervention after endovascular aneurysm repair (EVAR) range from 10% to 30%. We evaluated a single university center's experience with reinterventions in the context of Food and Drug Administration (FDA)-approved and trial devices.

Methods: Retrospective data collection was performed for patients who underwent infrarenal EVAR and required reintervention from 2000 to 2016. Trial devices included those used in FDA feasibility and pivotal trials. Time-to-event analysis was performed using Cox regression. Predictors of mortality and explantation were evaluated using logistic regression; survival analysis was performed using Kaplan-Meier methods.

Results: From 2000 to 2016, there were 1835 EVARs performed, and 137 patients (116 men; mean age, 72.2 ± 10.0 years) underwent reintervention with a mean aneurysm size of 5.9 ± 1.2 cm. The median follow-up was 5 years with an overall survival of 70.1%. The overall reintervention rate was 7.5%. FDA-approved devices had a reintervention rate of 6.4%, whereas trial devices had a rate of 14.4% ($P < .001$). For all devices, the most common cause of reintervention was type II endoleak (52.5%), followed by type I endoleak (18.2%), type III endoleak (9.5%), limb kink (7.3%), iliac occlusive disease (5.8%), endotension (1.5%), and other. The overall mean time to first reintervention was 2.3 ± 2.5 years, and univariate Cox regression identified male gender (hazard ratio, 1.91; 95% confidence interval [CI], 1.17-3.10; $P = .010$) and age at the time of EVAR (hazard ratio, 1.03; 95% CI, 1.01-1.05; $P = .006$) as risk factors for time to first reintervention. Among patients requiring reintervention, the mean number of reinterventions for trial devices was significantly greater than that for FDA-approved devices (2.18 vs 1.65; $P = .01$). Trial devices requiring reintervention had a nearly threefold higher odds for the need for more than two reinterventions (odds ratio, 2.88; 95% CI, 1.12-7.37; $P = .034$). Trial device, cause of reintervention, and type of reintervention were not predictive of the need for explantation or mortality, but the number of reinterventions was significantly associated with the need for explantation (odds ratio, 1.86; 95% CI, 1.17-2.96; $P = .012$). EVAR device and the need for explantation did not have an impact on mortality.

Conclusions: Despite the rigorous nature of patient enrollment in clinical trials and the development of newer iterations of investigational devices, patients undergoing EVAR with trial devices are more likely to undergo a greater number of reinterventions than with FDA-approved devices. Although mortality and the need for explantation were not significantly associated with trial devices, the finding of a greater number of reinterventions highlights the need to properly inform patients willing to partake in investigational device trials. (J Vasc Surg 2017;■:1-9.)

Since its introduction into the field of vascular surgery in 1991, endovascular aneurysm repair (EVAR) of abdominal aortic aneurysms (AAAs) has quickly gained acceptance as a minimally invasive alternative to open AAA repair. Despite studies demonstrating early benefit in terms of morbidity and mortality compared with open repair, reinterventions remain the Achilles heel after EVAR, with published rates ranging from 10% to 30%.[1-8] Assessment of these reinterventions is essential in understanding the causes of treatment failure, the contribution of device design, and the modes of improving the next generation of devices.

Throughout the early years of EVAR, numerous trials and iterations of commercial devices have entered the market, with some withdrawn because of a variety of problems. Yet, few argue that trial devices have been crucial for advancing the field to correct previous device failures and to treat challenging aortic anatomy for patients who are not ideal candidates for open repair.

From the Division of Vascular Surgery and Endovascular Therapy, Hospital of the University of Pennsylvania.

Author conflict of interest: none.

Presented during the aortic plenary session at the 2017 Vascular Annual Meeting of the Society for Vascular Surgery, San Diego, Calif, May 31-June 3, 2017.

Correspondence: Alexander S. Fairman, MD, Department of Surgery, Hospital of the University of Pennsylvania, 3400 Spruce St, 4 Silverstein Pavilion, Philadelphia, PA 19104 (e-mail: fairmana@uphs.upenn.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2017.08.058

Moreover, the introduction of new devices depends on the participation of patients in trials now when there are more than five Food and Drug Administration (FDA)-approved devices on the market and the technology for these contemporary devices is relatively stable. From the perspective of the patient, the vascular surgeon, and the FDA, there is a need to know of the potential risks of trial devices. Whereas there is a surfeit of data reporting on reinterventions after EVAR, a study focused on the comparison of reinterventions in trial vs FDA-approved devices has not been performed to date. This study was undertaken to describe the nature of reinterventions and outcomes after EVAR performed at a tertiary care institution with a breadth of experience in performing EVAR in the context of clinical trials and with commercially available devices.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, single-center cohort study
- **Take Home Message:** Reintervention rate at a median follow-up of 5 years was 7.5% after 1835 endovascular aneurysm repairs, significantly more frequent when trial devices were used than with Food and Drug Administration (FDA)-approved devices (14.4% vs 6.4%). Mortality and the need for explantation were not associated with trial devices.
- **Recommendation:** This study suggests that patients undergoing endovascular aneurysm repair with a trial device should be informed that they are more likely to require reinterventions than those receiving an approved device.

METHODS

We performed a retrospective review of patients undergoing reintervention after infrarenal EVAR from 2000 to 2016 at the University of Pennsylvania. Fenestrated or branched devices were excluded, whereas both trial (FDA feasibility and pivotal trials) and FDA-approved devices were included in this analysis.

For patients treated with commercially available devices, decisions about EVAR device selection were made by the attending surgeon. Follow-up after EVAR generally included computed tomography angiography imaging at 1 month, 6 months, and yearly intervals. For those with renal insufficiency, abdominal ultrasound or non-contrast-enhanced computed tomography scan of the abdomen and pelvis was performed. Any additional studies required of trial patients were done in accordance with those guidelines outlined by the particular trial.

Trial devices were compared with FDA-approved devices with respect to the following outcomes: type and cause of reintervention, mean number of reinterventions per device, time to each reintervention, freedom from explantation, and overall survival.

Continuous variables were evaluated graphically and using the skewness/kurtosis test to confirm normality. Demographics of the patients were analyzed and compared between groups using Student *t*-test for continuous variables and χ^2 analysis for categorical variables. Time-to-event analysis for reintervention was performed using Cox regression. Predictors of mortality and explantation were evaluated using logistic regression; survival analysis for freedom from explantation and freedom from all-cause mortality was performed using Kaplan-Meier methods. In all analyses, a P value $\leq .05$ was used to determine statistical significance. All statistical analyses were performed using Stata version 13 (StataCorp LP, College Station, Tex). This project was reviewed and approved by the University of Pennsylvania Institutional Review Board under expedited review and qualified for waiver of informed consent.

RESULTS

Demographics of patients and device specifics. During the study period, 1835 patients underwent index EVAR at the University of Pennsylvania. Of these, 137 patients underwent reintervention, and these composed our study group. The cohort comprised predominantly men, including 116 men with a mean aneurysm size of 5.9 ± 1.2 cm and an average age of 72.2 ± 10.0 years. Patients whose index EVAR was performed with a trial device did not differ significantly from patients treated with FDA-approved devices with respect to medical comorbidities, although trial patients were younger (68.6 ± 9.6 vs 73.6 ± 9.8 years; $P < .010$), were more frequently male (94.7% vs 80.8%; $P = .043$), and had a trend toward smaller aneurysms treated (5.6 ± 0.8 vs 5.9 ± 1.3 cm; $P = .158$). Coronary artery disease was present in a substantial number of patients overall (trial device, 60.5%; FDA-approved device, 55.1%; $P = .213$), whereas a smaller percentage had chronic obstructive pulmonary disease (trial device, 18.4%; FDA-approved device, 16.3%; $P = .768$). Chronic renal insufficiency was present in 10.5% of the trial group and 18.4% of the FDA-approved group ($P = .108$). Details of the patients' demographics for both trial and FDA-approved devices are summarized in Table I. Trial devices were kept deidentified for confidentiality purposes. FDA-approved devices included Ancure (Guidant, Menlo Park, Calif); Excluder (W. L. Gore & Associates, Flagstaff, Ariz); AneuRx, Talent, and Endurant (Medtronic, Santa Rosa, Calif); Powerlink and AFX (Endologix, Irvine, Calif); and Zenith (Cook Medical, Bloomington, Ind).

Reinterventions. The reintervention rate for all EVARs performed from 2000 to 2016 was 7.5%. Trial devices had a greater reintervention rate than FDA-approved