VASCULAR LITERATURE HIGHLIGHTS

SAFE-AAA Supports Initiation of Prospective Surveillance Program to Monitor Stent Graft–Related Safety Events

In an analysis comparing the safety of unibody and nonunibody aortic stent grafts implanted for intact abdominal aortic aneurysms (AAAs), Secemsky et al found that unibody AAA devices failed to meet noninferiority testing as compared with nonunibody devices. The study was designed in conjunction with the FDA. Results were published online in *Circulation*.[1]

The SAFE-AAA study aimed to longitudinally assess the safety of unibody aortic stent grafts compared with other approved endografts. Medicare fee-for-service beneficiaries aged ≥ 66 years were included in the study if they underwent endovascular aneurysm repair (EVAR) for an intact AAA with an aortic stent graft from August 1, 2011 to December 17, 2017, as determined by CPT claims codes. Patients were excluded if they underwent concomitant fenestrated aortic repair or placement of both unibody and nonunibody devices in the same procedure. A subgroup analysis was performed for patients who underwent stent graft placement between February 22, 2016 to December 31, 2017, to capture safety data after launch of the commercially available AFX2 system (Endologix, Inc.).

The primary endpoint was a composite of postindex procedure aneurysm rupture, aortic reintervention (graft relining, endograft extension, conversion to open repair), or all-cause mortality after EVAR. This was evaluated through December 31, 2019. Secondary endpoints included individual components of the primary endpoint, as well as perioperative morbidity and mortality.

KEY FINDINGS

- Unibody AAA devices failed to meet noninferiority testing as compared with nonunibody AAA devices through a median 3.4-year follow-up, driven by higher risks of all-cause mortality, conversion to open repair, and late aneurysm rupture with unibody devices.
- Sensitivity analyses, including falsification endpoints, supported the results of the primary analysis.
- A prespecified subgroup analysis of patients treated from February 22, 2016 to December 31, 2017, corresponding with the launch of the currently available AFX2 device, suggested persistent ongoing harm with unibody devices.
- Based on these and results of other studies and device safety data, a prospective, longitudinal surveillance program should be instituted to monitor safety events related to aortic endografts.

Imbalances in observed characteristics were adjusted for with inverse probability weighting, and the effects of confounding factors were assessed with sensitivity analyses, including falsification endpoint testing for hospitalization for congestive heart failure, stroke, and pneumonia.

ENDOVASCULAR TODAY ASKS…

We asked lead investigator Eric Secemsky, MD, with Beth Israel Deaconess Medical Center and Harvard Medical School in Boston, Massachusetts, about partnering with the FDA on the study design, use of claims-based analyses, and implications of the study's results.

One of the unique elements of this study is the involvement of FDA representatives among the investigators and authorship. How did the research partnership with FDA come to start?

This was a great partnership with FDA Officers from the office of the Center for Devices and Radiological Health. Our group at the Smith Center for Outcomes Research has

worked closely together with this group on the paclitaxel-coated device safety assessment, including the ongoing SAFE-PAD study (NCT04496544). As such, when this panel was being designed, we discussed what other sources could help identify longitudinal data among patients treated with unibody grafts, as many of the concerning studies had low sample sizes with short follow-up. Uniquely, the unibody stent grafts manufactured by Endologix have a specific CPT code to identify their use versus other grafts, which allowed for the identification of these devices in Medicare data and the foundation for the SAFE-AAA analysis.

Long-term durability is an increasingly focal topic in the field of aortic interventions for all implanted grafts, and the costs to conduct premarket approval trials with longer follow-up and/or conventional postmarket surveillance studies are challenging if not prohibitive. However, the findings of your work and other studies point to the need for longitudinal follow-up. What are some of the necessities any such surveillance program must include?

This is a critical and ongoing question. Key aspects include the ability to track a broad group of patients treated at all hospital types throughout the country. It is also imperative to require nonselective enrollment, as many registries and postmarket studies may fail to capture device implants if failures or adverse events occur and are not reported or excluded. There is a need to identify certain details at the time of implant, including aneurysm anatomy, device type, and whether this is consistent with the instructions for use directions. Lastly, we have a major need for understanding how postimplantation surveillance occurs, including how often patients are seen in follow-up and surveillance imaging for endoleak detection. Obviously, costs and feasibility are key and need to be considered when constructing any surveillance program.

Beyond the specific findings of the study, what is the potential for claims-based review of aortic endografts to assist in evaluating long-term outcomes in this field? How might claims-based analysis be merged or integrated with other registries, such as the Vascular Quality Initiative (VQI)? What are the inherent confounders in claims-based registries (eg, lack of specific codes for each device type), and can they be overcome or accounted for in another way?

The VQI has done a phenomenal job creating a registry that can capture many of these requirements discussed in the previous question. The strengths of the registry included the detailed data on the stent grafts implanted. The only caution is to ensure contributing centers from across the country and clinical settings are included, as well as procedures performed by nonsurgical operators. We have also discussed using case report forms with linked Medicare data as another vehicle to track broad device implantation, as this can supplement the granularity missing with insurance claims data and also create a system with limited resources and costs. These case report forms, which can be completed at the time of implantation and provide the procedural and anatomic data listed previously, could then be linked to Medicare data to assess follow-up patterns and outcomes.

Of 103,179 total patients, 87,163 (84.5%) from 2,146 hospitals were included for analysis, with 11,903 (13.7%) treated with a unibody device (mean age, 77.0 ± 6.7 years; 21.1% female; 93.5% White). Median follow-up was 3.3 and 3.4 years (maximum, 8.4 years for both) for patients treated with a unibody device versus a nonunibody device, respectively. At 8.4 years, the cumulative incidence of the primary outcome was 73.4% for unibody device treatment and 65.0% for nonunibody device treatment (adjusted hazard ratio [HR], 1.19; 95% CI, 1.15-1.22). Patients treated with unibody devices had a greater risk of all components of the primary endpoint as compared with nonunibody device–treated patients, including a greater risk of all-cause mortality, conversion to open repair, graft relining, endograft extension, and late aneurysm rupture.

In the subgroup analysis, 23,386 patients (26.8% of the total cohort) were treated with a stent graft, with 20,482 (87.6%) treated with a nonunibody device and 2,904 (12.4%) treated with a unibody device, the majority of which were AFX2 grafts. At 3.9 years, the cumulative incidence of the primary endpoint was 37.5% and 32.7% in the unibody and nonunibody device groups, respectively (HR, 1.06; 95% CI, 0.98-1.14).

Investigators concluded that based on these and results of other studies and device safety data, a prospective, longitudinal surveillance program should be urgently instituted to monitor safety events related to aortic endografts. ■

1. Secemsky ES, Song Y, Sun T, et al. Comparison of unibody and non-unibody endografts for abdominal aortic aneurysm repair in Medicare beneficiaries. Circulation. Published online March 3, 2023. doi: 10.1161/CIRCULATIONAHA.122.062123