From the Western Vascular Society

Adherence to endovascular aortic aneurysm repair device instructions for use guidelines has no impact on outcomes

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Objective: **Prior reports have suggested unfavorable outcomes after endovascular aortic aneurysm repair (EVAR) performed outside of the recommended instructions for use (IFU) guidelines. We report our long-term EVAR experience in a large multicenter registry with regard to adherence to IFU guidelines.**

Methods: **Between 2000 and 2010, 489 of 1736 patients who underwent EVAR had preoperative anatomic measurements obtained from the M2S, Inc, imaging database (West Lebanon, NH). We examined outcomes in these patients with regard to whether they had met the device-specific IFU criteria. Primary outcomes were all-cause mortality and aneurysm-related mortality. Secondary outcomes were endoleak status, adverse events, reintervention, and aneurysm sac size change.**

Results: **The median follow-up for the 489 patients was 3.1 years (interquartile range, 1.6-5.0 years); 58.1% (n = 284) had EVAR performed within IFU guidelines (IFU-adherent group), and 41.9% (n = 205) had EVAR performed outside of IFU guidelines (IFU-nonadherent group). Preoperative anatomic data showed that 62.4% of the IFU-nonadherent group had short neck length, 10.2% had greater angulation than recommended, 7.3% did not meet neck diameter criteria, and 20% had multiple anatomic issues. A small portion (n = 49; 10%) of the 489 patients were lost to follow-up because of leaving membership enrollment (n = 28), moving outside the region (n = 10), or discontinuing image surveillance (n = 11). There was no significant difference in any of the primary or secondary outcomes between the IFU-adherent and IFU-nonadherent groups. Aneurysm sac size change at any time point during follow-up also did not differ significantly between the two groups. A Cox proportional hazard model showed that IFU nonadherence was not predictive of all-cause mortality (hazard ratio, 1.0; $P = .91$). Similarly, IFU nonadherence was not identified as a risk factor for aneurysm-related mortality or adverse events in stepwise Cox proportional hazards models.**

Conclusions: **In our cohort of EVAR patients with detailed preoperative anatomic information and long-term follow-up, overall mortality and aneurysm-related mortality were unaffected by IFU adherence. In addition, rates of endoleak and reintervention after initial EVAR were similar, suggesting that lack of IFU-based anatomic suitability was not a driver of outcomes. (J Vasc Surg 2015;61:1151-9.)**

Since its first description in 1991, endovascular aortic aneurysm repair (EVAR) has become a commonplace and well-accepted alternative to open abdominal aortic aneurysm (AAA) repair.[1,2] Proper patient selection based on anatomic criteria has become critical to ensuring satisfactory long-term results. To that end, each endovascular device manufacturer publishes an instructions for use (IFU) guideline that specifies anatomic criteria for "correct" use of the EVAR device. These recommendations are made on the basis of preclinical engineering assessments and clinical study results. The guidelines specify appropriate aortic neck diameter, aortic neck length, aortic neck angle, and iliac artery morphology. Many clinicians believe that outcomes after EVAR largely depend on whether the devices are used in accordance with the IFU guidelines. A recent paper documented the incidence of IFU nonadherence in registry data sets but had notable gaps in availability of device-specific and patient outcome data.[3] We analyzed outcomes of EVAR patients in a longitudinal registry for whom detailed preoperative anatomic data were available, with the objective of determining whether IFU adherence affects outcomes after EVAR.

METHODS

Kaiser Permanente Northern California (KPNC) is an integrated health care delivery system that offers multispecialty care for more than 3 million members. Implementation of

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digital health records has allowed access to all arenas of clinical information. Data for 1736 patients who underwent EVAR procedures in 17 KPNC medical centers were collected in a clinical registry from 2000 to 2010. This study protocol was approved by the KPNC Institutional Review Board and was funded for one calendar year in 2011 by the KPNC Community Benefit Research Grant Program. This in-depth evaluation of IFU adherence was funded by the KPNC Residency Programs. Informed consent was waived by the local Institutional Review Board, given that the study was retrospective and the data de-identified for analysis.

Data collection and follow-up. Beginning in 2000, relevant clinical information for patients undergoing EVAR was collected by trained research nurses, with December 31, 2010, as the last follow-up date. Data collected from electronic medical records included baseline preoperative demographic data and clinical characteristics (sex, age, aneurysm sac size, comorbidities [coronary artery disease, diabetes mellitus, hypertension, hyperlipidemia, and peripheral vascular disease], smoking status, and statin history). Device type and operative details were collected from the operative report and device entry forms. Information on adjunctive maneuvers (placement of additional aortic cuffs or stents, graft limb extensions, exploratory laparotomy/conversion, renal stenting/snorkel, and femoral-femoral bypass) was also collected. Decisions regarding indications for surgery, suitability for endovascular repair, device selection, and need for secondary intervention were made at the discretion of the operating surgeon. Data recorded in our registry during the follow-up period were also collected and included aneurysm rupture, major adverse event (ie, conversion to open repair, major embolic event, graft infection requiring explantation, device migration, loss of device patency requiring reintervention, and other miscellaneous complications that substantially affected clinical outcome), types of reintervention, AAA sac size, endoleak, leaving KPNC membership, moving outside the region, and mortality.

Postoperative follow-up varied across medical centers but generally involved a 1-month postoperative computed tomography (CT) scan followed by serial CT imaging at regular intervals ranging from every 3 months to every 12 months as dictated by clinical circumstances. Imaging was accompanied by clinical follow-up. As follow-up progressed, there was a considerable amount of variability regarding the timing, modality, and use of contrast material in CT imaging. However, the preoperative and first postoperative imaging generally consisted of CT scans with and without contrast material and arterial and venous phases with 1.25-mm slices. In the absence of sac growth or endoleak, intravenous contrast material was sometimes withheld for subsequent examinations at the discretion of the treating physician. Device migration was reported if it required intervention or if adequate seal was lost, usually when reduced to <10 mm of the circumferential apposition length. Endoleak was classified according to established reporting standards[4] and was typically detected by CT scan, confirmatory angiography, or, more rarely, ultrasound.

Determination of adherence to IFU guidelines. Our clinical EVAR registry was cross-referenced with data from the M2S, Inc, imaging repository (West Lebanon, NH). The M2S anatomic registry (hereafter termed M2S) comprehensively assesses detailed anatomic data from CT scans submitted to them from the clinician. Using standardized algorithms, M2S creates three-dimensional computer models from CT images of aortic aneurysms with semiautomated quantification of multiple measurements of interest. Measurements of interest corresponded with major determinants of IFU adherence and therefore primarily involved the proximal infrarenal aortic neck (eg, neck length, diameter, and angulation).

This in-depth study was a subset analysis limited to patients whose initial EVAR procedures had relevant preoperative M2S analysis of CT imaging. These anatomic data and corresponding measurements were then used to determine adherence to IFU guidelines. Patients whose initial EVAR procedures were performed within the IFU guidelines were classified as the IFU-adherent group, and those outside the IFU guidelines as the IFU-nonadherent group. The evaluation of specific guidelines varied according to the specific device implanted.

Outcome variables. The primary outcomes were all-cause mortality and aneurysm-related mortality (ARM); the latter was defined as death within 30 days of the initial EVAR or of a secondary procedure related to aneurysm rupture or a major adverse event. Secondary outcome variables examined were type I or type III endoleak, major adverse events, need for reintervention, and change in aneurysm sac size over time. Sac size was assessed at several time points during follow-up (ie, 2 months, 6 months, 9 months, 12 months, 18 months, 2 years, 3 years, 4 years, and 5 years after the initial EVAR). Sac size measurements were accepted if performed within 1.5 months before or after each time point within the first 12 months or within 3 months before or after time points after 12 months.

Statistical methods. Rates of categorical demographic (sex, age groups, racial/ethnic groups) and clinical characteristics (comorbidities, smoking status, statin history, preoperative embolization, adjunctive maneuver or bifurcated graft during the initial EVAR procedure, and aneurysm sac growth status at various time points during follow-up) were compared between the IFU-adherent and IFU-nonadherent groups with χ^2 tests or Fisher exact tests as appropriate. Preoperative AAA sac size, age at initial EVAR, and M2S anatomic data (ie, neck length, neck diameter, neck angle, and femoral diameter) were not normally distributed; therefore, nonparametric Wilcoxon-Mann-Whitney tests were used to compare medians. Survival analysis was performed with the Kaplan-Meier method to estimate the survival function in 489 patients with M2S stratified by IFU guideline status (adherence vs nonadherence), and survival functions were compared between these two groups by the log-rank test.

Before fitting of the multivariable regression models, bivariate analyses were performed to evaluate the association of risk factors of interest (IFU adherence, sex, age, preoperative AAA sac size, history of statin, comorbidities, smoking status, preoperative embolization, operative