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Fenestrated endovascular aneurysm repair is associated with lower perioperative morbidity and mortality compared with open repair for complex abdominal aortic aneurysms

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ABSTRACT

Objective: The Zenith Fenestrated Endovascular Graft (ZFEN; Cook Medical, Bloomington, Ind) has expanded the anatomic eligibility of endovascular aneurysm repair (EVAR) for complex abdominal aortic aneurysms (AAAs). Current data on ZFEN mainly consist of single-institution experiences and show conflicting results. Therefore, we compared perioperative outcomes after repair using ZFEN with open complex AAA repair and infrarenal EVAR in a nationwide multicenter registry.

Methods: We identified all patients undergoing elective AAA repair using ZFEN, open complex AAA repair, and standard infrarenal EVAR between 2012 and 2016 within the American College of Surgeons National Surgical Quality Improvement Program targeted vascular module. Open complex AAA repairs were defined as those with a juxtarenal or suprarenal proximal AAA extent in combination with an aortic cross-clamping position that was above at least one renal artery. The primary outcome was perioperative mortality, defined as death within 30 days or within the index hospitalization. Secondary outcomes included postoperative renal dysfunction (creatinine concentration increase of >2 mg/dL from preoperative value or new dialysis), occurrence of any complication, procedure times, blood transfusion rates, and length of stay. To account for baseline differences, we calculated propensity scores and employed inverse probability-weighted logistic regression.

Results: We identified 6825 AAA repairs—220 ZFENs, 181 open complex AAA repairs, and 6424 infrarenal EVARs. Univariate analysis of ZFEN compared with open complex AAA repair demonstrated lower rates of perioperative mortality (1.8% vs 8.8%; $P = .001$), postoperative renal dysfunction (1.4% vs 7.7%; $P = .002$), and overall complications (11% vs 33%; $P < .001$). In addition, fewer patients undergoing ZFEN received blood transfusions (22% vs 73%; $P < .001$), and median length of stay was shorter (2 vs 7 days; $P < .001$). After adjustment, open complex AAA repair was associated with higher odds of perioperative mortality (odds ratio [OR], 4.9; 95% confidence interval [CI], 1.4-18), postoperative renal dysfunction (OR, 13; 95% CI, 3.6-49), and overall complication rates (OR, 4.2; 95% CI, 2.3-7.5) compared with ZFEN. Compared with infrarenal EVAR, ZFEN presented comparable rates of perioperative mortality (1.8% vs 0.8%; $P = .084$), renal dysfunction (1.4% vs 0.7%; $P = .19$), and any complication (11% vs 7.7%; $P = .09$). Furthermore, after adjustment, there was no significant difference between the odds of perioperative mortality, postoperative renal dysfunction, or any complication between infrarenal EVAR and ZFEN.

Conclusions: ZFEN is associated with lower perioperative morbidity and mortality compared with open complex AAA repair, and outcomes are comparable to those of infrarenal EVAR. Long-term durability of ZFEN compared with open complex AAA repair warrants future research. (J Vasc Surg 2019;69:1670-8.)

Keywords: Aortic diseases; AAA; Fenestration; FEVAR; Treatment outcome

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Since the introduction of endovascular aneurysm repair (EVAR) in 1991, the treatment paradigm has shifted from primarily open surgery to endovascular repair; currently, EVAR is the predominant treatment modality for infrarenal abdominal aortic aneurysms (AAAs).[1] Several clinical trials and large retrospective studies have demonstrated the benefit of infrarenal EVAR over open surgical repair in terms of perioperative mortality and complications.[2-4] However, complex AAAs—defined as those with a juxtarenal or suprarenal proximal extent—are more challenging for endovascular repair because of involvement or proximity of renal arteries. The proportion of AAA repairs that have a juxtarenal proximal extent has been estimated between 16% and 42% of all AAA repairs, whereas suprarenal AAAs are less common.[5,6]

Ongoing improvements in endovascular techniques and technologies have allowed surgeons to treat selected complex AAAs, including chimney/snorkel, branched, and fenestrated EVAR (FEVAR) devices. Custom-made FEVAR and physician-modified endografts allow the incorporation of visceral and renal arteries through fenestrations or scallops in the graft fabric, through which bare-metal or covered stents can be placed.[7-10] The Zenith Fenestrated Endograft (ZFEN; Cook Medical, Bloomington, Ind) received approval by the Food and Drug Administration in 2012 and remains the only such device currently approved in the United States. ZFEN devices are custom manufactured for each patient's specific anatomy and can contain up to three fenestrations or scallops. Use of ZFEN increased rapidly after its introduction, resulting in a ninefold increase in orders between 2012 and 2015.[11]

Comparisons between ZFEN and open complex AAA repair are limited and show conflicting results. One study reported lower mortality and morbidity after ZFEN, whereas another study showed equivalent results, and an international cohort study actually showed higher mortality with fenestrated repairs.[12-14] However, these studies were from the relatively early fenestrated repair experience, and the studies that demonstrated equivalent or worse mortality with fenestrated repairs were from high-volume open repair centers.[12,13] Previous multicenter database studies comparing endovascular with open repair of complex AAAs showed lower rates of mortality and morbidity after endovascular repair but were unable to distinguish FEVAR from other endovascular modalities.[15,16]

Therefore, we compared perioperative mortality and postoperative complications in patients receiving ZFEN and patients treated with open surgical repair for complex AAAs in a large nationwide registry. In addition, we evaluated differences in outcomes between ZFEN treatment and standard infrarenal EVAR to evaluate how treatment outcomes with ZFEN relate to the more widely used endovascular treatment of infrarenal AAAs.

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective analysis using the American College of Surgeons National Surgical Quality Improvement Program targeted vascular module.
- **Key Findings:** This study analyzed 30-day or in-hospital outcomes after 220 abdominal aortic aneurysm (AAA) repairs with Zenith Fenestrated endovascular aneurysm repair (EVAR) in a nationwide registry. Compared with 181 open juxtarenal AAA repairs and 6424 infrarenal EVARs, fenestrated EVAR was associated with lower perioperative morbidity and mortality compared with open juxtarenal AAA repair, but outcomes were comparable to those of infrarenal EVAR.
- **Take Home Message:** ZFEN is associated with lower perioperative morbidity and mortality compared with open complex AAA repair, and early outcomes are comparable to those of infrarenal EVAR.

METHODS

Data source. The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) is a national registry that contains prospectively collected clinical data from participating hospitals in the United States. The NSQIP includes >270 variables, including demographics, comorbidities, procedural characteristics, and postoperative outcomes, collected in the 30 days after the index procedure. Data collection is performed by trained clinical nurses and data abstractors. The reliability of the NSQIP registry has been validated previously.[17,18]

The vascular targeted module of the NSQIP was introduced in 2012 and captures additional procedure-specific data, with >60 hospitals participating in AAA repair data collection. Further information about the NSQIP data set is available at www.facs.org/quality-programs/acs-nsqip. The Institutional Review Board of Beth Israel Deaconess Medical Center approved this study and waived the need for informed consent because of the deidentified nature of the data set.

Cohort of patients. We identified all patients undergoing EVAR (both with and without visceral vessel involvement) or open complex AAA repairs within the targeted NSQIP registry between 2012 and 2016 using the *Current Procedural Terminology* (CPT) codes. Endovascular repairs were identified with CPT codes 34800, 34802, 34803, 34804, 34805, and 34825 and stratified into ZFEN patients (identified by the variable coding for the main body device) and infrarenal EVAR (patients who underwent repair for an aneurysm with an infrarenal extent and received a device other than ZFEN). Open complex AAA repair patients were identified as those with the CPT code 35091 in combination with a proximal aneurysm extent that was juxtarenal (defined by the NSQIP as AAAs that do not involve renal arteries but owing to proximity would require clamping above renal arteries), pararenal (defined as AAAs that involve the origin of the renal arteries), or suprarenal (defined as AAAs that begin above at least one renal artery but below the visceral segment). Complex open repairs were included only if aortic cross-clamping position was above at least one renal artery.

Patients who underwent nonelective repair were excluded (n = 2315 [22.6%]), as were patients with thoracoabdominal aneurysms or thoracic repairs (n = 38 [0.4%]) and procedures with an indication for surgery other than aneurysm diameter or symptomatic aneurysm (eg, dissection; n = 643 [6.3%]). EVAR devices for infrarenal repair that were used <100 times were excluded to avoid including experimental devices and to improve generalizability (n = 434 [4.2%]). Last, infrarenal EVARs with a concurrent CPT code for visceral vessel repair or open repair were excluded (n = 8 [0.1%]).

Clinical and outcome variables. Baseline characteristics included patients' demographics, comorbid conditions, and anatomic and procedural characteristics. Age was a continuous variable; however, patients older than 89 years in the NSQIP are recorded as 90 years old to maintain deidentification. Estimated glomerular filtration rate (eGFR) was calculated with the Chronic Kidney Disease Epidemiology Collaboration equation.[19] Preoperative renal function was categorized as eGFR ≥60 mL/min, eGFR 30 to 60 mL/min, eGFR <30 mL/min, and patients who were on dialysis (regardless of preoperative eGFR). As anatomic distinction between the NSQIP's definition of pararenal and suprarenal AAA extents could be subject to interpretation by the data abstractors and both extents are clinically similar (both would require renal artery bypass in case of open surgery) and are commonly considered the same, we combined those extents and refer to them as suprarenal.

The primary outcome of this study was perioperative mortality, defined as death within 30 days or within the index hospitalization. To assess the impact of proximal AAA extent on mortality, we additionally analyzed perioperative mortality for each proximal AAA extent for ZFEN and open repair. Secondary outcomes were perioperative complications (defined as occurrence of any complication within 30 days) and postoperative renal dysfunction (defined as an absolute creatinine concentration increase of >2 mg/dL from preoperative value [predefined variable] or new dialysis within 30 days), procedure time, length of stay (LOS), and intraoperative and postoperative blood transfusions. Further evaluation of individual complications included unplanned reintubations, failure to be weaned from ventilator within 48 hours, pneumonia, unplanned reoperation, myocardial infarction or cardiac arrest, septic shock, and ischemic colitis. All outcomes were compared between ZFEN vs open complex AAA repair and ZFEN vs infrarenal EVAR.

Statistical analysis. Categorical variables are presented as count and percentage and continuous variables as median plus interquartile range as not all variables were normally distributed. Differences in characteristics between groups were compared using χ^2 or Fisher exact tests where appropriate for categorical variables, and Mann-Whitney *U* tests were used for continuous variables.

The low event rates for the primary outcomes precluded robust multivariable adjustment through standard logistic regression. Consequently, we chose instead to calculate propensity scores and to employ inverse probability weighting to account for nonrandom assignment to treatments. To calculate propensity scores, we built logistic regression models where the outcome of interest is the treatment modality.[20] We built separate models for ZFEN vs open complex AAA repair and ZFEN vs infrarenal EVAR. Covariates were selected a priori and generously introduced into the model, including age, sex, white race, Hispanic ethnicity, smoking status, body mass index, insulin-dependent diabetes, hypertension (requiring medication), congestive heart failure, preoperative dyspnea, chronic obstructive pulmonary disease, eGFR, bleeding disorders, systemic inflammatory response syndrome, chronic steroid use, any functional dependence, ≥10% weight loss within 6 months preoperatively, disseminated cancer, prior abdominal aortic surgery, AAA diameter, American Society of Anesthesiologists class, and AAA symptom status. In the model comparing ZFEN vs infrarenal EVAR, we were able to adjust for additional variables because of the availability of additional endovascular-specific variables, including percutaneous femoral access, distal AAA extent, and hypogastric embolization. Inverse probability weights were calculated using the propensity score (p) as 1/p for open surgery and infrarenal EVAR and 1/(1 − p) for ZFEN. We tested these scores for adequacy of overlap by plotting the distribution of propensity scores in the treated and untreated groups. After weighting, the standardized differences were all ≤10% (the usual threshold).[21] Two sensitivity analyses were performed: one by adding the propensity score in the multivariable model as a covariate rather than as a weight; and a second one by truncating the weights below the 5th and above the 95th percentile to adjust for extreme weights.[22]

Missing data. Variables with >2% missing data were race (13.5%), ethnicity (14.4%), eGFR (3.5%), prior abdominal aortic surgery (7.2%), and distal AAA extent (15.1%). Missing data were equally distributed between repair modalities, which allowed the missing data to be

Table I. Baseline characteristics

Characteristic	ZFEN No.	ZFEN %	Open repair No.	Open repair %	Infrarenal EVAR No.	Infrarenal EVAR %	*P* value ZFEN vs open	*P* value ZFEN vs infrarenal
No.	220		181		6424			
Age, years, median (IQR)	75 (69.5-81)		72 (67-77)		74 (68-80)		**<.001**	.22
Female sex	39	17.7	43	23.8	1144	17.8	.14	.98
White race	174	95.1	138	94.5	5187	93.1	.82	.29
Current smoker	79	35.9	87	48.1	1987	30.9	**.014**	.12
Underweight (BMI <18.5 kg/m^2)	3	1.4	3	1.7	86	1.4	1	1
Obese (BMI ≥30 kg/m^2)	68	31.1	51	28.3	2189	34.4	.55	.31
IDDM	6	2.7	4	2.2	181	2.8	1	1
Hypertension	176	80.0	145	80.1	5143	80.1	.98	.98
CHF	7	3.2	1	0.6	81	1.3	.078	**.026**
Dyspnea	45	20.5	28	15.5	1158	18.0	.2	.36
COPD	49	22.3	34	18.8	1128	17.6	.39	.072
Renal function							.16	.2
eGFR ≥60 mL/min	133	63.3	107	60.5	4086	65.8		
eGFR 30-60 mL/min	75	35.7	62	35.0	1918	30.9		
eGFR <30 mL/min	2	1.0	6	3.4	151	2.4		
On dialysis	0	0	2	1.1	50	0.8		
Any functional dependence	3	1.4	3	1.7	137	2.1	1	.63
Chronic steroid use	11	5.0	7	3.9	268	4.2	.59	.55
Prior abdominal aortic surgery	59	28.1	54	31.8	1624	27.3	.44	.79
AAA diameter, cm, median (IQR)	5.6 (5.3-6.0)		5.8 (5.5-6.5)		5.5 (5.1-5.9)		**<.001**	**<.001**
Symptomatic AAA	7	3.2	8	4.4	204	3.2	.6	1
Proximal aneurysm extent							**<.001**	**<.001**
Infrarenal	70	32.7	–	–	6424	100		
Juxtarenal	110	51.4	107	59.1	–	–		
Suprarenal	34	15.9	74	40.9	–	–		
Distal aneurysm extent							**.001**	.41
Aortic	97	54.5	99	61.9	2731	50.1		
Common iliac	59	33.1	58	36.2	2046	37.5		
External iliac	7	3.9	2	1.2	302	5.5		
Internal iliac	15	8.4	1	0.6	337	6.9		
Percutaneous femoral access	60	27.4	–	–	2502	39.0	–	**<.001**
Hypogastric artery embolization	11	5.0	–	–	368	5.7	–	.65

AAA, Abdominal aortic aneurysm; *BMI*, body mass index; *CHF*, congestive heart failure; *COPD*, chronic obstructive pulmonary disease; *eGFR*, estimated glomerular filtration rate; *EVAR*, endovascular aneurysm repair; *IDDM*, insulin-dependent diabetes mellitus; *IQR*, interquartile range; *Open repair*, open complex abdominal aortic aneurysm repair; *ZFEN*, Zenith Fenestrated endovascular aneurysm repair.
Boldface *P* values represent significance ($P \leq .05$).

inserted in the multivariable model as dummies to maintain statistical power.

All analyses were performed using Stata 15.1 (StataCorp LLC, College Station, Tex).

RESULTS

Characteristics of the patients

A total of 6825 AAA repairs were identified, of which 220 were repaired with ZFEN, 181 were open repairs for complex AAAs, and 6424 were repairs with infrarenal EVAR. Baseline characteristics are presented in Table I. Compared with patients undergoing open complex AAA repair, patients receiving ZFEN were older (75 years [interquartile range, 69.5-81 years] vs 72 years [67-77 years]; $P < .001$) and less often active smokers (36% vs 48%; $P = .014$); they had smaller aneurysm diameters (5.6 cm [5.3-6.0 cm] vs 5.8 cm [5.5-6.5 cm]; $P < .001$) and more often had an AAA extent in the internal or external iliac artery (12.3% vs 1.8%; $P = .001$).

Compared with infrarenal EVAR, patients undergoing ZFEN more often had congestive heart failure (3.2% vs

1.3%; P = .026) and a larger AAA diameter (5.6 cm [5.3-6.0 cm] vs 5.5 cm [5.1-5.9 cm]; $P < .001$), and rates of percutaneous femoral access were lower (27% vs 39%; $P < .001$).

Outcomes

ZFEN vs open complex AAA repair. Compared with patients undergoing open complex AAA repair, those who underwent ZFEN experienced lower rates of perioperative mortality (1.8% vs 8.8%; P = .001) and less often had any perioperative complication (11% vs 33%; $P < .001$; Table II). For ZFEN, perioperative mortality stratified over AAA extent was similar between extents (infrarenal, 2.9%; juxtarenal, 1.8%; suprarenal, 0%; P = .82; Table III). Perioperative mortality trended toward significance for open juxtarenal AAA repair compared with open suprarenal repair (5.6% vs 13.5%; P = .065). Postoperative renal dysfunction (creatinine concentration increase >2 mg/dL from preoperative value or new dialysis) was less common in the ZFEN group (1.4% vs 7.7%; P = .002). Total operative time was similar (235 minutes [159.5-304 minutes] vs 240 minutes [186-308 minutes]; P = .24). However, patients undergoing ZFEN less often received blood transfusions (22% vs 73%; $P < .001$) and had a shorter LOS (2 days [1-4 days] vs 7 days [6-10 days]; $P < .001$). In addition, unplanned reoperations were almost three times more common after open complex AAA repair (4.5% vs 13%; P = .003). Furthermore, patients undergoing ZFEN experienced lower rates of unplanned reintubation, failure to be weaned from ventilator within 48 hours, pneumonia, myocardial infarction or cardiac arrest, and ischemic colitis (Table II).

After adjustment, using ZFEN as the reference group, open complex AAA repair was independently associated with perioperative mortality (odds ratio [OR], 4.9; 95% confidence interval [CI], 1.4-18; P = .015), postoperative renal dysfunction (OR, 13; 95% CI, 3.6-49; $P < .001$), and any complication (OR, 4.2; 95% CI, 2.3-7.5; $P < .001$; Table IV).

ZFEN vs infrarenal EVAR. Perioperative mortality was 1.8% after ZFEN and 0.8% after infrarenal EVAR (P = .084). Patients in both cohorts experienced similar rates of overall complications (ZFEN vs infrarenal EVAR, 11% vs 7.7%; P = .09) and renal dysfunction (1.4% vs 0.7%; P = .19; Table II). Procedural time was approximately twice as long in patients undergoing ZFEN (235 minutes [159.5-304 minutes] vs 118 minutes [92-156 minutes]; $P < .001$), blood transfusions were given more frequently (22% vs 5.5%, $P < .001$), LOS was longer (2 days [1-4 days] vs 1 day [1-2 days]; $P < .001$), and more patients were reintubated (2.3% vs 0.6%; P = .014).

Adjusted analysis comparing infrarenal EVAR with ZFEN showed no significant associations for perioperative mortality (OR, 0.6; 95% CI, 0.2-2.0; P = .42), renal dysfunction (OR, 0.4; 95% CI, 0.1-1.8; P = .24), or any complication (OR, 0.8; 95% CI, 0.5-1.3; P = .35; Table IV).

Sensitivity analyses

Addition of the propensity score as a covariable and truncation of extreme weights both yielded similar outcomes compared with our initial model.

DISCUSSION

In this study, using a nationwide registry, we were able to distinguish ZFEN procedures with high accuracy from other modes of endovascular repair. Therefore, we were able to compare ZFEN with the standard open treatment for complex AAAs. We found that rates of perioperative mortality, postoperative renal dysfunction, and any perioperative complication after ZFEN treatment were lower compared with open repair of complex AAAs, even after adjustment for baseline differences.

The perioperative mortality rate of 1.8% after ZFEN that we found is in line with rates that have been published previously. Three meta-analyses presented pooled 30-day mortality rates ranging between 1.4% and 4.1% after FEVAR.[23-25] In addition, the U.S. fenestrated trial showed no 30-day deaths,[26] and a recent contemporary single-center study reported a rate of 2%.[27] The 8.8% perioperative mortality we found for open complex AAA repair is higher compared with the 3.6% 30-day mortality reported in a recent study within the registry of the Vascular Study Group of New England (VSGNE).[28] This study included symptomatic patients, similar to our study. Contemporary series from high-volume centers showed 30-day mortality rates ranging between 0.8% and 6.1% for open complex AAA repair.[5,29-38] The higher mortality rate for open complex AAA repair in our study compared with the VSGNE is likely to be related to smaller numbers of complex open AAA repairs in our study and the fact that we included in-hospital deaths after 30 days. Nevertheless, because the mortality rate for complex open repair within the VSGNE is still higher than the rate we found for ZFEN, the overall message of lower perioperative mortality after ZFEN remains the same. In contrast to open repair, perioperative mortality after ZFEN did not differ between infrarenal, juxtarenal, and suprarenal proximal AAA extents, suggesting that mortality after ZFEN is not related to proximal AAA extent.

Several studies compared ZFEN and open complex AAA repair directly. Canavati et al[14] showed lower perioperative mortality and morbidity after ZFEN, in line with our findings. In contrast, Raux et al[12] compared 45 FEVAR procedures (of which 95% were ZFEN) performed in a French hospital with propensity-matched open complex AAA repairs performed in a center in the United States and found that FEVAR was associated with higher rates of mortality, complications, and graft-related complications. This study, however, compared relatively early experience of FEVAR with open repairs performed in a high-volume and very experienced open aortic repair center, and results are therefore likely not to be generalizable to other institutions performing open repair. The

Table II. Intraoperative and postoperative outcomes

Outcome	ZFEN No.	ZFEN %	Open repair No.	Open repair %	Infrarenal EVAR No.	Infrarenal EVAR %	*P* value ZFEN vs open	*P* value ZFEN vs infrarenal
No.	220		181		6424			
Perioperative mortality[a]	4	1.8	16	8.8	49	0.8	**.001**	.084
Total procedure time, minutes, median (IQR)	235 (159.5-304)		240 (186-308)		118 (92-156)		.24	**<.001**
Blood transfusion (intraoperative or postoperative)	49	22.3	132	72.9	351	5.5	**<.001**	**<.001**
LOS, days, median (IQR)	2 (1-4)		7 (6-10)		1 (1-2)		**<.001**	**<.001**
Any complication	24	10.9	59	32.6	497	7.7	**<.001**	.085
Unplanned reintubation	5	2.3	17	9.4	39	0.6	**.002**	**.014**
On ventilator >24 hours	2	0.9	22	12.2	20	0.3	**<.001**	.13
Pneumonia	3	1.4	14	7.7	34	0.5	**.002**	.1
Unplanned reoperation	10	4.5	23	12.7	222	3.5	**.003**	.35
MI or cardiac arrest	4	1.8	18	9.9	73	1.1	**<.001**	.35
Renal dysfunction	3	1.4	14	7.7	42	0.7	**.002**	.19
Creatinine increase >2 mg/dL	1	0.5	5	2.9	20	0.3		
Dialysis requirement	2	0.9	9	5.0	22	0.4		
Septic shock	2	0.9	8	4.4	17	0.3	**.048**	.13
Ischemic colitis	1	0.5	10	5.5	36	0.6	**.003**	1
Other complication	15	6.8	19	10.5	276	4.3	.19	.072
Aneurysm rupture	0	0.0	1	0.6	5	0.1		
Any wound complication	4	1.8	7	3.9	93	1.4		
Venous thrombosis	3	1.4	4	2.2	13	0.2		
Pulmonary embolism	0	0.0	1	0.6	11	0.2		
Stroke or CVA	1	0.5	0	0.0	11	0.2		
Lower extremity ischemia	4	1.8	4	2.2	75	1.2		
Urinary tract infection	3	1.4	3	1.7	73	1.1		
Sepsis	2	0.9	1	0.6	29	0.5		

CVA, Cerebrovascular accident; *EVAR*, endovascular aneurysm repair; *IQR*, interquartile range; *LOS*, length of stay; *MI*, myocardial infarction; *Open repair*, open complex abdominal aortic aneurysm repair; *ZFEN*, Zenith Fenestrated endovascular aneurysm repair.
Boldface *P* values represent significance ($P \leq .05$).
[a]Death within 30 days or within the index hospitalization.

Table III. Perioperative mortality stratified by proximal aneurysm extent

Perioperative mortality	Total No.	Total %	Proximal AAA extent: Infrarenal No.	Infrarenal %	Juxtarenal No.	Juxtarenal %	Suprarenal No.	Suprarenal %	*P* value
Zenith Fenestrated EVAR	4/214	1.9	2/70	2.9	2/110	1.8	0/34	0	.82
Open complex AAA repair	16/181	8.8	–	–	6/107	5.6	10/74	13.5	.065
Infrarenal EVAR	49/6424	0.8	49/6424	0.8	–	–	–	–	–

AAA, Abdominal aortic aneurysm; *EVAR*, endovascular aneurysm repair.

same hospital performing the open repairs later presented the early experience with ZFEN and compared outcomes with the open complex AAA repairs.[13] No 30-days deaths were recorded in either treatment group, and perioperative rates of morbidity, acute kidney injury, and 1-year survival were similar. Although the authors suggested that graft-related complications and secondary reinterventions were higher after ZFEN, no significant

Table IV. Multivariable analysis outcomes

	OR	95% CI	*P* value
30-Day mortality			
Procedure			
Zenith Fenestrated EVAR	Reference		
Open complex AAA repair[a]	4.9	1.4-18	**.015**
Infrarenal EVAR[a,b]	0.6	0.2-2.0	.42
Postoperative renal dysfunction			
Procedure			
Zenith Fenestrated EVAR	Reference		
Open complex AAA repair[a]	13	3.6-49	**<.001**
Infrarenal EVAR[a,b]	0.4	0.1-1.8	.24
Any complication			
Procedure			
Zenith Fenestrated EVAR	Reference		
Open complex AAA repair[a]	4.2	2.3-7.5	**<.001**
Infrarenal EVAR[a,b]	0.8	0.5-1.3	.35

AAA, Abdominal aortic aneurysm; *CI,* confidence interval; *EVAR,* endovascular aneurysm repair *OR,* odds ratio.
Boldface *P* values represent significance ($P \leq .05$).
[a]Adjusted for age, sex, race, ethnicity, smoking status, body mass index, insulin-dependent diabetes, hypertension, congestive heart failure, dyspnea, obstructive pulmonary disease, estimated glomerular filtration rate, functional dependence, chronic steroid use, prior abdominal aortic surgery, abdominal aortic aneurysm diameter, symptom status, American Society of Anesthesiologists class, bleeding disorder, disseminated cancer, systemic inflammatory response syndrome, and >10% weight loss within 6 months.
[b]Additionally adjusted for percutaneous femoral access, distal aneurysm extent, and hypogastric artery embolization.

difference was found, possibly because of the small sample size of ZFEN (n = 18). Again, generalizability of this study could be questioned because of extensive experience in complex open AAA repairs, especially compared with early experience with ZFEN.

Rao et al[25] systematically reviewed the literature on ZFEN and reported that rates of secondary reinterventions and renal failure after ZFEN were higher during follow-up compared with open juxtarenal AAA repair. However, patients undergoing ZFEN were on average 5 years older and presented with significantly higher rates of renal, cardiac, and respiratory comorbidities, likely substantially responsible for the worse outcomes. In accordance with our findings, this study found that rates of major complications were higher after open repair.

We found lower rates of postoperative renal dysfunction after ZFEN compared with open repair, even after adjustment for covariables. Other studies presented similar findings of relatively lower rates of postoperative renal dysfunction after ZFEN compared with open repair, although absolute rates were higher compared with our results (ZFEN, 9.8%-14.0%; open, 13.9%-20%).[22-24] The low rates in our study were most likely related to the narrow definition of renal insufficiency in the NSQIP (creatinine concentration increase of >2 mg/dL compared with preoperative value), in contrast to the definition that was mostly used in previously described studies (creatinine concentration increase of >0.5 mg/dL).[12,13,24] This narrow definition precluded identification of all patients with clinically significant postoperative renal dysfunction as creatinine concentration increase of ≥0.5 mg/dL was demonstrated to be associated with significantly lower 1- and 5-year survival, which is a limitation of our study.[39]

In contrast to the comparison between ZFEN and open complex AAA repair, we did not find different rates of perioperative mortality and morbidity between ZFEN and infrarenal EVAR. Whereas the low event rates and numbers of ZFEN patients may explain the lack of significance, the absolute adverse event rates were small, even if differences were to become significant with inclusion of more patients. We previously analyzed perioperative outcomes of all endovascular repairs of complex AAAs (including ZFEN, other fenestrated grafts, and parallel grafts) and compared them with infrarenal EVAR using the targeted NSQIP from 2011 to 2013.[15] In contrast to our current findings, complex endovascular repair was associated with higher morbidity and mortality than infrarenal EVAR. Subanalysis of ZFEN vs other endovascular complex AAA repair techniques showed a similar or possibly lower rate of perioperative mortality after ZFEN (1.2% vs 4.0%). However, the comparison of ZFEN vs open complex AAA repair or ZFEN vs infrarenal EVAR was not analyzed because of the small number of ZFEN procedures at the time. Given the higher procedural complexity and advanced extent of disease in patients with complex AAAs, probably resulting in longer operative times, we conclude that the ZFEN procedure performs well compared with infrarenal EVAR in the perioperative period.

Although the comparison between ZFEN and infrarenal EVAR is limited by anatomic differences and differences in instructions for use, there might be a cohort of patients for whom physicians do now have the choice between ZFEN and infrarenal EVAR as some grafts now have indications for short necks. Whereas our analysis cannot focus on this group and is likely therefore biased against ZFEN, no significant differences in outcomes were found. Thus, the more important factor in the decision of which graft to use should be long-term durability, which warrants further research.

Our study should be interpreted in context of its design. First, although the NSQIP collects data prospectively, we performed a retrospective cohort study. Selection bias for different procedures is likely as individual decision-making of operating surgeons based on nonrecorded variables in the registry, such as specific anatomic characteristics, could not be reviewed. In addition, 33% of the ZFEN cohort might have been candidates for infrarenal clamping in case of open repair. However, as mortality was similar for each proximal AAA extent in patients undergoing ZFEN, exclusion of those with infrarenal AAA extents would not lead to different outcomes. Second, we were not able to stratify between on-label and off-label use of the ZFEN device as no such variable was available within the registry. However, because the instructions for use for ZFEN require a proximal infrarenal neck length of at least 4 mm, it is likely that the ZFEN patients with suprarenal AAA extent were treated off-label. Third, there is no center or surgeon identification within the registry, and we were therefore not able to assess surgeon or hospital volume. Although the effect was highest after open repair for AAA, lower hospital volume also has been shown to be associated with higher perioperative mortality after infrarenal EVAR.[40] Given the higher complexity and less frequent use of ZFEN, there is likely also a relationship between volume and outcomes. Fourth, we were unable to determine specific graft configurations of ZFEN devices and number of visceral vessels involved. Nevertheless, a recent publication showed that additional fenestrations for the superior mesenteric artery or celiac trunk were not associated with increased perioperative mortality or morbidity.[41] Fifth, we only assessed the outcomes of ZFEN and open repair for complex AAAs. Other repair modalities, such as parallel stent grafts and physician-modified grafts, are also potential treatment modalities in these patients. However, the registry did not provide sufficient information to accurately distinguish these other treatment modalities. Finally, this study assessed the outcomes only within the perioperative period. Clarification on long-term durability of ZFEN and how this relates to other endovascular approaches as well as open repair of complex AAAs bears further research.

CONCLUSIONS

ZFEN is associated with lower perioperative mortality, complication rates, and renal dysfunction compared with open repair for complex AAAs. In contrast, outcomes after ZFEN repair are comparable to those of infrarenal EVAR. Therefore, ZFEN treatment is a safe alternative to open repair in treatment of complex AAA. Further research is warranted to address the long-term durability of ZFEN compared with open complex AAA repair.

AUTHOR CONTRIBUTIONS

Conception and design: RV, MS
Analysis and interpretation: RV, TO, NS, PL, CL, KU, AP, LD, HV, MS
Data collection: RV
Writing the article: RV
Critical revision of the article: RV, TO, NS, PL, CL, KU, AP, LD, HV, MS
Final approval of the article: RV, TO, NS, PL, CL, KU, AP, LD, HV, MS
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REFERENCES

1. Dua A, Kuy S, Lee CJ, Upchurch GR, Desai SS. Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010. J Vasc Surg 2014;59:1512-7.
2. Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F, Landon BE. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. N Engl J Med 2008;358:464-74.
3. Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med 2004;351:1607-18.
4. Greenhalgh R. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. Lancet 2004;364:843-8.
5. Sarac TP, Clair DG, Hertzer NR, Greenberg RK, Krajewski LP, O'Hara PJ, et al. Contemporary results of juxtarenal aneurysm repair. J Vasc Surg 2002;36:1104-11.
6. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation 2011;123:2848-55.
7. Ohrlander T, Sonesson B, Ivancev K, Resch T, Dias N, Malina M. The chimney graft: a technique for preserving or rescuing aortic branch vessels in stent-graft sealing zones. J Endovasc Ther 2008;15:427-32.
8. Lee JT, Greenberg JI, Dalman RL. Early experience with the snorkel technique for juxtarenal aneurysms. J Vasc Surg 2012;55:935-46.
9. Starnes BW. Physician-modified endovascular grafts for the treatment of elective, symptomatic, or ruptured juxtarenal aortic aneurysms. J Vasc Surg 2012;56:601-7.
10. Greenberg RK, Haulon S, Lyden SP, Srivastava SD, Turc A, Eagleton MJ, et al. Endovascular management of juxtarenal aneurysms with fenestrated endovascular grafting. J Vasc Surg 2004;39:279-87.
11. Simons JP, Shue B, Flahive JM, Aiello FA, Steppacher RC, Eaton EA, et al. Trends in use of the only Food and Drug Administration-approved commercially available fenestrated endovascular aneurysm repair device in the United States. J Vasc Surg 2017;65:1260-9.

12. Raux M, Patel VI, Cochennec F, Mukhopadhyay S, Desgranges P, Cambria RP, et al. A propensity-matched comparison of outcomes for fenestrated endovascular aneurysm repair and open surgical repair of complex abdominal aortic aneurysms. J Vasc Surg 2014;60:858-64.
13. Deery SE, Lancaster RT, Gubala AM, O'Donnell TF, Kwolek CJ, Conrad MF, et al. Early experience with fenestrated endovascular compared to open repair of complex abdominal aortic aneurysms in a high-volume open aortic center. Ann Vasc Surg 2018;48:151-8.
14. Canavati R, Millen A, Brennan J, Fisher RK, McWilliams RG, Naik JB, et al. Comparison of fenestrated endovascular and open repair of abdominal aortic aneurysms not suitable for standard endovascular repair. J Vasc Surg 2013;57:362-7.
15. Ultee KH, Zettervall SL, Soden PA, Darling J, Verhagen HJ, Schermerhorn ML. Perioperative outcome of endovascular repair for complex abdominal aortic aneurysms. J Vasc Surg 2017;65:1567-75.
16. Gupta PK, Brahmbhatt R, Kempe K, Stickley SM, Rohrer MJ. Thirty-day outcomes after fenestrated endovascular repair are superior to open repair of abdominal aortic aneurysms involving visceral vessels. J Vasc Surg 2017;66:1653-8.e1.
17. Davis CL, Pierce JR, Henderson W, Spencer CD, Tyler C, Langberg R, et al. Assessment of the reliability of data collected for the department of Veterans Affairs National Surgical Quality Improvement Program. J Am Coll Surg 2007;204:550-60.
18. Shiloach M, Frencher SK, Steeger JE, Rowell KS, Bartzokis K, Tomeh MG, et al. Toward robust information: data quality and inter-rater reliability in the American College of Surgeons National Surgical Quality Improvement Program. J Am Coll Surg 2010;210:6-16.
19. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A New equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604-12.
20. McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med 2013;32:3388-414.
21. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46:399-424.
22. Cole SR, Hernan MA. Constructing inverse probability weights for marginal structural models. Am J Epidemiol 2008;168:656-64.
23. Nordon IM, Hinchliffe RJ, Holt PJ, Loftus IM, Thompson MM. Modern treatment of juxtarenal abdominal aortic aneurysms with fenestrated endografting and open repair—a systematic review. Eur J Vasc Endovasc Surg 2009;38:35-41.
24. Katsargyris A, Oikonomou K, Klonaris C, Töpel I, Verhoeven EL. Comparison of outcomes with open, fenestrated, and chimney graft repair of juxtarenal aneurysms: are we ready for a paradigm shift? J Endovasc Ther 2013;20:159-69.
25. Rao R, Lane TRA, Franklin IJ, Davies AH. Open repair versus fenestrated endovascular aneurysm repair of juxtarenal aneurysms. J Vasc Surg 2015;61:242-55.e5.
26. Greenberg RK, Sternbergh WC, Makaroun M, Ohki T, Chuter T, Bharadwaj P, et al. Intermediate results of a United States multicenter trial of fenestrated endograft repair for juxtarenal abdominal aortic aneurysms. J Vasc Surg 2009;50:730-7.e1.
27. Wang SK, Gutwein AR, Gupta AK, Lemmon GW, Sawchuk AP, Motaganahalli RL, et al. Institutional experience with the Zenith Fenestrated aortic stent graft. J Vasc Surg 2018;68:331-6.
28. Deery SE, Lancaster RT, Baril DT, Indes JE, Bertges DJ, Conrad MF, et al. Contemporary outcomes of open complex abdominal aortic aneurysm repair. J Vasc Surg 2016;63:1195-200.
29. Jean-Claude JM, Reilly LM, Stoney RJ, Messina LM. Pararenal aortic aneurysms: the future of open aortic aneurysm repair. J Vasc Surg 1999;29:902-12.
30. Chiesa R, Marone EM, Brioschi C, Frigerio S, Tshomba Y, Melissano G. Open repair of pararenal aortic aneurysms: operative management, early results, and risk factor analysis. Ann Vasc Surg 2006;20:739-46.
31. West CA, Noel AA, Bower TC, Cherry KJ, Gloviczki P, Sullivan TM, et al. Factors affecting outcomes of open surgical repair of pararenal aortic aneurysms: a 10-year experience. J Vasc Surg 2006;43:921-8.e1.
32. Ockert S, Schumacher H, Böckler D, Malcherek K, Hansmann J, Allenberg J. Comparative early and midterm results of open juxtarenal and infrarenal aneurysm repair. Langenbecks Arch Surg 2007;392:725-30.
33. Pearce JD, Edwards MS, Stafford JM, Deonanan JK, Davis RP, Corriere MA, et al. Open repair of aortic aneurysms involving the renal vessels. Ann Vasc Surg 2007;21:676-86.
34. Knott AW, Kalra M, Duncan AA, Reed NR, Bower TC, Hoskin TL, et al. Open repair of juxtarenal aortic aneurysms (JAA) remains a safe option in the era of fenestrated endografts. J Vasc Surg 2008;47:695-701.
35. Chong T, Nguyen L, Owens CD, Conte MS, Belkin M. Suprarenal aortic cross-clamp position: a reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. J Vasc Surg 2009;49:873-80.
36. Landry G. Open abdominal aortic aneurysm repair in the endovascular era: effect of clamp site on outcomes. Arch Surg 2009;144:811.
37. Tsai S, Conrad MF, Patel VI, Kwolek CJ, LaMuraglia GM, Brewster DC, et al. Durability of open repair of juxtarenal abdominal aortic aneurysms. J Vasc Surg 2012;56:2-7.
38. Ferrante AM, Moscato U, Colacchio EC, Snider F. Results after elective open repair of pararenal abdominal aortic aneurysms. J Vasc Surg 2016;63:1443-50.
39. Zarkowsky DS, Hicks CW, Bostock IC, Stone DH, Eslami M, Goodney PP. Renal dysfunction and the associated decrease in survival after elective endovascular aneurysm repair. J Vasc Surg 2016;64:1278-85.e1.
40. Zettervall SL, Schermerhorn ML, Soden PA, McCallum JC, Shean KE, Deery SE, et al. The effect of surgeon and hospital volume on mortality following open and endovascular repair of abdominal aortic aneurysms. J Vasc Surg 2017;65:626-34.
41. Katsargyris A, Oikonomou K, Kouvelos G, Mufty H, Ritter W, Verhoeven EL. Comparison of outcomes for double fenestrated endovascular aneurysm repair versus triple or quadruple fenestrated endovascular aneurysm repair in the treatment of complex abdominal aortic aneurysms. J Vasc Surg 2017;66:29-36.

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