Comparison of Early and Mid-Term Outcomes After Fenestrated-Branched Endovascular Aortic Repair in Patients With or Without Prior Infrarenal Repair

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Abstract

Objective: The purpose of this study was to compare short- and mid-term outcomes of fenestrated-branched endovascular repair (F-BEVAR) of pararenal (PRAA)/thoracoabdominal (TAAA) aortic aneurysms in patients with or without prior endovascular/open (EVAR/OAR) infrarenal aortic repair.

Methods: Data from consecutive F-BEVAR (2010–2019) at two high-volume aortic centers were retrospectively reviewed. Primary endpoints were technical success, 30-day mortality, and overall survival. Secondary endpoints included 30-day major adverse events (MAE), freedom from type I/III endoleaks, reinterventions, sac expansion, and target vessel (TV) primary patency.

Results: A total of 222 consecutive patients were included for analysis; of these 58 (26.1%) had prior infrarenal repair (EVAR=33, OAR=25) and 164 (73.9%) had native PRAA/TAAA. At baseline, patients with prior infrarenal repair were older (mean age=75.1 vs 71.6 years, p=.005) and the proportion of females was lower (8.6% vs 29.3%, p=.002). Technical success was 97.8% (n=217) in the entire cohort, without any significant differences between study groups (94.8% vs 98.8%, p=.08). At 30 days, there were no significant differences between patients with prior infrarenal repair as compared with those without in rate of MAE (44.8% vs 54.9%, p=.59). The 5-year estimate of survival for those who underwent native aortic repair was 61.6%, versus 61.3% for those who had a previous repair (p=.67). The 5-year freedom from endoleaks I/III estimates were significantly lower in patients who had prior infrarenal repair as compared with patients undergoing treatment of native aneurysms (57.1% vs 66.1%, p=.03), mainly owing to TV-related endoleaks (ie, type IC and/or IIIC endoleaks). No significant differences were found between study groups in rates of reinterventions and TV primary patency. Five-year estimates of freedom from sac increase >5mm were significantly lower in patients who received F-BEVAR after previous infrarenal repair as compared with those who underwent treatment of native aneurysms (48.6% vs 77.5%, p=.002).

Conclusions: F-BEVAR is equally safe and feasible for treatment of patients with prior infrarenal repair as compared with those undergoing treatment for native aneurysms. Increased rates of TV-related endoleaks were observed which could lead to lower freedom from aneurysm sac shrinkage during follow-up. Nevertheless, the 5-year rates of reinterventions and TV patency were similar, thereby indicating that overall effectiveness of treatment remained satisfactory at mid-term.

Keywords

fenestrated-branched endovascular repair, pararenal, thoracoabdominal, aortic disease, secondary repair, reintervention, short-term, mid-term, outcomes

Introduction

Endovascular aortic repair (EVAR) has become the first-line treatment for aortic aneurysmal pathology in most patients with suitable anatomy and reasonable life expectancy.[1] Long-term durability of EVAR remains a concern, as the potential for adverse events over time mandates lifelong follow-up and reinterventions when needed.[2,3] Although considered more durable, secondary interventions may also be required after open aortic repair (OAR).[4] Open surgical conversion for failure after prior infrarenal procedures (either EVAR and/or OAR) is associated with significant technical challenges, as well as often prohibitive perioperative morbidity and mortality.[5] This is especially true among patients with previous EVAR, who may have been deemed at high risk for open surgery at the time of their original treatment. Meanwhile, complex EVAR techniques have emerged to address aneurysms that involve the renal-mesenteric vessels, including pararenal (PRAA) and thoracoabdominal (TAAA) aortic aneurysms. Fenestrated-branched EVAR (F-BEVAR) can be used in a secondary procedure for rescue of failing EVAR/OAR by raising the proximal sealing zone to the visceral or thoracic aorta.[6–9] However, the presence of an infrarenal surgical graft or endograft can increase the complexity of the F-BEVAR procedure which, in turn, may lead to lower technical success rates and worsened durability as compared with F-BEVAR for native aneurysms.

Our aim was to evaluate the early and mid-term outcomes of F-BEVAR in patients with prior infrarenal repair and compare these results against those that were obtained in patients who underwent treatment for native PRAA and TAAA.

Methods

Study Design

The study was performed with approval from the regional ethical review board. The main exposure variable was the presence of any prior infrarenal repair, either OAR or EVAR, which was noted, as was the indication for subsequent F-BEVAR. Therefore, the study cohort was divided into two groups for all subsequent analyses based on the presence or absence of prior infrarenal repair. Data of all consecutive F-BEVAR interventions performed after prior infrarenal repair at two tertiary academic institutions from Sweden (Uppsala University Hospital; Karolinska University Hospital) with high volume for complex endovascular aortic operations (>30 cases/year) from January 1, 2010, to July 1, 2019, were retrospectively reviewed and compared against primary F-BEVAR operations done at one of the two participating institutions (Uppsala University Hospital). Both centers shared similar patterns for referral, timing, and intervention in patients deemed suitable F-BEVAR candidates. Patients' demographics and comorbidities were recorded, in addition to the size and type of aneurysm repaired according to the Crawford-Safi classification.[10,11]

Surgical Practice

Details on surgical technique have been previously published; distal landing in the native or prosthetic infrarenal aorta was always selected when feasible to avoid standard iliac landing.[12] All F-BEVAR procedures were performed using Cook Medical endografts (Cook Medical Inc, Brisbane, Australia), including custom-made and off-the-shelf endografts, as well as those which were physician-modified. The status of the procedure, that is, acute or elective, was noted, in addition to operative and radiological data. Postoperative data, including hospital length-of-stay (LoS) and complications, were also noted. All preoperative imaging consisted of high-resolution computed tomography angiography (CTA), while the follow-up protocol consisted of CTA at 1 month and then annually, unless altered by indications for reintervention.

Definitions and Endpoints

The primary endpoints were technical success, 30-day mortality, and overall survival. The secondary endpoints included major adverse events (MAE) and access-site complications at 30 days, hospital LoS, freedom from type I/III endoleaks, freedom from reinterventions, and target vessel (TV) primary patency. Technical success was defined as successful deployment of the stent-graft by endovascular means only, the absence of type I/III endoleaks on completion angiography and patent TV. MAE were defined as per Society for Vascular Surgery reporting standards: cumulative endpoint of any-cause mortality, myocardial infarction, new-onset congestive heart failure, blood loss >1L, acute kidney injury, stroke, spinal cord ischemia, or bowel ischemia.[13] Loss of TV patency was diagnosed when thrombosis of the TV and/or bridging stent-graft was noted, or there was radiologic evidence of significant TV stenosis requiring reintervention.

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Statistical Analysis

All data were evaluated for normality with quantile-quantile plots. Continuous variables are expressed with either mean or median values, with corresponding standard deviation (SD) or interquartile range (IQR). Categorical variables are presented as number with percentage. Univariable analyses were carried out with either Student's *t* test or Mann–Whitney *U* test for continuous variables, and chi-square test or Fisher's exact test for categorical variables. Time-dependent outcomes were reported using life tables and presented as Kaplan-Meier curves; differences were determined by the log-rank test. Binary outcomes were evaluated first by univariable methods, with results reported as odds ratio (OR) with 95% confidence intervals (CI). Sensitivity analysis was carried out repeating all univariate analyses of interest in the restricted subgroup of patients who had been treated at one institution (Uppsala University Hospital), and for whom data on F-BEVAR procedures both with and without prior infrarenal repair were retrieved.

A multiple logistic regression model was built including significant covariates and confounders based on univariate screen or clinical significance (including aneurysm morphology). Stepwise backward selection was then performed with a removal criteria of .05 and the resulting parsimonious model was not statistically significantly different from the full model (likelihood ratio test, p=.91). The model discrimination was measured by the area under the operating curve, and the Hosmer-Lemeshow goodness-of-fit was not significant. Multivariable Cox proportional hazards was used to assess independent predictors for any-cause mortality, reinterventions, and endoleaks, with results reported as hazard ratio (HR) with 95% CI. Covariates for these models were selected based on previously described risk factors and univariate screen of all available potential confounders, using backward selection with a criterium of 0.25 to stay in the final models. The final models were tested for violation of proportional hazards assumptions using Schoenfeld residuals. By convention, statistical significance was set at p value of <0.05. Statistical analysis and graphing were performed with Stata/SE 16 software (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX, USA: StataCorp LLC).

Results

Study Population

A total of 222 consecutive patients were included for analysis; of these 58 (26.1%) had prior infrarenal repair (EVAR=33, OAR=25) and 164 (73.9%) had native PRAA/TAAA. Reasons for F-BEVAR after prior infrarenal repair included 27 cases of type IA endoleak (1 rupture), 2 cases of endograft migration, and 29 cases of proximal degeneration/pseudoaneurysm (2 ruptures).

At baseline, patients with prior infrarenal repair were older (mean age=75.1 vs 71.6 years, p=.005) and the proportion of females was lower (8.6% vs 29.3%, p=.002). Chronic obstructive pulmonary disease was less frequent in patient who had prior infrarenal repair (19% vs 32%, p=.04) and the largest aneurysm diameter before treatment was higher in those with prior OAR/EVAR (67.5 vs 60.0 mm, p<.001), but no other significant differences were found between study groups (Table 1).

A high proportion (about 40%) of patients undergoing F-BEVAR after prior infrarenal repairwere referred from other centers. For those patients with available data on their initial EVAR/OAR (N=54), the median time from primary repair was 5.0 (IQR=6) years, with 9 years (IQR=6.5) following OAR and 5 years (IQR=4) following EVAR.

Procedural Details

No significant differences were found in operative time (313 vs 372.5 minutes, p=.27) or fluoroscopy time (114.5 vs 95 minutes, p=.14), while contrast volume was significantly lower for F-BEVAR operations performed after prior infrarenal repair (133.5 vs 195 mL, p<0.001; Table 2). Also, no significant differences were found in the distribution of number of TV incorporated, but F-BEVAR procedures following prior infrarenal repair were done more often with a single straight tube (29% vs 9%, p=.001). No other major procedural differences were noted between study groups.

Technical success was 97.8% (n=217) in the entire cohort, without any significant differences between study groups (94.8% vs 98.8%, p=.08). There were two failures of left renal artery cannulation (both occurring in patients undergoing F-BEVAR for native aneurysms, one of which was performed using a physician-modified endograft in acute setting), one failure to cannulate the celiac trunk (in a patient undergoing elective F-BEVAR after prior endovaascular infrarenal repair), and two failures to cannulate the superior mesenteric artery (both occurring in patients undergoing F-BEVAR after prior infrarenal repair, one OAR and one EVAR, the former performed in acute setting using a physician-modified endograft). The two renal arteries that were not stented required an iliorenal bypass that was successful in restoring blood flow to the kidney. In the case where a branch to the celiac trunk could not be bridged, the branch was plugged using an Amplatzer Plug (Medtronic Inc, Santa Rosa, CA); the patient was readmitted one month later with acute mesenteric ischemia (owing to occlusion of the superior mesenteric artery bridging stent that had been compressed by the above plug), which resulted in death of the patient. The superior mesenteric artery was rescued in one case with bailout chimney stenting, while in the other case backflow filling from collaterals originating from the celiac trunk was evident on completion angiography, both

Table 1. Baseline Characteristics and Comorbidities for the 222 Patients, 2010–2019, Who Underwent Complex Endovascular Aortic Repair, Either as a Primary Repair or Following a Failed Previous Open or Endovascular Repair.

Variable	All patients (n=222)	Any previous infrarenal repair (n=58)	No previous infrarenal repair (n=164)	p value
Demographics				
Age, years (mean ± SD)	72.5 ± 8.2	75.1 ± 6.2	71.6 ± 8.7	0.005
Octogenarians (%)	40 (18.0)	14 (24.1)	26 (15.9)	0.16
Female sex (%)	53 (26.2)	5 (8.6)	48 (29.3)	0.002
BMI, kg/m^2 (median, IQR)	25.8 (5.9)	24.8 (5.4)	25.9 (5.9)	0.35
Obese (BMI>30) (%)	46 (20.8)	10 (21.7)	36 (22.0)	0.48
Comorbidities				
IHD (%)	74 (33.3)	23 (39.7)	51 (31.1)	0.24
Atrial fibrillation (%)	47 (21.2)	16 (27.6)	31 (18.9)	0.16
CHF (%)	30 (13.5)	7 (12.1)	23 (14.0)	0.71
Hypertension (%)	197 (88.7)	51 (87.9)	146 (89.0)	0.82
COPD (%)	64 (28.8)	11 (19.0)	53 (32.3)	0.04
DM (%)	22 (9.9)	5 (8.6)	17 (10.4)	0.70
Previous stroke/TIA (%)	21 (9.5)	6 (10.3)	15 (9.2)	0.79
Smoking (%)				
Never	39 (17.9)	9 (16.7)	30 (18.3)	1.00
Previous	110 (50.5)	29 (53.7)	81 (49.4)	1.00
Current	67 (30.7)	16 (29.6)	51 (31.1)	1.00
Baseline eGFR, mL/min/1.73m^2 (median, IQR)	73.3 (30.7)	74.9 (23.8)	73.6 (31.9)	0.65
CKD stage III–V (eGFR<60) (%)	51 (25.2)	8 (21.1)	43 (26.2)	0.51
Anatomy				
Largest AAA diameter, mm (median, IQR)	61.0 (12.0)	67.5 (19.0)	60.0 (8.5)	<0.001
Extent of disease				
Para/suprarenal AAA (%)	140 (63.1)	36 (62.1)	104 (63.4)	1.00
Extent 1-3 TAAA (%)	68 (30.6)	16 (31.0)	50 (30.5)	1.00
Extent 4 TAAA (%)	14 (6.3)	4 (6.9)	10 (6.1)	1.00

Continuous data are provided as mean values ± standard deviation or median values (interquartile range), while categorical values are given as absolute counts (percentages).

Abbreviations: AAA, abdominal aortic aneurysm; BMI, body mass index; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; IHD, ischemic heart disease; IQR, interquartile range; TAAA, thoracoabdominal aortic aneurysm; TIA, transient ischemic attack.

patients were discharged alive and did not develop any late abdominal complications.

Morbidity and Mortality

At 30 days, there were no significant differences between patients with prior infrarenal repair as compared to those without in the rates of overall mortality (3.5% vs 1.8%, p=.48), MAE (44.8% vs 54.9%, p=.59), or access-site complications (8.6% vs 13.4%, p=.16). In-depth analysis of all MAE revealed no significant differences between patients with prior infrarenal repair as compared to subjects without, except for blood loss >1L which represents 78% of all MAE (Table 3). Total hospital LoS was shorter in patients with previous infrarenal procedures (5 vs 6 days, p=.01). In multivariate analysis (Supplementary Table 1), significant predictors for MAE included aortic diameter (OR for each additional 5mm increase=1.18, 95% CI: 1.02–1.37, p=.03) and TAAA (OR=2.61, 95% CI: 1.24–5.49, p=.01). Prior infrarenal repair was not an independent predictor for in-hospital major morbidity.

The 5-year estimate of survival for the entire cohort was 61.3% (95% CI: 51.1–70.1). For those who underwent treatment of native PRAA-TAAA, the estimate was 61.6% (95% CI: 50.0–71.4), while for those who had a previous infrarenal repair, the estimate was 61.3% (95% CI: 39.4–77.4). There was no statistical significance in survival probability between the two groups (p=.67; Figure 1). After multivariate adjustments detailed in Supplementary Table 2, presence of larger aneurysm diameter remained as a significant predictor of any-cause mortality (HR for each additional 5mm increase=1.23, 95% CI: 1.10–1.36, p<001; respectively). Presence of previous infrarenal repair was not associated with increased hazards of mortality.

Table 2. Procedural Details for All Complex Endovascular Aortic Repairs.

Variable	All patients (n=222)	Any previous infrarenal repair (n=58)	No previous infrarenal repair (n=164)	p value
Status (%)				
Elective	193 (86.9)	49 (84.5)	161 (98.8)	1.00
Subacute	17 (7.7)	6 (10.3)	11 (6.7)	1.00
Acute	12 (5.4)	3 (5.2)	9 (5.5)	1.00
Total operation time, minutes (Median, IQR)	354 (224)	313 (171)	372.5 (234)	0.27
Total fluoroscopy time, minutes (Median, IQR)	101.5 (61)	114.5 (77)	95 (57.5)	0.14
Contrast volume, mL (Median, IQR)	180 (118)	133.5 (117.5)	195 (108)	$<$0.001
Proximal Landing Zone (%)				
Proximal Thoracic	58 (26.1)	12 (20.7)	46 (28.1)	0.82
Mid Thoracic	32 (14.4)	11 (19.0)	21 (12.8)	0.75
Distal Thoracic	132 (59.5)	35 (60.3)	97 (59.2)	1.0
Type of device (%)				
Custom-made	179 (80.6)	45 (77.6)	134 (81.7)	1.0
Off-the-shelf	36 (16.2)	11 (19.0)	25 (15.2)	1.0
Physician-modified	7 (3.2)	2 (3.5)	5 (3.1)	1.0
Design of device (%)				
Fenestrations Only	154 (69.4)	39 (67.2)	115 (70.1)	1.0
Branches Only	52 (23.4)	16 (27.6)	36 (22.0)	1.0
Combined	16 (7.2)	3 (5.2)	13 (7.9)	1.0
Number of target vessels (%)				
2	37 (16.7)	5 (8.6)	32 (19.5)	0.17
3	89 (40.1)	24 (41.4)	65 (39.6)	1.0
4 or more	96 (43.2)	29 (50.0)	67 (40.9)	1.0
Infrarenal distal landing zone (%)	26 (12.9)	11 (29.0)	15 (9.2)	0.001
Percutaneous groin access (%)				
Unilateral	95 (47.0)	12 (31.6)	83 (50.6)	0.10
Bilateral	68 (33.7)	17 (44.7)	51 (31.1)	0.68
Brachial Access (%)	71 (32.0)	20 (34.5)	51 (31.1)	0.64
Prophylactic spinal drain (%)	87 (39.2)	25 (43.1)	62 (37.8)	0.48

Continuous data are provided as mean values ± standard deviation or median values (interquartile range), while categorical values are given as absolute counts (percentages).
Abbreviation: IQR, interquartile range.

Type I-III Endoleaks, Reinterventions, Target Vessels Patency, and Aneurysm Sac Changes

As shown in Figure 2, the 5-year freedom from endoleaks I/III estimates were significantly lower in patients undergoing F-BEVAR after prior infrarenal repair as compared with patients undergoing treatment of native aneurysms (57.1% vs 66.1%, p=.03). On aggregate analysis of the specific types of type I/III endoleaks observed, 64.7% (n=22) were type IC (n=9) or type IIIC (n=13) that resulted from inadequate seal at the junction of a bridging stent-graft with a TV or from inadequate seal of a fenestration/branch with a bridging stent-graft, respectively. There was a significant difference (p=.03) between patients with previous infrarenal repair (n= 10; 17.2%) or without (n=12;7.3%). Proximal (type IA) or distal (type IB) seal failure occurred in only 5.0% (n=11) of all patients studied, without any difference between patients with or without prior infrarenal repair (p=.93). After multivariate adjustments detailed in Supplementary Table 3, presence of prior infrarenal repair was not found as independent predictor for the occurrence of type I/III endoleaks.

No significant differences were found between study groups in rates of reinterventions and TV primary patency (Figures 3 and 4), and prior EVAR/OAR was not confirmed as independent predictor for the occurrence of either event (Supplementary Tables 4 and 5). However, aneurysm size was associated with higher hazards of reinterventions after multivariate adjustment (HR for each additional 5 mm increase=1.16, 95% CI: 1.05–1.30, p=.006).

The 5-year estimates of freedom from sac increase $>$5mm were significantly lower in patients who received F-BEVAR after previous infrarenal repair as compared with those who underwent treatment of native aneurysms (48.6% vs 77.5%, p=.002; Figure 5). After multivariate adjustments detailed in Supplementary Table 6, prior infrarenal repair was independently associated with higher risk

Table 3. Thirty-Day Outcomes.

Variable	All patients (n=222)	Any previous infrarenal repair (n=58)	No infrarenal repair (n=164)	p value
Technical Success (%)	217 (97.8)	55 (94.8)	162 (98.8)	0.08
Any MAE (%)	116 (52.3)	26 (44.8)	90 (54.9)	0.19
Mortality (%)	5 (2.3)	2 (3.5)	3 (1.8)	0.48
EBL>1000 mL (%)	90 (40.7)	17 (29.3)	73 (44.8)	0.04
MI (%)	5 (2.3)	2 (3.5)	3 (1.8)	0.48
New CHF (%)	2 (0.9)	0	2 (1.2)	0.40
Respiratory failure (%)	22 (9.9)	2 (3.5)	20 (12.2)	0.06
Stroke (%)	8 (3.6)	3 (5.2)	5 (3.1)	0.46
SCI (%)				
Transient	10 (4.5)	1 (1.7)	9 (5.5)	0.71
Permanent	7 (3.2)	2 (3.5)	5 (3.1)	1.0
Any SCI	17 (7.7)	3 (5.2)	14 (8.5)	0.41
AKI (%)				
Without dialysis	23 (10.4)	4 (6.9)	19 (11.6)	1.0
New-onset dialysis	14 (6.3)	2 (3.4)	12 (7.3)	1.0
Any AKI	37 (16.7)	6 (10.3)	31 (18.9)	0.13
Bowel Ischemia (%)				
No resection	5 (2.3)	1 (1.7)	4 (2.4)	1.0
With resection	5 (2.3)	1 (1.7)	4 (2.4)	1.0
Any bowel ischemia	8 (4.5)	2 (3.5)	8 (4.9)	0.65
Access-site major complications (%)	27 (12.2)	5 (8.6)	22 (13.4)	0.56
Total LoS, days (Median, IQR)	6.0 (5.0)	5.0 (5.0)	6.0 (6.0)	0.01

Continuous data are provided as mean values ± standard deviation or median values (interquartile range), while categorical values are given as absolute counts (percentages).
Abbreviation: MAE, major adverse events; EBL, estimated blood loss; CHF, congestive heart failure; SCI, spinal cord ischemia; AKI, acute kidney injury; LoS, length of stay; IQR, interquartile range.

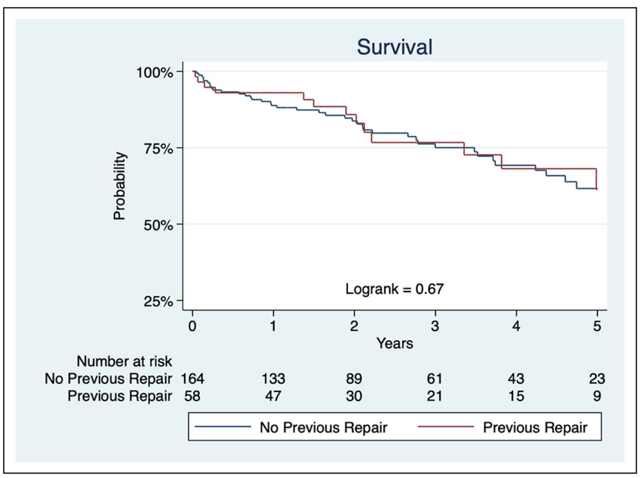

Figure 1. Kaplan-Meier estimates of overall survival.

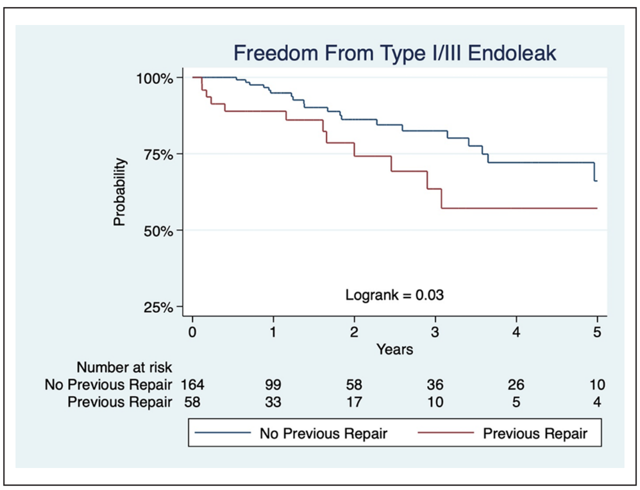

Figure 2. Kaplan-Meier estimates of freedom from type I/III endoleaks.

for late sac expansion (HR=3.28, 95% CI: 1.35–7.97, p=.009).

Sensitivity analysis as previously specified in the restricted subgroup of patients from one institution confirmed the original findings (data not shown).

Discussion

It is well documented that both EVAR and OAR, albeit with differing incidence and etiology, are associated with

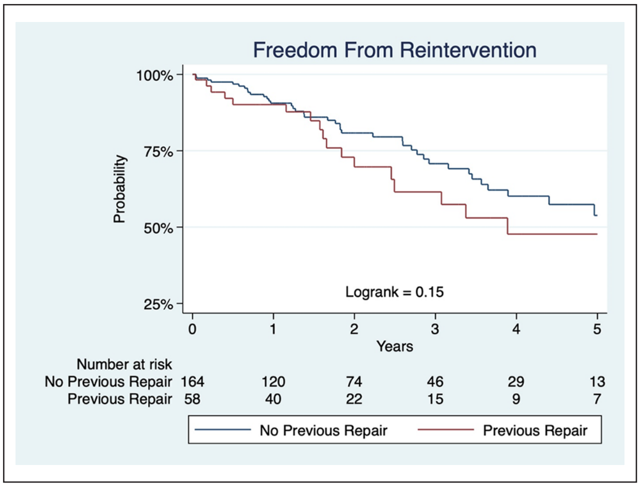

Figure 3. Kaplan-Meier estimates of freedom from reinterventions.

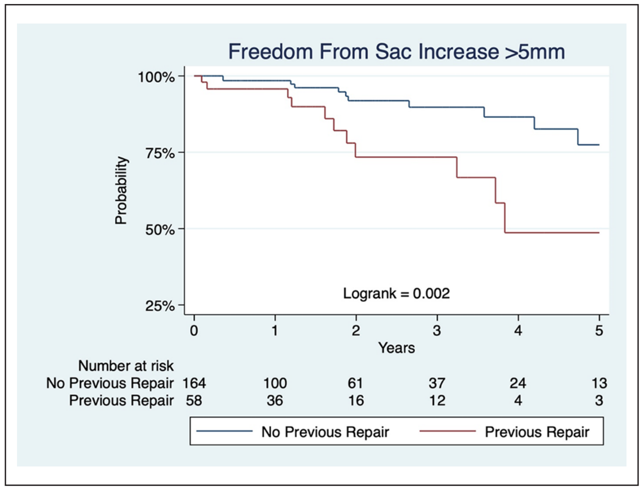

Figure 5. Kaplan-Meier estimates of freedom from sac expansion>5mm.

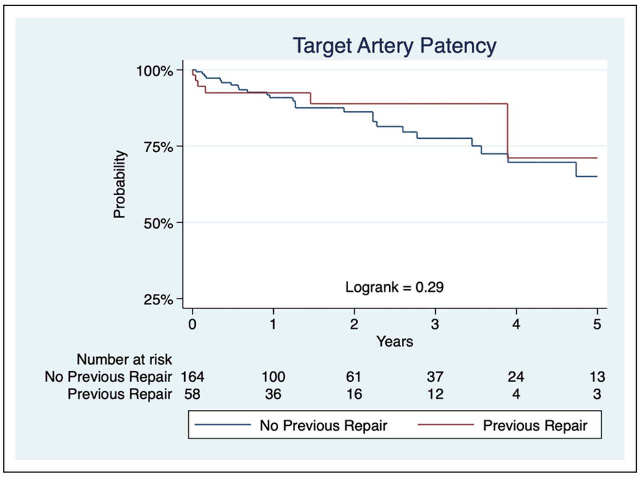

Figure 4. Kaplan-Meier estimates of target vessels primary patency.

secondary complications and indications for secondary interventions.[14] These secondary interventions are not without operative risks, and they are often technically demanding due to the presence of prior grafts and endografts. These patients are typically older and less fit than they were at the time of their initial repair, partially explaining the high morbidity of open surgical conversion, particularly under urgent circumstances.[15–20] Meanwhile, F-BEVAR has progressively become the first-line option for management of PRAA-TAAA over the last decade, mainly owing to its reduced invasiveness, thereby extending potential treatment to patients who would have been deemed unfit for open surgical repair.[21–23] With increasing experience, as well as persistent technological refinements, F-BEVAR indications have expanded to include secondary rescue of failures after prior infrarenal procedures, but relevant outcomes in this clinical scenario have only recently emerged.[24,25]

The main findings of this study, obtained at two high-volume aortic centers over 10 years, were that the use of F-BEVAR in patients with prior EVAR/OAR did not differ significantly regarding early and mid-term outcomes as compared with those undergoing treatment for native aortic aneurysms. Indeed, F-BEVAR in patients with prior infrarenal procedures (either open or endovascular) was equally safe and feasible, and its effectiveness remained satisfactory over a median follow-up of 3 years, with no differences noted in the rates of TV patency loss and need for reinterventions. Although type I/III endoleaks occurred more frequently after failure of previous infrarenal procedures, the analysis of specific types of I/III endoleaks revealed that only a minority resulted from inadequate proximal seal while a higher proportion of endoleaks from TV-endograft junctions were noted in the group of subjects receiving F-BEVAR following prior infrarenal repair. When evaluated in the clinical context, this is highly relevant, as the main indication for F-BEVAR after prior infrarenal repair in the study cohort was loss of, or inadequate, proximal seal from the prior infrarenal procedure; therefore, it is reasonable to conclude that F-BEVAR procedures were successful for the specific indications for which they were applied and the higher incidence of TV-related endoleaks could be related to the expected increased level of technical complexity. Owing to the overall low number of adverse events that were reported, no other specific explanations could be reasonably hypothesized to explain the increased number of TV-related endoleaks among F-BEVAR procedures performed in patients who had prior infrarenal repair. Further research could shed further light on the specific risk factors for such endoleaks and how to possibly prevent their occurrence. Until then, this potential safety signal could alert physicians to the potential need for stricter follow-up in patients undergoing F-BEVAR after prior infrarenal repair. Nevertheless, since all these endoleaks could be successfully managed with new endovascular interventions, they would not detract from the minimal invasiveness and overall effectiveness of treatment, provided they are readily detected and adequately managed.

These results are in line with previously published series evaluating the role of F-BEVAR after failed infrarenal repair,[26–29] supporting the notion of F-BEVAR as the first-line option for rescue of infrarenal failure in anatomically suitable patients. There are, however, scenarios where open surgical treatment will remain the preferred treatment. For instance, in the presence of graft/endograft infections, classical surgical treatment can provide definitive control and eradication of the infective focus.[30,31] Although complex endovascular techniques have recently been reported as a feasible alternative solution in selected cases, more experience and longer follow-up are warranted before any definitive conclusion can be reached.[32] Another limitation to the use of custom-made devices might be the presence of symptoms or frank rupture, given the time delay required for manufacturing and delivery. In this setting, other endovascular techniques (including chimneys-snorkels,[33,34] off-the-shelf multibranched stent-grafts,[35] and physician-modified endografts) may all play a role as bridging measures to stabilize the patient, but these should be employed by adequately trained physicians in patients without other reasonable options.

This study also highlights that, at highly specialized endovascular aortic centers, a significant proportion of patients undergoing F-BEVAR receive this treatment after failed EVAR or OAR (almost one fourth of all F-BEVAR treated patients in this series), and the proportion seems to be increasing over time (Supplementary Figure 1). Several factors may contribute to this phenomenon, including increasing expertise with complex endovascular techniques as well as more liberal use of stent-grafts outside their instructions-for-use or the intrinsically progressive nature of aneurysmal disease, although caution should be exercised when drawing conclusions.[36] Thereby, it is likely that a learning curve effect for these secondary procedures had already been achieved by performing physicians given the high volume of aortic cases at participating institutions. As many patients were referred from other centers with details of the primary procedures lacking, it is not possible to delineate factors predicting the need for F-BEVAR after prior infrarenal repair. More secondary F-BEVAR procedures were performed after prior EVAR (n=33) than OAR (n=25), but a detailed analysis of differences is not possible given the limited number of cases. Although OAR does not completely protect against the need for future F-BEVAR, our data would suggest that time to proximal regrafting might be longer as compared with standard EVAR.

Whereas F-BEVAR after prior infrarenal repair is safe, feasible, and effective with encouraging short-term and mid-term outcomes which are largely comparable with those obtained in native PRAA/TAAA, caution is needed not to interpret these findings as justification to push the boundaries of conventional infrarenal repair; especially with EVAR devices placed in cases with hostile or dubious aortic anatomy or outside their instructions-for-use. In fact, in patients with a reasonably long life expectancy, more complex repairs in the first place might offer potential savings in terms of clinical efficacy and cost-effectiveness.[37] In that sense, the goal of treatment must always be for the first operation to be the right operation.[38] With no strict "instructions for use" among fenestrated and branched devices, adequate proximal sealing is typically equated with a goal of achieving two sealing stents, regardless of whether it is a primary or secondary procedure. When a prior infrarenal repair is already present, the proximal sealing might sometimes be (at least partly) achieved in the previously placed graft/endograft. Regarding the distal sealing, we always aim to achieve a $>$20mm-zone to ensure durability of repair. Although this can at times be achieved within the infrarenal aorta, it is more commonly seen when a prior graft-endograft is already present and could explain why a significantly higher proportion of F-BEVAR devices could be planned as straight tube (without need for a distal bifurcated body) in the group of patients with prior infrarenal repair. This technique could contribute to reduce technical complexity and costs, and should be carefully considered when morphologically suitable.

When performing F-BEVAR procedures in the presence of prior infrarenal grafts/endografts, higher technical complexity should be anticipated, and several anatomical challenges can be expected. Presence of suprarenal bare stent from prior EVAR can make TV cannulation more difficult because of suprarenal stent struts encroaching on the TV origins (Supplementary Figure 2). However, whether rates of technical failure of TV-related endoleaks might be higher in patients who had prior EVAR with suprarenal fixation (versus those that were originally treated using EVAR devices with infrarenal fixation) could not be ascertained in the current study owing to the overall low number of cases and would require further research endeavors.

Another difficulty in the setting of F-BEVAR after prior infrarenal repair might be related to the short distance between the proximal anastomosis or edge of endograft and the graft/endograft bifurcation. The incessant improvements of endovascular technology along with increased skills and confidence from operators have improved the capabilities of overcoming most issues that can be encountered. In our practice, we usually implement dual diameter-reducing ties when planning F-BEVAR devices for patients with prior infrarenal repair, to better accommodate the need for rotational adjustments in the already placed graft-endograft. Furthermore, in the last years we have introduced routine application of steerable sheaths for cannulation of target vessels and intraoperative navigation with fusion imaging technology for all f-BEVAR interventions. Other advanced techniques, such as the use of preloaded and indwelling wires and catheters or low-profile devices, are also made available on a case-by-case basis when needed to accommodate specific anatomic challenges. As ever the case in endovascular procedures, and even more so with complex ones, meticulous preoperative planning, careful intraoperative manipulation, and strict postoperative surveillance are all key to achieving technical success and sustained durability.

Designing initial OAR/EVAR ahead of potential secondary endovascular interventions might offer some advantages. In that sense, avoiding placement of short main body during infrarenal reconstructions might allow easier F-BEVAR if required later during follow-up, although use of F-BEVAR devices with inverted limbs can often be helpful in this setting (Supplementary Figure 3). Also, manipulation of the F-BEVAR device while working through a relatively stiff graft/endograft can hinder the ability to rotate the device freely. Despite these considerations, no obvious differences were found in this study in regard to main procedural metrics and technical success rates, thereby highlighting that with accurate preoperative planning and careful intraoperative manipulation satisfactory and durable results can still be expected by experienced operators. Nevertheless, the observed higher incidence of TV-related endoleaks in patients receiving F-BEVAR after prior infrarenal repair would suggest a more cautious approach be endorsed during follow-up of these subjects, as these endoleaks might lead to sac size increase in the long-run.

Maximal aortic diameter was found to be an independent predictor for perioperative adverse events as well as mortality during follow-up. Although these findings have been reported by previous studies of infrarenal EVAR,[39–41] others have not confirmed such association,[42] and caution should be exercised before drawing conclusions. Whether aneurysm size has a causal relationship with worse outcomes or is a marker of something else is still a matter of debate: patients with larger aneurysms are usually older, have more comorbidities, and are at higher surgical risk; all these factors could explain why these patients experience increased morbidity and mortality. In that sense, it is meaningful to notice that the baseline aneurysm diameter was larger in patients undergoing F-BEVAR interventions after prior infrarenal repair, and several explanations might be offered to analyze this finding. On one side, patients experiencing EVAR/OAR failure might have been those with lower compliance to follow-up protocols which could explain in itself the larger sac size as compared with screening-detected native aneurysms. However, this might also be related to the older age and perceived higher complexity of subjects considered for F-BEVAR regrafting, which could lead physicians to consider a higher size threshold for treatment referral. Nevertheless, larger aneurysm size could be regarded as a negative prognostic marker both in the perioperative phase as well as during follow-up in order to implement proper pathways of care.

Study Limitations

Findings from this study must be interpreted in the context of its limitations. The study was retrospective, with a relatively small sample size and limited follow-up owing to the increase of F-BEVAR cases performed in patients who had prior infrarenal repair in the later years of experience. Nevertheless, we report on >200 consecutive patients treated over a 10-year period with a median follow-up of 3 years and virtually complete survival assessment due to cross-linkage with national death registry data, rendering the conclusions clinically accurate and meaningful. All patients included in this series were treated at two highly specialized endovascular aortic centers, which may limit the generalizability of study findings to less experienced operators. Although statistical significance was not reached likely reflecting type II error owing to the small sample size, more technical failures were noted in the group of patients undergoing F-BEVAR after prior infrarenal repair; for the same reasons, regression analysis for this outcome could not be performed. The low number of patients with prior EVAR or OAR did not allow any specific subanalysis for these subgroups, and detailed information on prior procedures was not available for this study thereby making it impossible to analyze the risk factors that led to failure of prior infrarenal repairs. Although we attempted to correct for known confounders using multivariate analysis, it is possible that unmeasured confounders still remained.

Conclusions

F-BEVAR is equally safe and feasible for treatment of patients with prior infrarenal repair as compared with those undergoing treatment for native aneurysms. A higher level of technical complexity can be expected, and increased rates of TV-related endoleaks were observed which could lead to lower freedom from aneurysm sac shrinkage during follow-up. Nevertheless, the 5-year rates of reinterventions and TV patency were similar, thereby indicating that overall effectiveness of treatment remained satisfactory at mid-term. These results could support extended use of F-BEVAR as first-line option for treatment of OAR/EVAR failures in well-selected patients with suitable anatomy. The increasing proportion of F-BEVAR interventions performed in patients with prior infrarenal repair over time highlights the need for larger multicentric studies with extended follow-up to allow sufficient power for further analyses.

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Supplemental Material

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References

1. Wanhainen A, Verzini F, Van Herzeele I, et al. Editor's choice—European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg*. 2019;57(1):8–93.
2. Antoniou GA, Antoniou SA, Torella F. Editor's choice—Endovascular vs open repair for abdominal aortic aneurysm: systematic review and meta-analysis of updated peri-operative and long-term of randomized controlled trials. *Eur J Vasc Endovasc Surg*. 2020;59:385–397.
3. Li B, Khan S, Salata K, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal aortic aneurysm. *J Vasc Surg*. 2019;70(3):954–969.
4. D'Oria M, Mastrorilli D, Calvagna C, et al. Secondary endovascular repair of recurring lesion and perioperative complications after open aortic repair: the complementary role of different technical solutions. *Ann Vasc Surg*. 2020;63:99–107.
5. Rinaldi E, Kahlberg A, Carta N, et al. Late open conversion following failure of EVAR and TEVAR: "State of the Art." *Cardiovasc Intervent Radiol*. 2020;43(12):1855–1864
6. Katsargyris A, Yazar O, Oikonomou K, et al. Fenestrated stent-grafts for salvage of prior endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg*. 2013;46:49–56.
7. Martin Z, Greenberg RK, Mastracci TM, et al. Late rescue of proximal endograft failure using fenestrated and branched devices. *J Vasc Surg*. 2014;59(6):1479–1487
8. Marques de Marino P, Malgor RD, Verhoeven EL, et al. Rescue of proximal failure of endovascular abdominal aortic aneurysm repair with standard and fenestrated grafts. *J Cardiovasc Surg (Torino)*. 2019;60(2):159–166
9. D'Oria M, Griselli F, Mastrorilli D, et al. Novel application of custom-made stent-grafts with inner branches for secondary treatment after stent-graft migration of previous infrarenal endovascular aortic repair. *Ann Vasc Surg*. 2020;66:665.e9–665.e15.
10. Crawford ES, Crawford JL, Safi HJ, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg*. 1986;3(3):389–404
11. Safi HJ, Miller CC III. Spinal cord protection in descending thoracic and thoracoabdominal aortic repair. *Ann Thorac Surg*. 1937–1939; discussion 1953–1958.
12. D'Oria M, Budtz-Lilly J, Wanhainen A, et al. Short-term and mid-term outcomes after use of the native infrarenal aorta as distal landing zone for fenestrated-branched endovascular aortic repair. *Ann Vasc Surg*. 2021;72:114–123.
13. Oderich GS, Forbes TL, Chaer R, et al. Reporting standards for endovascular aortic repair of aneurysms involving the renal-mesenteric arteries. *J Vasc Surg*. 2021;73(1):4S–52S.
14. Gallitto E, Gargiulo M, Freyrie A, et al. Fenestrated and branched endograft after previous aortic repair. *Ann Vasc Surg*. 2016;32:119–127.
15. Xodo A, D'Oria M, Squizzato F, et al. Fifteen-year multicentric experience of Early and mid-term outcomes following open surgical conversion for failed endovascular aneurysm repair from the "Italian North-easT RegIstry of surgical Conversion AfTer Evar" (INTRICATE) [published online ahead of print June 25, 2021]. *J Vasc Surg*. doi:10.1016/j.jvs.2021.05.053.
16. Ultee KHJ, Soder PA, Zettervall SL, et al. Conversion from endovascular to open abdominal aortic aneurysm repair. *J Vasc Surg*. 2016;64:76–82.
17. Kansal V, Nagpal S, Jetty P. Editor's choice—Late open surgical conversion after endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg*. 2018;55(2):163–169.
18. Davidovic LB, Palombo D, Treska V, et al. Late open conversion after endovascular abdominal aortic aneurysm repair: experience of three high-volume centers. *J Cardiovasc Surg (Torino)*. 2020;61(2):183–190.
19. Perini P, Gargiulo M, Silingardi R, et al. Twenty-two year multicentre experience of late open conversion after endovascular abdominal aneurysm repair. *Eur J Vasc Endovasc Surg*. 2020;59(5):757–765.
20. Goudeketting SR, Fung Kon Jin PHP, Ünlü Ç, et al. Systematic review and meta-analysis of elective and urgent late open conversion after failed endovascular aneurysm repair. *J Vasc Surg*. 2019;70(2):615–628.
21. Verhoeven EL, Katsargyris A, Bekkema F, et al. Editor's choice—ten-year experience with endovascular repair of thoracoabdominal aortic aneurysms: results from 166 consecutive patients. *Eur J Vasc Endovasc Surg*. 2015;49(5):524–531.
22. Schanzer A, Simons JP, Flahive J, et al. Outcomes of fenestrated and branched endovascular repair of complex abdominal and thoracoabdominal aortic aneurysms. *J Vasc Surg*. 2017;66(3):687–694.
23. Oderich GS, Ribeiro M, de Souza LR, et al. Endovascular repair of thoracoabdominal aortic aneurysms using fenestrated and branched endografts. *J Thorac Cardiovasc Surg*. 2017;153:S32–S41.

24. Gallitto E, Faggioli G, Mascoli C, et al. Impact of previous open aortic repair on the outcome of thoracoabdominal fenestrated and branched endografts. *J Vasc Surg*. 2018;68(6):1667–1675.
25. Sveinsson M, Kristmundsson T, Dias N, et al. Juxtarenal endovascular therapy with fenestrated and branched stent-grafts after previous infrarenal repair. *J Vasc Surg*. 2019;70(6):1747–1753.
26. Wang SK, Drucker Na Sawchuk AP, Lemmon GW, et al. Use of the Zenith platform to rescue failing endovascular and open aortic reconstructions is safe and technically feasible. *J Vasc Surg*. 2018;68:1017–1022.
27. Manunga J, Stanberry LI, Alden P, et al. Technical approach and outcomes of failed infrarenal endovascular aneurysm repairs rescued with fenestrated and branched endografts. *CVIR Endovacular*. 2019;2:34.
28. Gallitto E, Sobocinski J, Mascoi C, et al. Fenestrated and branched thoraco-abodminal endografting after previous open abdominal aortic repair. *Eur J Vasc Endovasc Surg*. 2020;60:843–852.
29. Schanzer A, Beck AW, Eagleton M, et al. Results of fenestrated and branched endovascular aortic aneurysm repair after failed infrarenal endovascular aortic aneurysm repair. *J Vasc Surg*. 2020;72(3):849–858.
30. Antonello RM, D'Oria M, Cavallaro M, et al. Management of abdominal aortic prosthetic graft and endograft infections. *J Infect Chemother*. 2019;25(9):669–680.
31. Chakfè N, Diener H, Lejay A, et al. Editor's choice—European Society for Vascular Surgery (ESVS) 2020 clinical practice guidelines on the management of vascular graft and endograft infections. *Eur J Vasc Endovasc Surg*. 2020;59:339–384.
32. Gavali H, Mani K, Furebring M, et al. Branched endovascular aortic plug in patients with infrarenal aortic graft infection and hostile anatomy. *J Endovasc Ther*. 2020;27(2):328–333.
33. Adovasio R, Chiarandini S, Calvagna C, et al. Treatment of complex abdominal aortic aneurysms with parallel graft-endovascular aneurysm repair. *Ann Vasc Surg*. 2018;47:260–265.
34. Reyes A, Donas KP, Pitoulias G, et al. Complementary role of fenestrated/branched endografting and the chimney technique in the treatment of pararenal aneurysms after open abdominal aortic repair. *J Endovasc Ther*. 2016;23(4):599–605.
35. Eleshra A, Oderich GS, Spanos K, et al. Short-term outcomes of the t-Branch off-the-shelf multibranched stent-graft for reintervention after previous infrarenal aortic repair. *J Vasc Surg*. 2020;72(5):1558–1566.
36. Juraszek A, Rylski B, Kondov S, et al. Late surgical conversions after abdominal aortic endovascular aortic repair: underlying mechanisms, clinical results and strategies for prevention. *Interact Cardiovasc Thorac Surg*. 2019;29:944–949.
37. D'Oria M, Wanhainen A, DeMartino R, et al. A scoping review of the rationale and evidence for cost-effectiveness analysis of fenestrated-branched endovascular repair for intact complex aortic aneurysms. *J Vasc Surg*. 2020;72(5):1772–1782.
38. Schanzer A, Messina L. Two decades of endovascular abdominal aortic aneurysm repair: enormous progress with serious lessons learned. *J Am Heart Assoc*. 2012;1(3):e000075.
39. Huang Y, Gloviczki P, Duncan AA, et al. Maximal aortic diameter affects outcome after endovascular repair of abdominal aortic aneurysms. *J Vasc Surg*. 2017;65(5):1313–1322.
40. Deery SE, Ergul EA, Schermerhorn ML, et al. Aneurysm sac expansion is independently associated with late mortality in patients treated with endovascular aneurysm repair. *J Vasc Surg*. 2018;67(1):157–164.
41. O'Donnell TFX, Deery SE, Boitano LT, et al. Aneurysm sac failure to regress after endovascular aneurysm repair is associated with lower long-term survival. *J Vasc Surg*. 2019;69(2):414–422.
42. Ramos C, Pujari A, Rajani RR, et al. Perioperative outcomes for abdominal aortic aneurysm repair based on aneurysm diameter. *Vasc Endovascular Surg*. 2020;54(4):341–347.