Outcomes of fenestrated endovascular repair of juxtarenal aortic aneurysm

Thorarinn Kristmundsson, MD, PhD, Björn Sönesson, MD, PhD, Nuno Dias, MD, PhD, Per Törnqvist, MD, Martin Malina, MD, PhD, and Timothy Resch, MD, PhD, Malmö, Sweden

Objective: To evaluate late outcomes after fenestrated endovascular aortic repair (f-EVAR) in a tertiary European referral center.

Methods: In 2009, we published short- and midterm results after f-EVAR in the first 54 patients treated with this technique at our center between September 2002 and June 2007. In this paper, we provide long-term follow-up of the same patient cohort with the main focus on target vessel (TV) patency, renal function, reinterventions, and survival.

Results: A total of 54 patients were included in this study. Median age was 72 years (interquartile range [IQR], 68-76 years) at primary operation, and 85% were men. Median preoperative aneurysm diameter was 60 mm (IQR, 53-66 mm). One hundred thirty-four vessels were targeted (mean, 2.5 per patient), and 96 TV stents were placed. The median clinical follow-up was 67 months (IQR, 37-90 months), and computed tomography follow-up was 60 months (IQR, 35-72 months). Aneurysm diameter decreased ≥5 mm in 39% ± 7% at 12 months, 64% ± 8% at 36 months, and 71% ± 8% at 60 months. Primary TV patency was 94% ± 2% at 12 months, 91% ± 3% at 36 months, and 90% ± 3% at 60 months. Glomerular filtration rate decreased by 17% at 59 months (IQR, 26-73 months) follow-up (60 [IQR, 46-79] vs 50 [IQR, 38-72] mL/min/1.73 m²; P < .001), and one patient became dialysis-dependent secondary to a renal stent occlusion. Reintervention-free survival was 88% ± 5% at 12 months, 69% ± 7% at 36 months, and 56% ± 5% at 60 months. At least one reintervention was done in 37% of patients, of which 29% were endoleak-related, 26% TV-related, 13% graft-limb-related, and 32% due to other causes. The majority of reinterventions (68%) were based on complications detected on routine follow-up. Estimated overall survival was 93% ± 4% at 12 months, 76% ± 6% at 36 months, and 60% ± 7% at 60 months. In total, 54% of the patients died during the 10-year study period, where 9% died of aneurysm-related causes.

Conclusions: Long-term mortality after f-EVAR is high, but most patients die from nonaneurysmal causes. Aneurysm-related mortality is associated with technical complications that can be reduced with increased experience. Reinterventions are common, and most complications are detected on routine follow-up. (J Vasc Surg 2014;59:115-20.)

The Zenith fenestrated abdominal aortic aneurysm endovascular graft was approved by the U.S. Food and Drug Administration (FDA) in April 2012, and consequently, an explosive increase in fenestrated endovascular aortic repair (f-EVAR) is to be expected in the United States. At our center, the first f-EVAR was performed in late 2002, and the number of patients treated with this method has gradually increased, with close to 50 procedures performed annually during the past few years. In 2009, we published short- and midterm results of our initial experience with the fenestrated device, which included a learning curve for the procedure. Since then, numerous authors have published promising short-term results, but long-term follow-up is lacking. In this paper, we provide long-term follow-up of our initial experience for better understanding of late complications and mortality in this patient group.

METHODS

All patients treated with f-EVAR between September 2002 and June 2007 were prospectively enrolled in a database incorporating multiple variables such as stent graft design and patient demographics. Work-up consisted of clinical exam and high-resolution spiral computed tomography (CT) scans, which were reconstructed in a vascular three-dimensional workstation (www.terarecon.com). During this period, all patients who were anatomically unfit for standard infrarenal EVAR and deemed at high risk for open aneurysm repair were considered for f-EVAR. The Zenith device (William Cook Europe, Bjaeverskov, Denmark) formed the foundation of the fenestrated graft in all cases. Follow-up consisted of clinical exam at 1 month as well as CT scans and plain abdominal films after 1 month, 1 year, and yearly thereafter. As part of the follow-up protocol, medical records and follow-up images were electronically linked to our center for evaluation by the operating surgeon and the corresponding author. Deaths were verified through a national register, and medical records were obtained for further analysis when aneurysm-related death was suspected. End points were target vessel (TV) stenosis or occlusion, secondary
intervention, or death. Aneurysm-related death was defined as all deaths occurring within 30 days from the initial procedure as well as late deaths associated with stent graft complications. Endoleaks, changes in aneurysm size, and changes in glomerular filtration rate (GFR) over time were also registered. Aneurysm diameter changes were considered significant when ≥5 mm. A detailed study method has been published earlier and covers our initial experience with fenestrated devices.

Statistics. Continuous data are presented as median with interquartile range in parenthesis. The Wilcoxon signed-rank test was used for analyzing changes in aortic diameter and GFR. Estimations of mortality, TV patency, changes in aortic diameter, and reintervention-free survival were done with Kaplan-Meier and life-table analysis (presented as percentages ± standard error). SPSS version 20.0 (SPSS Inc, Chicago, Ill; www.spss.com) was used for all statistical analysis, and $P < .05$ was considered statistically significant.

RESULTS

A total of 54 patients were included in the study. Median age was 72 (range, 68-76) years, and 85% were men. All patients were asymptomatic and were anatomically unsuitable for infrarenal EVAR. The median clinical follow-up was 67 (range, 37-90) months, CT follow-up was 60 (range, 35-72) months, and GFR follow-up was 59 (range, 26-73) months. Patient demographics, operative results, and short-term outcomes have been published earlier.

Aneurysm diameter. Median aortic diameter was 60 (range, 53-66) mm on the preoperative CT scan, 54 (range, 46-64) mm after 1 year, 51 (range, 39-61) mm after 3 years, and 50 (range, 39-50) mm after 5 years ($P < .001$). Aneurysm diameter decreased ≥5 mm in 39% ± 7% of patients at 12 months, 64% ± 8% at 36 months, and 71% ± 8% at 60 months. Changes in aortic diameter over time are presented in Fig 1.

Endoleaks. Large balloon-expandable stents were used intraoperatively to treat type I ($n = 11$) or type III ($n = 3$) endoleaks in 13 patients. Completion angiography showed type I endoleaks in three patients, two proximal and one distal. The proximal leaks had resolved on pre-discharge CT scans, and the distal leak was treated with a giant Palmaz stent on postoperative day 4. Late type I endoleaks were observed in five patients. All leaks were associated with the distal sealing zones and successfully treated with distal extensions after their appearance on 1-month, 1-year, 2-year, 3-year, and 5-year CT scans. Three of the patients required treatment bilaterally.

Type II endoleaks were observed in 13 patients on completion angiography and persisted in three patients at 1 year. One patient was treated with coil embolization of the inferior mesenteric artery after 44 days (endoleak on 1-month CT scan) and another with glue embolization of lumbar arteries after 553 days (expanding aneurysm sac). Both endoleaks reappeared on 3-year CT scans. In the first case, the leak was successfully treated with glue embolization, but in the second case, the patient died of nonaneurysm-related causes prior to any reintervention. No other type II endoleaks were treated.

One patient had a type III endoleak on the completion angiography but died from complications due to bowel ischemia prior to any control angiography. One patient with an expanding aneurysm sac without signs of endoleak during follow-up died from aneurysm rupture secondary to a separation of the proximal and bifurcated components 3 years postoperatively after emergency conversion to open repair.

TV patency. One hundred thirty-four vessels were targeted (mean, 2.5 per patient), and 96 TV stents were placed (all balloon-expandable, 72% uncovered, 28% covered). Estimated primary TV patency was 94% ± 2% at 12 months, 91% ± 3% at 36 months, and 90% ± 3% at 60 months, with primary-assisted patency of 96% ± 2% at 12 months and 93% ± 2% at 36 and 60 months. Seven renal angiographies were performed, leading to three reinterventions at 1 year, one reintervention at 2 years, and one reintervention at 4 years. Two unstented renal arteries early in the series became partially covered by the stent graft fabric without causing a hemodynamically significant stenosis or occlusion during the follow-up period. Two other stented renal arteries had a significant stenosis on 1-year CT follow-up and were not treated. In one case, the patient had disseminated malignant disease, and in the other case, the kidney had shrunked and was non-functional at the time of diagnosis. Additionally, one superior mesenteric artery (SMA) was stented due to an asymptomatic stenosis detected at 6-year follow-up (3.6% of unstented SMA scallops).
Eight (6%) of the TVs occluded: three SMAs and five renal arteries. Two SMAs occluded prior to the 12-month CT scan and one 6 months postoperatively (10.7% of unstented SMA scallops). In all cases, the patients were asymptomatic, and no further intervention was necessary. One renal artery was sacrificed to seal a type I endoleak intraoperatively, one occluded prior to a 12-month CT scan, and three occluded after 3 years (all stented primarily through 6- × 8-mm renal fenestrations). Of those late occlusions, one patient became dialysis-dependent due to a reduced arterial circulation in the other kidney without any signs of stenosis on angiography. TV patency over time is presented in Fig 2.

**Renal function.** One patient was on dialysis prior to endografting. The median preoperative GFR was 60 (range, 46-79) mL/min/1.73 m², and 50% of the patients had a baseline renal dysfunction at the time of the initial procedure (GFR <60). Nineteen patients (35%) developed at least a transient decrease in GFR (>30%) in the immediate postoperative period. At last follow-up, GFR decreased to 50 (38-72; P < .001) in the whole patient cohort, and seven (26%) of the patients with normal preoperative renal function had developed a decrease in GFR >30%. Of those, one patient had developed a renal stenosis with assisted primary patency after 24 months. The remaining six patients had no signs of decreased renal perfusion on CT angiography during follow-up. Of the patients with preoperative renal dysfunction, one patient became dialysis-dependent due to a renal artery occlusion 3 years postoperatively, and six patients (22%) deteriorated successively with >30% decrease in GFR without any signs of decreased perfusion on CT angiography during follow-up. Changes in renal function over time are presented in Fig 3.

**Reinterventions.** Reintervention-free survival rate was 88% ± 5% at 1 year, 69% ± 7% at 3 years, and 56% ± 5% at 5 years (Fig 4). Thirty-one reinterventions were done in 20 (37%) patients. Of those, 29% were endoleak-related, 26% TV-related, 13% graft-limb-related, and 32% due to other causes. The majority of reinterventions (68%) were based on complications detected on routine follow-up. Reinterventions are presented in Table I.

**Survival.** Estimated overall survival was 93% ± 4% at 1 year, 76% ± 6% at 3 years, and 60% ± 7% at 5 years. Twenty-nine patients died during the follow-up period (54%), and two of those within 30 days of the initial procedure (3.7%). One patient developed bowel ischemia secondary to mesenteric artery embolization and died after 13 days from multiorgan failure. One patient died after 15 days from complications secondary to retroperitoneal bleeding, which was caused by a renal artery perforation during the procedure. Three late deaths were aneurysm-related. One patient died from massive bleeding at an outside hospital 6 months after the primary procedure during surgery of the groin related to infection. One patient died of aneurysm rupture due to separation of the proximal and bifurcated components after 35 months, and one patient died of bowel ischemia secondary to graft infection after 72 months. In total, 9% of all deaths were aneurysm-related. Patient demographics and graft configuration of the cohort remaining in the study at 1, 3, and 5 years is presented in Table II, and survival function for all-cause mortality is given in Fig 5.

**DISCUSSION**

The Zenith fenestrated abdominal aortic aneurysm endovascular graft has been on the market in the European Union since late 2005 and was FDA approved in the U.S. in April 2012. As with most endovascular treatments,
f-EVAR has the appeal of the minimally invasive approach, and data until now have confirmed that this method works in the short- to midterm. Due to the novelty of this technique, reports on long-term follow-up in this patient group are lacking.

Operative mortality has been reported between 0.2% and 2.6%,2-8 with a pooled proportion mortality rate of 2.0% in meta-analysis.9 This compares favorably with that of open surgical repair of short neck aneurysm, which has operative mortality rates of 2.5% to 5.8%.10,11 In our series, operative mortality occurred in two patients (3.7%), and both deaths were secondary to technical complications during the procedure, indicating that catheterization and stenting of TVs add a level of complexity. With increased experience, technical failures are likely to decrease, as no operative deaths occurred from technical failures at our center in the 100 consecutive patients treated (unpublished data). A major concern is the late aneurysm deaths and overall mortality in our series. In one case, death occurred secondary to device failure missed on routine follow-up. Separation of the proximal and bifurcated components resulted in repressurization of the aneurysm sac with

### Table I. Reinterventions during follow-up

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number</th>
<th>Reintervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I endoleak</td>
<td>5</td>
<td>Distal limb extensions (5; 3 bilaterally)</td>
</tr>
<tr>
<td>Type II endoleak</td>
<td>4</td>
<td>Glue embolization (2), coiling IMA (1), untreated (1)</td>
</tr>
<tr>
<td>TV stenosis</td>
<td>8</td>
<td>Renal PTA (5), SMA PTA (1), untreated (2)</td>
</tr>
<tr>
<td>Graft limb stenosis</td>
<td>1</td>
<td>Stenting (1)</td>
</tr>
<tr>
<td>Graft limb occlusion</td>
<td>3</td>
<td>Thrombectomy and patch in CFA (1), femoro-femoral crossover (2)</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>Pressure measurements in nonshrinking aneurysm (5), endostapling due to migration (1), coiling of renal artery bleeding (1), drainage of hematoma (1), drainage of infection (1), thrombolyis of graft occlusion (1)</td>
</tr>
</tbody>
</table>

### Table II. Comorbidities and number of fenestrations in patients remaining in the study at 12, 36, and 60 months of follow-up

<table>
<thead>
<tr>
<th></th>
<th>12 months</th>
<th>36 months</th>
<th>60 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>12%</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>43%</td>
<td>45%</td>
<td>49%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>14%</td>
<td>14%</td>
<td>9%</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>60%</td>
<td>62%</td>
<td>58%</td>
</tr>
<tr>
<td>Chronic obstructive</td>
<td>41%</td>
<td>36%</td>
<td>33%</td>
</tr>
<tr>
<td>pulmonary disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>50%</td>
<td>49%</td>
<td>40%</td>
</tr>
<tr>
<td>Mean number of fenestrations</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
</tbody>
</table>

CFA, Common femoral artery; IMA, inferior mesenteric artery; PTA, percutaneous transluminal angioplasty; SMA, superior mesenteric artery; TV, target vessel.
The majority of reinterventions (68%) were based on findings on routine CT follow-up.

Fig 4. Kaplan-Meier estimate of the reintervention-free survival. Majority (68%) of reinterventions were based on findings detected on routine computed tomography (CT) follow-up.

Fig 5. Kaplan-Meier estimate of the survival function for all-cause mortality. Overall mortality in the study period was 54%, with abdominal aortic aneurysm-related mortality of 9%.
a secondary rupture and death 3 years after the initial procedure despite an emergency open repair. The possibility of distal movement of the bifurcated component after f-EVAR is indeed deliberate to avoid displacement of the proximal fenestrated graft, which might result in crushing of the TV bridging stents. When the component overlap is insufficient, especially in a large aneurysm sac, total dislocation of the components can occur. Even if clinical consequences are rare, reported intercomponent migration is found in up to 13% of patients during follow-up, making detailed evaluation of component overlap necessary on follow-up CT scans. In this particular patient, component separation (<2 stent overlap) was only noted retrospectively. We now routinely evaluate intercomponent migration between the fenestrated and bifurcated components by measuring the distance between gold markers on plain abdominal films and/or CT reconstructions during follow-up. Other late aneurysm-related deaths were secondary to infection. In one case, the patient died at an outside hospital due to bleeding associated with abscess drainage in the groin, and in the other case, the visceral segment of the graft occluded in a patient with a chronic stent graft infection.

Additionally, 24 (44%) of the patients died of other causes, making overall mortality 54% at a median follow-up of 67 months. Although survival was better than in an untreated cohort of patients unfit for open surgery, the mortality rate is in line with overall mortality in patients with peripheral vascular disease, indicating severe comorbidities in this patient group. This might partially reflect the fact, that during this time period, only patients deemed unfit for open surgery were considered for fenestrated repair. Considering the high operative mortality after open surgery, we now offer f-EVAR as the first-line treatment in all patients with juxtarenal aneurysm, which might increase survival in the long term.

As reported in our previous publication, most TVs are successfully catheterized during the procedure. At 1 year, estimated primary patency of all TVs was 94% ± 2% and primary-assisted patency 96% ± 2%, which compares well to earlier reports of fenestrated and branched devices. Of eight TV occlusions, five occurred in the first postoperative year, but late occlusions did occur in three stented renal arteries (two bare stents, one covered stent) where no signs of stenosis were apparent during follow-up. This was probably related to distal migration of the fenestrated component resulting in fractures in the bridging renal stents. Despite most TV occlusion being asymptomatic, close evaluation of TV stents during follow-up is to be recommended using appropriate CT reconstructions.

One concern regarding f-EVAR is the potential negative effect on renal function. This has been described earlier, with a decrease in renal function in about one-fifth of patients postoperatively. In our series, 50% of patients had a baseline renal dysfunction prior to treatment, and the median GFR decreased significantly over time in 26% of the patients. Only 14% of patients with significant impairment had signs of decreased renal blood flow during follow-up, including one patient with renal stent occlusion that became dialysis-dependent. For the remaining patients at least, renal impairment is probably associated with the natural course of the aneurysmal disease. Reports on infrarenal EVAR describe renal deterioration over time, regardless of whether bare fixation stents across the renal arteries are used or not. This even applies to open repair, where renal function is negatively affected in the immediate postoperative period in a large number of patients. Series that have compared open and endovascular repair report conflicting results, most likely due to selection bias. Renal status is also negatively correlated to longer operation time and more proximal clamp positioning, which is likely to negatively affect patients undergoing open surgery for juxtarenal aneurysms.

Estimated freedom from reintervention was significantly lower than after infrarenal EVAR in the contemporary setting, with many reinterventions being endoleak- and TV-related. Late type I endoleaks were exclusively associated with the distal sealing zone appearing at different time intervals during follow-up. This emphasizes that, for long-term durability of the repair, the distal sealing zone has to be of good quality as progression of the aneurysmal disease can be expected in the common iliac arteries. If both common iliacs are dilated, we now apply unilateral iliac branch with coil- or covered stent placement. Most TV occlusions were distal to the pelvis and left colon. Still, a majority of reinterventions were due to causes other than endoleak and TV failures, with a large portion being pressure measurements in nonshrinking and expanding aneurysms as part of an ongoing study. In most cases, no further intervention was needed, and this procedure is now almost entirely conserved for expanding aneurysm without apparent cause, endoleak embolization, or aspiration and culture where graft infection is suspected. Thus, one can expect the reintervention rate to be significantly reduced in the contemporary setting.

CONCLUSIONS
f-EVAR is a procedure with good short-, mid-, and long-term results. Long-term mortality is high but mostly nonaneurysm-related. Aneurysm-related mortality is associated with technical complications that can be reduced with increased experience and better understanding of the stent graft behavior. Reinterventions are common, and most complications are detected on routine CT follow-up. Knowledge of failure mechanisms is vital to adequately evaluate postoperative imaging.

AUTHOR CONTRIBUTIONS
Conception and design: TK, BS, ND, PT, MM, TR
Analysis and interpretation: TK, BS, ND, PT, MM, TR
Data collection: TK
Writing the article: TK, TR
Critical revision of the article: TK, BS, ND, PT, MM, TR
Final approval of the article: TK, BS, ND, PT, MM, TR
Statistical analysis: TK
Obtained funding: Not applicable
Overall responsibility: TK

REFERENCES


