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1 **Risk factors for early and late mortality following complex aneurysm repair with F-**  
2 **BEVAR**

3  
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18

19 **Conflict of Interest:**

20 SH, is a consultant for Cook Medical, GE Healthcare, and Bentley.

21

22 **Key words:** aorta, aneurysm, endovascular repair, fenestrated

- 1 This work was presented at the international session of the 2017 Vascular Annual Meeting in
- 2 San Diego, CA.
- 3

1 **ABSTRACT**

2

3 **Background:** To evaluate outcomes following fenestrated and branched endovascular repair (F-  
4 BEVAR) performed in high-risk patients to treat para-renal (PR) and thoracoabdominal (TAAA)  
5 aneurysms, and to identify those patients likely to benefit from this treatment.

6 **Methods:** A prospective single-centre review of patients treated electively for PR and TAAA  
7 repair using F-BEVAR between 2004 and 2016 was performed. Survival was estimated utilizing  
8 the Kaplan-Meier method. Risk factors associated with 30-day mortality and mortality during  
9 follow-up were determined using multivariate statistical techniques and a Cox regression model  
10 including all variables that were significant on univariate analysis ( $p < 0.05$ ).

11 **Results:** 468 patients (median age 71.6 years) were identified with American Society for  
12 Anaesthesiology score  $\geq 3$  in 94.7%. There were 221 (47.2%) type 1-3 TAAA and 247 (52.8%)  
13 Type 4, 5 and PR aneurysms, with a median diameter of 58 mm. Technical success for target  
14 vessel stenting was 99.1% (1493/1506). The 30-day mortality rate was 4.9% (23 patients). The  
15 spinal cord ischemia rate was 3.8% (18 patients). Twenty patients (4.3%) required postoperative  
16 dialysis and four patients (0.8%) long-term dialysis after discharge. Median follow-up was 29  
17 months. Survival at one, three and five years was 86.7% (IC95% = 83.1 – 89.6), 73.3% (IC95%  
18 = 68.3 – 77.6) and 59.6% (IC95% = 53.4 – 65.2) respectively. Freedom from any target vessel  
19 occlusion and from secondary procedures were 96.2% (IC95% = 93.8 – 97.7) and 88.2% (IC95%  
20 = 84.8 – 90.9) at one year, and 90.0% (IC95% = 84.5 – 91.9) and 70.2% (IC95% = 63.9 – 75.6)  
21 at five years respectively. In multivariate analysis, early mortality was associated with procedure  
22 time (HR=1.007 per minute; IC95% = 1.003 – 1.010;  $p < 0.001$ ), TAAA pre-operative diameter  
23 (HR = 1.053 per mm; IC95% = 1.020 – 1.087;  $p = 0.001$ ) and chronic kidney disease (CKD)

1 (HR = 3.139; IC95% = 1.369 – 7.196; p = 0.007). Mortality during the first 24 months of  
2 follow-up was associated with Crawford type I-III (HR = 1.526; IC95% = 1.061 – 2.196; p =  
3 0.023) as compared with infra diaphragmatic repairs, CKD (HR = 1.874; IC95% = 1.294 –  
4 2.712; p <0.001) and TAAA pre-operative diameter (HR = 1.027 per mm; IC95% = 1.010 –  
5 1.044; p = 0.002). In addition to the previous risk factors, mortality after 24 months of follow-up  
6 was also associated with age at repair (HR = 1.055 per year; IC95% = 1.021 – 1.090; p = 0.001).

7  
8 **Conclusion:** F-BEVAR performed in high risk patients is associated with favourable outcomes.  
9 Judicious patient selection should take into consideration the reported risk factors associated with  
10 early and late mortality.

11

12

1

**2 INTRODUCTION:**

3

4 Fenestrated and branch endografts have been progressively utilized to treat complex aneurysms  
5 involving visceral and renal arteries. The technique has matured, and the use of fenestrated and  
6 branched endovascular repair (F-BEVAR) has evolved for the treatment of varieties of complex  
7 anatomical aneurysms. F-BEVAR has been shown to be safe and effective with high technical  
8 success and low mortality rates as reported in large series specialized centers.<sup>1-6</sup>

9 Although open remains standard of care in most centers, it is associated with high morbidity and  
10 mortality rates and remains an excessive challenge in high risk patients. Contemporary F-  
11 BEVAR has emerged as a promising modality in this patient population.<sup>7-10</sup>

12 Prospective analysis of a large standard EVAR database identifies a number of factors associated  
13 with peri-operative mortality. These include age, a history of congestive heart failure, aneurysm  
14 diameter at treatment, and chronic renal insufficiency.<sup>11</sup> To date, the limited populations  
15 reported for F-BEVAR make it difficult to draw or refute equivalent conclusions. The  
16 identification of these risk factors is paramount to the development of selection criteria and  
17 management strategies for patients offered F-BEVAR.

18

19 This study presents a single center experience of 468 high-risk patients and is intended to shed  
20 light on the short and long-term outcomes after F-BEVAR and to elucidate factors that predict  
21 poor outcomes in this fragile population.

1

## 2 MATERIAL AND METHODS

3

### 4 Study population

5 The study was conducted as a retrospective analysis of prospectively collected data at the Aortic  
6 Center of CHU Lille, France. All patients with para-renal (PR, including AAA with necks  
7 <10mm long, juxta renal aneurysms, and aneurysms with no normal aorta between upper extent  
8 of aneurysm and renal arteries) or thoracoabdominal (TAAA) aneurysms who underwent  
9 endovascular aneurysm repair with branched (BEVAR) or fenestrated (FEVAR) devices between  
10 October 2004 and December 2016 were included. The indication for PR or TAAA aneurysm  
11 repair was a maximum aneurysm diameter  $\geq 50$  mm or a rapidly expanding aneurysm ( $> 10$   
12 mm/year). F-BEVAR was restricted to elective cases because of the delay required to design and  
13 manufacture these custom-made devices (CMD). Aneurysms were classified according to the  
14 extent of aortic stent graft coverage into categories TAAA Crawford type 1 to 5 and PR  
15 aneurysm. All patients signed pre-operative informed consent for the collection of their data in  
16 our study database and for the future use of these data for scientific research. The choice between  
17 open and endovascular repair of complex aneurysms was made during a weekly  
18 multidisciplinary Aortic conference involving vascular and cardiac surgeons, cardiologists,  
19 radiologists and anaesthetists. This retrospective study was undertaken as a clinical audit  
20 according to our centres' local regulations. IRB approval was not required.

21

22 Pre-operative variables collected included demographics, co-morbidities and cardiovascular risk  
23 factors, cardiovascular drug intake, previous aortic surgery, maximum aortic diameter and the

1 presence of Marfan's syndrome or previous aortic dissection. Chronic kidney disease (CKD)  
2 was defined as an estimated glomerular filtration rate (eGFR) less than 60 ml min<sup>-1</sup>.

3

#### 4 **Eligibility for endovascular repair and device design**

5 Anatomical suitability for endovascular repair was determined by the treating surgeon during a  
6 dedicated planning meeting. Images from high-resolution thin-sliced CTA were analysed using  
7 TeraRecon AquariusNet (TeraRecon, San Mateo, CA, USA). All procedures were performed  
8 with custom-made (CMD) fenestrated or branched devices, or with off-the-shelf branched  
9 devices (Zenith t-Branch), all of which were manufactured by Cook Medical (Bloomington,  
10 IND, USA). The choice between a fenestrated, branched, or mixed graft was based on aortic and  
11 target vessel morphology, including the extent of the aneurysm and the diameter of the aortic  
12 lumen at the level of the visceral vessels.

13

14 Bridging stent configurations were selected during the planning meetings with consideration of  
15 the type of endograft and the morphology of the target vessel lumen, including diameter and  
16 distance from the ostium to the first major branch. Fenestrations were aligned with balloon-  
17 expandable covered stents such as the Advanta V12<sup>®</sup> (Atrium Medical, Maquet, New Hampshire,  
18 USA) and the second generation BeGraft Peripheral Stent Graft<sup>®</sup> (Bentley InnoMed GmbH,  
19 Hechingen, Germany) the latter after October 2015. Branches were aligned with self-expandable  
20 covered stents such as the Fluency<sup>®</sup> Vascular Stent Graft (Bard, Tempe, USA), with distal  
21 relining with a self-expandable bare-metal stent such as the E-Luminexx<sup>®</sup> Endovascular Stent  
22 (Bard, Tempe, USA).

1 Late target vessel instability was defined as a composite outcome including target vessel  
2 occlusion and target vessel reintervention during follow-up.

3

#### 4 **Procedures**

5 Procedures were initially performed in a standard operating room with a mobile C-arm (GE  
6 Healthcare, Buc, France). After October 2012, all interventions were performed in a dedicated  
7 hybrid operating room using the Discovery IGS 730 module (GE Healthcare, Buc, France).

8 Radiation exposure was minimized in accordance to the ALARP principle, including the use of  
9 fusion images, shielding, collimation, low-dose settings, and digital zoom instead of actual  
10 magnification.

11

12 Procedures were performed under general or spinal anesthesia. Preventive measures for spinal  
13 cord ischemia (post-operative paraparesis or paraplegia) were implemented according to a  
14 standardized protocol. Spinal cord protection with cerebrospinal fluid (CSF) drainage was used  
15 in type 1-3 TAAA.<sup>12</sup> Most spinal drains were inserted the day before the intervention.

16 Additional preventive measures included early limb reperfusion during surgery, permissive  
17 hypertension (target mean arterial pressure of 90mmHg) and liberal transfusion in cases of  
18 postoperative hemoglobin < 10g/dl.

19

20 The decision to perform percutaneous transfemoral access or surgical cutdown was based on the  
21 patient's body habitus, the localization of the femoral bifurcation and the quality of the vessel on  
22 preoperative CTA. In cases of percutaneous approach, two 6F Perclose ProGlide® Suture-  
23 Mediated Closure Systems (Abbott Vascular, Ill, USA) were used per punctured artery.

1

**2 Follow-up**

3 Post-operative 3D imaging before discharge was performed in all patients, either by early post-  
4 operative multi-detector computer tomography (MDCT) scans or by peri-operative Cone Beam  
5 computer tomography (CBCT). Duplex ultrasound (mostly contrast enhanced) was performed in  
6 all patients before discharge. Clinical and radiological follow-up was organized at 6, 12, 18 and  
7 24 month intervals and yearly thereafter. MDCT scans, duplex ultrasound, plain radiographs and  
8 eGFR assessments were obtained.

9

10 Cause of late death was determined from verbal or written communication with the treating  
11 doctor at the time of death.

12

13 Post-operative diagnosis of acute renal failure (ARF) was defined as a decrease in estimated  
14 glomerular filtration rate (eGFR) of more than 25 %, based on the RIFLE classification using  
15 eGFR evaluated during the first 72 hours after the procedure. Severe acute renal failure was  
16 defined as more than 50 % decrease in eGFR.

17

**18 Statistical analysis**

19 Data were collected in a prospective database with retrospective analyses using SAS software v  
20 9.4 (SAS Institute Inc., Cary, NC, USA). Continuous variables were expressed as median with  
21 their 25<sup>th</sup> and 75<sup>th</sup> percentiles. Categorical variables were presented as absolute numbers and  
22 percentages.

1 Population means were compared using Student's t tests or Mann Whitney U tests (according to  
2 normality assessed by the Shapiro-Wilk test in case of small sample sizes) and using the chi-  
3 square test of Fisher's test, as appropriate, for proportions of a categorical variable.

4 Predictive factors for early and late mortality were identified with multivariate Cox analysis.

5 Patients with peri-operative mortality were excluded from late mortality analysis.

6 The linear relationship between the outcome and a continuous covariate and proportional hazard  
7 assumption were tested by supremum tests. In case of a non-linear relationship, the continuous  
8 variable was dichotomized, the cut-off value being visually established and minimizing  
9 Schwarz's Bayesian Criterion. If proportional hazard assumption was not respected, a piecewise  
10 model was used to model the hazard ratio (HR) as a step function of time, the cut-off value being  
11 visually established.

12 The multivariate model was built by first including all predictors and then using different  
13 backward selection to reduce the model.

14 A two-tailed type I error rate of 0.05 was considered for statistical significance.

15

16

## 1 **RESULTS**

2

### 3 **Patients and aneurysms characteristics**

4 A total of 468 consecutive patients were treated with FEVAR or BEVAR from October 21<sup>st</sup> 2004

5 to December 31<sup>st</sup> 2016, including 441 males (94.2%) and 27 females (5.8%). Median age was

6 71.6 (65; 77) years, including 59 octogenarians (12.6 %).

7 Clinical and anatomical characteristics are listed in Table I. American Society for

8 Anaesthesiology score was  $\geq 3$  in 443 patients (94.7 %). Coronary artery disease (CAD) was

9 identified in 209 patients (44.7%), chronic obstructive pulmonary disease (COPD) in 172

10 patients (36.7%) and chronic kidney disease (CKD) in 112 patients (23.9 %), including 3

11 dialysis-dependent patients (0.6%). One hundred and twenty-seven patients (27.1%) had prior

12 aortic surgery.

13 Aneurysm classification according to aortic coverage was TAAA type I-II-III in 221 cases (47.2

14 %) and TAAA type IV, V and PR in 247 cases (52.8 %). Post-dissection aneurysm repair was

15 performed in 21 cases (4.5 %). Median maximum aortic diameter was 58 mm (53.75; 64).

16

### 17 **Stent graft design and adjunct devices**

18 Device specific details are outlined in Table II. Devices with fenestrations only, branches only,

19 and a combination of both were used in respectively 375 (80.1 %), 43 (9.2 %) and 50 (10.7%) of

20 patients. A total of 1519 fenestrations or branches were designed with a mean of 3.2 +/- 0.9

21 vessels per device. In addition, one hundred and ninety-four scallops were incorporated in 189

22 devices (40.4%).

23

1 Adjunct distal devices included bifurcated stentgrafts in 353 patients (75.4 %), mono-iliac grafts  
2 in 7 patients (1.5 %) and internal iliac branch devices in 12 patients (2.6 %). Thoracic endografts  
3 were used in 92 patients (19.7 %) during the same procedure and in 11 patients (2.3 %) during a  
4 first-stage procedure. In 1 case (0.2%) a simultaneous left carotid to subclavian transposition was  
5 performed, and in 12 cases (2.6%) during a first-stage procedure. One patient had a transcatheter  
6 aortic valve implantation (TAVI) during the same procedure.

7

### 8 **Procedure details**

9 Table III shows the procedural details. In one patient (0.2 %) an occluded left iliac artery was  
10 recanalized prior to inserting the endograft.

11 Nine target vessels (9/1519, 0.6 %) were occluded at initiation of the procedure, and therefore  
12 catheterization was not attempted. These vessels included 6/233 celiac arteries (2.6 %), 2/445  
13 right renal arteries (0.4 %) and 1/446 left renal arteries (0.2 %). All those vessels had severe  
14 stenosis depicted on the pre-operative CT scan. The fenestration or branch designed for those  
15 target vessels was plugged during the same procedure in 3 patients; no additional maneuvers  
16 were performed in 5/6 celiac arteries fenestrations located at the top of the endograft, and the left  
17 renal artery fenestration was plugged during a secondary procedure. Three other target vessels,  
18 both renal arteries and the superior mesenteric arteries were not stented because the patient died  
19 from aneurysm rupture before the device was implanted.

20 Taking into account the 1507 target vessels that were eligible for catheterization and stenting,  
21 technical success of target vessel stenting was 99.1% (1494/1507). Failure to catheterize and  
22 stent a target vessel occurred in 2 right renal arteries (0.5 %), 1 left renal artery (0.2 %), 9 celiac  
23 arteries (4.0 %) and 1 accessory renal artery. In 1 patient with preoperative CKD in whom we

1 failed to access the right renal artery, an immediate ilio-renal bypass was performed to reduce the  
2 risk of postoperative dialysis.

3 Additional target vessel ballooning or stenting was performed in 29 patients (6.2%) because of  
4 target vessel or bridging stent kinking, dissections or ruptures, and in 27 patients (5.8%) because  
5 of endoleaks.

6  
7 One patient (0.2%) developed hemodynamic instability just after device insertion. Aortography  
8 showed aortic rupture. The patient died during surgery despite urgent laparotomy for  
9 hemostasis. Three other patients (0.6%) needed conversion because of arterial or venous iliac  
10 bleeding and in 1 case an external iliac artery rupture was treated by covered stenting.

11 Conversion from a bifurcated aortic endograft to a mono-iliac endograft with a femorofemoral  
12 crossover graft was performed in 3 cases (0.6%).

13

#### 14 **Early morbidity and mortality**

15 The 30-day mortality rate was 4.9% (23 patients) and early complications occurred in 267  
16 patients (57.1%). These are listed in Table IV.

17 The most common complication was acute renal failure, which was diagnosed in 109 patients  
18 (23.3%), 85 patients (38%) with type I-III TAAA and 24 (9.7%) in the rest of the cohort. The  
19 majority of acute renal failures were limited to RIFLE stage 1 (12.4 %). Severe acute renal  
20 failure (> 50 % decrease in estimated glomerular filtration rate) appeared in 51 patients (10.9%).

21 Twenty patients (4.3%) required postoperative dialysis (17 patients (7.7%) with type I-III TAAA  
22 and 3 (1.2%) in the rest of the cohort), and 4 (0.8%) needed long-term dialysis after discharge.

1 Eighteen patients (3.8%) suffered from spinal cord ischemia. Half of the episodes occurred less  
2 than 24 hours after surgery. In 4 patients with delayed (>24 hours) spinal cord ischaemia, there  
3 was complete recovery, 3 patients had partial improvement (2 with early and one with delayed  
4 onset) and 11 patients had no improvement of symptoms. Spinal cord ischaemia rate was  
5 diagnosed in 17 patients (7.6%) with type I-III TAAA and 1 patient (0.04%) with PR and type  
6 IV TAAA.

7  
8 Early occlusion was diagnosed in 10/1494 of the stented target vessels (0.7 %). Percutaneous  
9 recanalization was performed in 1 patient with RRA occlusion and 3 patients with LRA  
10 occlusion. All 3 patients with early SMA occlusion underwent urgent re-intervention, including  
11 1 endovascular SMA recanalization, 1 laparotomy for bowel resection and 1 endovascular  
12 recanalization in combination with laparotomy for bowel resection.

13  
14 **Late outcome (>30 days): target vessel occlusions, endoleaks, sac changes, limb occlusions.**

15 Median follow up was 29 months (8.7; 51,1). Six patients (1.3%) were lost to follow-up after  
16 discharge (five of those 6 patients live abroad).

17 There were 126 late deaths (29.5 %), including 90 non-aortic related, 11 aortic-related, and 25  
18 undetermined causes (Table V). Estimated survival at one, three and five years was 86.7% (95%  
19 CI = 83.1 – 89.6), 73.3% (95% CI = 68.3 – 77.6), and 59.6% (95% CI = 53.4 – 65.2)  
20 respectively. Survival curves according to type of aneurysm (type 1-2-3 versus 4-5 and  
21 pararenals) are shown in Figure 1.

22

23 Late target vessel occlusion and late target vessel instability:

1 Late occlusion was diagnosed in 30/1351 stented target vessels (2.2 %) in 22/424 patients  
2 (5.2%), including 11 right renal arteries (2.7 %), 9 left renal arteries (2.2 %), 4 superior  
3 mesenteric arteries (1.2 %), 4 celiac arteries (2.1%), and 2 accessory renal and other  
4 fenestrations (10 %). Eighteen patients (4.2%) had 1 target vessel occlusion, 2 patients (0.5%)  
5 had 2 target vessel occlusions, and 2 patients (0.5 %) had 3 target vessel occlusions. During  
6 follow-up, six patients (1.4%) underwent 8 reinterventions, including 5 target vessel  
7 recanalizations, 1 bilateral ilio-renal bypass, 1 open embolectomy and 1 laparotomy for bowel  
8 resection in combination with percutaneous target vessel revascularization. Branch occlusion  
9 during follow-up resulted in permanent dialysis in 5 patients.

10 Freedom from late target vessel occlusion at 1, 3 and 5 years was respectively 97.7 % (95 % CI =  
11 95.6 – 98.8), 93.9 (95 % CI = 90.5 – 96.1) and 92.3 (95 % CI = 88.4 – 94.6).

12 Freedom from target vessel occlusion and from late target vessel instability are reported figure 2  
13 and 3.

14

#### 15 **Endoleaks and sac changes during follow-up**

16 Clinical data on endoleaks, sac changes and limb occlusions during follow-up (> 30 days) were  
17 obtained for 402 patients. Endoleaks during follow-up were identified in 118 patients by CTA or  
18 color duplex ultrasound. Ninety-eight patients had 1 endoleak, whereas 17 patients had 2  
19 different endoleaks and 5 patients had 3 different endoleaks. Type 1a, 1b and 1c endoleaks were  
20 diagnosed in respectively 10, 13 and 3 patients. Ninety-one patients had a type 2 endoleak.  
21 Twenty-six patients were identified with a total of 29 type 3 endoleaks.

22

1 Pre-operative diameters were compared to the last post-operative diameter. Overall, sac  
2 shrinkage (> 5 mm) occurred in 218 patients (54.2 %) and sac enlargement was seen in 38  
3 patients (9.4 %). One hundred and forty-six patients had stable diameters (36.3 %). Treatment of  
4 endoleak types I and/or III was performed during follow-up in respectively 5/218 (2.3%), 17/38  
5 (44.7%), and 8/146 (5.5%) of the patients in the sac shrinkage, sac enlargement, and stable  
6 groups respectively.

7  
8 Limb occlusion was identified in 6 patients during follow-up. One additional patient was  
9 diagnosed with full bifurcated graft thrombosis including both iliac limbs. Surgical intervention  
10 was performed in all patients, except 1 patient with unilateral asymptomatic limb occlusion.

## 11 12 **Secondary interventions**

13 A list of early and late reinterventions is displayed in Table VI. A total of 130 re-interventions  
14 were performed in 99 (21.2 %) of 467 patients, excluding the one patient that died during  
15 surgery. Ninety-two interventions are classified as aortic procedures versus 35 non-aortic  
16 procedures. Three interventions were combined aortic and non-aortic interventions, i.e. 2  
17 laparotomies for bowel resection in combination with percutaneous target vessel  
18 revascularization and 1 type 1b endoleak treatment in combination with a crossover bypass for  
19 lower limb ischemia.

20  
21 Freedom from secondary intervention at 1, 3 and 5 years were 88.2 % (95 % CI = 84.8-90.9),  
22 78.8 (95% CI = 74.0 – 82.8) and 70.2 % (95% CI = 63.9 - 75.6) (Figure 4).

23

## 1 **Predictive factors for 30-day mortality**

2 Predictive factors for early mortality according to univariate and multivariate analysis are listed  
3 respectively in Table VII and Table VIII. According to univariate analysis, age (HR= 1.079 per  
4 year; 95% CI = 1.19 – 1.143; p = 0.009), male gender (HR = 4.742; 95% CI = 1.760 – 12.774; p  
5 = 0.002), maximum pre-operative aneurysm diameter (HR = 1.054 per mm; 95 % CI = 1.024 –  
6 1.085; p < 0.001), chronic kidney disease ( HR = 3.055; 95% CI = 1.348-6.923; p = 0.007),  
7 procedure time (HR = 1.007 per minute; 95 % CI = 1.004 – 1.010; p < 0.001), spinal cord  
8 ischemia (HR = 5.567; 95 % CI = 1.893 – 16.367; p= 0.002) and ASA score 4 (HR = 0.175; 95%  
9 CI 0.065 – 0.47; p 0.001) were significant risk factors for 30-day mortality. Multiple logistic  
10 regression analysis confirmed a significant association between 30-day mortality and chronic  
11 kidney disease (HR = 3.139; 95 % CI = 1.369 – 7.196; p = 0.007), procedure time (HR = 1.007  
12 per minute; 95 % CI = 1.003 – 1.010; p < 0.001) and aneurysm diameter (HR = 1.053 per mm;  
13 95 % CI = 1.020 – 1.087; p = 0.001).

14

## 15 **Predictive factors for late mortality**

16 Maximum pre-operative aneurysm diameter (HR = 1.029 per mm; 95 % CI = 1.013 – 1.046; p =  
17 0.001), chronic kidney disease (HR = 1.903; 95 % CI = 1.315 – 2.752; p = 0.001), procedure  
18 time (HR = 1.003 per minute; 95 % CI = 1.001 – 1.005; p = 0.015), spinal cord ischemia (HR =  
19 2.410; 95 % CI = 1.173 – 4.953; p = 0.017) and type 1-2-3 TAAA (HR = 1.698; 95 % CI = 1.185  
20 – 2.432; p = 0.004) are significant risk factors for late mortality according to univariate analysis.  
21 Age is another significant risk factor for late mortality, but the effect is time-dependent. Up to 24  
22 months after surgery, age is not a significant predictive factor (HR = 1.004 per year; 95 % CI =  
23 0.971 – 1.039; p = 0.815), whereas after 24 months of follow-up, age becomes a significant risk

1 factor (HR = 1.052 per year; 95 % CI = 1.019 – 1.087; p = 0.002). Multivariate logistic  
2 regression analysis confirms this variable effect of age on late mortality, with age being an  
3 independent risk factor for late mortality only after 24 months after surgery (HR = 1.055 per  
4 year, 95 % CI 1.021 – 1.090; p = 0.001). In contrast, Crawford type 1-2-3 TAAA, chronic  
5 kidney disease and maximum preoperative aneurysm diameter are all significant independent  
6 risk factors for late mortality before and after 24 months of follow-up.

7

8

## 1 DISCUSSION

2  
3 The current study represents early and late results of a large consecutive series at a single centre  
4 of F-BEVAR for complex aortic aneurysms. With the majority (94.7%) of patients having an  
5 ASA score of 3 or above with significant co-morbidities; this cohort characterises outcomes of  
6 high risk patients reflecting pragmatic clinical practice conditions. Our findings suggest that F-  
7 BEVAR can be performed in high risk patients with excellent technical success (99.1%), low 30-  
8 day mortality rate (4.9%), low rates of spinal cord ischemia and permanent dialysis, and freedom  
9 from target vessel occlusion that extends to 5 years (92.3%). Furthermore, our results confirm  
10 that early mortality was associated with preoperative TAAA diameter and CKD among  
11 additional factors. Long term mortality at 24 months continued to demonstrate the association of  
12 these factors and also included Crawford Type I-III TAAA as a significant risk factor.

13  
14 30 day mortality rates have been reported between 3.7% to 8.9% in series examining patients  
15 with PR and TAAA aneurysms.<sup>13 2,14,15</sup> Despite offering F-BEVAR only to patients that were  
16 denied open surgical repair, these outcomes are similar. This also compares favourably to  
17 perioperative mortality rates of 5 % to 8.7% in series of open surgical repair of similar  
18 anatomical aneurysms.<sup>7 16-18</sup> Baseline CKD has been strongly predictive of perioperative  
19 mortality in standard EVAR and continues to be a significant risk factor for patients undergoing  
20 F-BEVAR.<sup>11</sup> Furthermore, procedure time and aneurysm diameter are also associated with early  
21 mortality. These outcomes reflect technical factors related to the complexity of repair. With the  
22 evolution of experience, our standard approach includes the use of a preloaded system when  
23 performing F-BEVAR. Two 6 French sheaths are positioned in the ipsilateral main delivery

1 system to create a stable platform to cannulate branches and provide access to branches from the  
2 ipsilateral side. The contralateral access site is utilized only for the SMA and celiac. This method  
3 both reduces procedure time and also limits limb and pelvic ischemia by allowing perfusion past  
4 the relatively smaller access sheaths. Moreover, in order to contain procedure time, and to  
5 avoid access via the supra aortic trunks (and thus reduce the risk of stroke), wherever possible  
6 we limit branched grafts for the treatment of type II TAAA repairs. With experience (especially  
7 since steerable sheaths became available) we have found that most type I and III TAAA can be  
8 treated with fenestrated grafts if the aortic lumen at the origin of the visceral vessels is not  
9 excessive (i.e. if the fenestration can be positioned within 10mm of the aortic wall). In the  
10 reported cohort, branches were utilized in 42% of type I-III TAAA repairs.

11  
12 As it is a relatively newly adopted technique, there are few large published F-BEVAR series with  
13 long term survival data. Despite losing 8.8% of our series follow up, our five-year estimated  
14 survival rate was 59.6%. This is in line with other series that describe similar high-risk cohorts  
15 with a 58% to 60% survival rate.<sup>3 1</sup> The majority of late deaths are attributed to non-device, non-  
16 aortic related causes in keeping with the natural history of the patients that comprise the cohort.  
17 There were few aortic-related deaths, including four that were secondary to late aortic rupture.  
18 As aneurysm rupture remains the largest contributor to aneurysm related mortality in standard  
19 EVAR at 8 years, longer follow-up is required to determine whether the low late aneurysm-  
20 related mortality in the F-BEVAR group persists beyond 5 years.<sup>19</sup> Both CKD and aneurysm  
21 diameter remain significant predictors of long term, non-aortic mortality. In addition, patients  
22 with Crawford Type I-III aneurysms do worse than those with type IV-VI TAAA aneurysms. We  
23 suggest that these patients reflect more extensive underlying pathology and/or technical

1 demands, and a greater risk of SCI.

2 Somewhat surprisingly, patient age at the time of repair becomes predictive of late non-aortic  
3 mortality only beyond 24 months post-operatively.

4

5 In keeping with our previously published F-BEVAR series, the majority of target visceral vessels  
6 are successfully stented at the time of initial procedure (99.1%).<sup>2</sup> The stenting of target visceral  
7 vessels has become standard practice in order to align fenestrations, avoid target vessel occlusion  
8 and provide seal. Covered stents are recommended for bridging due to their resistance to  
9 intimal hyperplasia, improved patency rates, and need to seal the fenestration or branch in  
10 order to avoid endoleaks. Target vessel patency has been reported to be between 84%-93.3% at  
11 5 years which compares favourably to our rate at 92.3%.<sup>3 4,20</sup> Recent work on branch instability  
12 has highlighted the importance of this indicator as a comprehensive evaluator of target vessels.  
13 Oderich et. al. report a freedom of branch instability of 93% at 1 year which is comparable to our  
14 rate at the same follow up (96%).<sup>5</sup> Furthermore, the freedom from late 5-year target instability  
15 was 83% - a modest improvement (70% at 5 years) from the comparable cohort from Mastracci  
16 et. al.<sup>20</sup> This may be attributed to that groups' practice evolving from uncovered to covered  
17 stents during the study follow up, whereas our study utilized covered stents exclusively.

18

19 This strength of this study lies in the large cohort of prospectively collected patient data,  
20 extensive follow up, and systematic approach to pre-operative planning, execution, and  
21 surveillance. Nonetheless, important limitations should be highlighted. This study is a  
22 comprehensive review of a 12-year period at a high volume aortic centre and thus reflects a  
23 transformation in practice and techniques. Our early results may not be reflective of more

1 contemporary practice. Although this cohort has been described as high risk, it is difficult to  
2 draw conclusions with a comparable open surgical group.

3 We did not find any striking changes in FEVAR outcomes over the time of this study because  
4 patient selection evolved gradually. We have incrementally raised the technical challenge  
5 associated with these procedures by taking on progressively difficult cases as our experience and  
6 confidence has grown, but there has been no “before and after” step-change in our practice.

7 During the initial learning curve, we limited ourselves to 2 and 3 target vessel FEVAR. With  
8 increasing experience, and with access to a hybrid room, we performed more complex  
9 procedures including routine 4 vessel FEVAR and BEVAR. However, with specific respect to  
10 the TAAA repairs, our previous report<sup>12</sup> shows that our outcomes improved significantly after  
11 2010 when we revised our spinal cord protection strategy. We optimized the implantation  
12 procedure (to include the early restoration of pelvic and lower limb perfusion, aggressive  
13 revascularization of the left subclavian and the internal iliac arteries, and staging repairs  
14 whenever possible) together with systematic CSF drainage, assiduous blood pressure  
15 management, and a strategy of pre-emptive of blood, plasma and platelet transfusion. We  
16 attribute this pro-active spinal cord protective protocol together with the fluency of a high-  
17 volume practice to a significant reduction in the incidence of SCI after endovascular TAAA  
18 repair.

19 We opine that these procedures can be offered safely, even in high risk patients. However, this  
20 mandate high-volume centers prepared to invest in the incrementally complex learning curve that  
21 this technology and these patients demand. Furthermore, we suggest that it is past time for the  
22 industry to invest in clinical trials in USA centers of excellence to avail currently disadvantaged  
23 north American patients of these technologies.

1  
2 **Conclusion:** F-BEVAR performed in high risk patients is associated with favourable outcomes.  
3 Patient selection should take into consideration the reported patient and aneurysm factors  
4 associated with early and late mortality.

5

## 6 **REFERENCES**

7

- 8 1. Kristmundsson T, Sonesson B, Dias N, Törnqvist P, Malina M, Resch T. Outcomes of  
9 fenestrated endovascular repair of juxtarenal aortic aneurysm. *Journal of Vascular*  
10 *Surgery*. 2014 Jan;59(1):115–20.
- 11 2. Amiot S, Haulon S, Becquemin JP, Magnan PE, Lermusiaux P, Goueffic Y, et al.  
12 Fenestrated endovascular grafting: the French multicentre experience. *Eur J Vasc*  
13 *Endovasc Surg*. 2010 May;39(5):537–44.
- 14 3. Verhoeven ELG, Vourliotakis G, Bos WTGJ, Tielliu IFJ, Zeebregts CJ, Prins TR, et al.  
15 Fenestrated stent grafting for short-necked and juxtarenal abdominal aortic aneurysm:  
16 an 8-year single-centre experience. *Eur J Vasc Endovasc Surg*. 2010 May;39(5):529–  
17 36.
- 18 4. Eagleton MJ, Follansbee M, vascular KWJO, 2016. Fenestrated and branched  
19 endovascular aneurysm repair outcomes for type II and III thoracoabdominal aortic  
20 aneurysms. *jvascsurgorg*

- 1 5. Oderich GS, Ribeiro M, Hofer J, Wigham J, Cha S, Chini J, et al. Prospective,  
2 nonrandomized study to evaluate endovascular repair of pararenal and  
3 thoracoabdominal aortic aneurysms using fenestrated-branched endografts based on  
4 supraceliac sealing zones. *Journal of Vascular Surgery*. 2017 May;65(5):1249–  
5 1259.e10.
- 6 6. Oderich GS, Greenberg RK, Farber M, Lyden S, Sanchez L, Fairman R, et al. Results  
7 of the United States multicenter prospective study evaluating the Zenith fenestrated  
8 endovascular graft for treatment of juxtarenal abdominal aortic aneurysms. *Journal of*  
9 *Vascular Surgery*. 2014 Dec;60(6):1420–8.e1–5.
- 10 7. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Experience with 1509  
11 patients undergoing thoracoabdominal aortic operations. *Journal of Vascular Surgery*.  
12 1993 Feb;17(2):357–68–discussion368–70.
- 13 8. Sarac TP, Clair DG, Hertzner NR, Greenberg RK, Krajewski LP, O'Hara PJ, et al.  
14 Contemporary results of juxtarenal aneurysm repair. *Journal of Vascular Surgery*. 2002  
15 Dec;36(6):1104–11.
- 16 9. Cambria RP, Clouse WD, Davison JK, Dunn PF, Corey M, Dorer D.  
17 Thoracoabdominal aneurysm repair: results with 337 operations performed over a 15-  
18 year interval. *Annals of Surgery*. 2002 Oct;236(4):471–9–discussion479.
- 19 10. Cox GS, O'Hara PJ, Hertzner NR, Piedmonte MR, Krajewski LP, Beven EG.  
20 Thoracoabdominal aneurysm repair: a representative experience. *Journal of Vascular*  
21 *Surgery*. 1992 May;15(5):780–7–discussion787–8.

- 1 11. Giles KA, Schermerhorn ML, O'Malley AJ, Cotterill P, Jhaveri A, Pomposelli FB, et  
2 al. Risk prediction for perioperative mortality of endovascular vs open repair of  
3 abdominal aortic aneurysms using the Medicare population. *Journal of Vascular*  
4 *Surgery*. 2009 Aug;50(2):256–62.
- 5 12. Maurel B, Delclaux N, Sobocinski J, Hertault A, Martin-Gonzalez T, Moussa M, et al.  
6 The impact of early pelvic and lower limb reperfusion and attentive peri-operative  
7 management on the incidence of spinal cord ischemia during thoracoabdominal aortic  
8 aneurysm endovascular repair. *Eur J Vasc Endovasc Surg*. 2015 Mar;49(3):248–54.
- 9 13. Clough RE, Modarai B, Bell RE, Salter R, Sabharwal T, Taylor PR, et al. Total  
10 Endovascular Repair of Thoracoabdominal Aortic Aneurysms. *European Journal of*  
11 *Vascular & Endovascular Surgery*. 2012 Mar;43(3):262–7.
- 12 14. Marzelle J, Presles E, Becquemin JP, WINDOWS trial participants. Results and factors  
13 affecting early outcome of fenestrated and/or branched stent grafts for aortic  
14 aneurysms: a multicenter prospective study. *Annals of Surgery*. 2015 Jan;261(1):197–  
15 206.
- 16 15. Guillou M, Bianchini A, Sobocinski J, Maurel B, D'elia P, Tyrrell M, et al.  
17 Endovascular treatment of thoracoabdominal aortic aneurysms. *Journal of Vascular*  
18 *Surgery*. 2012 Jul;56(1):65–73.
- 19 16. Coselli JS, Conklin LD, LeMaire SA. Thoracoabdominal aortic aneurysm repair:  
20 review and update of current strategies. *Ann Thorac Surg*. 2002 Nov;74(5):S1881–4–  
21 discussionS1892–8.

- 1 17. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal  
2 aortic aneurysms. *Ann Thorac Surg*. 2007 Feb;83(2):S862–4–discussionS890–2.
- 3 18. LeMaire SA, Price MD, Green SY, Zarda S, Coselli JS. Results of open  
4 thoracoabdominal aortic aneurysm repair. *Ann Cardiothorac Surg*. 2012 Sep;1(3):286–  
5 92.
- 6 19. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM, EVAR trial investigators.  
7 Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up  
8 of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised  
9 controlled trial. *Lancet*. 2016 Nov 12;388(10058):2366–74.
- 10 20. Mastracci TM, Greenberg RK, Eagleton MJ, Hernandez AV. Durability of branches in  
11 branched and fenestrated endografts. *Journal of Vascular Surgery*. 2013  
12 Apr;57(4):926–33–discussion933.
- 13  
14

1 **Figure legends**

2

3

4 Figure 1: Survival curves (Kaplan-Meier) of 468 patients undergoing F-BEVAR for types 1-2-3  
5 thoracoabdominal aneurysms (TAAA) versus type 4 TAAA and pararenal aneurysms (PR).

6

7 Figure 2: Freedom from target vessel occlusion/patient (Kaplan-Meier) for types 1-2-3  
8 thoracoabdominal aneurysms (TAAA) versus type 4 TAAA and pararenal aneurysms (PR).

9

10 Figure 3: Freedom from late target vessel instability per patient (Kaplan Meier) for types 1-2-3  
11 thoracoabdominal aneurysms (TAAA) versus type 4 TAAA and pararenal aneurysms (PR).

12

13 Figure 4: Freedom from secondary intervention

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Table 1: Clinical and anatomical characteristics of all cohort

Variable	Median (IQ25-75) or Number of patients (%)
<b>Demographics</b>	
Age (years)	71.6 (65;77)
Age ≥ 80 years	59 (12.6)
Male gender	441 (94.2)
<b>Cigarette smoking (*)</b>	
Never Smoked	58 (12.7)
Active smoker	124 (26.6)
Former smoker	282 (69.9)
<b>Comorbidities</b>	
Coronary artery disease	209 (44.7)
Chronic obstructive pulmonary disease	172 (36.7)
Chronic kidney disease	112 (23.9)
Diabetes mellitus	93 (19.8)
<b>Prior aortic surgery</b>	127 (27.1)
<b>Preoperative medication</b>	
Anti-platelet drugs	376 (80.3)
Anticoagulant drugs	58 (12.4)
Statins	346 (73.9)
<b>ASA classification</b>	
Class I	0
Class II	25 (5.3)
Class III	419 (89.5)
Class IV	24 (5.1)
<b>Aneurysms characteristics</b>	
Maximum diameter	58 (53.75;64)
Aneurysm Classification	
Type 1 TAAA	11 (2.3)
Type 2 TAAA	44 (9.4)
Type 3 TAAA	166 (35.5)
Type 4 TAAA	138 (29.5)
Type 5 TAAA	14 (3.0)
Pararenal aneurysm	95 (20.3)
Post-dissection aneurysm	21 (4.5)

Table 2: Device characteristics

<b>Device design</b>	N (%)
Fenestrations only	375 (80.1)
Branches only	43 (9.2)
Combination	50 (10.7)
<b>Fenestrations</b>	
Total	1286
RRA	399
LRA	407
SMA	303
CA	154
Accessory renal arteries	21
Other fenestrations*	2
<b>Branches</b>	
Total	233
RRA	46
LRA**	39
SMA	69
CA	79
<b>Scallops</b>	
Total	194
RRA	5
LRA	1
SMA	85
CA	103

\* including 1 splenic artery fenestration and 1 inferior mesenteric artery fenestration

\*\* including 1 left pelvic kidney artery branch

Table 3: Procedural details

Variable	Number of patients (%)
<b>Approach</b>	
<i>Femoral access</i>	
Surgical cutdown	432 (92.3)
Bilateral percutaneous access	24 (5.1)
Unilateral percutaneous access + contralateral cutdown	4 (0.8)
<i>Retroperitoneal access</i>	
Unilateral, without conduit	5 (1.1)
Bilateral, without conduit	1 (0.2)
Unilateral, with iliac conduit	2 (0.4)
<i>Others</i>	
Aorto-uni-femoral graft	1 (0.2)
<b>Procedure</b>	Median (25 and 75 percentile)
Operation time (min)	180 (150; 225)
Contrast Volume (ml)	120 (92; 155)
Fluoroscopy time (sec)	2252 (1673; 3145)
<b>Embolization</b>	
Hypogastric artery	18 (3.8)
Inferior mesenteric artery	15 (3.2)
Accessory renal artery	7 (1.5)
Splenic artery	2 (0.4)
Left gastric artery	1 (0.2)
Left subclavian artery	1 (0.2)
Left renal artery (patient on dialysis)	1 (0.2)
<b>Other interventions</b>	
Conversion to laparotomy	1 (0.2)
Conversion for iliac bleeding arterial/venous	3 (0.6)
Conversion from bifurcated to mono-iliac endograft with femoro-femoral cross over bypass	3 (0.6)
Iliofemoral or femorofemoral graft	10 (2.1)
<b>Target vessels</b>	
<i>Adjunct target vessel interventions</i>	
Extra ballooning/ stenting for endoleak	29 (6.2)
Extra ballooning/stenting for kink, dissection or rupture	27 (5.8)
<i>Technical success of target vessel stenting</i>	Number of target vessels (%)
Overall success:	
Success of RRA stenting	1494/1507 (99.1)*
Success of LRA stenting	440/442 (99.5)
Success of SMA stenting	444/445 (99.8)
Success of CA stenting	371/371 (100)
Success of accessory renal artery stenting	217/226 (96,0)
Success of other target vessel stenting	20/21 (95.2)
	2/2 (100)

\* Exclusion of 9 target vessels that were occluded at the beginning of the procedure and 3 target vessels of the patient that died during surgery before device implantation from aneurysm rupture.

Table 4: Early complications (&lt; 30days) in 467 patients \*

	Number of patients (%)
<b>Any complication</b>	267 (57.1)
<b>Cardiovascular</b>	
New onset arrhythmia	16 (3.4)
Cardiac failure	6 (1.3)
Cardiac arrest / cardiogenic shock	6 (1.3)
Resistant hypertension	3 (0.6)
Myocardial ischemia NSTEMI	3 (0.6)
Myocardial ischemia STEMI	2 (0.4)
New onset AV block with the need for pacemaker implantation	2 (0.4)
Endocarditis	1 (0.2)
<b>Respiratory</b>	
Pneumonia	27 (5.8)
Pneumonia requiring antibiotics	19 (4.1)
Pneumonia requiring antibiotics and invasive ventilation	8 (1.7)
Respiratory insufficiency	13 (2.8)
Mild insufficiency with or without non-invasive therapy and/or diuretics	7 (1.5)
With mechanical ventilation > 24 hours postoperative or re-intubation	6 (1.3)
Bronchitis requiring antibiotics	1 (0.2)
Sub-segmental pulmonary embolism	1 (0.2)
Pneumothorax requiring thoracic drain	1 (0.2)
<b>Acute Renal Failure</b>	
RIFLE 1	58 (12.4)
RIFLE 2	30 (6.4)
RIFLE 3	15 (3.2)
RIFLE 4	5 (1.1)
RIFLE 5	1 (0.2)
New onset dialysis	20 (4.3)
- Temporary	16 (3.4)
- Permanent	4 (0.8)
<b>Urinary</b>	
Urinary tract infection +/- urinary sepsis	40 (8.6)
Urinary retention requiring bladder catheter	7 (1.5)
Macroscopic hematuria (without urinary tract infection)	7 (1.5)
<b>Gastro-intestinal</b>	
Paralytic ileus	14 (3)
Intestinal ischemia	10 (2.1)
Gastro-intestinal bleeding	5 (1.1)
Bowel obstruction/sub-obstruction	6 (1.3)
Acute pancreatitis	2 (0.4)
Diarrhea without ischemia or infection	2 (0.4)
Flair-up of Chron's ileitis	1 (0.2)
Obstructive icterus	1 (0.2)
<b>Neurological</b>	
Spinal cord ischemia	18 (3.8)

Stroke	9 (1.9)
Post CSF drainage headache – medical treatment	7 (1.5)
Post CSF drainage headache – bloodpatch	1 (0.2)
Miscellaneous **	13 (2.8)
<b>Vascular</b>	
Iliac limb or ilio-femoral occlusion/sub occlusion/kink	9 (1.9)
Cholesterol embolization lower limbs	4 (0.9)
Thrombosis left axillary artery	1 (0.2)
Pseudo-aneurysm radial artery	1 (0.2)
<b>Non-access site hematoma (+/- hypovolemic shock)</b>	
Perinefric hematoma	10 (2.1)
Other retroperitoneal hematoma's	5 (1.1)
Intraperitoneal hematoma	1 (0.2)
Intramesenteric hematoma	1 (0.2)
Cervical hematoma after central catheter	1 (0.2)
Postoperative hypovolemic shock without active bleeding	1 (0.2)
<b>Sepsis with positive hemocultures (non-urolological, non-respiratory)</b>	
Gastro-intestinal sepsis (due to mesenteric ischemia or cholecystitis)	9 (1.9)
Catheter sepsis	7 (1.5)
Sepsis without origin	7 (1.5)
<b>Access-site ***</b>	
Medical treatment	49 (10.5)
Surgical treatment	11 (2.4)
<b>Target vessel occlusions (as a percentage of stented target vessels)</b>	
RRA	3/440 (0.7)
LRA	4/444 (0.9)
SMA	3/371 (0.8)
TC	0/217
Accessory renal arteries	0/20
Other target vessels	0/2
<b>Early endoleak requiring therapy</b>	
Type 1c endoleak	1 (0.2)
Type 3 endoleak	2 (0.4)
<b>Other complications ****</b>	13 (2.8)

\* excluding 1 patient that died during surgery

\*\*including temporary sensory deficits or motor deficits without evidence of spinal cord ischemia or stroke, neuropathic pain, persistent paresthesia, episode of peripheral diabetic neuropathy, convulsion due to alcohol abstinence, delirium tremens.

\*\*\*Including hematoma, seroma, dehiscence, pseudo-aneurysm, persistent bleeding

\*\*\*\* including severe epistaxis, seborrheic dermatitis, episode of polyarthritis nodosa, flair-up of pilonidal sinus inflammation, skin rash, urticaria, houlder contusion after accidental fall during hospitalization, acute knee arthritis, gout episode, voice alteration due to post-intubation glottitis, bleeding hemorrhoids.

Table 5: Causes of late death (> 30days) in 427 patients\* treated with fenestrated and branched endografts for thoracoabdominal and pararenal aneurysms.

	Number of patients (%)
Total number of late deaths	126 (29.5)
<b>Non-aortic related causes</b>	90 (21.1)
Malignancy	23 (5.4)
Cardiac	19 (4.4)
General deterioration **	16 (3.7)
Infection/sepsis	10 (2.3)
Advanced renal insufficiency	7 (1.6)
Respiratory insufficiency	7 (1.6)
Cerebrovascular accident	3 (0.7)
Intestinal ischemia/obstruction/perforation	4 (0.9)
Pulmonary embolism	1 (0.2)
<b>Aortic related causes</b>	11 (2.6)
Target vessel thrombosis with MOF	4 (0.9)
Secondary aortic rupture	4 (0.9)
Aorto-oesophageal fistula	1 (0.2)
Graft infection with MOF	1 (0.2)
Graft thrombosis	1 (0.2)
<b>Undetermined causes</b>	25 (5.9)

\* excluding patients with early mortality, patients lost to follow-up after discharge or patients with no follow-up after 30 days because of recent surgery

\*\*including 2 patients who died as a direct consequence of post-procedural deterioration, but > 30 days after surgery.

Table 6: Early and late reinterventions in 467 patients treated with BEVAR/FEVAR for TAAA and PR aneurysms.

Variable	Number of patients (%)			Number of procedures
	All n = 467 *	< 30 days n = 467 *	>30days n = 427	
<b>Aortic</b>				
Endoleak	37 (7.9)	3 (0.6)	36 (8,4)	48
Type 1A	3 (0.6)	0	3 (0.7)	3
Type 1B	6 (1.3)	0	6 (1.4)	6
Type 1C	2 (0.4)	1 (0.2)	1 (0.2)	2
Type 2	13 (2.8)	0	13 (3.0)	14
Type 3	14 (3.0)	2 (0.4)	13 (3.0)	18
Combined endoleaks treatments **	5 (1.1)	0	5 (1.2)	5
Target vessel stenosis	15 (3.2)	0	15 (3.5)	17
Target vessel occlusion	9 (1.9)	3 (0.6)	6 (1.4)	11
Target vessel stent fracture	3 (0.6)	0	3 (0.7)	3
Target vessel pseudo-aneurysm	1 (0.2)	0	1 (0.2)	1
Iliac limb occlusion	10 (2.1)	5 (1.1)	5 (1.2)	10
Fully thrombosed endograft	1 (0.2)	0	1 (0.2)	1
Aorto-esophageal fistula	1 (0.2)	0	1 (0.2)	1
All aortic procedures	73 (15.6)	12 (2.7)	63 (14.7)	92
<b>Non aortic</b>				
Acces site complications	12 (2.6)	11(2.4)	1 (0.2)	12
Lower limb ischemia (non-iliac limb)	6 (1.3)	4 (0.9)	3 (0.7)	8
Laparotomy ( bowel resection or hematoma drainage)	10 (2.1)	10 (2.1)	0	10
Nephrectomy	1 (0.2)	1 (0.2)	0	1
Drainage iliac fossa hematoma	2 (0.4)	2 (0.4)	0	2
Percutaneous embolisation bleeding arteries	29 (6.2)	26 (5.6)	4 (0.9)	34
All non-aortic procedures				
<b>Combined aortic + non aortic surgery</b>				
Endoleak 1b treatment + revascularisation ischemic limb	1 (0.2)	0	1 (0.2)	1
Percutaneous target vessel stenosis or occlusion + laparotomy for bowel resection	3 (0.6)	1 (0.2)	2 (0.5)	3
All mixed procedures:	4 (0.9)	1 (0.2)	3 (0.7)	4
<b>All reinterventions</b>	<b>99 (21.2)</b>	<b>38 (8.1)</b>	<b>71 (16.6)</b>	<b>130</b>

\* excluding 1 patient who died during surgery before device implantation

\*\*Combined type endoleak treatment: type 1b and type 1c, type 1b and 2, type 1b and type 3, type 2 and type 1c, type 2 and type 3

Table 7: Univariate Cox models for the risk of early mortality in the study population.

Variable	HR	95 % CI	p
Age (per year)	1.079	[1,19- 1.143]	0.009
Male gender	4.742	[1.760 – 12.774]	0.002
Maximum aneurysm diameter (per mm)	1.054	[1.024 -1.085]	< 0.001
Diabetes	0.841	[0.286- 2.471]	0.753
Smoking	0.947	[0.530-1.693]	0.854
Coronary artery disease	1.632	[0.716-3.721]	0.244
Chronic obstructive pulmonary disease	1.115	[0.483 – 2.576]	0.799
Chronic kidney disease	3.055	[1.348 – 6.923]	0.007
Preoperative anti-platelet therapy	0.556	[0.229 - 1.352]	0.196
Preoperative statin therapy	0.539	[0.233 – 1.244]	0.148
Preoperative anticoagulant therapy	1.054	[0.313 – 3.546]	0.933
Marfan syndrome	0.049	[0 - 460141]	0.712
Post-dissection aneurysm	0.046	[0 - 270]	0.488
Procedure time (per minute)	1.007	[1.004 – 1.010]	< 0.001
Postoperative spinal cord ischemia	5.567	[1.893 – 16.367]	0.002
ASA score 1,2,3 versus 4	0.175	[0.065 – 0.472]	0.001
Aneurysm type Crawford type 1,2,3 versus 4,5,6	1.778	[0.769 – 4.107]	0.178

For all the variables tested, nor proportional hazard assumption, nor log linearity assumption were met.

HR: hazard ratio. CI: confidence interval

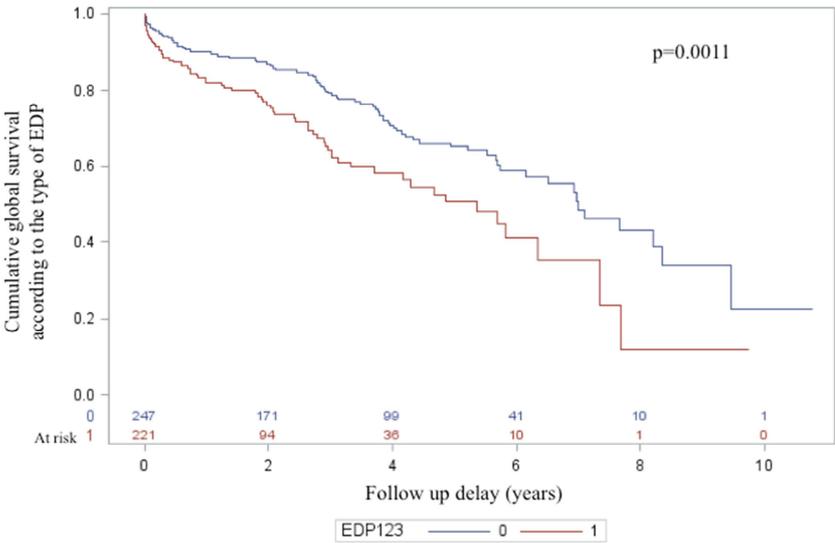
Table 8: Multivariable Cox model for the risk of early mortality in the study population

Variable	HR	95 % CI	p
Procedure time (per minute)	1.007	[1.003-1.010]	< 0.001
Maximum aneurysm diameter (per mm)	1.053	[1.020- 1.087]	0.001
Chronic kidney disease	3.139	[1.369 – 7.196]	0.007

For all the variables tested, nor proportional hazard assumption, nor log linearity assumption were met.

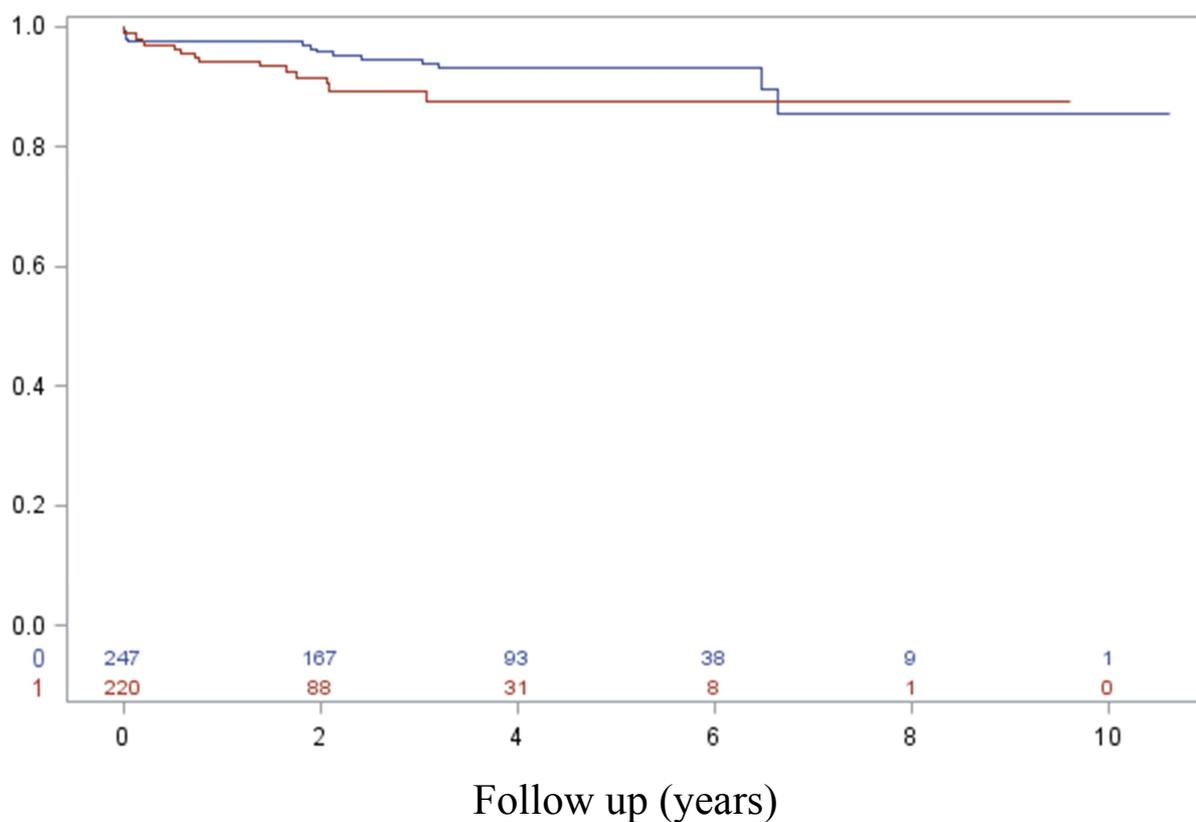
HR: hazard ratio. CI: confidence interval

Figure 1: Survival curve (Kaplan-Meier) of 468 patients undergoing F-BEVAR for types 1-2-3 thoracoabdominal aneurysms (TAAA) versus type 4-5 TAAA and pararenal aneurysms (PR).



	1 month	1 year	2 years	3 years	4 years	5 years
<b>Survival (%)`</b>						
EDP 123	93.55	82.18	76.15	64.34	58.25	50.75
EDP 456	96.32	90.32	86.91	79.37	70.72	65.24
<b>CI 95%</b>						
EDP123	89.35 – 96.13	75.99 – 86.90	68.96 –81.88	55.46 -71.89	48.64-66.68	39.87-60.63
EDP 456	93.04 – 98.07	85.79 – 93.46	81.78 –90.68	73.19-84.27	63.49-76.77	57.44-71.96
<b>Deaths (n)</b>						
EDP 123	14	35	43	55	60	64
EDP 456	9	23	30	44	57	64
<b>Patients at risk (n)</b>						
EDP 123						
EDP 456	194	134	94	62	36	25
	234	199	171	144	99	72

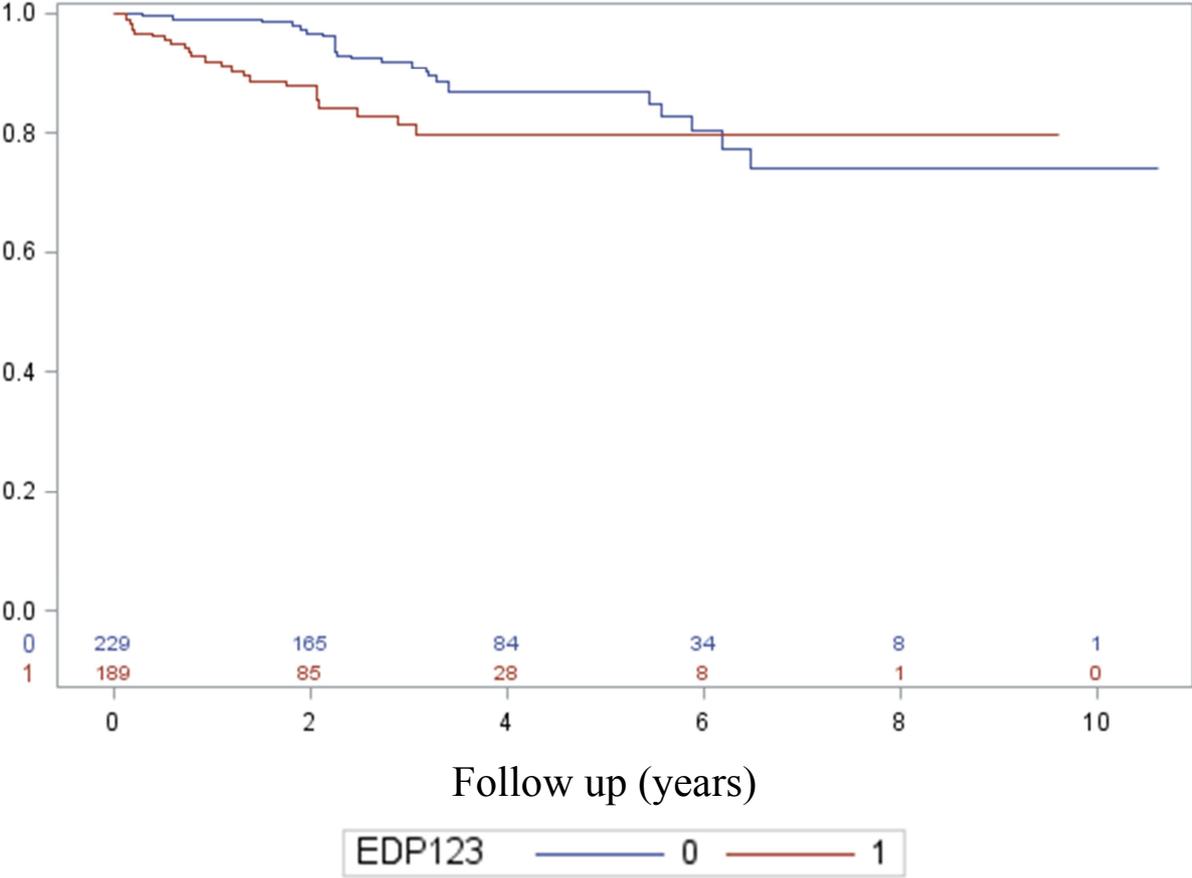
Figure 2: Freedom from target vessel occlusion/patient (Kaplan-Meier) of patients undergoing F-BEVAR for types 1-2-3 thoracoabdominal aneurysms (TAAA) versus type 4 TAAA and pararenal aneurysms (PR).



EDP123 — 0 — 1

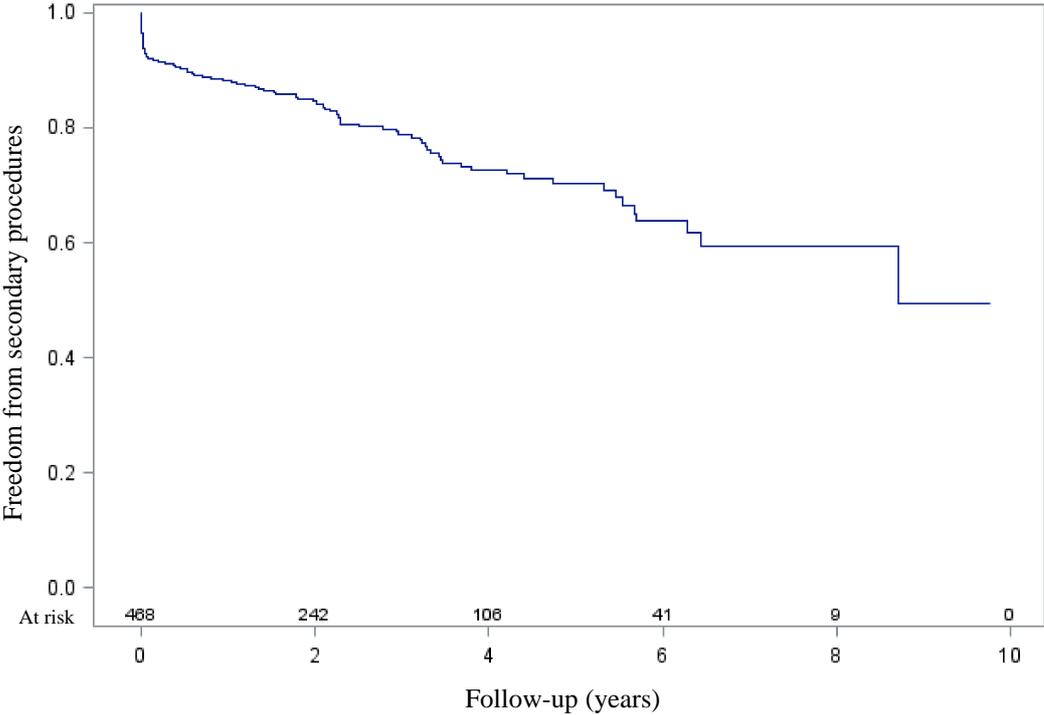
	1 month	1 year	2 years	3 years	4 years	5 years
TAAA 123	99.55	94.35	91.64	89.32	87.60	87.60
TAAA 4 + PR	99.19	97.54	95.83	94.62	93.12	93.12
<b>CI 95%</b>						
TAAA 123	96.82 – 99.93	89.68 – 96.94	85.78 – 95.15	82.42 – 93.61	79.66 – 92.58	79.66 – 92.58
TAAA 4 + PR	96.80 – 99.79	94.60 – 98.89	92.07 – 97.83	90.40 – 97.02	88.26 – 96.15	88.26 – 96.15

Figure 3: freedom from branch instability (Kaplan-Meier) of patients undergoing F-BEVAR for types 1-2-3 thoracoabdominal aneurysms (TAAA) versus type 4 TAAA and pararenal aneurysms (PR).



	1 year	2 years	3 years	4 years	5 years
TAAA 123	91.23	87.70	81.42	79.72	79.72
TAAA 4 + PR	99.06	96.75	91.78	86.92	86.92
<b>CI 95%</b>					
TAAA 123	85.55 – 94.74	80.99 – 92.16	72.66 – 87.60	70.35 – 86.41	70.35 – 86.41
TAAA 4 + PR	96.29 – 99.76	92.88 – 98.53	86.48 – 95.07	80.30 – 91.44	80.30 – 91.44

Figure 4: Freedom from secondary intervention



	1 month	1 year	2 years	3 years	4 years	5 years
FF secondary procedures (%)	92.1	88.2	84.7	78.8	72.7	70.2
CI 95%	89.2 – 94.2	84.8 – 90.9	80.7 – 87.9	74.0 – 82.9	66.9 – 77.6	63.9 – 75.6
Secondary procedures (n)	36	51	62	77	88	91
Patients at risk (n)	399	306	242	177	106	75