

## Editor's Choice – Pre-Operative Moderate to Severe Chronic Kidney Disease is Associated with Worse Short-Term and Mid-Term Outcomes in Patients Undergoing Fenestrated-Branched Endovascular Aortic Repair

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### WHAT THIS PAPER ADDS

Analysis of 202 consecutive patients treated with fenestrated-branched endovascular repair (F-BEVAR) for pararenal and thoraco-abdominal aortic aneurysms showed that, despite similarly low peri-operative mortality, subjects with a history of moderate to severe chronic kidney disease (CKD) have higher rates of acute kidney injury than those with unimpaired renal function. Prior CKD was independently associated with renal function decline and poorer survival at midterm follow up. Presence of pre-operative moderate to severe CKD must be considered during decision making for complex endovascular aortic interventions, and efforts made to optimise outcomes in the immediate peri-operative period as well as in the long term.

**Objective:** To review experience of fenestrated-branched endovascular aortic repair (F-BEVAR) for pararenal/thoraco-abdominal aortic aneurysms (PRAA/TAAA) and to assess the association between pre-operative moderate to severe chronic kidney disease (CKD) and post-operative outcomes.

**Methods:** All consecutive patients undergoing (elective and non-elective) F-BEVAR at a single centre (1 January 2011 – 1 July 2019) were identified. Renal function was calculated as the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease formula. Accordingly, presence of moderate to severe CKD was defined as eGFR < 60 mL/min/1.73m<sup>2</sup>.

**Results:** Overall, 202 consecutive patients (mean age 72 ± 8 years; 25% women) underwent F-BEVAR for the treatment of PRAA/TAAA during the study period. Of these, 51 had a history of moderate to severe CKD (none on chronic haemodialysis). No statistically significant differences were found in demographics and major comorbidities between patients with or without a history of CKD. The overall peri-operative mortality rate was 2%, without statistically significant differences between study groups ( $p = .26$ ). Patients with prior CKD had statistically significantly higher rates of acute kidney injury (AKI) (37% vs. 12%,  $p < .001$ ). At three years, overall survival was statistically significantly lower in patients with history of CKD compared with those without pre-operative CKD (57% vs. 82%,  $p = .010$ ). Similarly, freedom from renal function decline at three years was statistically significantly poorer in patients with prior history of CKD compared with those without pre-operative CKD (43% vs. 80%,  $p = .020$ ). In a multivariable analysis CKD was independently associated with higher odds of peri-operative AKI (OR 2.8, 95% CI 1.9 – 5.8,  $p = .030$ ), renal function decline (OR 4.9, 95% CI 1.7 – 9.2,  $p = .003$ ), and all cause mortality (HR 3.2, 95% CI 1.2 – 8.6,  $p = .020$ ).

**Conclusion:** Despite low peri-operative mortality rates that are comparable to patients with unimpaired renal function, occurrence of AKI was statistically significantly higher in subjects with pre-existing moderate to severe CKD. History of CKD was independently associated to renal function decline and poorer midterm survival.

**Keywords:** Acute kidney injury, Aortic aneurysm, Chronic kidney disease, Fenestrated-branched endovascular aortic repair, Midterm, Short term

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### INTRODUCTION

Endovascular techniques have continued to gain popularity over the last two decades, mainly because of their reduced invasiveness compared with open surgical repair, and

especially in high risk surgical candidates.<sup>1,2</sup> Fenestrated-branched endovascular aortic repair (F-BEVAR) is a less invasive method to treat pararenal (PRAA) and thoraco-abdominal (TAAA) aneurysms, which is now regarded as

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the first line treatment for repair of complex aortic pathology in patients with suitable anatomy, even more so in those deemed unsuitable for open surgical repair because of high comorbidity burden and poor health status.<sup>3,4</sup> The avoidance of prolonged visceral and renal ischaemia during the procedure may reduce the morbidity that ensues from bowel ischaemia and acute kidney injury (AKI) after open surgical repair of extensive aortic disease, which will in turn substantially increase peri-operative morbidity.

From prior studies, it is known that presence of pre-operative chronic kidney disease (CKD) may significantly worsen the early and late outcomes after both open or endovascular treatment of aortic disease.<sup>5–7</sup> Currently, there is a paucity of data that have examined the impact of pre-operative CKD on early and late morbidity and mortality after complex endovascular aortic procedures. However, recent studies have suggested that although a major contraindication for open surgical repair, baseline renal dysfunction may not be as prohibitive a risk factor for endovascular repair in patients with history of CKD.<sup>8</sup>

Therefore, the purpose of this study was to review experience with F-BEVAR for PRAA/TAAA and to assess the association between pre-operative moderate to severe CKD and post-operative outcomes in the short and midterm compared with patients with unimpaired renal function.

## METHODS

### Study design

Ethical approval was received for this retrospective study. All consecutive patients treated between 1 January 2011 and 1 July 2019 who received F-BEVAR for PRAA/TAAA were identified. Patient information was retrieved retrospectively, including baseline demographics and clinical characteristics, operative details, peri-operative outcomes, and follow up data. Details on surgical technique and follow up protocols at the study institution have been published previously.<sup>9</sup> Follow up consisted of computed tomography angiography (CTA) within one month of the index intervention and at one year in all patients, followed by imaging evaluation annually thereafter in the absence of technical defects using CTA or non-enhanced CT with duplex ultrasound of the visceral and aorto-iliac territory in patients with normal or impaired renal function, respectively.

The main exposure variable for this study was presence of pre-operative moderate to severe CKD. All patients had pre-operative renal function assessment. Renal function was calculated as the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease formula; this equation has been studied extensively and is the preferred method of estimating GFR.<sup>10</sup> Presence of moderate to severe CKD was defined as eGFR < 60 mL/min/1.73m<sup>2</sup>, while patients with eGFR ≥ 60 mL/min/1.73 m<sup>2</sup> were considered to have normal renal function. CKD was grouped into stages of severity; the CKD stages developed by the National Kidney Foundation were used in this study.<sup>11</sup> Accordingly, CKD stages III, IV, and V were defined as eGFR values of 30 – 60, 15 – 30, and < 15, respectively.

### Definitions and endpoints

The primary endpoints for this study were peri-operative acute kidney injury (AKI) and overall survival. To ensure 100% survival follow up, mortality was assessed by cross linkage of data using the unique personal identification number of each study individual with the national Swedish population registry. AKI was classified using the RIFLE system proposed by the Acute Dialysis Quality Initiative group for patients with and without CKD. This classification system stages acute renal dysfunction into five grades: Risk (R), Injury (I), Failure (F), Loss (L), and End stage (E).<sup>12</sup>

Secondary endpoints included peri-operative major adverse events (MAE) and access site complications, freedom from renal function decline, renal artery (RA) primary patency, and freedom from re-interventions. 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 > 1 L, AKI, stroke, spinal cord ischaemia, or bowel ischaemia.<sup>13</sup> According to prior studies, renal function decline was defined differently for patients with and without CKD.<sup>14</sup> For those without baseline CKD, renal function decline was defined as a drop in GFR to < 60 mL/min/1.73m<sup>2</sup> (i.e. progression to CKD stage 3 or higher). For patients with baseline CKD, an eGFR decline > 20% or progression in CKD stage (e.g. from stage 3 to stage 4) was considered as renal function decline. Loss of RA patency was diagnosed when thrombosis of the target vessel and/or bridging stent graft was noted, or there was radiological evidence of significant stenosis requiring re-intervention.

### Statistical analysis

Continuous variables were tested for normality, with results reported as frequencies for categorical variables, and mean ± standard deviation (SD) or median with interquartile range (IQR) for continuous variables. The Pearson's chi square or Fisher's exact test were used for analysis of categorical variables. Differences between means were tested with two sided Student *t* test, or Wilcoxon rank sum test. Time dependent outcomes were reported using life tables and presented as Kaplan–Meier curves with standard error < 10%. Differences were determined by the log rank test. As a higher rate of AKI was expected in patients with history of CKD, and it was hypothesised that this could represent a collinear risk factor for loss of renal function and reduced survival, a sensitivity analysis was performed after removing patients with peri-operative AKI from life tables. Also, given that it was anticipated that loss of RA patency could represent an independent predictor for worsening renal function over time, a further sensitivity analysis was performed after excluding patients with any loss of primary RA patency from life tables.

Binary outcomes were evaluated first by univariable methods, with results reported as odds ratio (OR) with 95% confidence intervals (CI). A multiple logistic regression model was built including significant covariables and confounders based on univariable screen or because of clinical significance. Stepwise backward selection was then performed with a removal criterion of .05 and the resulting

**Table 1.** Demographics, comorbidities, anatomy, and medications in 202 patients who underwent fenestrated-branched endovascular aortic repair stratified on the basis of normal baseline renal function ( $n = 151$ ) or pre-operative chronic kidney disease (CKD) ( $n = 51$ )

Variable	No pre-operative CKD ( $n = 151$ )	Pre-operative CKD ( $n = 51$ )	<i>p</i> value
<i>Demographics</i>			
Age – y	72 ± 9	73 ± 5	.26
Age ≥ 80	28 (18)	7 (13)	.29
Women	39 ± 25	14 ± 27	.48
BMI – kg/m <sup>2</sup>	26 ± 4	28 ± 6	.020
Obesity, BMI ≥ 30	26 (17)	18 (35)	.008
<i>Comorbidities</i>			
Ischaemic heart disease	46 (30)	20 (39)	.16
Prior aortic repair	46 (36)	17 (34)	.48
Congestive heart failure	18 (12)	11 (22)	.070
Chronic atrial fibrillation	33 (22)	9 (18)	.34
Hypertension	133 (88)	48 (94)	.17
Current or previous smoking	121 (79)	42 (82)	.080
COPD	41 (27)	15 (29)	.44
Diabetes mellitus	13 (9)	6 (12)	.34
Pre-operative haemoglobin – g/dL	13.5 ± 2	13 ± 2	.15
Pre-operative anaemia*	37 (24)	18 (35)	.090
Solitary functioning kidney	12 (8)	15 (29)	<.001
Pre-operative creatinine – mg/dL	80.4 ± 15	128.2 ± 30	<.001
Pre-operative eGFR – mL/min/1.73m <sup>2</sup>	84.2 ± 17	48.9 ± 9	<.001
ASA class ≥ 3	124 (82)	50 (98)	.002
<i>Anatomy</i>			
Maximum aortic diameter – mm	64 ± 12	64 ± 10	.87
<i>Extent of disease</i>			
Pararenal	54 (36)	20 (39)	
Thoraco-abdominal	97 (64)	31 (61)	
Post-dissection aneurysm	9 (6)	4 (8)	.42
Bilaterally patent HA	131 (87)	41 (80)	.25
<i>Medications</i>			
Aspirin	100 (67)	31 (63)	.39
Clopidogrel	13 (9)	6 (12)	.31
Warfarin	21 (14)	10 (20)	.19
Statin	118 (79)	35 (71)	.19
Diuretics	38 (19)	24 (49)	.002
ACE/ARB	105 (70)	35 (71)	.50
CCB/BB	119 (79)	44 (90)	.070

Data are presented as  $n$  (%) or mean ± standard deviation. BMI = body mass index; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; ASA = American Society of Anesthesiology; HA = hypogastric artery; ACE/ARB = angiotensin converting enzyme inhibitors/angiotensin receptor blockers; CCB/BB = calcium channel blockers/beta blockers.

\* Pre-operative haemoglobin in females < 12 g/dL or in males < 13 g/dL.

parsimonious model was not statistically significantly different from the full model (likelihood ratio test,  $p = .91$ ). The model discrimination, measured by the area under the operating curve, was 0.66 and the Hosmer-Lemeshow goodness of fit was not significant ( $p = .27$ ). Multivariable Cox proportional hazards was used to assess independent predictors for any cause mortality with results reported as hazard ratio (HR) with 95% CI. Covariables for these models were selected based on previously described risk factors and the univariable screen of all available potential confounders, using backwards selection with a criterion of 0.25 to stay in the final models. The final models were tested for violation of proportional hazards assumptions using Schoenfeld residuals.

The outcomes of interest were analysed in the whole cohort of treated patients, but subgroup analyses were

carried out to evaluate separately the primary patency rates of renal fenestrations vs. renal branches, and in patients undergoing repair for PRAA vs. patients undergoing repair for TAAA. Statistical significance was defined as a  $p$  value < .050. All statistical analyses were performed using SPSS statistical software version 24.0.

## RESULTS

### Study cohort

Overall, 202 consecutive patients (mean age 72 ± 8 years; 25% women) underwent F-BEVAR for treatment of PRAA/TAAA during the study period. Of these, 51 had a prior history of moderate to severe CKD and the vast majority ( $n = 49$ ) were in stage III; only two patients were in stage IV/V (none on chronic haemodialysis). While there was a

**Table 2.** Operative details in 202 patients who underwent fenestrated-branched endovascular aortic repair stratified on the basis of normal baseline renal function ( $n = 151$ ) or pre-operative chronic kidney disease (CKD) ( $n = 51$ )

Variable	No pre-operative CKD ( $n = 151$ )	Pre-operative CKD ( $n = 51$ )	<i>p</i> value
<i>Status</i>			.61
Elective	131 (87)	42 (82)	
Non-elective	20 (13)	9 (18)	
General anaesthesia	149 (99)	49 (96)	.26
Staged repair	19 (13)	10 (20)	.15
Prophylactic spinal drain	56 (37)	18 (35)	.48
<i>Design</i>			.83
Only fenestrations	105 (70)	35 (68)	
Only branches	34 (22)	13 (25)	
Both fenestrations and branches	12 (8)	3 (6)	
<i>Device</i>			.43
Custom made	119 (80)	41 (80)	
Off the shelf	28 (18)	7 (14)	
Physician modified	4 (3)	3 (6)	
Target vessels – <i>n</i>	3.2 ± 0.7	3.1 ± 0.7	.45
≥ 4 target vessels	64 (42)	16 (31)	.11
RRA stent diameter – mm	6.7 ± 0.6	6.9 ± 0.5	.25
LRA stent diameter – mm	6.7 ± 0.5	6.7 ± 0.5	.46
<i>Proximal landing zone</i>			.67
Proximal thoracic	41 (27)	13 (25)	
Mid thoracic	19 (13)	9 (17)	
Distal thoracic	91 (60)	29 (56)	
Percutaneous access	85 (56)	22 (43)	.24
Brachial access	47 (31)	18 (35)	.35
Median operating time (IQR) – min	354 (224)	372.5 (234)	.27
Median fluoroscopy time (IQR) – min	101.5 (61)	114.5 (77)	.84
Median contrast volume (IQR) – mL	195 (108)	180 (118)	.63

Data are presented as *n* (%) or mean ± standard deviation unless stated otherwise. RRA = right renal artery; LRA = left renal artery; IQR = interquartile range.

progressive increase in the total number of F-BEVAR procedures per year, the percentage of CKD cases remained stable over time (Supplementary Fig. S1).

At baseline, no significant differences were found in the distribution of age, sex, and major comorbidities between patients without prior history of CKD compared with subjects with known renal dysfunction (Table 1). Patients with pre-operative CKD had a statistically significantly higher body mass index compared with those without a history of CKD ( $28 \pm 6$  vs.  $26 \pm 4$ ,  $p = .020$ ), as well as being

statistically significantly more likely to be obese (35% vs. 17%,  $p = .008$ ). Also, the proportion of patients with a solitary functioning kidney was statistically significantly greater in patients with pre-operative CKD (29% vs. 8%,  $p < .001$ ). Most patients in both groups were treated electively (82% vs. 87%,  $p = .61$ ).

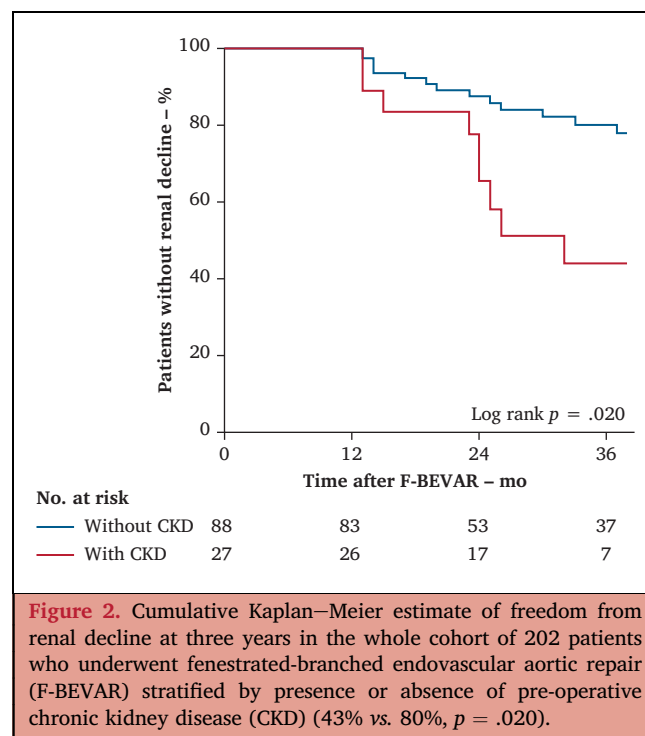
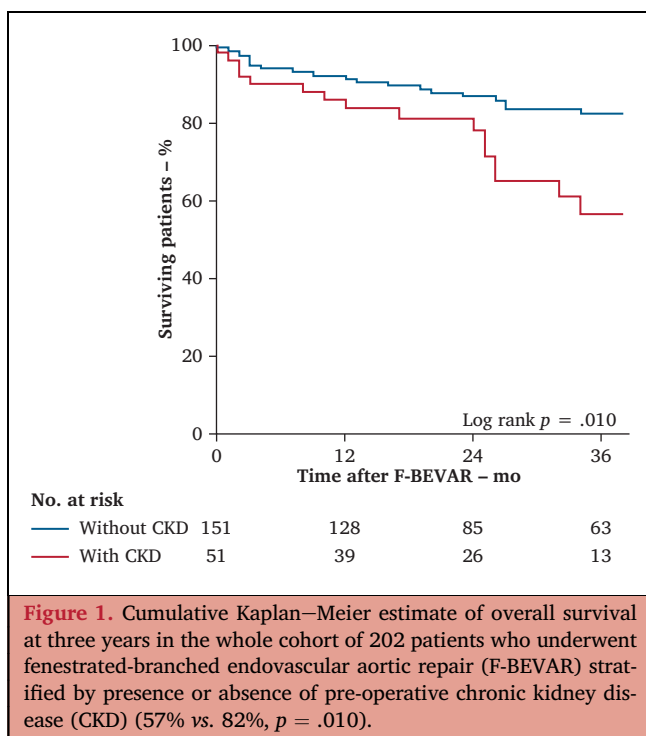
#### Operative details and peri-operative morbidity

Procedural metrics and operative details, including extent of aortic disease, operating time, fluoroscopy time, and

**Table 3.** Early outcomes (< 30 d or in hospital) in 202 patients who underwent fenestrated-branched endovascular aortic repair stratified on the basis of normal baseline renal function ( $n = 151$ ) or pre-operative chronic kidney disease CKD ( $n = 51$ )

Variable	No pre-operative CKD ( $n = 151$ )	Pre-operative CKD ( $n = 51$ )	<i>p</i> value
<i>Any major adverse event</i>	74 (49)	35 (69)	.010
Death	2 (1)	2 (4)	.26
Acute kidney injury	18 (12)	19 (37)	<.001
New dialysis	6 (4)	8 (15)	<.001
Myocardial infarction	3 (2)	2 (4)	.37
Respiratory failure	14 (7)	8 (15)	.20
New onset CHF	2 (1)	0 (0)	.79
Stroke	5 (3)	2 (4)	.99
Bowel ischaemia	3 (2)	5 (9)	.020
Estimated blood loss > 1 L	66 (44)	23 (45)	.99
Spinal cord injury	10 (6)	6 (12)	.24
Access site complications	17 (12)	9 (17)	.23
Unplanned re-interventions	27 (18)	13 (25)	.30

Data are presented as *n* (%). CHF = congestive heart failure.



contrast volume, were not statistically significantly different between groups (Table 2).

The overall peri-operative mortality rate was 2% (elective: 1%; non-elective: 7%), without statistically significant differences between groups ( $p = .26$ ).

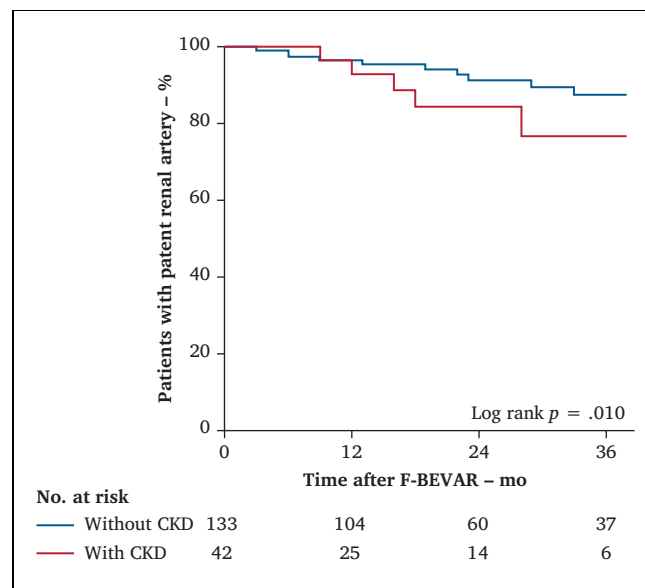
Patients with history of CKD had significantly more peri-operative MAE compared with subjects without prior CKD (69% vs. 49%,  $p = .010$ ; Table 3). Analysis of individual MAE showed that patients with prior CKD had statistically significantly higher rates of AKI (37% vs. 12%,  $p < .001$ ), new onset temporary dialysis (15% vs. 4%,  $p < .001$ ), and bowel ischaemia (9% vs. 2%,  $p = .020$ ). Non-elective repair (OR 4.5, 95% CI 1.3 – 7.2,  $p = .010$ ), history of CKD (OR 2.8, 95% CI 1.9 – 5.8,  $p < .001$ ), and age  $\geq 80$  (OR 2.7, 95% CI 1.5 – 4.4,  $p = .020$ ) were independently associated with post-operative AKI on multivariable analysis (Supplementary Table S1).

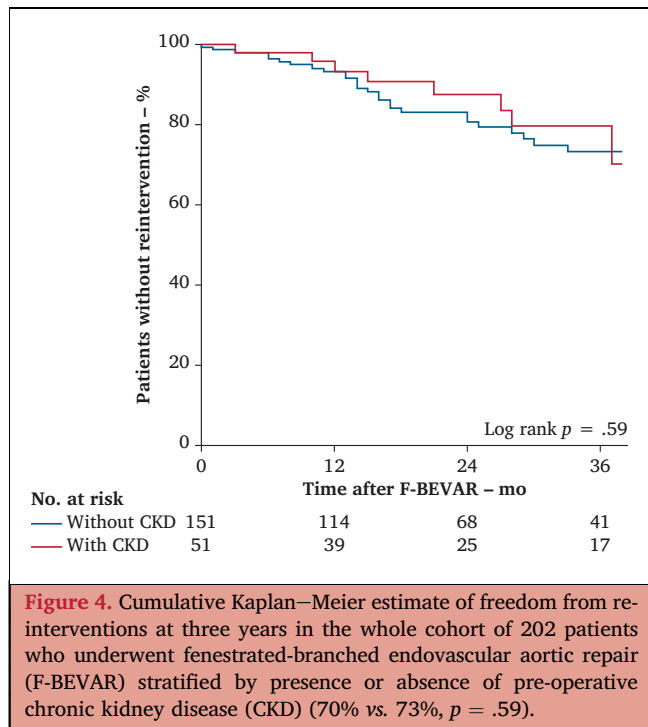
### Survival, renal function decline, renal artery patency, and re-interventions

The duration of follow up was similar between patients with and without baseline CKD (mean 32.8 months, 95% CI 27.6 – 36.0 vs. mean 33.6 months, 95% CI 26.5 – 35.6;  $p = .13$ ).

At three years, overall survival was statistically significantly lower in patients with a prior history of CKD compared with those without pre-operative CKD (57% vs. 82%,  $p = .010$ ; Fig. 1). These results of the initial model were confirmed in sensitivity analysis after excluding those who developed peri-operative AKI (Supplementary Fig. S2). In the subgroup of patients with uninterrupted RA primary patency, statistically significantly lower survival was still noted in subjects with baseline CKD compared with those with normal baseline renal function (at three years: 60% vs. 81%,  $p = .030$ ). When

assessing patients undergoing repair for PRAA or TAAA separately, the results remained consistent, with a trend towards lower three year survival in patients with pre-operative CKD (PRAA: CKD 63% vs. non-CKD 81%,  $p = .090$ ; TAAA: CKD: 43% vs. non-CKD: 81%,  $p = .050$ ). On multivariable analysis, female sex (HR 2.1, 95% CI 1.3 – 3.7,  $p = .003$ ), history of CKD (HR 3.2, 95% CI 1.2 – 8.6,  $p < .001$ ), ASA class  $> 3$  (HR 2.5, 95% CI 1.2 – 5.1,  $p = .001$ ), and age  $\geq 80$  (HR 2.8, 95% CI 1.6 – 5.1,  $p =$





.020) were independently associated with all cause mortality (Supplementary Table S2).

Freedom from renal decline at three years was statistically significantly lower in patients with a prior history of CKD compared with those without pre-operative CKD (43% vs. 80%,  $p = .020$ ; Fig. 2). The results of the initial model were confirmed in sensitivity analysis after excluding those who developed peri-operative AKI (Supplementary Fig. S3). In the subgroup of patients with uninterrupted RA primary patency, statistically significantly lower freedom from renal function decline was still noted in subjects with baseline CKD compared with those with normal baseline renal function (at three years: 48% vs. 82%,  $p = .001$ ). When assessing patients undergoing repair for PRAA or TAAA separately, the results remained consistent, with a trend towards lower three year freedom from renal decline for patients with pre-operative CKD (PRAA: CKD 54% vs. non-CKD 82%,  $p = .050$ ; TAAA: CKD: 44% vs. non-CKD: 69%,  $p = .050$ ). On multivariable analysis, history of CKD (HR 4.9, 95% CI 1.7 – 9.2,  $p = .003$ ), post-operative AKI (HR 2.8, 95% CI 1.9 – 8.7,  $p = .030$ ), female gender (HT 2.3, 95% CI 1.1 – 5.2,  $p = .004$ ), and loss of RA patency (HR 4.4, 95% CI 1.2 – 7.5,  $p = .001$ ) were independently associated with renal function decline (Supplementary Table S3).

No statistically significant differences were found in the three year estimates of RA primary patency (CKD: 77% vs. non-CKD: 87%,  $p = .10$ ; Fig. 3) and freedom from re-interventions (70% vs. 73%,  $p = .59$ ; Fig. 4) between study groups. No significant differences were found in the three year estimates of RA primary patency between renal fenestrations vs. renal branches (89% vs. 69%, respectively;  $p = .12$ ) and freedom from re-interventions (84% vs. 68%, respectively;  $p = .090$ ).

## DISCUSSION

As technology continues to evolve, so does the ability to treat complex aortic pathology with a total endovascular approach such as F-BEVAR, which is currently regarded as the first line option for treatment of PRAA/TAAA at high volume dedicated centres,<sup>15</sup> and is also endorsed by current clinical practice guidelines.<sup>16</sup> Moving the bar towards optimisation of early and late results, coupled with the need for optimisation of cost effectiveness of treatment,<sup>17</sup> there is a need for a better understanding of how health status can impact outcomes to provide appropriate patient selection during decision making and individualise follow up algorithms. In that sense, CKD remains a prevalent pathological condition among patients with aortic aneurysms, and pre-operative assessment of kidney function is recommended in all patients undergoing endovascular treatment with referral to a renal physician when significant renal impairment is detected.<sup>16</sup>

The main findings from this study, reporting a single centre nine year experience with F-BEVAR for treatment of PRAA/TAAA in 202 consecutive patients, were that history of pre-operative moderate to severe CKD was strongly and independently associated with worse clinical outcomes in the immediate post-operative period as well as during follow up. Indeed, patients with baseline CKD had significantly higher rates of peri-operative AKI, as well as lower survival and increased risk of renal function worsening in the long term.

These results are largely comparable with those reported in other recent series on this topic, although some differences must be noted. Khoury and colleagues reported that F-BEVAR is an effective and safe procedure for patients with complex aortic disease even among patients with CKD, but that worsening of renal function was more frequent among patients with pre-existing CKD.<sup>14</sup> However, they did not find significant mortality among subjects with prior renal dysfunction. The study did not report any significant difference in the frequency of post-operative AKI between patients with or without history of CKD. Also, Cajas-Monson and associates showed that advanced CKD (i.e., stage 4–5) was not a major risk factor for lower survival during midterm follow up.<sup>8</sup> While these results would encourage extended application of F-BEVAR even to CKD patients, some notable differences between these studies and the present research must be noted. Indeed, follow up in both studies was shorter, thereby potentially hindering evaluation of clinical outcomes over the long term. Also, both studies excluded some notable categories of patients (such as those undergoing urgent/emergency repair, and those with solitary functioning kidney) that might be at higher risk of worse renal outcomes. These differences may partly explain some of the differences noted with the present findings. Although the present study included only a few patients ( $n = 2$ ) with end stage CKD (i.e., NKF-QDOQI stage 4–5), and caution should be exercised before drawing any strong conclusions, given the observation that patients with already moderate CKD had significantly worse post-

operative outcomes compared with those with normal baseline renal function, it is unlikely that those with even more advanced renal dysfunction would fare better. As noted by Gallitto *et al.* who recently reported that presence of CKD represents a significant risk factor for worse outcomes in the setting of elective F-BEVAR but also in that of acute interventions,<sup>18</sup> its clinical meaning would be different in these two clinical scenarios. Indeed, while in the setting of elective F-BEVAR the detection of CKD should be considered in the decision making process, in the setting of acute interventions it should be seen as a marker for increased odds of post-operative complications in a higher risk patient.

As shown in prior research, AKI remains one of the most common peri-operative complications after F-BEVAR for PRAA/TAAA.<sup>19</sup> Although certainly multifactorial in nature, the rate of AKI was higher in patients with baseline CKD, with advanced age and pre-existing renal function impairment as the main risk factors for its occurrence.<sup>20</sup> Therefore, appropriate multimodal strategies for renal protection should target predominantly those subgroups of patients at higher pre-operative risk of this complication, with peri-operative intravenous hydration using 0.9% saline, withdrawal of nephrotoxic drugs and minimisation of intra-operative iodinated contrast medium (ICM) being the mainstay in that sense. The use of image fusion technology is an important tool to reduce the need for large ICM volumes during complex EVAR.<sup>21</sup> Additionally, use of CO<sub>2</sub> as contrast is a novel and promising tool for prevention of AKI, as recently shown in a case series of 15 FEVAR procedures performed with CO<sub>2</sub> angiography coupled with fusion imaging.<sup>22</sup> The authors compared the post-operative outcome between these patients and those undergoing standard procedures and found that FEVAR with CO<sub>2</sub> allowed them to use a lower volume of ICM as well as to preserve post-operative renal function. Although these preliminary experiences of the use of CO<sub>2</sub> angiography during advanced EVAR showed very promising results, the technique must be further improved, standardised, and tested before it can be implemented into routine clinical practice.

Lastly, although previous studies have reported that AKI after endovascular procedures is associated with decreased short term and long term survival,<sup>18,23</sup> whether it is causative or just associated with this phenomenon remains to be elucidated. In this study, AKI was not found to be an independent predictor of all cause mortality, while the sensitivity analysis confirmed that patients with baseline CKD had poorer midterm life expectancy even after removal of early AKI events from the survival estimates. Therefore, although the main goal of the present study was not to develop a risk scoring tool for post-operative death after F-BEVAR, the results offer strong evidence that any degree of CKD should be regarded as a marker for worse prognosis in the long term and routinely incorporated into the clinical decision making process. The European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms<sup>16</sup>

suggest that elective repair should be considered primarily in patients with an expected survival of at least two to three years; in this context, it can be noted that patients with history of CKD had an estimated three year survival rate of 57% in the current cohort, thereby highlighting the relevant prognostic impact of renal function deterioration in the treatment algorithm. This might conceivably be the case also in patients with extensive thoraco-abdominal aortic pathology, who would require more complex repair, and future guidelines might further incorporate CKD among the tools used to evaluate the overall risk benefit ratio of the procedure, on top of perceived technical complexity and expected post-operative outcomes.

Chronic renal function worsening after endovascular aortic procedures is a well known phenomenon,<sup>24</sup> described as occurring more frequently compared with open surgical repair.<sup>25</sup> Nevertheless, prior studies have shown that complex endovascular repair does not impair renal function more (often) than open surgery for PRAA.<sup>26</sup> Although limited in the ability to provide any definite explanation, it is likely that CKD per se was the culprit for the lower survival rates that were observed in patients with pre-existing renal function deterioration. Indeed, in their study of 275 patients who underwent standard EVAR (8% women; mean age 75 years; median follow up nine years), Charles *et al.* showed that almost half of those with normal baseline renal function would experience a > 20% reduction of eGFR in the years after the intervention, which was thereby strongly associated with increased long term mortality (odds ratio 3.3,  $p < .001$ ).<sup>24</sup> These results seem largely comparable with the present findings, which indicate that worsening renal function was independently linked to poorer survival in the long term. Given the much higher rates of renal function decline in patients with pre-existing CKD, it is reasonable to assume that history of CKD represents a significant marker for poorer long term survival as does any worsening of renal function that is encountered during follow up. Based on the study results, it is suggested that follow up after F/BEVAR should incorporate more structured assessment of renal function and especially so in patients with prior CKD.

Several risk factors for renal function deterioration following endovascular aortic interventions which are consistent with the present findings have been described previously,<sup>27,28</sup> but it remains unclear whether this risk is intrinsic to the high risk profile of these patients, or whether procedure related factors (including micro-embolisation caused by intra-operative manipulation especially when concomitant shaggy aorta exists) might play a substantial role.<sup>29,30</sup> In that sense, in the present study, renal function worsening was observed even in patients with normal baseline status. Recently, Orrico *et al.* showed that use of branches was associated with a greater decrease in the eGFR than use of fenestrations, which was already evident on three month renal scintigraphy and stable at one year, but the evolution and clinical significance of these data still need to be documented.<sup>31</sup> Therefore, although use of fenestrations over branches might be warranted for

incorporation of renal arteries based on these preliminary data, it should always be borne in mind that selection of stent graft design is often mandated by the need to accommodate the aortic anatomy at the level of target vessel origin. In fact, durability of both fenestrations and branches after complex EVAR procedures remains a debated issue,<sup>32</sup> even after the introduction of newer generation bridging stent grafts<sup>33–35</sup> and refined assessment of their geometrical configuration,<sup>36–38</sup> and future research should focus on risk prediction models for loss of RA patency that could better inform how to structure adequate follow up protocols. Further refinement in technique and technology of complex endovascular aortic repair might also contribute to improve the patency rates of incorporated renal arteries.

Other mechanisms, including repeated contrast exposure (either because of repeated imaging or secondary interventions) and loss of RA patency, may be reasonably linked to renal function decline during long term follow up. Nevertheless, after multivariable adjustments baseline CKD remained a strong independent risk factor for accelerated renal function worsening over time, and its worse prognostic impact was further confirmed using *ad hoc* sensitivity and subgroup analyses. Post-operative AKI and RA occlusion were the other independent predictors of renal function worsening and, although unable to precisely assess their interplay with CKD, it is reasonable to assume that patients with already impaired kidney function would probably benefit from stricter protocols focused on prevention of immediate renal damage after the intervention, assurance of unrestricted renal perfusion, and incorporation of serial renal function evaluation especially when lower RA target patency rates might be anticipated on the basis of challenging RA anatomy (including small, angulated, or diseased vessels).<sup>39,40</sup>

### Study limitations

The findings from this study must be interpreted within the context of its inherent limitations. First, the study was retrospective, with relatively small sample size and limited follow up. Nevertheless, it reported on > 200 consecutive patients treated over nine years with a median follow up of almost three years, which makes the results clinically meaningful and comparable with prior studies. Not all patients included in the study received renal function assessment during follow up, as this was estimated in retrospectively and only in those surviving at least six months after the index procedure with at least one creatinine examination available for review. However, the proportion of patients available for this analysis was comparable between study groups (baseline CKD: 53% vs. non-baseline CKD: 58%;  $p = .43$ ) and therefore unlikely to influence study results. Furthermore, the study cohort represents a well selected group of CKD patients as not all those with renal function decline and aortic aneurysmal disease were offered repair. As no information was available on patients who were denied repair, this study is not representative of the entire population of patients with CKD

and aortic aneurysm pathology. Also, the extremely low number of patients with very advanced CKD (i.e. stage 4–5) at baseline did not allow any specific subanalysis for this group. However, it is reasonable that clinical outcomes would not be better in subjects with more advanced baseline renal dysfunction, which may further strengthen the relevance of the findings. Lastly, although attempts were made to correct for known confounders using multi-variable analysis, it remains possible that some unmeasured confounders might have remained. The results were confirmed using multiple sensitivity and subgroup analyses (although the absence of statistically significant differences in the latter could be attributed to type II error because of lack of statistical power given the smaller sample sizes that were available within subgroups), thereby strengthening the association between baseline CKD and poorer clinical outcomes in the short and midterm after F-BEVAR.

### Conclusion

Although F-BEVAR for treatment of PRAA/TAAA in patients with baseline moderate to severe CKD enjoys low peri-operative mortality rates that are comparable with patients with unimpaired renal function, occurrence of AKI was significantly higher in subjects with pre-existing CKD. Furthermore, history of CKD was independently associated to renal function decline and poorer survival at midterm follow up. Therefore, presence of pre-operative moderate to severe CKD must be considered during decision making, and efforts made to optimise outcomes in the immediate peri-operative period as well as in the long term.

### CONFLICT OF INTEREST

None.

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### APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejvs.2021.08.033>.

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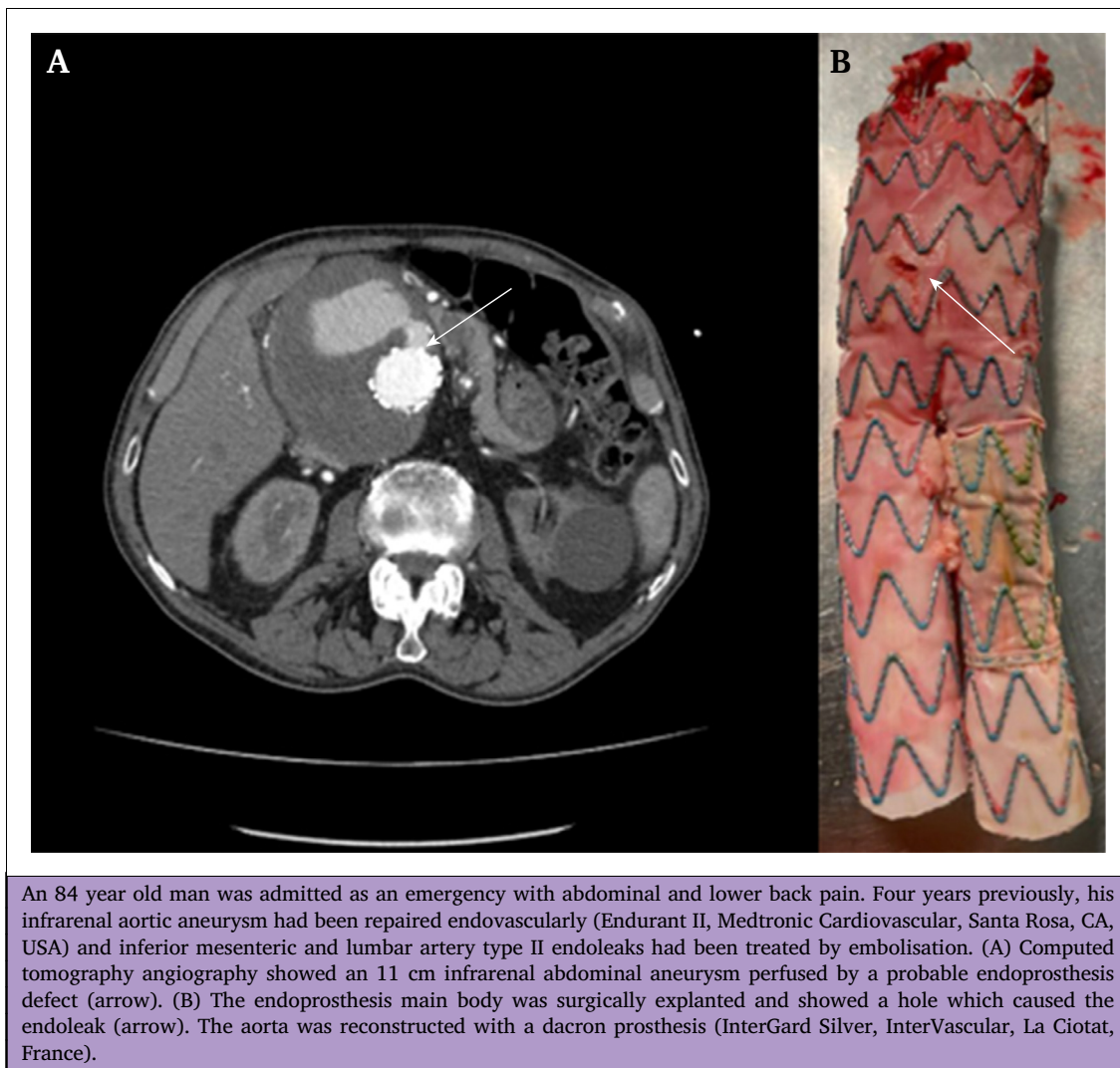
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## COUP D'OEIL

### Fabric Failure: an Old Problem in Modern Stent Grafts

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