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How Does Female Sex Affect Complex Endovascular Aortic Repair? A Single Centre Cohort Study

Christian-Alexander Behrendt [*], **Giuseppe Panuccio, Jenny Kuchenbecker, Fiona Rohlffs, Franziska Heidemann, E. Sebastian Debus, Konstantinos Spanos, Tilo Kölbel**

German Aortic Centre Hamburg, Department of Vascular Medicine, University Heart and Vascular Centre UKE Hamburg, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany

WHAT THIS PAPER ADDS

There is a paucity of evidence concerning a suggested female patient disadvantage in complex endovascular aortic repair. In this single centre cohort study including 445 patients treated consecutively by elective fenestrated or branched endovascular aortic repair for either thoraco-abdominal or pararenal aneurysm, an independent impact of female sex was observed on overall in hospital mortality, post-procedural complication, and spinal cord ischaemia. The current study provides clinical evidence that peri-procedural outcomes after complex aortic repair of pararenal aortic aneurysm in females are worse. Future studies should confirm these findings and sex specific outcomes should be implemented more generally in vascular research.

Objective: There is growing evidence of a female patient disadvantage in complex endovascular aortic repair using fenestrated and branched endografts (FB-EVAR) primarily related to peri-procedural events including ischaemic and access vessel complications. This study aimed to determine the impact of sex differences on treatment patterns, and in hospital outcomes in a single centre cohort.

Methods: This was a retrospective cross sectional single centre cohort study of all consecutive FB-EVAR procedures provided to patients with asymptomatic pararenal and thoraco-abdominal aortic aneurysm (TAAA) between 1 January 2010 and 28 February 2021. Adjusted multivariable logistic regression models were developed using backward (Wald) elimination of variables to determine the independent impact of female sex on short term outcomes.

Results: In total, 445 patients (24.3% females, median age 73.0 years, IQR 66, 78) were included. Female patients had a smaller aneurysm diameter, less frequent coronary artery disease (29.6% *vs.* 44.8%, $p = .007$) and history of myocardial infarction (2.8% *vs.* 15.4%, $p < .001$) when compared with males. Females were more frequently treated for TAAA than males (49.1% *vs.* 25.2%, $p < .001$). The median length of post-procedural hospital stay was 10 days in females and 9 in males. In adjusted analyses, female sex was independently associated with higher mortality (odds ratio [OR] 10.135, 95% CI 2.264 – 45.369), post-procedural complications (OR 2.500, 95% CI 1.329 – 4.702), spinal cord ischaemia (OR 4.488, 95% CI 1.610 – 12.509), sepsis (OR 4.940, 95% CI 1.379 – 17.702), and acute respiratory insufficiency (OR 3.283, 95% CI 1.015 – 10.622) after pararenal aortic aneurysm repair during the hospital stay.

Conclusion: In this analysis of consecutively treated patients, female sex was associated with increased in hospital mortality, peri-procedural complications, and spinal cord ischaemia after elective complex endovascular repair of pararenal aortic aneurysm, while no differences were revealed in the TAAA subgroup. These results suggest that sex related patient selection and peri-procedural management should be studied in future research.

Keywords: Aneurysm, Aortic disease, Endovascular techniques, Health services research, Outcome research, Sex
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* Corresponding author. German Aortic Centre Hamburg, Department of Vascular Medicine, University Heart and Vascular Centre UKE Hamburg, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany.
E-mail address: behrendt@hamburg.de (Christian-Alexander Behrendt).
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INTRODUCTION

There is growing evidence for differences between the sexes in the diagnosis and treatment of vascular diseases. Interestingly, while recent studies failed to show worse long term survival after peripheral revascularisations or abdominal aortic aneurysm repair in females, some unfavourable major events including peri-operative ischaemic and bleeding complications were associated with female sex.[1–5]

During the past decade, complex endovascular aortic repair using fenestrated or branched endografts (FB-EVAR) has gradually replaced open repair to treat thoracoabdominal (TAAA) and pararenal aortic aneurysm. Advanced techniques and innovative medical devices have enabled the operative treatment of patient populations at prohibitive risk of open repair. However, although these developments appear encouraging, there is also evidence for a female patient disadvantage and an under representation of females in vascular trials.[6–9] It appears likely that technical innovations were predominantly developed and evaluated in males while sex specific anatomy,[5] treatment, and outcomes in females were considered less. In previous studies including registry data on FB-EVAR procedures, higher rates of major bleeding complications, acute limb ischaemia, and spinal cord ischaemia were revealed in the female subgroup.[10–12] Female sex could be associated with increased rotational deviation of branched endografts after implantation,[13] and higher rates of type IA endoleaks.[5]

In the light of these results, the American Heart Association (AHA) recently issued a call to action to further emphasise the need for sex related research in cardiovascular disease.[14,15]

This study aimed to determine the impact of female sex on patient selection, treatment patterns, and in hospital outcomes after complex endovascular aortic repair. Therefore, consecutive patients treated for complex aortic aneurysms at a tertiary referral centre were analysed with a focus on sex specific data.

METHODS

Study design

This was a retrospective cross sectional single centre cohort study covering all patients treated by FB-EVAR for asymptomatic TAAA and pararenal aortic aneurysm between 1 January 2010 and 28 February 2021 at one large multidisciplinary centre in Northern Germany. Details of the centre and results from the registry have been published elsewhere.[13,16,17]

The reporting of the current study follows the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement.[18]

Study variables

For the current study, information was collected on dichotomised sex (female, male), age (in years), year of procedure (2010 – 2021), maximum aneurysm diameter (in cm), concomitant occurrence of an aortic dissection, confirmed diagnosis of any genetic aortic syndrome (e.g., Marfan, Loeys-Dietz, Ehlers-Danlos), body mass index (in kg/m^2), American Society of Anaesthesiologists class (I – VI), history of coronary artery disease (CAD), cardiac dysrhythmias, atrial fibrillation, hypertension, dyslipidaemia, smoker (active, former, never), chronic obstructive pulmonary disease (COPD), stroke, myocardial infarction (ever, within 30 days), congestive heart failure, coronary bypass surgery (ever, within six months), percutaneous coronary intervention (ever, within six months), coronary stent angioplasty, diabetes, serum creatinine before surgery (in mg/dL), chronic renal failure, chronic dialysis dependency, cancer, peripheral arterial occlusive disease, previous abdominal or thoracic aortic procedures (endovascular, open surgery), any previous abdominal surgery, previous cervical debranching, and aneurysm extent (thoraco-abdominal, pararenal). Further information included the post-operative length of stay (days), length of intensive care unit stay (days), spinal fluid drainage, operation time (minutes), contrast volume (millilitres), dose area product ($cGy*cm^2$), fluoroscopy time (minutes), type of implanted endograft (fenestrated, branched, both), and existence of any endoleak on final angiography.

As outcomes, information was collected on peri-procedural mortality during the in hospital stay and after 30 days, any early peri-procedural re-intervention, prolonged intensive care unit stay $>$ 48 hours, systemic inflammatory response syndrome (SIRS) or sepsis, acute myocardial infarction, acute respiratory insufficiency (pathologically increased respiratory rate or abnormal blood gases), stroke or transient ischaemic attack (TIA), spinal cord ischaemia, acute renal failure (abrupt post-interventional decrease in kidney function), new dysrhythmia, colonic ischaemia, bleeding complication (occurrence of bleeding from access vessels, iliac artery, or aorta), any access vessel complication, and wound infection (surgical site infection with presence of microbes causing a local or systemic response). As a composite endpoint, the occurrence of either complication was additionally analysed in one variable.

Protocol and standards for complex endovascular aortic repair at the study centre

Patients who were included in the study cohort were previously seen at the university outpatient department to evaluate the treatment indication and modality. The general threshold for repair of asymptomatic pararenal and thoracoabdominal aortic aneurysm was 55 mm considering further individual morphological factors, comorbidities, and patient preference to decrease or increase that threshold. In female patients, the threshold was decreased by a maximum of 5 mm according to current guidelines.[19] Endovascular repair was the preferred treatment modality in patients with suitable anatomy and without confirmed or suspected genetic aortic syndrome also taking patient preference into account. Using computed tomography angiography (CTA), the appropriate procedure was planned and prepared according to local standards. According to the local standard operating

procedure, spinal fluid drainage was established on the day of the intervention if two of four territories would be compromised after the planned repair: 1) impairment of left subclavian artery perfusion, 2) long thoracic aortic coverage $\geq$ 20 cm, 3) previous abdominal aortic repair, 4) impairment of iliac perfusion. No sex specific thresholds or standard operating procedures were applied.

Ethical considerations

This retrospective study was in accordance with the Declaration of Helsinki. All patients treated at the study centre gave their explicit informed consent to process personal data for quality assurance and health service research. The data extraction and processing of personal data for quality assurance purposes was lawful in accordance with the European Union General Data Privacy Regulation (EU-GDPR).

Statistical analysis

In descriptive analyses, means with standard deviations (SD) or medians with interquartile ranges (IQR) are presented for continuous variables. Similarly, proportions and 95% confidence intervals (CI) are presented for categorical variables. Tests of normality were conducted using the Kolmogorov–Smirnov test. In bivariable analyses, the Mann–Whitney *U* test and Kruskal–Wallis *H* test were used for non-normally

Table 1. Baseline characteristics of the cohort including 445 patients with elective fenestrated or branched endovascular aortic repair

	Female (n = 108; 24.3%)	Male (n = 337; 75.7%)	p value
Median age – y	72 (66–78)	74 (69–78)	.21
Octogenarians	19 (17.6)	52 (15.4)	.65
Aneurysm diameter – cm	5.9 (5.4–6.4)	6.0 (5.5–6.8)	.011
Occurrence of dissection	5 (4.6)	24 (7.1)	.50
Aneurysm location			<.001
Thoraco-abdominal aneurysm	53 (49.1)	85 (25.2)	
Pararenal aneurysm	55 (50.9)	252 (74.8)	
Genetic aortic syndrome	3 (2.9)	5 (1.5)	.11
Body mass index – kg/m^2	24.5 (22.1–28.6)	26.0 (23.7–29.0)	.014
American Society of Anaesthesiologists class			.73
ASA class III	79 (78.2)	247 (78.4)	
ASA class IV	10 (9.9)	20 (6.3)	
History of coronary artery disease	32 (29.6)	151 (44.8)	.007
History of cardiac dysrhythmias	9 (8.3)	29 (8.6)	1.0
History of atrial fibrillation	21 (19.4)	65 (19.3)	1.0
Hypertension	93 (86.1)	286 (84.9)	.88
Dyslipidaemia	28 (25.9)	99 (29.4)	.54
Current smoker	26 (24.1)	80 (23.7)	1.0
Ever smoker	36 (33.3)	124 (36.8)	.57
History of chronic obstructive pulmonary disease	27 (25.0)	56 (16.6)	.064
History of stroke	6 (5.6)	37 (11.0)	.13
History of myocardial infarction	3 (2.8)	52 (15.4)	<.001
Myocardial infarction within 30 days	0	0	N/A
History of congestive heart failure	13 (12.0)	37 (11.0)	.73
History of coronary bypass surgery	14 (13.0)	42 (12.5)	.87
Coronary bypass surgery within six months	1 (0.9)	3 (0.9)	1.0
History of any coronary intervention			.21
Any intervention	16 (14.8)	76 (22.6)	
Coronary artery stent angioplasty	3 (2.8)	11 (3.3)	
Coronary intervention within six months	2 (1.9)	10 (3.0)	.74
Diabetes	12 (11.1)	55 (16.3)	.22
Chronic renal failure			.342
No dialysis dependency	19 (17.6)	80 (23.7)	
Dialysis dependency	1 (0.9)	4 (1.2)	
Serum creatinine – mg/dL	0.91 (0.77–1.10)	1.10 (0.95–1.40)	<.001
History of cancer	24 (22.2)	60 (17.8)	.32
Peripheral arterial occlusive disease	15 (13.9)	59 (17.5)	.46
History of a previous aortic procedure	49 (45.4)	135 (40.1)	.37
Previous endovascular aorto-iliac repair	17 (15.7)	80 (23.7)	.083
Previous open surgical aortic repair	35 (32.4)	82 (24.3)	.10
Previous thoracic aortic repair	40 (37.0)	68 (20.2)	.001
Any previous abdominal surgery	14 (13.0)	51 (15.1)	.64
Previous cervical debranching	16 (14.8)	23 (6.8)	.017

Data are presented as n (%) or median (interquartile range). N/A = not applicable.
*p values < .050 were considered to be statistically significant.

distributed data. Rates and differences in proportions were estimated using the Pearson χ^2 test and the Fisher exact test.

To address the impact of aneurysm extent (TAAA *vs.* pararenal aneurysm), the cohort was separated into two strata. In a consensus meeting of clinical relevance and interpretation of the bivariable analyses, multivariable logistic regression models were developed for each outcome described under "study variables" including the following variables in a stepwise backward elimination (Wald) of variables: female sex (*vs.* male sex), higher age (increase per year), coronary artery disease, chronic obstructive pulmonary disease, myocardial infarction, previous aortic surgery or intervention, dyslipidaemia, current smoker, stroke, diabetes, chronic renal failure, and peripheral arterial occlusive disease. Odds ratios (OR) are presented with 95% CI.

Missing values (< 5%) were excluded from the analysis using complete case exclusion. A p value of < .050 was considered to be statistically significant. Data processing was performed with SPSS version 25 (IBM Corporation, New York, NY, USA).

RESULTS

In total, 445 consecutively hospitalised patients were identified (24.3% females, median age 73.0 years, IQR 66, 78) having elective invasive treatment between 1 January 2010 and 28 February 2021. Between 2011 and 2020, the monthly number of treated patients varied between < 1 and > 6 in 2020 with a monthly mean of 3.16 patients.

The baseline characteristics of the cohort by female *vs.* male sex are presented in Table 1. Female patients were treated with smaller aneurysm diameter (5.9 *vs.* 6.0 cm, p = .011) and more frequently for TAAA (49.1% *vs.* 25.2%, p < .001) when compared with males.

Risk profile and pre-existing comorbidities

Concerning the risk profile at the time of treatment, females had a lower body mass index (24.5 *vs.* 26.0, p = .014) and serum creatinine (0.91 *vs.* 1.10, p < .001), and less often had coronary artery disease (29.6% *vs.* 44.8%, p = .007) and history of myocardial infarction (2.8% *vs.* 15.4%, p < .001) than males.

More often, females had pre-treatment with thoracic endovascular aortic repair (TEVAR) (37.0% *vs.* 20.2%, p = .001) and cervical debranching (14.8% *vs.* 6.8%, p = .017) than males.

Peri-operative details and complex endovascular procedures

The peri-operative and procedural details are presented in Table 2. The median length of intensive care unit stays was three days (IQR 2, 5) for both sexes. The proportion of procedures with spinal fluid drainage was 64.8% in females and 52.2% in males.

The crude unadjusted in hospital (9.3% *vs.* 2.7%) and 30 day mortality rates (12.0% *vs.* 3.3%) were three times higher in females compared with males. The rates of spinal cord ischaemia were 19.4% in females and 9.5% in males (results not shown in tables). The crude unadjusted outcomes stratified by TAAA *vs.* pararenal aortic aneurysm are presented in Tables 3 and 4.

Multivariable logistic regression models

The results of the adjusted multivariable regression models are presented in Tables 5 and 6.

In the pararenal aneurysm stratum, female sex was significantly associated with in hospital mortality (OR 10.135, 95% CI 2.264 − 45.369, p = .002), occurrence of post-procedural complication (OR 2.500, 95% CI 1.329 − 4.702, p = .004), spinal cord ischaemia (OR 4.488, 95% CI 1.610 − 12.509, p = .004), SIRS or sepsis (OR 4.940, 95% CI 1.379 − 17.702, p = .014), and acute respiratory insufficiency (OR 3.283, 95% CI 1.015 − 10.622, p = .047).

In the thoraco-abdominal aneurysm stratum, no statistically significant impact of female sex was observed.

DISCUSSION

In this cross sectional cohort study of a tertiary referral centre, 445 patients (24% females) were included who were treated consecutively by elective FB-EVAR for TAAA and pararenal

Table 2. Unadjusted peri-operative and procedural details of the cohort including 445 patients with elective fenestrated or branched endovascular aortic repair

	Female (n = 108; 24.3%)	Male (n = 337; 75.7%)
Length of post-operative hospital stay − d	10 (7–15)	9 (7–14)
Length of intensive care unit stay − d	3 (2–5)	3 (2–5)
Spinal fluid drainage	70 (64.8)	176 (52.2)
Total operation time − min	292 (235–369)	260 (202–330)
Contrast volume − mL	132 (108–157)	118 (96–150)
Dose area product − cGy*cm^2	17 285 (10 016–26 676)	23 800 (13 900–44 945)
Total fluoroscopy time − min	63 (49–106)	68 (52–96)
Fenestrated endograft	44 (40.7)	204 (60.5)
Branched endograft	50 (46.3)	106 (31.5)
Fenestrated and branched endograft	14 (13.0)	27 (8.0)
Existence of any endoleak on final angiogram	20 (18.5)	93 (27.6)

Data are presented as n (%) or median (interquartile range).

Table 3. Unadjusted post-operative outcomes after elective complex endovascular aortic repair of pararenal aortic aneurysm during the hospital stay in 307 patients with elective fenestrated or branched endovascular aortic repair

	Female (n = 55; 17.9%)	Male (n = 252; 82.1%)
In hospital mortality	5 (9.1)	3 (1.2)
30 day mortality	7 (12.7)	5 (2.0)
Occurrence of any complication	23 (41.8)	63 (25.0)
Spinal cord ischaemia	8 (14.5)	15 (6.0)
Any endoleak at final angiography	10 (18.2)	72 (28.6)
Intensive care unit stay > 48 h	35 (63.6)	149 (59.1)
Any early re-intervention	6 (10.9)	18 (7.1)
SIRS or sepsis	5 (9.1)	5 (2.0)
Myocardial infarction	0 (0.0)	4 (1.6)
Acute respiratory insufficiency	5 (9.1)	9 (3.6)
Stroke or TIA	0 (0.0)	2 (0.8)
Acute renal failure	10 (18.2)	26 (10.3)
New dysrhythmia	3 (5.5)	14 (5.6)
Colonic ischaemia	1 (1.8)	3 (1.2)
Bleeding complication	5 (9.1)	16 (6.3)
Any access vessel complication	6 (10.9)	16 (6.3)
Wound infection	4 (7.3)	9 (3.6)

Data are presented as n (%). SIRS = systemic inflammatory response syndrome; TIA = transient ischaemic attack.

Table 4. Unadjusted post-operative outcomes after elective complex endovascular aortic repair of thoraco-abdominal aortic aneurysm during the hospital stay in 138 patients with elective fenestrated or branched endovascular aortic repair

	Female (n = 53; 38.4%)	Male (n = 85; 61.6%)
In hospital death	5 (9.4)	6 (7.1)
30 day mortality rate	6 (11.3)	6 (7.1)
Occurrence of any complication	26 (49.1)	41 (48.2)
Spinal cord ischaemia	13 (24.5)	17 (20.0)
Any endoleak at final angiography	10 (18.9)	21 (24.7)
Intensive care unit stay > 48 h	35 (66.0)	60 (70.6)
Any early re-intervention	6 (11.3)	10 (11.8)
SIRS or sepsis	3 (5.7)	7 (8.2)
Myocardial infarction	0 (0.0)	1 (1.2)
Acute respiratory insufficiency	3 (5.7)	5 (5.9)
Stroke or TIA	4 (7.5)	3 (3.5)
Acute renal failure	8 (15.1)	18 (21.2)
New dysrhythmia	5 (9.4)	6 (7.1)
Colonic ischaemia	1 (1.9)	2 (2.4)
Bleeding complication	7 (13.2)	10 (11.8)
Any access vessel complication	4 (7.5)	6 (7.1)
Wound infection	2 (3.8)	6 (7.1)

Data are presented as n (%). SIRS = systemic inflammatory response syndrome; TIA = transient ischaemic attack.

aortic aneurysm. Both the median age and risk profile were remarkably similar between sexes except for higher rates of coronary artery disease and myocardial infarction in males. The aneurysm extent and pre-treatment of aortic disease differed with more TAAA (*vs.* pararenal aneurysm) and higher rates of TEVAR and cervical debranching in females. Remarkably, the distribution of TAAA *vs.* pararenal aneurysm was 50:50 in females, while it was 25:75 in males. In correspondingly stratified and adjusted analyses, female sex was independently associated with higher rates of in hospital mortality, occurrence of post-procedural complication, spinal cord ischaemia, SIRS or sepsis, and acute respiratory insufficiency after FB-EVAR for pararenal aneurysm, while no statistically significant differences were revealed in patients treated for thoraco-abdominal aortic aneurysm.

O'Donnell and colleagues used a device specific multicentre registry to determine five year survival in 1 263 patients (11% females) treated by standard EVAR for AAA. After matching, they observed higher rates of any type IA endoleak through five years (10% *vs.* 1%, $p < .001$) and an overall more challenging anatomy in females.[5] In another retrospective review of all TEVAR procedures included in the Vascular Quality Initiative registry from 2011 to 2015, females had smaller aortic diameters and fewer cardiac risk factors. Mortality was higher for females at 30 days.[20] Although complex endovascular procedures were excluded by those previous studies, interesting results were confirmed by the present study.

Given the growing evidence concerning thoracic and abdominal aortic aneurysm repair,[21,22] it appears remarkable that only few studies to date specifically addressed sex disparities in complex endovascular aortic procedures. Most available studies into this target population focused on rather technical parameters and overall outcomes but did not report meaningful outcomes stratified by sex.[23–30] Grandi and colleagues used a single centre database including 268 patients (26% females) treated with an off the shelf multibranched endograft. The overall anatomical and vascular access feasibility was lower in females (22% *vs.* 45%, $p = .001$).[31] This also confirmed data from another device specific study, where an increased rotational deviation of multibranched endografts after implantation was revealed in females.[13] Interestingly, the current study revealed that sex differences were limited to the pararenal subgroup, in which a higher rotational error during deployment of fenestrated and branched endografts may impact outcomes because of misalignment of fenestrations and branches in a narrow or kinked visceral segment. Limited iliac access in female patients may play a causative role for their worse outcome, may be less important in the thoraco-abdominal subgroup in which branched endografts are used predominantly, which are well known for their forgiving nature in cases of misalignment.[13] De Guerre and colleagues recently used data derived from the National Surgical Quality Improvement Program (NSQIP) targeted vascular module in the United States to determine the impact of female sex on outcomes after complex aneurysm repairs (56% endovascular, thereof 21.4% females). Female

Table 5. Impact of female sex (reference) on peri-operative outcomes after elective complex endovascular aortic repair of pararenal aortic aneurysm in adjusted analyses of the cohort including 445 patients with elective fenestrated or branched endovascular aortic repair

	Independent impact of female sex (*vs.* male sex)	
	OR (95% CI)	*p**
In hospital mortality	10.135 (2.264–45.369)	.002
Occurrence of any complication	2.500 (1.329–4.702)	.004
Spinal cord ischaemia	4.488 (1.610–12.509)	.004
SIRS or sepsis	4.940 (1.379–17.702)	.014
Acute respiratory insufficiency	3.283 (1.015–10.622)	.047
Any endoleak at final angiography	0.558 (0.257–1.211)	.14
ICU stay > 48 h	1.376 (0.728–2.603)	.33
Any early re-intervention	1.125 (0.365–3.472)	.84
Stroke or TIA	N/A	N/A
Acute renal failure	2.282 (0.957–5.442)	.063
New dysrhythmia	1.822 (0.418–7.936)	.42
Colonic ischaemia	N/A	N/A
Bleeding complication	1.444 (0.442–4.713)	.54
Any access vessel complication	1.714 (0.564–5.207)	.34
Wound infection	4.008 (0.972–16.526)	.055

Analyses were adjusted for female sex, higher age, coronary artery disease, chronic obstructive pulmonary disease, myocardial infarction, previous aortic surgery or intervention, dyslipidaemia, current smoker, stroke, diabetes, chronic renal failure, peripheral arterial occlusive disease). OR = odds ratio; CI = confidence interval; ICU = intensive care unit; SIRS = systemic inflammatory response syndrome; TIA = transient ischaemic attack; N/A = not applicable.
*p values < .050 were considered statistically significant.

Table 6. Impact of female sex (reference) on peri-operative outcomes after elective complex endovascular aortic repair of thoraco-abdominal aortic aneurysm in adjusted analyses of the cohort including 445 patients with elective fenestrated or branched endovascular aortic repair

	Independent impact of female sex (*vs.* male sex)	
	OR (95% CI)	*p*
In hospital mortality	1.057 (0.249–4.480)	.94
Occurrence of any complication	1.165 (0.545–2.491)	.69
Spinal cord ischaemia	1.187 (0.469–3.007)	.72
SIRS or sepsis	0.422 (0.088–2.027)	.28
Acute respiratory insufficiency	0.402 (0.052–3.116)	.38
Any endoleak on final angiogram	0.705 (0.276–1.801)	.47
ICU stay > 48 h	0.960 (0.425–2.168)	.92
Any early re-intervention	1.128 (0.327–3.883)	.85
Stroke or TIA	4.634 (0.527–40.744)	.17
Acute renal failure	1.155 (0.369–3.616)	.80
New dysrhythmia	1.828 (0.412–8.120)	.43
Colonic ischaemia	0.544 (0.005–63.555)	.80
Bleeding complication	1.652 (0.474–5.766)	.43
Any access vessel complication	1.962 (0.398–9.677)	.41
Wound infection	0.441 (0.068–2.839)	.39

Analyses were adjusted for female sex, higher age, coronary artery disease, chronic obstructive pulmonary disease, myocardial infarction, previous aortic surgery or intervention, dyslipidaemia, current smoker, stroke, diabetes, chronic renal failure, peripheral arterial occlusive disease. OR = odds ratio; CI = confidence interval; ICU = intensive care unit; SIRS = systemic inflammatory response syndrome; TIA = transient ischaemic attack.

sex was associated with higher rates of peri-operative mortality and major complications after complex endovascular repair compared with male patients, which was not apparent after complex open surgical repair.[32] Torsello and colleagues used a registry collecting multicentre experience with the chimney technique. Among 412 patients, 17% were female, and no statistically significant differences were observed during a three year follow up between sexes. The authors concluded that given these results, the chimney technique may provide benefits for females considering the potentially higher risk of access complications demonstrated in previous studies.[33]

A devastating complication after FB-EVAR of pararenal aneurysm was associated with female sex, as clearly confirmed by previous multicentre studies using administrative multicentre registries from Germany.[10,11] Twice as many females exhibited spinal cord ischaemia when compared with their male counterparts with overall equivalent event rates in administrative and clinical registries (11.9% in the current study *vs.* 10.9% in previous studies), emphasising the validity of this striking observation. Bisdas *et al.* included a consecutive cohort of 142 patients with TAAA to determine risk factors associated with the occurrence of spinal cord ischaemia. Among that cohort, 16% developed spinal cord ischaemia and 8% suffered from paraplegia. The authors found that thoracic aortic coverage was the only risk factor significantly associated with this complication.[34] Confirming previous reports, an interaction between female sex, spinal cord ischaemia, and in hospital mortality was revealed. Although the underlying causal factors remain unknown, this clearly demands further investigation. Females were more frequently selected for TAAA treatment, while males were predominantly treated for pararenal aneurysm. This finding was in accordance with a retrospective registry study, in which thoracic aortic aneurysms were more common among women with abdominal aortic aneurysms.[35] Correspondingly, females were more often pre-treated by TEVAR and cervical debranching. The multivariable models were stratified and adjusted accordingly, and the independent impact of female sex on major peri-operative events remained statistically significant in the pararenal stratum. This underlines that concomitant factors were more important and that the observed disadvantage of females could not be explained by aneurysm extent alone.

Another aspect that deserves careful reflection is the considerably high mortality observed in the present study. Interestingly, previous studies have reported mortality rates after FB-EVAR that ranged from far below standard infrarenal endovascular aortic repair procedures to slightly above those in the present study.[12,29,30,32] Certainly, it appears challenging to compare the remarkable heterogeneous

cohorts and varying definitions of outcomes used in previous studies. That said, future observational research should follow existing reporting standards to improve the comparability of results.[36]

Besides the many strengths of this study, there are limitations. First, the merely observational design does not allow for drawing any causal conclusions. The growing evidence for differences between female and male patients makes it necessary to apply high quality trials further examining the research hypotheses derived by observational studies. Second, although the current study included all consecutively treated patients, the rather small event size and residual confounding limit the generalisability of certain conclusions to nationwide or even global reality. Another inherent limitation is related to the fact that this cohort can only describe a study population that was treated invasively with fenestrated or branched devices, while the patients turned down or ineligible for complex endovascular aortic repair were not in the scope of the present study. This selection bias is probably relevant for all procedure related registries and deserves a critical discussion by the community. Furthermore, while the interesting concept of body surface area thresholds for aortic repair has recently gained more attention by the vascular community, it was not implemented in local practice by the present authors and was not available.[37] An impact of anatomical measures that acknowledge sex differences on prevalence and outcomes can be expected. Lastly, it appears challenging for transregional referral centres to follow all patients after they return home to their usual care system. The numerous considerations related to ethics and data protection exacerbate a complete data collection beyond 30 days. To assure complete data and avoid bias, the present study reported only outcomes after 30 days, although there is an ongoing debate concerning the complementary value of mid- and long term outcomes.

Conclusion

In this large consecutive cross sectional cohort study from a tertiary centre, an independent association was observed between female sex and both higher in hospital mortality and spinal cord ischaemia after elective complex endovascular repair of pararenal aortic aneurysm, while no statistically significant differences were revealed in patients treated for thoraco-abdominal aortic aneurysm. Future trials should address the peculiarities and underlying differences between the sexes.

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CONFLICT OF INTEREST

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