

Women undergoing endovascular thoracoabdominal aortic aneurysm repair differ significantly from their male counterparts preoperatively and postoperatively

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ABSTRACT

Objective: A rational approach to the management of aortic aneurysm disease relies on weighing the risk of aneurysm rupture against the complications and durability of operative repair. In men, seminal studies of infrarenal aortic aneurysm disease and its endovascular management can provide a reasoned argument for the timing and modality of surgery, which is then extrapolated to the management of thoracoabdominal aortic aneurysms (TAAAs). In contrast, there is less appreciation for the natural history of TAAA disease in women and its response to therapy.

Methods: We used a retrospective cohort design of women, all men, and matched men, fit for complex endovascular thoracoabdominal aneurysm repair at two large aortic centers. We controlled for preoperative anatomic and comorbidity differences, and assessed technical success, postoperative renal dysfunction, spinal ischemia, and early mortality. Women and matched men were reassessed at follow-up for long-term durability and survival.

Results: Assessing women and all men undergoing complex endovascular aortic reconstruction, we demonstrate that these groups are dissimilar before the intervention with respect to comorbidities, aneurysm extent, and aneurysm size; women have a higher proportion of proximal Crawford extent 1, 2, and 3 aneurysms. Matching men and women for demographic and anatomic differences, we find persistent elevated perioperative mortality in women (16%) undergoing endovascular thoracoabdominal aneurysm repair compared with matched men (6%); however, at the 3-year follow-up, both groups have the same survival. Furthermore, women demonstrate more favorable anatomic responses to aneurysm exclusion, with good durability and greater aneurysm sac regression at follow-up, compared with matched men.

Conclusions: Women and unmatched men with TAAA disease differ preoperatively with respect to aneurysm extent and comorbidities. Controlling for these differences, after complex endovascular aneurysm repair, there is increased early mortality in women compared with matched men. These observations argue for a careful risk stratification of women undergoing endovascular thoracoabdominal aneurysm treatment, balanced with women's good long-term survival and durability of endovascular aneurysm repair. (*J Vasc Surg* 2019;■:1-10.)

Keywords: Thoracoabdominal; Aortic aneurysm; Branched/fenestrated; Endovascular; Sex differences

Our current understanding of aortic aneurysm disease, both its natural history and response to open or endovascular therapy, has historically relied primarily on data unsegregated on the basis of sex, with most study participants composed of men.¹⁻³ The paucity of data in female patients has spurred recent interest in delineating more precise indications for, and outcomes of, treatment. A rational approach to aneurysm management in women must balance the hazards of repair with the probability

of mortality from aneurysm rupture; data are needed to weigh these risks.

The rationale for examining women undergoing aortic aneurysm repair relates to perceived increased risk relating to access complications, mortality, suitability for standard endovascular aneurysm repair (EVAR), and rupture risk in women scaled to maximal aneurysm diameter and body size. A recent meta-analysis of open (open surgical repair) and endovascular infrarenal

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aneurysm repair in women demonstrated that, compared with men, women have increased perioperative mortality (open surgical repair 5.37% vs 2.82%, EVAR 2.31% vs 1.37%), although EVAR maintains its early survival advantage in both sexes.⁴ These data are most salient in the context of turn-down rates for infrarenal EVAR in women owing to anatomic unsuitability.⁵ Pooled estimates of infrarenal EVAR suitability differ significantly between men and women,⁴ and women are less likely than men to undergo EVAR electively for intact aneurysms.⁶

It has been posited that outcome differences in women undergoing EVAR relate to advanced age and burden of comorbidities; this supposition has not been universally borne out in the literature. Studies that control for age, comorbidities, ethnicity, and hospital volume, note poorer outcomes in women, including perioperative mortality, length of stay, and readmission.⁷ Indeed, although female patients undergoing EVAR tend to be older, they are also healthier, having fewer diagnosed instances of heart disease, diabetes, concurrent smoking, chronic obstructive pulmonary disease (COPD), and chronic renal dysfunction.⁸ There have been several studies where controlling for age, urgency at presentation, comorbidities, and risk factors has resulted in equipoise of perioperative and 1-year mortality.⁶

There is interplay between a patient's comorbidities and their aneurysm anatomy, which ultimately determines long-term outcome: successful aneurysm exclusion, prevention of rupture, aneurysm-related mortality, and overall survival. Female sex has been noted to predict failure of abdominal aortic aneurysm (AAA) exclusion with resultant ongoing risk of rupture.⁹ Given the conflicted literature with respect to infrarenal EVAR, we wanted to directly compare outcomes of endovascular repair for more extensive aortic aneurysm disease, in men and women at two aortic centers, as a matched cohort. We felt that fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR) or branched endovascular thoracoabdominal aneurysm repair (BEVAR), with its increasing complexity, greater physiologic demand, greater risk of access complications, or postoperative complications, might exaggerate differences between men and women with respect to EVAR. These data could then be used to rationalize differing approaches to treatment, possibly with respect to timing of intervention or preferred approach, stratified by sex.

METHODS

Population. This retrospective cohort series used data collected prospectively from two independent centers for aortic surgery (Royal Free Hospital, London, UK; Lille University Hospital, Lille, France.) All patients, male and female, undergoing FEVAR or BEVAR between 2006 and 2017 were identified, and demographic data,

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter retrospective cohort
- **Key Findings:** Complex endovascular thoracoabdominal aortic aneurysm repair in 50 fit female and 50 matched male patients was associated with infrequent perioperative complications in both groups, but elevated 30-day mortality in women (16% vs 6%). At long-term follow-up, women have predominantly type II endoleaks and a decrease in aneurysm diameter compared with matched men. Matched men and women after complex endovascular thoracoabdominal aneurysm repair have the same 3-year survival rate.
- **Take Home Message:** Endovascular thoracoabdominal aortic aneurysm repair in women is associated with increased perioperative mortality, but acceptable survival and durability at long-term follow-up.

including sex, smoking status, coronary artery disease, COPD, and chronic renal impairment, were collected prospectively, as were details of individual operations. Patients were only included if they underwent a planned FEVAR or BEVAR; ruptured, urgent or symptomatic cases, and dissections were excluded, as were cases where only an infrarenal device was implanted. Thus, only patients with thoracoabdominal aneurysms of Crawford extents 1 to 5 (Safi modification), and pararenal aneurysms, denoted here as extent 6, were studied. Retrospectively, all female patients (female all-comers) undergoing FEVAR or BEVAR were matched to case control male patients on the basis of age, aneurysm extent, smoking status, presence of ischemic heart disease, and diagnosis of COPD. Surgery was undertaken by two aortic surgeons (T.M., S.H.) on patients deemed anatomically suitable for FEVAR/BEVAR by standard criteria for use for these devices, and physiologically appropriate for endovascular intervention with an acceptable risk for general anesthesia, through a preoperative anesthetic consultation and multidisciplinary team approach, "fit" patients. Threshold maximal diameter for intervention was determined by the treating surgeon, but most often followed the rules of more than 6.0 cm diameter for thoracoabdominal aneurysms and more than 5.5 cm for pararenal aneurysms. Measurements were made on centerline of flow reconstructed computed tomography (CT) scans. Female and matched male patients were equally distributed by operating surgeon (female: TM 23, SH 27; male: TM 28, SH 22), and the groups were matched in distribution over the time interval of assessment from 2006 to 2017. The endovascular devices used for repair included custom-made branched and/or fenestrated devices from Cook Medical (Bloomington, Ind) and were designed and

implanted at the discretion of the local surgeons. As is standard practice in the United Kingdom, this research project was adjudicated through the MRC/HRA decision-making tool (<http://www.hra-decisiontools.org.uk/research/>) and deemed not to require ethical review board oversight. As such, this project was registered as a local clinical audit, patient consent was waived, and ethics procedures adhered to according to local governance.

Variables. Patient demographics, comorbidities, preoperative aneurysm anatomy by Crawford extent, and aneurysm diameter were gathered for all-comers. Aneurysm extent and diameter were assessed by preoperative contrast-enhanced CT scan, reformatted to centerline measurements. As is standard practice at both institutions, following an early postoperative CT assessment within 3 months of the index procedure, patients undergo, at minimum, yearly CT imaging and duplex arterial assessment of their endovascular repairs. Postoperative aneurysm diameter was assessed as the maximal aneurysm diameter at the patient's last follow-up, by contrast-enhanced CT scan, again through center of flow measurement. Endoleaks were also assessed from these contrast-enhanced CT scans and Duplex ultrasound examination, and were reported if perigraft flow was noted by either modality. Endoleaks were assessed for all follow-up scans and are reported as positive if any endoleak was ever present for an individual patient at any time during follow-up. Target vessel patency and reinterventions are reported for any stenosis/occlusion reported by either duplex ultrasound examination or CT angiography at any time during follow-up. Renal dysfunction/acute kidney injury was assessed by estimated glomerular filtration rate (eGFR; calculated using the MDRD (Modification of Diet in Renal Disease) equation) at 24 hours after the procedure, and clinical follow-up regarding dialysis dependence thereafter, to produce Risk Injury Failure Loss End-Stage Kidney Disease scores.¹⁰

Statistical analysis. Categorical variables are presented as percentages, with raw data in adjacent parentheses, and continuous variables as the mean \pm standard deviation. Differences between groups were assessed using the χ^2 test, Student *t*-test, or analysis of variance. All tests were two-sided and considered significant if the *P* value was less than .05. Statistical analysis was performed using SPSS Statistical Analytics software (IBM Analytics, New York, NY).

RESULTS

Preoperative assessment. A cohort of all female patients undergoing endovascular repair for thoracoabdominal aortic aneurysm (TAAA), from 2006 to 2017 at two treating centers was assembled, 50 patients total (8% of all patients undergoing endovascular TAAA

Table 1. Female patients undergoing fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR) or branched endovascular thoracoabdominal aneurysm repair (BEVAR) are demographically dissimilar from male patients

	Female patients	Matched male cohort	Male all-comers
Mean age (SD)	71.9 (9.7)	72.3 (8.8)	72 (8.6)
Smoking status			
Never	26	16	13.6 ^a
Current	30	30	23.6 ^a
Former	42	54	62.9 ^a
Diabetes mellitus	4	8	20.1 ^a
Coronary artery disease	28	34	50 ^a
COPD	30	32	27.1
Chronic renal insufficiency	16	40 ^b	43.6 ^a

COPD, Chronic obstructive pulmonary disease; SD, standard deviation. Values are presented as percentages unless otherwise noted. Female patients undergoing FEVAR or BEVAR differ significantly from all male patients undergoing FEVAR/BEVAR, but can be matched according to comorbidities and aneurysm extent.
^a*P* < .01.
^b*P* < .05.

repair). These women were classified as requiring complex aortic repair, because they were anatomically unsuitable for infrarenal EVAR, requiring a custom-made fenestrated (FEVAR; 36 patients) or branched (BEVAR; 14 patients) device. Patients undergoing emergency intervention were excluded from this analysis. Female patients were then matched to a 50-patient cohort of male patients distributed over the same surgical sites and time period, and requiring complex EVAR (FEVAR 39 patients; BEVAR 11 patients). They were further matched on the basis of medical comorbidities including the diagnosis of coronary artery disease, COPD, diabetes mellitus, and smoking status (Table 1), as well as their aneurysm extent (modified Crawford criteria, with pararenal aneurysms delineated as category 6 in this article). The male and female matched cohorts (100 patients total) were compared with the entire cohort of male patients undergoing complex aortic repair during the same time period (541 patients). Because this research project, adjudicated through MRC/HRA, was recognized as a clinical audit, patient consent was waived and procedures adhered to according to local ethics governance.

Female patients undergoing FEVAR or BEVAR (Table 1) are the same age ($\mu = 71.9 \pm 9.7$) as their male (unmatched) counterparts ($\mu = 72 \pm 8.6$), however, they differ significantly with respect to percentage of patients currently using cigarettes, albeit a higher proportion of these women have never smoked (*P* < .01 by χ^2 between female and male all-comer cohorts). Women undergoing

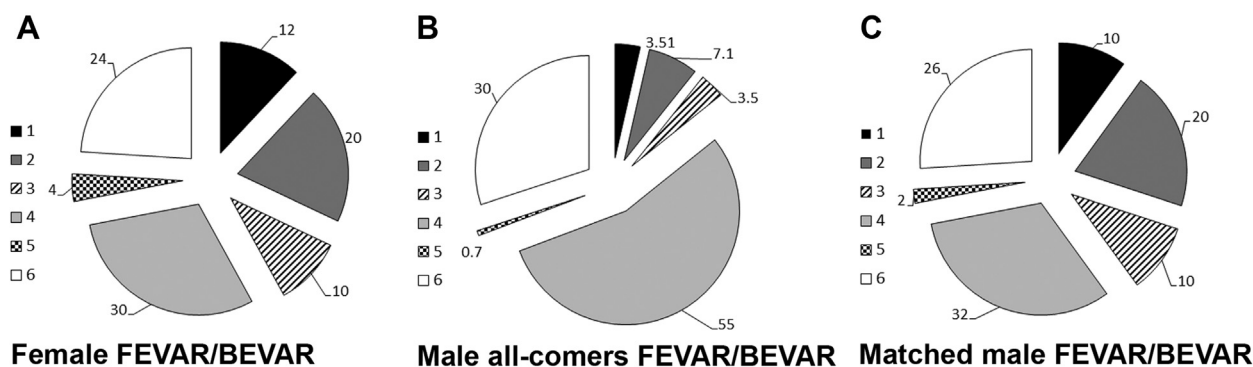


Fig 1. Female patients undergoing complex endovascular aortic repair have a different anatomic distribution of aneurysm than their male counterparts. Preoperative anatomic distribution of aneurysm extent in women (**A**), by modified Crawford criteria, with pararenal aneurysms denoted as category 6, and in (**B**) all male patients undergoing fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR)/branched endovascular thoracoabdominal aneurysm repair (BEVAR). Female patients can be (**C**) matched to a male cohort by aneurysm extent and comorbidities.

complex aortic repair, compared with all men, are also less likely to be diabetic, suffer from coronary artery disease or chronic renal insufficiency ($P < .01$). The male cohort of FEVAR/BEVAR patients, matched to our female cohort for age, smoking status, COPD, and diabetes mellitus remains statistically more heavily burdened by chronic renal insufficiency ($P < .05$, by χ^2 between matched male and female patients).

An assessment of preoperative distribution of aneurysm extent in women by modified Crawford criteria, with pararenal aneurysms delineated as extent 6 (Fig 1, A), demonstrates a representation of all aneurysm categories, with a predominance of extent 4 thoracoabdominal aneurysms (15/50), followed by extent 2 (10/50; percentages of each group next to wedges). In contrast (Fig 1, B), in all male patients undergoing FEVAR/BEVAR, patients have predominantly extent 4 TAAA and 6 (pararenal) aneurysms (77/140 and 42/140, respectively), with a paucity of more extensive/cephalad aneurysms ($P < .05$). Female patients can be matched to a male cohort by aneurysm extent and comorbidities, and no longer differ significantly with respect to Crawford aneurysm class (Fig 1, C).

Perioperative events. Technical success, defined as aneurysm exclusion, without immediate type I or III endoleak, and with perfusion to visceral, renal, and lower extremity arterial beds, was 100% in both female and male matched patients at the termination of each procedure. Intraoperative complications in both groups were rare. These consisted of failure to catheterize and stent the celiac artery, dissection of the celiac, thoracic or visceral aorta, left subclavian artery, or external iliac, and type II endoleak. There were no intraoperative deaths.

Early perioperative complications are infrequent, and similar, between women and matched men (Table II).

Postoperative mean renal function (eGFR) within 24 hours of FEVAR or BEVAR (Table II) in matched men and women is unchanged. For the minority of patients suffering any renal impairment postoperatively (women 14/47, men 13/48; NS), as expressed by Risk Injury Failure Loss End-Stage Kidney Disease score, change in postoperative eGFR does not differ significantly either in degree of eGFR decline, or in total loss of renal function requiring dialysis, between male and female patients. Patients developing renal impairment were primarily in the risk category (women 9/47, men 9/48), expressing a decrease in eGFR of less than 25%, from which all patients recovered. Very few patients (2% total) require new institution of dialysis either temporarily or indefinitely.

Spinal cord injury (Table II), either immediate or delayed, is also uncommon in patients undergoing FEVAR/BEVAR (9% of all patients), and there is no significant difference between matched men (12%) and women (6%), given the small cohort, and low frequency of this complication. Spinal cord injury was more often delayed (>24 hours) in both matched men and women (>24 hours 6/100 patients, <24 hours 3/100 patients).

Perioperative/early 30-day mortality is higher in women (16%) than matched men (6%) ($P < .05$). The causes of perioperative mortality are primarily attributable to the procedure, including cerebrovascular postoperative events, retrograde type A dissection, sepsis, and multiorgan failure, as well as cardiovascular causes (Table III). In female and matched male patients (Table III), a detailed assessment of events resulting in mortality demonstrates an association with more proximal/extensive aneurysm disease, presence of a TEVAR (placed as a staged procedure or concurrently), and placement of a BEVAR. These subgroup findings cannot be corroborated statistically in this study, given the small patient numbers. There was no difference in perioperative mortality rate by surgical site.

Table II. Perioperative complication rates are infrequent and similar between women and matched men undergoing fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR) or branched endovascular thoracoabdominal aneurysm repair (BEVAR)

Complications	Female	Male	Significance
Renal function			
Mean percent change eGFR	0.94 (0.3)	0.98 (0.6)	—
Renal outcomes by RIFLE score	(n = 47)	(n = 48)	—
0	33	35	—
1 Risk	9	9	—
2 Injury	4	2	—
3 Failure	0	1	—
4 Loss	0	0	—
5 ESRD	1	1	—
Spinal cord injury	(n = 50)	(n = 50)	
Total incidence	3	6	—
Immediate (<24 hours)	1	2	—
Delayed (>24 hours)	2	4	—
30-Day mortality			
Death within 30 days	8 (16%)	3 (6%)	<.05
Death attributable to intervention	7	3	—
Contributors to perioperative death			
Mesenteric ischemia	1	1	—
Cerebrovascular accident	3	0	—
Cardiac (arrhythmia/MI/arrest)	2	1	—
Sepsis	2	2	—
Multorgan failure	2	1	—

eGFR, Estimated glomerular filtration rate; ESRD, end-stage renal disease; MI, myocardial infarction; RIFLE, Risk Injury Failure Loss End-Stage Kidney Disease.

Postoperative follow-up. Postoperatively, women and matched men underwent follow-up for a median of 957 and 820 days, respectively. Follow-up of all patients consisted of clinical assessment, contrast-enhanced CT, and duplex assessment of visceral vessels, with measures of durability, including target vessel patency, secondary reinterventions, aneurysm diameter, and the presence of endoleak, as well as patient survival. At both institutions, a follow-up CT scan is performed at approximately 1 month postoperatively, and then by CT and duplex examination at a minimum on a yearly basis, barring indications for more aggressive surveillance.

Preoperatively, women and men statistically have the same maximal aneurysm diameter, albeit with the largest aneurysms (>8 cm) belonging exclusively to matched men (Fig 2, A). However, postoperatively, aneurysm maximal diameters in women are significantly smaller (women μ = 52.1, men μ = 62.9; P < .01), and they have a significantly larger decrease in mean aneurysm diameter (Fig 2, A: women mean, large dashes μ = -8.3 mm, matched men mean small dots μ = -2.8 mm; P < .05). In contrast, endoleaks occurred more frequently at any time during follow-up in women

(Fig 2, B); indeed, 42% of women demonstrated an endoleak recorded at any time during their follow-up. These were predominantly type 2 endoleaks (Fig 2, B; raw numbers of patients adjacent to wedges). In matched men after FEVAR/BEVAR, there were fewer endoleaks overall, occurring in 25% of patients; however, their distribution was predominantly of type Ib or Ic (Fig 2, C). Coordinate with this data, there were more reinterventions of any kind over the entire follow-up period in matched men compared with women (18 reinterventions in 15 men vs 16 reinterventions in 14 women), but this difference was not significant. Visceral vessel reinterventions at any time during follow-up are rare, and were required in seven visceral vessels in women and nine visceral vessels in men.

Although we have suggested that 30-day survival after FEVAR/BEVAR is decreased in women versus men, thereafter, survival by Kaplan-Meier analysis (Fig 3, A) is not statistically different between the groups; many patients are, however, lost to follow-up at 5 years (Fig 3, B). Patient mean survival, by days confirmed alive, is also the same, at 1114 days (3.05 years) for women and 855 days (2.3 years) for men (Fig 3, C; P = .17).

Table III. Perioperative complications in deceased male and female patients undergoing fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR) or branched endovascular thoracoabdominal aneurysm repair (BEVAR) frequently involve proximal/complex repairs

Time of death (days postoperative)	Cause of death	Associated perioperative complications	Crawford extent	TEVAR	BEVAR or FEVAR	Related to TAAA repair
Female perioperative deaths						
1	Cerebrovascular accident	Retrograde type A dissection, cardiac failure	1	Y	BEVAR	Y
1	Multiorgan failure	Iliac rupture, cerebrovascular accident	6	N	FEVAR	Y
3	Cardiac failure	—	2	Y	BEVAR	Y
3	Spinal cord injury	Acute renal failure	3	Y	BEVAR	Y
16	Cerebrovascular accident	Intracerebral hemorrhage	2	Y	BEVAR	Y
24	Multiorgan failure	Sepsis, mesenteric ischemia	2	Y	BEVAR	Y
27	Sepsis (pneumonia)	Spinal cord injury, acute renal failure	1	Y	BEVAR	Y
30	Cardiac failure	—	2	Y	BEVAR	N
Male perioperative deaths						
0	Multiorgan failure	Sepsis, ischemic leg	3	Y	BEVAR	Y
1	Embolization	Spinal ischemia, mesenteric ischemia, sepsis	3	N	BEVAR	Y
30	PEA arrest	Spinal ischemia, acute renal failure	2	Y	BEVAR	Y

PEA, Pulseless electrical activity; TAAA, thoracoabdominal aortic aneurysm; TEVAR, thoracic endovascular aneurysm repair.

DISCUSSION

This retrospective cohort study of complex endovascular aortic repair at two centers compared female, matched male, and all male patients fit for repair.

The cohort of women undergoing TAAA repair in our series is fundamentally different from all male patients undergoing intervention for this disease at our institutions. Although it has often been reported that female patients treated with infrarenal EVAR are older than their male counterparts,⁶ we found that, for more extensive thoracoabdominal aortic disease in our cohort, this is not true. Women do, however, have a different burden of medical comorbidities. Current smoking is more common in our female patients and is a recognized risk factor for aneurysm enlargement, rupture, and worse perioperative or long-term outcomes after EVAR.^{11,12} COPD, which is a predictor of AAA development, expansion, poor perioperative outcome, and rupture risk, is not different between our female patients and all male patients.^{13,14} Diabetes mellitus, chronic renal disease, and coronary artery disease have all been reported to influence perioperative outcome after endovascular AAA repair, or to influence rupture risk for infrarenal AAA¹⁵⁻¹⁷ and had a higher prevalence among all male patients than our female patients. These comorbidities represent complex and competing influences on aneurysm growth, rupture risk, and complications associated with

aneurysm repair. Sex differences in comorbidities or their management, rather than an intrinsic sex-related difference in aneurysm pathophysiology, may more accurately explain differences observed in rupture risk, perioperative, and long-term outcome reported for women in the literature.

It is compelling that the anatomic distribution of thoracoabdominal pathology differs significantly between unmatched men and women in our cohort; women who are fit for surgery have more proximal aortic disease, with higher proportions of Crawford extent 1, 2, and 3 aneurysms, in contrast with a higher prevalence of extent 4 and pararenal aneurysms in all male patients. If the difference in anatomic distribution is reflective of the total population, it would imply that these women are likely at increased risk of spinal ischemia, proximal arch complications, and visceral/renal complications owing to the more extensive nature of their repair and an increased number of visceral vessels receiving intervention.¹⁸ It is possible that the general view that endovascular aortic surgery in women is more complex and associated with poorer outcome, is in fact determined by more complex anatomy. Conversely, selection bias toward harder women may influence anatomic distribution and subsequent perioperative course. Without knowledge of all patients who defer surgery at each institution, this generalization is difficult to make.

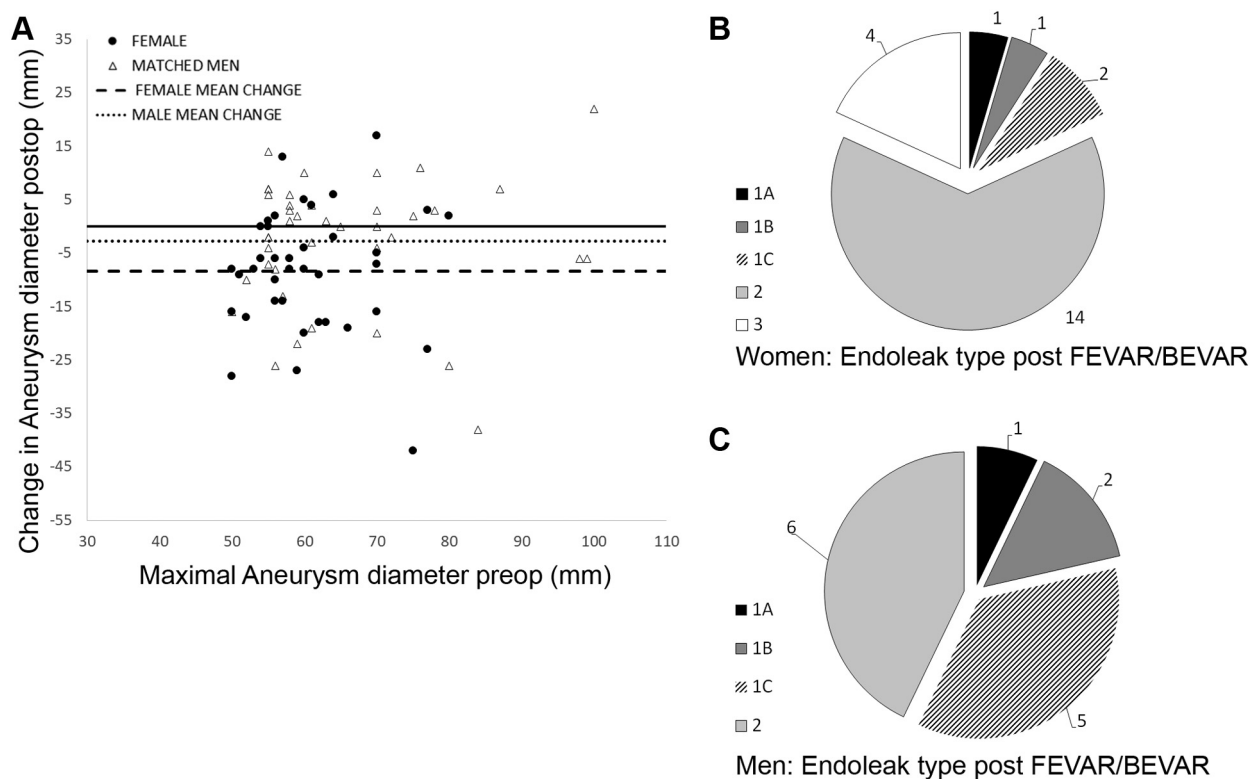


Fig 2. Postoperatively, women and matched male patients have dissimilar maximal aneurysm diameters, and a different distribution of endoleak type. Preoperatively, **(A)** women and men have the same maximal aneurysm diameter, but the mean diameter at latest follow-up differs postoperatively, as does the mean change in aneurysm diameter (female mean = *dashed line*; male mean = *dotted line*). **(B)** Endoleaks occurred more frequently at any time during follow-up in women and differed by type from those demonstrated in men **(C)**. BEVAR, Branched endovascular thoracoabdominal aneurysm repair; FEVAR, fenestrated endovascular thoracoabdominal aneurysm repair.

It has also been noted that absolute aneurysm size preoperatively is an independent predictor of cardiovascular death, whether or not the aneurysm is repaired.¹⁹ Although matched male patients in our study had the same mean preoperative aneurysm diameter, the largest aneurysms overall belonged to the matched male cohort. Women and matched men in our study, however, had similar long-term survival after repair, an effect that may reflect lower statistical power at longer follow-up owing to patient dropout.

It is salient that, although there is a relatively low incidence of perioperative complications in our matched male and female patients, there is initially increased mortality in women. The reasons for this are not immediately clear. New-onset renal failure was extremely uncommon in both groups, as was spinal cord ischemia, despite the extensive operations undertaken. Reports of perioperative renal failure after endovascular thoracoabdominal aneurysm repair vary widely in the literature; some studies report up to 32% of endovascular thoracoabdominal patients demonstrating acute renal insufficiency,²⁰ although in a larger study, only 5% of patients undergoing FEVAR and 9% of patients undergoing EVAR developed a decline in eGFR of greater than

25%.²¹ Preoperative renal dysfunction is a known risk factor for postoperative renal impairment in aneurysm patients, and we could not match female and male patients for the presence of renal dysfunction preoperatively, yet both groups had low rates of renal impairment. We cannot account for the effect of renal impairment on patient outcomes in this study. Matched men suffered more frequently from this comorbidity, but had lower perioperative mortality, and, thus, it seems unlikely to have had a negative impact. Similarly, one might expect a higher risk of spinal ischemia in women, compared with the male aneurysm patient, owing to more extensive disease. However, when matched for aneurysm extent, neither women or men in our study suffered from high rates of spinal cord dysfunction. Reported rates of spinal cord injury in the literature range from 2% to 10% after thoracoabdominal repair, and are stratified by aneurysm, and hence coverage, extent.^{22,23} The spinal cord event rates in our series concur with those data; they are also reassuring given the extensive nature of aneurysm disease presented here.

The extensiveness of aortic coverage in our patients compared with all patients with thoracoabdominal aneurysm disease is likely a contributor to their increased

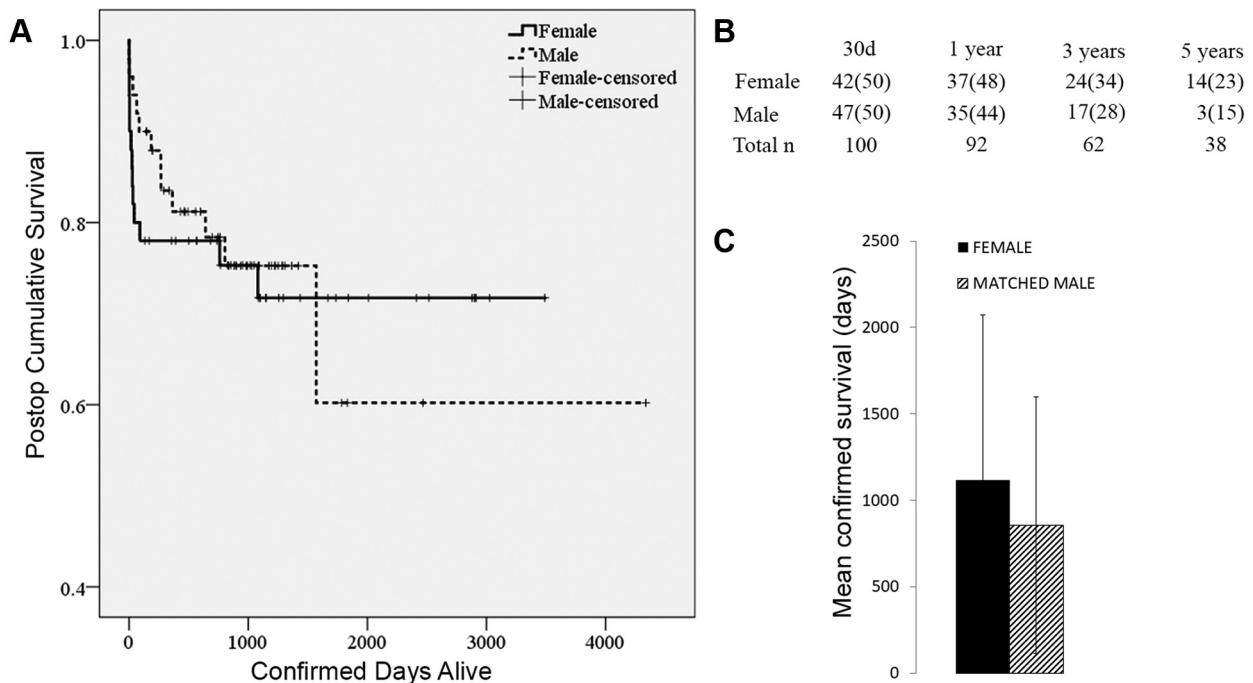


Fig 3. Survival after fenestrated endovascular thoracoabdominal aneurysm repair (FEVAR)/branched endovascular thoracoabdominal aneurysm repair (BEVAR) in men and women is similar. Early (**A**) Kaplan-Meier assessment of postoperative cumulative survival demonstrates a decreased early survival in women post FEVAR/BEVAR versus men; however, thereafter, survival is not significantly different between groups. **B**, Raw survival data for female and matched male patients post FEVAR/BEVAR demonstrates low patient follow-up at 5 years; however, **(C)** mean confirmed days alive in patients who undergo follow-up is the same in both groups at 1114 days (3.05 years) for women, and 855 days (2.3 years) for men.

perioperative mortality, with disproportionate impact on the basis of sex. Women suffering death within 30 days of FEVAR/BEVAR in the majority represented individuals with proximal/extensive aneurysm disease of Crawford extents 1 to 3, requiring branched endovascular devices. The small numbers of female patients undergoing FEVAR/BEVAR in this cohort does not allow for a subgroup analysis of mortality on the basis of sex and aneurysm extent, or an assessment of operative complexity. The literature regarding open repair of thoracoabdominal aneurysms would support elevated perioperative mortality in extent 2 aneurysms, with predictors including age, renal insufficiency, and transfusion requirement.^{24,25} The explanation for an increased perioperative mortality in women undergoing FEVAR/BEVAR, placed in the context of extensive aneurysm disease, may suggest that the assessment of interventional complexity, including factors assessing operative time, access site use, and difficulty of target vessel interventions, may be required to risk stratify women undergoing these procedures. These observations suggest that women with complex proximal aortopathy and multiple comorbidities require in-depth discussions of risk.

Although the mean preoperative aneurysm diameter was the same in matched men and women in our study,

significant sex-based differences were observed after repair. Women were more likely to suffer from any endoleak, although the majority of these were type II, whereas matched male patients with endoleaks were of types Ib or Ic. This finding is likely also related to our observation that the female cohort had a significant decrease in mean aneurysm diameter postoperatively, and the more distal phenotype of anatomic extent observed in men. There continues to be some debate regarding the significance of type II endoleak; however, without aneurysm sac enlargement, these are generally regarded as benign.²⁶ In contrast, the presence of type Ib, and Ic endoleaks, which results in repressurization of the aneurysm sac, should intuitively be associated with continued aneurysm expansion, or at least stabilization of aneurysm diameter. Indeed, this is borne out in our results, because matched male patients, on average, had a decrease in aneurysm diameter after the intervention of only 2.9 mm, in contrast with female patients, with a decrease of 9.3 mm. Perhaps this finding suggests that we should more aggressively treat ectatic iliac anatomy in men, because it is a likely source of diminished durability. However, the clinical sequela of this observation remains undetermined, because we measured only overall survival, as opposed to aneurysm-related mortality. With

increasing patient numbers and longer follow-up durations, one might expect divergence in these measures; however, this unfortunately remains a limitation of this study. At least at follow-up to 5 years, there is no significant difference in overall survival between matched male and female patients.

CONCLUSIONS

We have demonstrated that TAAA disease differs significantly in women and all men fit for complex endovascular repair at two large centers; women have more extensive proximal aortopathy and a different complement of comorbidities. Our current understanding of aneurysm pathophysiology, including development, expansion, and rupture risk, acknowledges the influence of medical comorbidities and their treatment. This finding implies that a comparison of unmatched women and men may attribute intraoperative and perioperative outcomes to differences in sex-based aortic physiology rather than the protective and disrupting influences of medical comorbidities on aneurysm pathophysiology and response to endovascular therapy. Controlling for anatomic and physiologic variables, both women and matched men undergoing complex aortic reconstruction have low perioperative complication rates. There is, nevertheless, a higher 30-day mortality in women associated with extensive aortic endovascular intervention. Fortunately, survival up to 3 years is not different between the groups, and women have low reintervention rates and favorable reductions in aneurysm size over time. Delineating the preoperative phenotypic components, sex and non-sex based, in patients that lead to poor perioperative and long-term outcome after endovascular thoracoabdominal repair, is fundamental to reasoned risk stratification and rational decision making.

AUTHOR CONTRIBUTIONS

Conception and design: MW, DC, TMG, SH, TM
Analysis and interpretation: MW, DC, TM
Data collection: MW, DC, TMG, KC, MD, AP, SH, TM
Writing the article: MW, DC, TM
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