








ORIGINAL RESEARCH

Male–Female Differences in Acute Type B Aortic Dissection

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BACKGROUND: Acute type B aortic dissection is a cardiovascular emergency with considerable mortality and morbidity risk. Male–female differences have been observed in cardiovascular disease; however, literature on type B aortic dissection is scarce.

METHODS AND RESULTS: A retrospective cohort study was conducted including all consecutive patients with acute type B aortic dissection between 2007 and 2017 in 4 tertiary hospitals using patient files and questionnaires for late morbidity. In total, 384 patients were included with a follow-up of 6.1 (range, 0.02–14.8) years, of which 41% (n=156) were female. Women presented at an older age than men (67 [interquartile range (IQR), 57–73] versus 62 [IQR, 52–71]; $P=0.015$). Prior abdominal aortic aneurysm (6% versus 15%; $P=0.009$), distally extending dissections (71 versus 85%; $P=0.001$), and clinical malperfusion (18% versus 32%; $P=0.002$) were less frequently observed in women. Absolute maximal descending aortic diameters were smaller in women (36 [IQR: 33–40] mm versus 39 [IQR, 36–43] mm; $P<0.001$), while indexed for body surface area diameters were larger in women (20 [IQR, 18–23] mm/m² versus 19 [IQR, 17–21] mm/m²). No male–female differences were found in treatment choice; however, indications for invasive treatment were different ($P<0.001$). Early mortality rate was 9.6% in women and 11.8% in men ($P=0.60$). The 5-year survival was 83% (95% CI, 77–89) for women and 84% (95% CI, 79–89) for men ($P=0.90$). No male–female differences were observed in late (re)interventions.

CONCLUSIONS: No male–female differences were found in management, early or late death, and morbidity in patients presenting with acute type B aortic dissection, despite distinct clinical profiles at presentation. More details on the impact of age and type of intervention are warranted in future studies.

Key Words: gender ■ sex ■ Stanford type B dissection ■ thoracic aortic dissection

Acute thoracic aortic dissection (TAD) is a clinical emergency¹ with an annual estimated incidence of 4.6 to 6.0 cases per 100,000 citizens.^{2,3} Acute Stanford type B aortic dissection (TBAD) is defined as a TAD that does not involve the ascending aorta^{4,5} and accounts for ≈33% of TAD cases.⁶ The in-hospital

mortality rate of acute TBAD ranges from 10% to 30%,^{6,7} and it is associated with a poor long-term prognosis; the reported long-term survival is around 80%.^{8,9} Current guidelines recommend conservative treatment with anti-impulse therapy for acute TBAD, unless the dissection is complicated.^{5,10}

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CLINICAL PERSPECTIVE

What Is New?

- In this multicenter retrospective cohort study on male–female differences in acute type B aortic dissection, no significant differences in early and late death and morbidity between men and women were observed and in the endovascular treatment group specifically.
- Female patients presented at an older age with smaller absolute descending aortic diameters, while male patients more often had a history of abdominal aortic aneurysm, DeBakey IIIb (distal extension below zone 5), and clinical malperfusion.
- In treatment strategy, no significant differences were observed, yet the indication for invasive treatment was different: occlusion of a major aortic branch was a more common indication for men.

What Are the Clinical Implications?

- Important male–female differences in clinical profile at presentation and comorbidities should be acknowledged; however, these results do not support a need for male–female-specific care of acute type B aortic dissection patients, because the reported clinical outcomes were comparable.
- No male–female differences were observed in safety profile for thoracic endovascular repair for acute type B aortic dissection.
- Investigation of male–female-specific imaging or blood biomarkers might provide more insight into the pathophysiological processes and distinct clinical profile in type B aortic dissection.

Nonstandard Abbreviations and Acronyms

TAD	thoracic aortic dissection
TBAD	type B aortic dissection

To increase our understanding of this complex clinical entity, as well as to improve treatment results through offering a more patient-specific management, detailed insights are needed concerning male–female differences, not only in presentation but also in treatment and outcomes. Unfortunately, no specific data are available concerning male–female differences in acute TBAD. In acute coronary syndromes, women are known to have less favorable outcomes^{11,12} and a distinct symptom presentation compared with men.¹³ Furthermore, worse outcomes are described for female patients undergoing endovascular repair for abdominal aortic aneurysms.^{14,15} Research on

male–female differences in aortic dissection has been focusing on TAD in general or on type A aortic dissections specifically.¹⁶

The aim of this study was to identify differences between male and female patients with acute TBAD in presentation, management, morbidity, and early and late death to identify the need for patient-specific care.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Study Population

In this retrospective multicenter cohort study, patients were included from 4 cardiothoracic centers in the Netherlands: the Erasmus University Medical Center Rotterdam, the Radboud University Medical Center in Nijmegen, the Catharina Hospital in Eindhoven, and the St. Antonius Hospital in Nieuwegein.

Adult patients (≥ 18 years old) who presented with acute TBAD and were treated at one of the participating centers between January 1, 2007, and December 31, 2017, were included. This time cohort was chosen to provide for a recent cohort with sufficient follow-up time. Traumatic, iatrogenic, and nonacute dissections were excluded.

The study was approved by the ethics committee (MEC-2018-1535) of the Erasmus University Medical Center Rotterdam and the other participating centers with a waiver for informed consent for the retrospective data collection and constructed, performed, and supervised following current local and international good clinical practice guidelines. Written informed consent was obtained from patients to request follow-up data from their treating physician.

Definitions

All included variables are defined in Data S1. Sex was defined as biological, that is, the sex at birth. Acute was defined as diagnosed within 14 days after symptom onset.¹⁷ Stanford type B dissection is defined as a dissection that does not involve the ascending aorta, including dissections that involve the aortic arch without involvement of the ascending aorta. DeBakey classification IIIa or IIIb was defined as extension of the dissection below the diaphragm (IIIb), that is, distally extending to zone 6 and beyond.^{4,5} Aortic side branches were considered involved when originating from the false lumen or when the dissection extends in the side branch. Clinical malperfusion was defined as an occlusion or dysfunction of any peripheral/visceral artery as observed on imaging and leading to symptoms. In case of presence of an intramural hematoma or penetrating aortic ulcer, TBAD was considered nonclassical. The Dubois–Dubois formula was used

to calculate body surface area (BSA).¹⁸ Aortic diameters were indexed for BSA: aortic size index=aortic diameter (mm)/body surface area (m²). Patients who received a hybrid procedure including open thoracotomy were assigned to the surgical treatment group. When patients received an endovascular procedure due to visceral or peripheral ischemia, yet no thoracic endovascular aortic repair, they were included in the surgical treatment group. Early death and morbidity was defined as during admission or within 30 days after the day of admission.

Data Collection

Eligible acute patients with TBAD were identified through searches with national diagnostic codes for thoracic aortic disease used by the cardiology, cardiothoracic surgery, and vascular surgery departments and verified with existing local research databases in each center. In Data S1, the diagnostic codes and search strategy are explained. The mortality status was checked in the municipal personal records database on November 18, 2021. Data were collected from the hospitals' digital patient files using an anonymized standardized case report form in OpenClinica (OpenClinica, LLC, version 3.6).

The maximal diameter of the descending aorta was measured in the axial plane on the first available scan after symptom onset (cardiac tomography angiography or magnetic resonance imaging when cardiac tomography angiography not available), during hospital stay and before any intervention. To ensure measurement of the true orthogonal diameter, the widest part of the descending aorta was identified, and subsequently the smallest diameter at that level was measured. Additionally, DeBakey class IIIa/IIIb was checked by examination of the imaging scans. The presence of intramural hematoma or penetrating atherosclerotic ulcer was determined using the medical and radiological records.

Late morbidity was collected from the hospital digital patient files of the participating hospitals. All patients who were alive were sent questionnaires regarding their cardiovascular status. In case of self-report of an event, the events were verified with information of the treating physician.

Treatment Strategies

In the Netherlands, patients with acute TBAD are treated according to the European guidelines for aortic disease.^{5,10} In case thoracic endovascular aortic repair was performed in the context of a clinical trial, this was reported.

Statistical Analysis

The data analysis was performed with statistical and computing program R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive analyses were used for the patient and procedural

characteristics. For continuous variables, normality was checked visually with the use of density plots and tested with the Shapiro–Wilk test. Normally distributed continuous data were presented as the mean and SD and compared using Student's *t* test. Skewed continuous data were presented as median and 25th to 75th percentile and were compared using the Mann–Whitney *U* test. For categorical data, the variables were presented as percentages or frequencies, and the chi-square test or Fisher exact test were used as appropriate.

A multivariable logistic regression model for early mortality was constructed with sex and age as independent risk factors. Odds ratios with their corresponding 95% CIs were presented. For death and morbidity during follow-up, Kaplan–Meier estimates with the time from admission to the time of death, (re) intervention or follow-up with the *survival* package were calculated excluding early events. The survival curves were compared with the log-rank test or the Peto and Peto Gehan Wilcoxon test, when appropriate. Overall and late death (excluding early death) were depicted separately, and stratification for endovascular and medical treatment was performed.

A risk factor analysis for late mortality was performed with Cox proportional hazards analysis in which the baseline hazard was stratified by study center. Baseline variables and variables at presentation were first tested in a univariable analysis for the whole cohort and men and women separately. The variables with a *P* value <0.20 on univariable analysis that were considered clinically relevant were examined for the multivariable model. Multicollinearity of predictor variables was assessed with correlation plots. The multivariable models were constructed with backward selection, in which sex and age were forced and variables with *P*<0.20 were kept in the final model. Complete case analysis was performed as the missing data pattern was assumed to be completely at random. For late mortality, hazard ratios with their corresponding 95% CIs were presented. For the final models, the Cox proportional hazards assumption and possible nonlinearity of age were checked.

In both the logistic regression analysis and the Cox regression analysis for early and late death, the interaction between sex and age was checked comparing the models with and without interaction.

A 2-sided *P* value of <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The study population consisted of 384 patients, of which 40.6% (n=156) were women. Patient characteristics at

presentation are shown in [Table 1](#). No significant male–female differences were observed in symptoms as depicted in [Figure 1](#). The imaging characteristics and laboratory values at presentation are shown in [Table 2](#). Other laboratory values are depicted in [Table S1](#).

Management

In [Table 3](#), the management for female and male patients is shown. Indications for endovascular or surgical treatment for female and male patients are depicted in [Figure 2](#) and were significantly different ($P=0.001$).

Early and Late Mortality

The early death and morbidity for the whole cohort are shown in [Figure 3](#). Early death was 9.6% ($n=15$) in female patients and 11.8% ($n=27$) in male patients ($P=0.603$). Also after adjustment for age (odds ratio, 1.03 [95% CI, 1.00–1.06], $P=0.068$), sex was not a risk factor for early death (odds ratio, 0.74 [95% CI, 0.37–1.43]; $P=0.372$). No significant interaction between age and sex was observed in the logistic regression analysis for early mortality ($P=0.365$). Early mortality stratified per treatment group and the causes of death are presented in [Table S2](#).

When considering late death, the median follow-up time was 6.1 (range, 0.02–14.8) years for the whole cohort; 6.2 (range, 0.15–14.7) years for women and 6.9 (0.02–14.8) years for men. The Kaplan–Meier estimates stratified by sex are shown in [Figure 4](#). During follow-up excluding early death, 43 female patients and 65 male patients died, resulting in a late 5-year survival of 0.83 (95% CI, 0.77–0.89) for women and 0.84 (95% CI, 0.79–0.89) for men ($P=0.90$). For 1 male patient, the mortality status could not be obtained. Excluding early mortality, also no male–female differences in late mortality were observed in the endovascular and medical treatment group separately ([Figure S1](#)).

The results of the multivariable Cox proportional hazards analyses for late death in the whole study population and the subgroup of female and male patients are presented in [Table 4](#). All the tested variables are shown in [Table S3](#). No significant interaction between age and sex was observed in the Cox regression analysis for late mortality ($P=0.149$).

Early and Late Morbidity

The median admission time was 14.0 days (interquartile range [IQR], 9.0–20.0) for women and 14.0 (IQR, 9.0–20.8) for men ($P=0.976$). Additionally, the early reoperations are described in [Table S4](#) and were not significantly different for women and men: 8.6% for women versus 15.6% in men ($P=0.353$).

In [Figure S2](#), Kaplan–Meier estimates for late reintervention and late intervention are depicted, and in

[Table S5](#), the indications for intervention are shown. Of the patients who received endovascular or surgical treatment in the early phase excluding early death ($n=162$), data on reintervention were available for 142 of 160 patients during a median follow-up time of 4.1 (range, 0.06–13.2) years. In the endovascular or surgically treated group, 32 of 142 patients (22.5%; 13 women, 19 men) had a reintervention during follow-up, resulting in a 5-year freedom from reintervention of 78% (95% CI, 67–90) for women and 77% (95% CI, 68–88) for men (log-rank $P=0.61$).

For patients who received medical treatment and survived in the early phase ($n=180$), data on late intervention were available for 162 of 182 patients during a median follow-up time of 3.5 (range, 0.09–13.9) years. During follow-up, 37 of 162 patients (22.8%; 14 women, 23 men) had a late intervention, resulting in a 5-year freedom from intervention of 80% (95% CI, 69–92) for women versus 76% for males (95% CI, 68–86) (log-rank $P=0.85$).

Imaging characteristics during follow-up are shown in [Table S6](#) and clinical events in [Table S7](#). The median follow-up time until the last imaging scan was 3.5 (range, 0.03–12.7) years for women and 4.1 (range, 0.11–13.2) years for men ($P=0.104$). The maximal thoracic aortic diameter during follow-up ($n=266$) was 42 mm (IQR, 38–49) for women and 44 mm (IQR, 38–49) for men ($P=0.119$). For the abdominal aorta ($n=189$), a maximal diameter of 31 mm (IQR, 24–38) and 37 mm (IQR, 31–47) was observed for women and men ($P<0.001$).

DISCUSSION

In this multicenter retrospective cohort study, an extensive overview of male–female differences for patients with an acute TBAD was provided. Female patients presented at an older age, while male patients more often had a history of abdominal aortic aneurysm and clinical malperfusion. Furthermore, female patients had distally extended acute TBAD less often, while they presented with smaller absolute descending aortic diameters and intramural hematoma more often. Indexed for BSA, aortic dimensions were larger in women. Although no significant male–female difference in treatment strategy was detected, significant differences in the indication of invasive treatment were found: occlusion of a major aortic branch was more common among men. In early and late death and morbidity, no significant male–female differences were found and also after adjustment for important parameters.

Comorbidities and Clinical Presentation

In our study, the male–female ratio was 1.5:1, corresponding with other studies on male–female differences in acute TBAD.^{19–22} In population-based studies

Table 1. Patient Characteristics at Presentation

	All patients (n=384)	Women (n=156)	Men (n=228)	P value	Missing %
Patient demographics					
Age, y	65.0 (54.0–72.0)	67.0 (57.0–73.0)	62.0 (52.0–71.0)	0.015*	0.0
BMI	26.4±4.6	25.7±5.0	27.0±4.2	0.015*	23.2
BSA	1.95±0.2	1.80±0.17	2.07±0.18	<0.001*	23.2
History of hypertension	203 (53.1)	82 (53.2)	121 (53.1)	1.000	0.5
Hyperlipidemia	85 (22.4)	52 (22.9)	33 (21.6)	0.856	1.0
Diabetes	16 (4.2)	8 (5.2)	8 (3.5)	0.585	0.5
COPD	35 (9.2)	14 (9.1)	21 (9.2)	1.000	0.5
History of CVA	35 (9.2)	17 (11.0)	18 (7.9)	0.388	0.5
History of MI	19 (5.0)	4 (2.6)	15 (6.6)	0.094†	0.8
Chronic kidney disease	19 (5.0)	8 (5.2)	11 (4.8)	1.000	0.5
Smoking				0.355	41.4
Never	66 (29.3)	31 (34.4)	35 (25.9)		
Currently	99 (44.0)	38 (42.2)	61 (45.2)		
In past	60 (26.7)	21 (23.3)	39 (28.9)		
Prior thoracic aortic aneurysm	37 (9.7)	19 (12.3)	18 (7.9)	0.211	0.8
Prior aortic dissection‡	8 (2.1)	4 (2.6)	4 (1.8)	0.719†	0.5
Prior cardiac surgery	35 (9.2)	12 (7.7)	23 (10.1)	0.539	0.5
Prior aortic surgery				0.107†	0.3
Other than descending thoracic aorta§	49 (12.8)	13 (8.4)	36 (15.8)		
Descending thoracic aorta	3 (0.8)	2 (1.3)	1 (0.4)		
Descending thoracic aorta+other§	6 (1.6)	3 (1.9)	3 (1.3)		
Prior AAA	43 (11.2)	9 (5.8)	34 (14.9)	0.009*	0.3
Operated AAA	25 (6.8)	5 (3.3)	20 (9.3)	0.034*	4.9
Connective tissue disease	22 (6.7)	12 (9.0)	10 (5.2)	0.257	15.1
Clinical presentation					
Abrupt onset of symptoms	299 (89.3)	123 (86.6)	176 (91.2)	0.247	12.8
Onset during exercise	40 (30.1)	15 (28.3)	25 (31.2)	0.865	65.4
Clinical malperfusion	96 (26.1)	26 (17.6)	70 (31.8)	0.002*	4.2
Shock	18 (5.0)	8 (5.4)	10 (4.7)	0.972	6.0
CVA/TIA	3 (0.8)	2 (1.3)	1 (0.5)	0.569†	4.7
Renal failure	22 (6.3)	9 (6.2)	13 (6.3)	1.000	8.9
Collapse	21 (6.0)	7 (4.8)	14 (6.9)	0.555	8.6
Resuscitation	6 (1.6)	4 (2.6)	2 (0.9)	0.231†	3.6
Ventilation support	7 (1.9)	2 (1.3)	5 (2.3)	0.705†	4.4
Antihypertensive medication	317 (94.6)	124 (91.2)	193 (97.0)	0.039*	12.8
Diuretics	85 (25.8)	31 (22.8)	54 (28.0)	0.352	14.3
Vasodilator	151 (45.2)	58 (42.3)	93 (47.2)	0.442	13.0
Blood pressure				0.685	10.2
Normotensive	61 (17.7)	28 (19.7)	33 (16.3)		
Hypotensive	21 (6.1)	9 (6.3)	12 (5.9)		
Hypertensive	263 (76.2)	105 (73.9)	158 (77.8)		
BP difference L-R	36 (22.9)	15 (24.2)	21 (22.1)	0.912	59.1
Time from onset to diagnosis, h				0.415	46.6
<6	113 (55.1)	46 (53.5)	67 (56.3)		
6–12	35 (17.1)	11 (12.8)	24 (20.2)		

Continued

Table 1. Continued

	All patients (n=384)	Women (n=156)	Men (n=228)	P value	Missing %
12–24	12 (5.9)	6 (7.0)	6 (5.0)		
24–48	3 (1.5)	2 (2.3)	1 (0.8)		
>48	42 (20.5)	21 (24.4)	21 (17.6)		
Type of pain				0.061 [†]	58.1
No pain	2 (1.2)	1 (1.3)	1 (1.2)	1.000 [†]	
Tearing	29 (18.0)	19 (25.0)	10 (11.8)	0.048	
Sharp	55 (34.2)	20 (26.3)	35 (41.2)	0.069	
Oppressive	75 (46.6)	36 (47.4)	39 (45.9)	0.976	

Normally distributed continuous variables are expressed as mean±SD, skewed continuous variables are expressed as median and 25th to 75th percentile (IQR), and categorical values are expressed as percentages. AAA indicates abdominal aortic aneurysm; BMI, body mass index; BP, blood pressure; BSA, body surface area; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular disease; IQR, interquartile range; L-R, left-right; MI, myocardial infarction; and TIA, transient ischemic attack.

* P values <0.05.

[†]Fisher’s exact test.

[‡]Prior aortic dissections included type A (n=6) and type B (n=2).

[§]Other than descending aorta includes procedures on all other parts of the thoracic aorta and the abdominal aorta.

on acute TAD, hypertension and smoking were the main risk factors for incident TAD.^{2,23} Our study showed no significant male–female differences in the prevalence of comorbidities, apart from a more prevalent history of abdominal aortic aneurysms in male patients. Interestingly, female patients presented at ≈5 years older age than male patients, in line with other literature in aortic dissection.^{19,20,22} Estrogen is suggested to have a protective effect on cardiovascular disease in premenopausal women,²⁴ which probably explains the low incidence of aortic dissections in younger women.

In acute coronary syndrome, male–female differences in presenting symptoms have been identified: In women, nausea, retrosternal pain, and dyspnea seem more common.²⁵ In our cohort of patients with acute TBAD, no significant male–female differences were found in symptoms or time to diagnosis. In 2 studies encompassing both type A and type B TADs, women

more often presented with altered consciousness, and the time to diagnosis was longer.^{19,21} Another study suggested that TAD was less likely to be recognized in women by physicians.²⁶ Based on our study, there are no male- or female-specific symptoms for clinicians to take into account in the recognition and diagnosis of acute TBAD. It remains pertinent to consider the diagnosis of TBAD and perform imaging when a patient presents with acute pain and no signs of coronary ischemia.

At diagnostic imaging, female patients were diagnosed with DeBakey class IIIa (extension until zone 6) more frequently than male patients, and male patients more often had clinical malperfusion at presentation. Two other studies on acute TBAD confirm these findings: They found more renal insufficiency in men^{20,21} and paraplegia as adverse event during hospital stay.²⁰ Besides involvement of the dissection in aortic side branches, the clinical malperfusion in men might be explained by

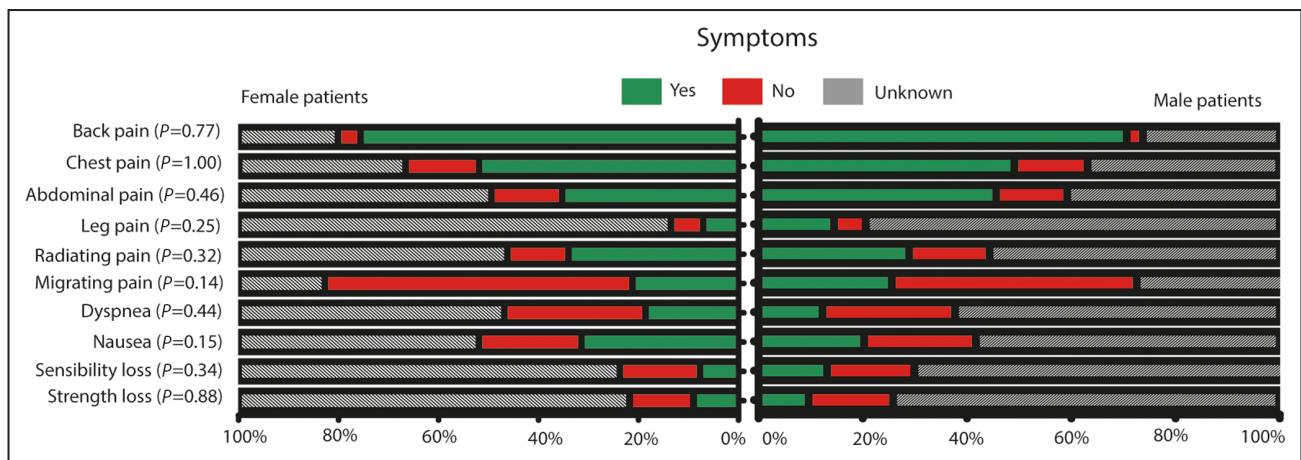


Figure 1. Symptoms in female and male patients.

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Table 2. Imaging and Laboratory Values at Presentation

	All patients (n=384)	Women (n=156)	Men (n=228)	P value	Missing %
Imaging method					
CTA	376 (99.7)	153 (100.0)	223 (99.6)		1.8
TTE	128 (34.4)	44 (28.9)	84 (38.2)		3.1
TEE	5 (1.3)	2 (1.3)	3 (1.4)	...	1.8
MRI	5 (1.3)	2 (1.3)	3 (1.4)	...	2.3
CAG	18 (4.8)	4 (2.6)	14 (6.3)	...	1.8
Signs on diagnostic imaging					
DeBakey class				0.001*	2.6
DeBakey IIIa (extension until zone 6)	77 (20.6)	44 (29.3)	32 (15.5)		
DeBakey IIIb (extension zone 6–11)	297 (79.4)	106 (70.7)	180 (84.5)		
Start of dissection				0.598	16.4
Aortic arch (zone 1–2)	30 (9.3)	14 (10.8)	16 (8.4)		
Descending thoracic aorta (zone 3–5)	291 (90.7)	116 (89.2)	175 (91.6)		
TBAD type				<0.001*†	2.1
TBAD	259 (68.9)	86 (55.8)	173 (77.9)	<0.001*	
IMH	51 (13.6)	31 (20.1)	20 (9.0)	0.003*	
TBAD+IMH	36 (9.6)	18 (11.7)	18 (8.1)	0.326	
IMH+PAU	20 (5.3)	11 (7.1)	9 (4.1)	0.281	
TBAD+IMH+PAU	6 (1.6)	5 (3.2)	1 (0.5)	0.044*†	
TBAD+PAU	2 (0.5)	1 (0.6)	1 (0.5)	1.000†	
PAU	2 (0.5)	2 (1.3)	0 (0.0)	0.167†	
Rupture	42 (11.2)	22 (14.4)	20 (9.0)	0.142	2.1
Maximum diameter descending aorta	37.6 (34.3–42.0)	36.0 (33.0–40.2)	38.9 (35.9–42.7)	<0.001*	7.6
Indexed for BSA, mm/m ²	19.7 (17.7–21.6)	20.2 (18.2–22.7)	19.2 (17.4–21.0)	0.001*	28.6
Involvement renal arteries	156 (59.8)	44 (48.4)	112 (65.9)	0.009*	32.0
Involvement celiac trunk	75 (27.9)	24 (26.1)	51 (28.8)	0.742	29.9
Involvement SMA	54 (20.1)	16 (17.4)	38 (21.5)	0.528	29.9
Involvement IMA	33 (20.0)	8 (13.3)	25 (23.8)	0.156*	57.0
Laboratory values					
CKD-EPI GFR with maximum 90, mL/min per 1.73m ²	74.2±23.8	75.3±25.3	73.4±25.3	0.457	7.6
CK, U/L	96.00 (67.50–146.50)	73.00 (54.50–108.00)	120.50 (80.00–191.00)	<0.001*	47.1
Lactate, mmol/L	1.60 (1.00–2.58)	1.40 (0.90–2.00)	1.80 (1.10–2.70)	0.006*	43.2
Leukocytes, 10 ⁹ /L	11.00 (8.72–13.80)	10.95 (8.75–13.17)	11.15 (8.78–14.12)	0.548	8.9
CRP >6.0 mg/L	236 (71.5)	106 (76.8)	130 (67.7)	0.092	14.1
D-dimer >4.0 µg/mL	40 (51.9)	14 (37.8)	26 (65.0)	0.031*	79.9

Normally distributed continuous variables are expressed as mean±SD, skewed continuous variables are expressed as median and 25th to 75th percentile (IQR), and categorical values are expressed as percentages. BSA indicates body surface area; CAG, coronary angiography; CK, creatine kinase; CKD-EPI GFR, Chronic Kidney Disease Epidemiology Collaboration glomerular filtration rate; CRP, C-reactive protein; CTA, computed tomography angiography; IMA, inferior mesenteric artery; IMH, intramural hematoma; IQR, interquartile range; MRI, magnetic resonance imaging; PAU, penetrating aortic ulcer; SMA, superior mesenteric artery; TBAD, acute type B aortic dissection; TEE, transesophageal echocardiogram; and TTE, transthoracic echocardiography.

* P values <0.05.

†Fisher’s exact test.

the higher proportion of intramural hematoma in women in our population, which seem to have a lower risk of end-organ malperfusion or lower-extremity ischemia

compared with classical TBAD.²⁷ Differences in the aortic wall or blood flow dynamics might explain the more frequently reported distal extension below zone 5 in males.

Table 3. Treatment Characteristics

	All patients (n=384)	Women (n=156)	Men (n=228)	P value	Missing, %
Treatment strategy				0.793*	0.0
No treatment	4 (1.0)	2 (1.3)	2 (0.9)		
Medical	190 (49.5)	73 (46.8)	117 (51.3)		
Endovascular	170 (44.3)	72 (46.2)	98 (43.0)		
Surgical†	20 (5.2)	9 (5.8)	11 (4.8)		
	All patients	Women	Men		
	(n=190)	(n=81)	(n=109)		
Endovascular or surgical treatment					
Urgency treatment				0.096*	0.5
Acute	94 (49.7)	35 (43.2)	59 (54.6)		
Urgent	90 (47.6)	42 (51.9)	48 (44.4)		
Elective	5 (2.6)	4 (4.9)	1 (0.9)		
Adjunctive procedure	61 (34.3)	22 (28.6)	39 (38.6)	0.215	6.3
Concomitant surgery				0.463*	6.3
None	163 (91.6)	71 (91.0)	92 (92.8)		
Gastrointestinal surgery	11 (6.2)	4 (5.1)	7 (6.2)		
Other	4 (2.2)	3 (3.8)	1 (1.0)		
	All patients	Women	Men		
	(n=171)	(n=72)	(n=99)		
TEVAR procedures					
Number of TEVAR stents				0.544	3.5
One	89 (54.3)	37 (52.1)	52 (55.9)		
Two	63 (38.4)	27 (38.0)	36 (38.7)		
Three	12 (7.3)	7 (9.9)	5 (5.4)		
Extended with open stent	28 (17.1)	14 (20.0)	14 (14.9)	0.516	3.5
Left carotid to subclavian artery bypass	20 (12.1)	6 (8.5)	14 (14.9)	0.310	2.9
LSA covered by stent	85 (55.2)	34 (51.5)	51 (58.0)	0.528	9.4
Spinal tab placed	24 (15.6)	10 (14.7)	14 (16.3)	0.965	9.4

Categorical values are expressed as percentages. Acute, within 24 h; elective, >2 weeks; and urgent, within 2 weeks or during hospital stay. LSA indicates left subclavian artery; and TEVAR, thoracic endovascular repair.

*Fisher's exact test.

†Endovascular procedure but no TEVAR (n=3); hybrid procedure (n=3).

Male sex was found to be associated with increased wall thickness of the descending thoracic aorta,²⁸ and aortic blood flow patterns in the thoracic aorta were significantly different between men and women.²⁹

Furthermore, female patients had smaller absolute descending aortic diameters at presentation, while the BSA-corrected diameters were larger. Previous literature in the general population also found smaller descending aortic diameters in women compared with men.^{30,31} In TBAD, no strong association with the aortic diameter is observed.³² A median diameter of 38 mm was found in our cohort, in line with Zafar et al,³² Who found a median size of 41 mm in TBAD, as opposed to descending thoracic aortic rupture, which occurs at dimensions above 50 mm. Therefore, current size thresholds for intervention in descending thoracic aortic

aneurysms at ≥ 55 mm cannot protect from TBAD. In descending thoracic and thoracoabdominal aneurysms, male sex was associated with slower growth,³² and in thoracic aortic aneurysm, male sex was protective for rupture or dissection.³³ Male–female-specific research into other parameters such as wall shear stress or blood biomarkers might provide more insight into risk stratification for acute TBAD than the aortic diameter.

Management

In treatment strategies, no significant differences were found for male and female patients. In previous literature, it was described that female patients more often were treated conservatively.^{19,20} In these studies, the female patients had more comorbidities, which might explain the

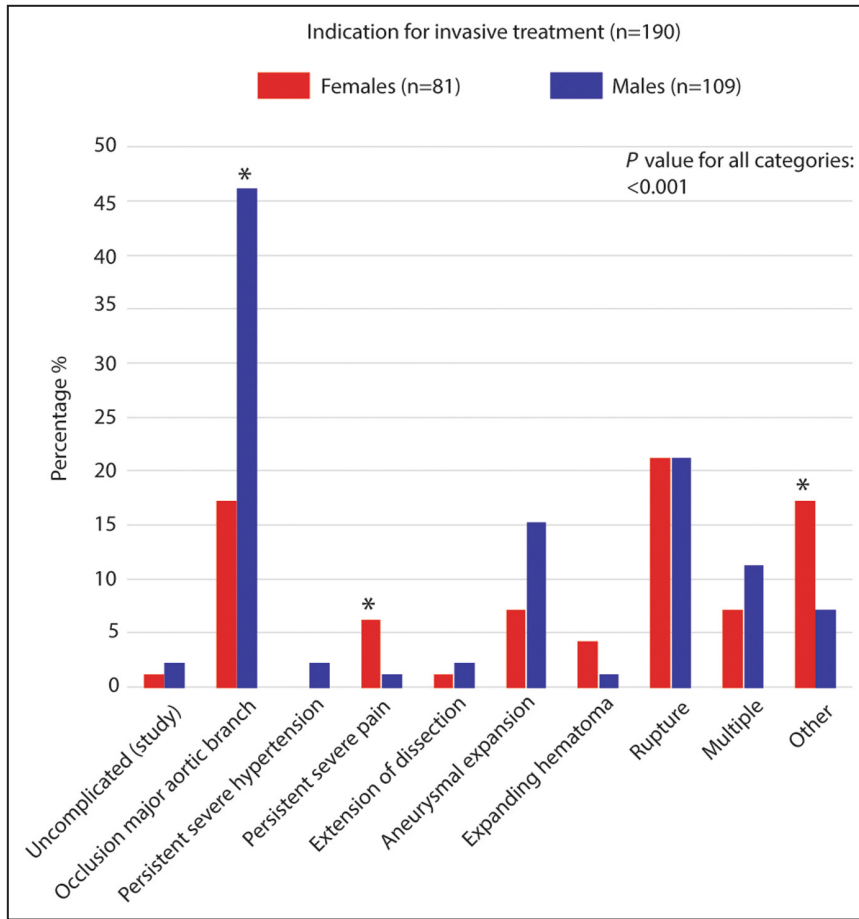


Figure 2. Indication for invasive treatment.
*P value for individual category <0.05.

more conservative approach. Interestingly, there was a significant difference in the indication for invasive treatment: Occlusion in a major aortic branch vessel was more

common in male patients compared with female patients. This corresponds with the fact that acute TBAD in male patients more frequently extended below the diaphragm and presented with clinical malperfusion more often.

The optimal timing for endovascular treatment of uncomplicated TBAD for both men and women remains to be elucidated. Unfortunately, our study design does not provide for insights on this question, as it was not possible to score the criteria for complicated/uncomplicated TBAD retrospectively. Still, after initial medical management, late intervention during follow-up was common: 37 of 162 (23%), with aneurysmal expansion as main indication. In 2 studies on male–female differences in surgically treated type A dissections, distal reinterventions seemed more common in male patients.^{34,35} Therefore, the fate of the distal aorta in both the complicated and uncomplicated TBAD group during follow-up should be closely monitored and also with regard to male–female differences.

Several studies on endovascular or open repair for abdominal aortic aneurysms show that women have worse outcomes compared to men.^{14,36} In contrast, a recent study on thoracic endovascular aortic repair for complicated acute TBAD showed no male–female differences in early or late morbidity or death.³⁷ In our

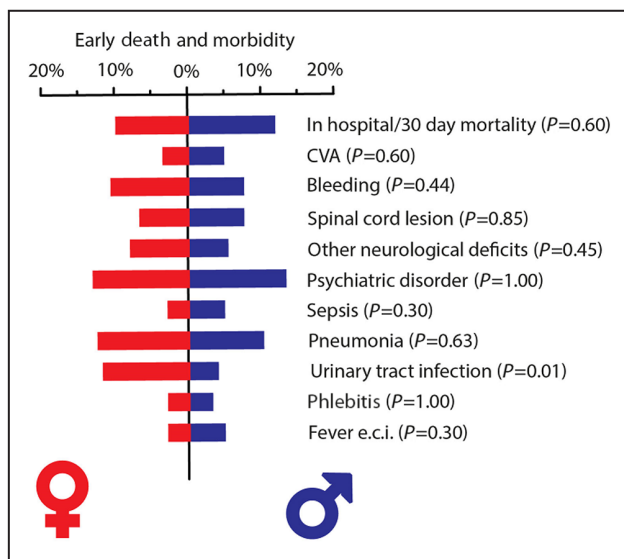


Figure 3. Early mortality and morbidity.
CVA indicates cerebrovascular accident; and e.c.i., e causa ignota (of unknown origin).

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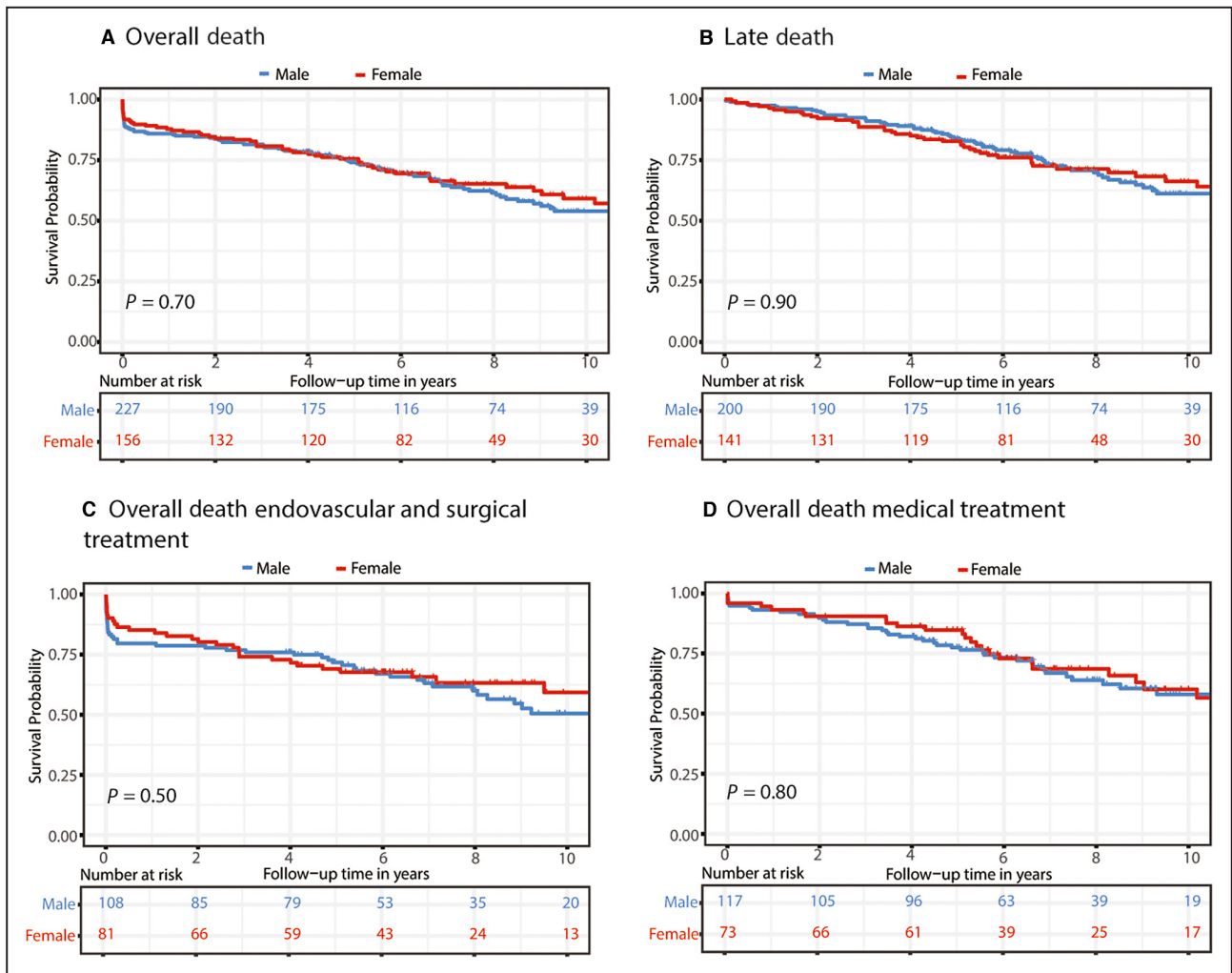


Figure 4. Kaplan–Meier estimates for death stratified by sex.

The 4 panels show: **(A)** Kaplan–Meier estimates for overall death including early death for all patients stratified by sex; **(B)** Kaplan–Meier estimates for late mortality excluding early death for all patients stratified by sex; **(C)** Kaplan–Meier estimates for overall mortality including early death for the endovascular and surgical treatment groups stratified by sex; **(D)** Kaplan–Meier estimates for overall death including early death for the medical treatment group stratified by sex. The *P* values depict the log-rank test or the Peto and Gehan Wilcoxon test, as appropriate.

study, early and late death were not found to be different for women compared with men in the endovascular and surgical treatment group. Possibly, women present with a more challenging anatomy in abdominal aortic aneurysms³⁸ associated with less favorable results, which might not be the case for endovascular treatment of TBAD and thoracic aortic aneurysm.

Late Death

No significant difference in late death between male and female patients was observed, even though male patients were younger at presentation. Compared with the sex- and age-matched general Dutch population, survival seems lower after acute TBAD for both women and men: In 2012, the 5-year survival estimates were 0.95 for women and 0.95 for men.³⁹ In multivariable analysis for

late death, age was the most important risk factor, in line with other TBAD literature.^{8,40,41} In our cohort, chronic obstructive pulmonary disease and a history of thoracic aortic aneurysm seemed strong prognostic factors for women, whereas hypertension and a history of abdominal aortic aneurysms had a strong effect in men. Distinct pathophysiologic processes might contribute to the progression of TBAD in male and female patients.

Limitations

Limitations of our study were mainly caused by its retrospective nature. Data available from the patient files were used, and missing data were unavoidable. As the participating centers were tertiary referral centers, the generalizability of our findings might be limited. The medically managed patients with TBAD treated

Table 4. Cox Proportional Hazards Analysis for Late Death

Variable	All patients (n=341)				Women (n=141)				Men (n=200)			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Demographics												
Female sex	0.97 (0.66–1.42)	0.868†	0.76 (0.50–1.17)	0.215
Male sex (reference)												
Age, y (per 1 y increase)	1.09 (1.07–1.11)	<0.001*†	1.10 (1.07–1.13)	<0.001*	1.12 (1.08–1.16)	<0.001*†	1.14 (1.08–1.20)	<0.001*	1.08 (1.05–1.11)	<0.001*†	1.09 (1.06–1.12)	<0.001*
History of hypertension	2.46 (1.62–3.74)	<0.001*†	2.10 (1.05–4.19)	0.035*†	2.63 (1.54–4.51)	<0.001*†	1.78 (0.97–3.29)	0.065
History of hyperlipidemia	2.26 (1.48–3.46)	<0.001*†	1.82 (0.90–3.68)	0.094†	2.59 (1.50–4.45)	<0.001*†
COPD	2.22 (1.20–4.09)	0.011*†	2.99 (1.26–7.11)	0.013*†	1.62 (0.64–4.10)	0.309
Prior CVA	1.73 (0.93–3.20)	0.082†	1.12 (0.39–3.20)	0.835	2.58 (1.20–5.57)	0.016*†
Prior MI	2.38 (1.23–3.37)	0.010*†	1.74 (0.85–3.57)	0.127	4.93 (1.65–14.8)	0.004*†	3.53 (1.05–11.9)	0.042*	1.59 (0.67–3.75)	0.289
Chronic kidney disease	2.47 (1.27–4.79)	0.007*†	1.98 (0.99–3.95)	0.053	2.33 (0.71–7.67)	0.165†	2.73 (0.69–10.8)	0.153	2.26 (0.99–5.14)	0.052†
History of thoracic aortic aneurysm	2.04 (1.19–3.50)	0.009*†	2.30 (1.28–4.11)	0.005*	3.28 (1.59–6.76)	0.001*†	4.01 (1.60–10.1)	0.003*	1.05 (0.95–2.65)	0.910
History of abdominal aortic aneurysm	3.09 (1.89–5.06)	<0.001*†	2.66 (0.90–7.84)	0.076*†	3.33 (1.86–5.97)	<0.001*†
DeBakey IIIb	0.45 (0.28–0.72)	<0.001*†	0.61 (0.32–1.17)	0.138†	2.46 (1.06–5.72)	0.037*	0.30 (0.17–0.54)	<0.001*†
DeBakey IIIa (reference)												
Maximum diameter descending aorta (per 1 unit)	1.07 (1.04–1.10)	<0.001*†	1.07 (1.03–1.12)	<0.001*†	1.05 (1.01–1.10)	0.011*†

Univariable and multivariable Cox regression analysis for all patients and females and males separately are shown. HRs and corresponding 95% CIs are presented. COPD indicates chronic obstructive pulmonary disease; CVA, cerebrovascular disease; HR, hazard ratio; and MI, myocardial infarction.

*P values <0.05.

†Variables entered in the full model for backward selection of final multivariable model.

at smaller centers might especially be underrepresented.⁴² Finally, due to the limited number of events at follow-up, an extensive multivariable analysis for late death could not be constructed.

CONCLUSIONS

Although some differences were found in clinical profiles at presentation and comorbidities, no male-female differences were found in treatment choice, early or late death, and morbidity in patients presenting with acute TBAD. The proportion of male patients presenting with distally extending acute TBAD was significantly higher as well as the clinical manifestation of malperfusion compared with female patients. Also, women presented with smaller absolute aortic dimensions, while BSA-indexed dimensions were larger.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1
Tables S1–S7
Figures S1–S2

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