

## The influence of gender on mortality in patients after thoracic endovascular aortic repair

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### Abstract

**Objectives:** The aim of this study was to determine if gender affects mortality in patients after thoracic endovascular aortic repair (TEVAR). **Methods:** We retrospectively analyzed 286 consecutive patients undergoing TEVAR at our institution during a 12-year period (female 29%, median age 69 years). Chronic health conditions, risk factors, as well as early and long-term outcome were assessed. Follow-up data were available in all patients. **Results:** For female gender, 1-year survival and 5-year survival was 84% and 56% versus 83% and 60% for male gender. No significant gender influence was observed (odds ratio (OR) 0.96, 95% confidence interval (CI) 0.59–1.56). Furthermore, no significant gender influence could be observed according to the individual indication – atherosclerotic aneurysms (OR 0.78 95%CI 0.41–1.47), acute type B dissections (OR 0.78 95%CI 0.21–2.83), penetrating atherosclerotic ulcers/intramural hematoma (OR 1.48 95%CI 0.53–4.19), and traumatic aortic lesions (OR 1.48 95%CI 0.53–4.19). Age (OR 3.6 95%CI 1.24–10.45) and chronic obstructive pulmonary disease (COPD; OR 3.09 95%CI 0.98–9.73) were independent predictors of mortality in females. **Conclusions:** Gender does not affect mortality in patients after TEVAR irrespective of the underlying indication, atherosclerotic aneurysms, acute type B dissections, penetrating ulcers/intramural hematoma, and traumatic aortic lesions. Classical risk factors such as age and the presence of COPD at the time of TEVAR remain the most important risk factors in females.

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**Keywords:** TEVAR; Gender; Outcome

### 1. Introduction

Thoracic endovascular aortic repair (TEVAR) is gaining increased popularity for the repair of various acute and chronic thoracic aortic pathologies [1–6]. Mid-term results have been encouraging and several analyses have shown risk factors for durability and survival such as arch involvement, length of landing zones, and number of prostheses [3,7,8]. Interestingly, no report to date has focused on the influence of gender on outcome.

The aim of this study was to determine if gender affects mortality in patients after TEVAR.

### 2. Methods

#### 2.1. Design

We retrospectively analyzed 286 consecutive patients undergoing TEVAR at our institution during a 12-year period (female 29%, median age 69 years). Indications for TEVAR were atherosclerotic aneurysms in 115 patients (41%), type B dissections in 75 patients (26%), penetrating atherosclerotic ulcers (PAUs)/intramural hematoma (IMH) in 73 patients (25%), and traumatic aortic lesions in 23 patients (8%).

#### 2.2. Patient data

Clinical risk factors according to EuroSCORE stratification were recorded (European System for Cardiac Operative Risk Evaluation, EuroSCORE) [9]. Logistic EuroSCORE levels were applied to estimate individual risk. Descriptive

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Table 1. Descriptive characteristics of the cohort.

	N overall = 286	
<b>Demographics</b>		
Age, median (IQR)	67	(58–74)
Female, <i>n</i> (%)	83	(29%)
<b>Chronic health conditions and risk factors</b>		
Chronic obstructive pulmonary disease, <i>n</i> (%)	89	(32%)
Diabetes, <i>n</i> (%)	23	(8%)
Coronary artery disease, <i>n</i> (%)	68	(24%)
Extracardiac arteriopathy, <i>n</i> (%)	147	(51%)
Previous aortic surgery, <i>n</i> (%)	42	(15%)
<b>In-hospital clinical assessment</b>		
Emergency, <i>n</i> (%)	136	(48%)
Suitable for open surgery, <i>n</i> (%)	59	(21%)
LV dysfunction (LVEF < 50%), <i>n</i> (%)	10	(3%)
<b>Classification</b>		
Aneurysm, <i>n</i> (%)	115	(41%)
Dissection, <i>n</i> (%)	75	(26%)
PAU/IMH, <i>n</i> (%)	73	(25%)
Traumatic, <i>n</i> (%)	23	(8%)
<b>EuroSCORE risk score</b>		
Additional, median (IQR)	9	(7–11)
Logistic, median (IQR)	17	(11–29)
<b>Outcome</b>		
Follow-up in months, median (IQR)	13	(3–41)
In-hospital, <i>n</i> (%)	18	(6%)
Overall mortality, <i>n</i> (%)	79	(28%)

Unless otherwise indicated, data are number (percentage). IQR, interquartile range; classification of chronic health conditions and risk factors according to EuroSCORE criteria.

characteristics of the patient cohort are shown in Table 1. Patient characteristics according to gender are shown in Table 2. Follow-up data were available in all patients. Ninety percent of patients were followed up by our own outpatient clinic. The remaining 10% were followed up by well-known referring physicians, who apply the exact follow-up algorithm as we do and who send us a detailed work-up of the clinical course as well as the completion computed tomography (CT) scans for our records.

### 2.3. Definitions

Chronic obstructive pulmonary disease (COPD) was defined as long-term use of bronchodilators or steroids for lung disease. Previous myocardial infarction was defined as enzyme infarction with morphological or functional correlate in coronary angiography or echocardiography. Peripheral arterial occlusive disease was defined as one or more of claudication, carotid occlusion or >50% stenosis, planned intervention on the abdominal aorta, limb arteries, or carotids. Renal insufficiency was defined as serum creatinine  $\geq 2$  mg dl<sup>-1</sup> in repeated measurements. Diabetes mellitus was defined as serum hyperglycemia requiring sulfonyleurea intake or insulin substitution. Previous cerebrovascular events were defined as previous minor or major neurologic adverse events, irrespective of origin with and without remaining morphological or functional correlate. Previous

Table 2. Distribution of patients by different chronic health conditions and hospital risk assessment stratified to gender.

	Female (N = 83) versus male (N = 203)		<i>p</i>
<b>Demographics</b>			
Age, median (IQR)	69 (61–75)	66 (57–74)	0.11
<b>Chronic health conditions and risk factors</b>			
Chronic obstructive pulmonary disease, <i>n</i> (%)	25 (30%)	64 (32%)	0.72
Diabetes, <i>n</i> (%)	6 (7%)	17 (8%)	0.71
Coronary artery disease, <i>n</i> (%)	16 (19%)	52 (26%)	0.25
Extracardiac arteriopathy, <i>n</i> (%)	49 (59%)	98 (48%)	0.14
Previous aortic surgery, <i>n</i> (%)	20 (24%)	22 (11%)	0.004
<b>In-hospital assessment</b>			
Emergency, <i>n</i> (%)	33 (40%)	103 (51%)	0.12
Unsuitable for open surgery, <i>n</i> (%)	49 (59%)	143 (70%)	0.03
Logistic EuroScore, median (IQR)	18 (12–28)	17 (10–29)	0.31
Stentgraft, median (Range)	2 (1–5)	2 (1–6)	0.54
Femoral access, <i>n</i> (%)	60 (72%)	158 (78%)	0.09
Periprocedural complications, <i>n</i> (%)	3 (4%)	4 (2%)	0.42
<b>Outcome</b>			
Endoleak, <i>n</i> (%)	15 (18%)	28 (14%)	0.36
In-hospital, <i>n</i> (%)	7 (8%)	11 (5%)	0.34
Aortic-related death, <i>n</i> (%)	4 (5%)	11 (5%)	0.84
Overall mortality, <i>n</i> (%)	24 (29%)	55 (27%)	0.75

Unless otherwise indicated, data are number (percentage). IQR, interquartile range; classification of chronic health conditions and risk factors according to EuroSCORE criteria.

heart surgery was defined as open-heart surgery irrespective of indication. Suitable for conventional surgery was defined as suitability for conventional thoracic aortic surgery according to preoperative risk stratification.

### 2.4. Statistical analysis

Continuous data are presented as the median and interquartile range (IQR; range from the 25th to the 75th percentile). Discrete data are given as counts and percentages. Comparisons of continuous data were performed by Mann–Whitney *U* tests and groups of categorical data were compared by Chi-square tests.

Univariate Cox regression analysis was primarily performed to assess the prognostic impact of female gender upon outcome stratified to the classification of aortic disease. Then, a multivariate time-dependent Cox regression model was applied to assess the strongest independent risk factor of outcome for female patients after adjustment for possible confounding factors. Baseline variables were entered into the model if they appeared imbalanced when indicated by a *p*-value <0.2 or if they were clinically established risk factors for adverse outcome. Results of the logistic regression model are given as the odds ratio (OR) and the 95% confidence interval (95%CI). Regression diagnostics and overall model fit were performed according to standard procedures. A two-sided *p*-value <0.05 was considered statistically significant. Calculations were performed with SPSS for Mac OsX (version 16.0).

### 3. Results

#### 3.1. Chronic health conditions and risk factors

The incidence of COPD was balanced in both males and females (32% vs 30%,  $p = 0.72$ ). The incidence of previous aortic surgery was significantly higher in women (24% vs 11%,  $p = 0.004$ ). Men were more likely to be unsuitable for conventional surgery (70% vs 59%,  $p = 0.03$ ).

#### 3.2. All-cause mortality

There was no significant difference in in-hospital mortality between males and females (5% vs 8%,  $p = 0.34$ ). Overall mortality during a median period of 13 months (IQR: 3–41) was comparable (27% vs 29%,  $p = 0.75$ ). Fig. 1 shows the all-cause mortality during follow-up.

There were no differences regarding mortality between males and females according to the individual indication. For female gender, 1-year survival and 5-year survival was 84% and 56% versus 83% and 60% for male gender. No significant gender influence was observed (OR 0.96 95%CI 0.59–1.56).

##### 3.2.1. Aneurysms

For female gender, 1-year survival and 5-year survival was 91% and 55% versus 82% and 53% for male gender. No significant gender influence was observed (OR 0.78 95%CI 0.41–1.47).

##### 3.2.2. Dissections

For female gender, 1-year survival and 5-year survival was 82% and 82% versus 89% and 67% for male gender. No significant gender influence was observed (OR 0.78 95%CI 0.21–2.83).

##### 3.2.3. PAUs/IMH

For female gender, 1-year survival was 72% versus 79% and 5-year survival of 56% for male gender. No significant gender influence was observed (OR 1.48 95%CI 0.53–4.19).

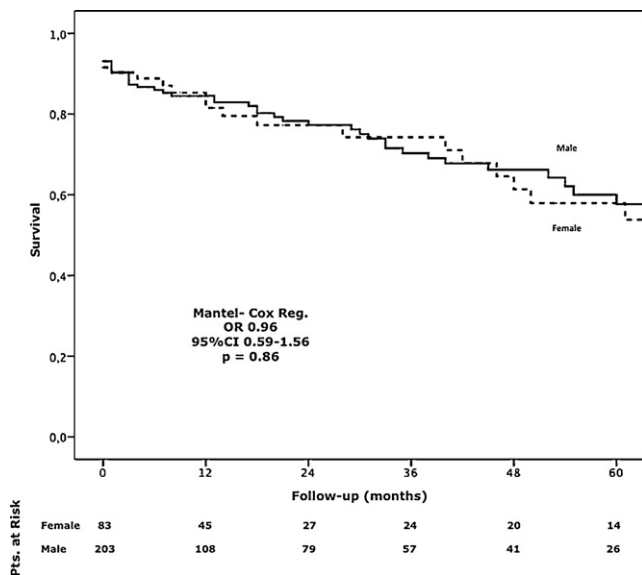


Fig. 1. All-cause mortality of patients after TEVAR.

#### 3.2.4. Traumatic lesions

No significant gender influence was observed (OR 1.48 95%CI 0.53–4.19).

#### 3.3. Aortic-related mortality

For female gender, 1-year survival and 5-year survival was 95% versus 97% and 91% for male gender (Fig. 2). No significant gender influence was observed (OR 0.65 95%CI 0.18–2.34). Accordingly, no differences were observed regarding the individual indication: Aneurysms (OR 0.02 95%CI 0.0–49.21), dissections (OR 2.50 95%CI 0.35–17.86), PAUs/IMH (OR 2.50 95%CI 0.16–40.01), and traumatic lesions (OR 0.05 95%CI 0.0–1.63) (Table 3).

#### 3.4. Multivariate logistic regression analysis

The strongest independent risk factor for overall mortality stratified to female gender was age (OR 3.60 95%CI 1.24–10.45) as well as the presence of COPD at the time of TEVAR (OR 3.09, CI 0.98–9.73) (Table 4). Extracardiac arteriopathy (OR 0.81 95%CI 0.24–2.79), previous aortic surgery (OR 1.58 95%CI 0.54–4.60), and emergency TEVAR (OR 1.65 95%CI 0.48–5.64) did not affect mortality.

### 4. Discussion

Gender does not affect mortality in patients after TEVAR irrespective of the underlying indication, atherosclerotic aneurysms, acute type B dissections, PAUs/IMH, and traumatic aortic lesions. Classical risk factors such as age and the presence of COPD at the time of TEVAR remain the most important risk factors in females.

An increasing number of reports on mid- and long-term results after TEVAR are now available revealing conflicting data regarding mortality. In a recent report at 4.5 years of

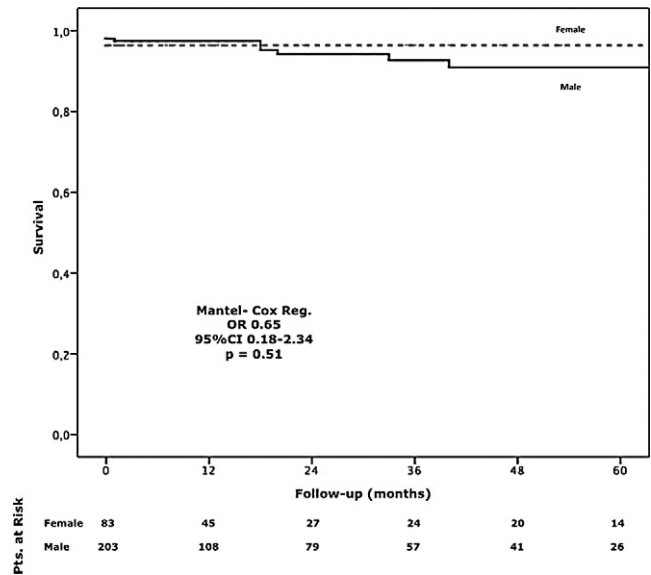


Fig. 2. Aortic-related mortality of patients after TEVAR.

Table 3. Distribution of female patients by different chronic health conditions and in-hospital risk assessment stratified to aortic disease morphology/etiology.

	Aneurysm N = 38 (46%)	Dissection N = 23 (28%)	PAU/IMH N = 21 (25%)	Traumatic * N = 1 (1%)	p
<b>Demographics</b>					
Age, median (IQR)	73 (69–77)	61 (48–69)	68 (61–77)	61	0.40
<b>Chronic health conditions and risk factors</b>					
Chronic obstructive pulmonary disease, n (%)	19 (50%)	1 (4%)	4 (19%)	0 (0%)	<0.001
Diabetes, n (%)	5 (13%)	1 (4%)	0 (0%)	0 (0%)	0.15
Coronary artery disease, n (%)	12 (32%)	2 (9%)	2 (10%)	0 (0%)	0.04
Extracardiac arteriopathy, n (%)	33 (87%)	8 (35%)	8 (38%)	0 (0%)	<0.001
Previous aortic surgery, n (%)	13 (34%)	3 (13%)	4 (19%)	0 (0%)	0.15
<b>In-hospital assessment</b>					
Emergency, n (%)	4 (11%)	17 (74%)	11 (52%)	0 (0%)	<0.001
Suitable for open surgery, n (%)	2 (5%)	6 (26%)	1 (4%)	1 (100%)	<0.001
Logistic EuroScore, median (IQR)	18 (12–28)	14 (10–26)	28 (13–39)	7	0.35
Stentgraft, median (Range)	2 (1–5)	1 (1–4)	1 (1–2)	1	0.003
Femoral access, n (%)	25 (66%)	21 (91%)	13 (62%)	1 (100%)	0.008
Periprocedural complications, n (%)	1 (3%)	1 (4%)	1 (5%)	0 (0%)	0.89
<b>Outcome</b>					
Endoleak, n (%)	11 (29%)	2 (9%)	2 (6%)	0 (0%)	0.07
30-day mortality, n (%)	2 (5%)	2 (9%)	3 (14%)	0 (0%)	0.49
Aortic disease related death, n (%)	1 (3%)	2 (9%)	1 (5%)	0 (0%)	0.57

Unless otherwise indicated, data are number (percentage). IQR, interquartile range; classification of chronic health conditions and risk factors according to EuroSCORE criteria. \*Excluded from group comparison.

follow-up, actuarial survival at 1, 5, and 8 years was 82%, 49%, and 27%, respectively [10]. By contrast, others report actuarial survival rates after 3.6 years of follow-up at 1, 3, and 5 years of 96%, 86%, and 69% [2]. The main difference seems to be evolving technology and better indications as the first report merely included first-generation devices and patients being treated early in TEVAR history. However, gender was not addressed, due to the low patient number. In this series, overall mortality compared favorably with the recent literature [10, 11]. No gender-related difference could be found with regard to mortality, indicating no increased risk in females such as after other cardiovascular interventions [12].

Several known risk factors contribute to the development of acute and chronic thoracic aortic pathology. COPD may act as the most important risk factor due to recurring episodes of abrupt changes in intrathoracic pressure. Advanced disease stages may prevent conventional open surgical treatment. In

this series, 30% of females as well as males suffered from severe COPD. Severe COPD, defined as forced expiratory volume in 1 s (FeV1) below 0.7 l, has been shown to be an independent predictor of mortality independent of aortic pathology by others [13, 14].

Women had a lower incidence of extracardiac arteriopathy but a higher incidence of previous aortic surgery. The first finding seems reasonable, as age was comparable between females and males. It is known that women are affected by atherosclerosis 10 years later than males [15]. It may be a specific finding of this report that more women had undergone previous aortic surgery. When analyzing our data, we found that the majority of women had undergone ascending or hemiarch replacement and the number of infrarenal replacements was low.

Women were more likely to be suitable for conventional open aortic surgery than men. Suitability for open repair remains a subjective decision of the treating physician to date. Several factors contribute to the decision. One of the most important details of this decision-making process may be the avoidance of deep hypothermic circulatory arrest (DHCA), which is associated with bleeding disorders as well as impaired gas exchange, especially in the left lung in the immediate postoperative period [16]. As previous ascending or hemiarch replacement may compel the utilization of DHCA, this fact may have well contributed to this result. Logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) levels showed no tendency toward higher levels in women. This is interesting as female gender *per se* is associated with increased risk in the EuroSCORE stratification system [9].

We have seen a well-balanced proportion of endoleaks regarding types and numbers as well as consequence

Table 4. Multivariate Cox-regression model assessing the strongest independent risk factor for overall mortality in female patients.

Risk factor for mortality	Odds ratio	95%CI	p-Value
Female gender			
Age > 75 years	3.60	1.24–10.45	0.01
Chronic obstructive pulmonary disease	3.09	0.98–9.73	0.05
Diabetes	0.91	0.16–5.24	0.91
Coronary artery disease	0.39	0.10–1.49	0.17
Extracardiac arteriopathy	0.81	0.24–2.79	0.74
Previous aortic surgery	1.58	0.54–4.60	0.41
Emergency	1.65	0.48–5.64	0.43
Stentgraft > 1	0.81	0.76–2.41	0.71
Endoleak	1.02	0.34–3.12	0.97

between males and females. Results of individual indications regarding these parameters as well as need for secondary surgical interventions are addressed in detail in other reports from our group [7,17]. A more detailed description of these parameters would – in our impression – defocus the article and would exceed its frame. Actually, cumulative rate of endoleak formation was comparable throughout the entire study period. Our rate of endoleak formation is acceptably low and well comparable with recent reports [18]. Improved understanding of factors associated with endoleak formation requiring treatment has contributed to these stable results. Most importantly, aortic-related mortality was low.

Age turned out to be an independent risk factor in females, most likely due to the increased frailty and limited natural life expectancy of advanced age in combination with an underlying thoracic aortic pathology even after successful treatment [19]. Furthermore, COPD was an independent predictor of mortality in females. This has also been shown in several investigations in patients without thoracic aortic pathology [13,14].

## 5. Strengths and limitations

This study is the first addressing gender aspects after TEVAR. Nevertheless, this analysis should be viewed in the light of its limitations. First, this study is a single-center study and retrospective in its nature. Furthermore, a more detailed analysis with regard to gender-specific risk according to the individual indication for TEVAR is warranted. However, this study is a first step to shed light on this important field of evolving knowledge.

Summarizing, gender does not affect mortality in patients after TEVAR irrespective of the underlying indication, atherosclerotic aneurysms, acute type B dissections, PAUs/IMH, and traumatic aortic lesions. Classical risk factors such as age and the presence of COPD at the time of TEVAR remain the most important risk factors in females.

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