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Editor's Choice — Sex Related Differences in Peri-operative Mortality after Elective Repair of an Asymptomatic Abdominal Aortic Aneurysm in the Netherlands: a Retrospective Analysis of 2013 to 2018

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WHAT THIS PAPER ADDS

This paper retrospectively analysed contemporary data of a mandatory, nationwide registry in the Netherlands and showed that women had a significantly higher peri-operative mortality than men following elective open surgical repair of an asymptomatic abdominal aortic aneurysm. By contrast, endovascular aneurysm repair demonstrated favourably low rates of peri-operative mortality for both women and men.

Objective: The aim was to compare peri-operative (30 day and/or in hospital) mortality between women and men in the Netherlands after elective repair of an asymptomatic abdominal aortic aneurysm (AAA).

Methods: This was a retrospective study using data from the Dutch Surgical Aneurysm Audit (DSAA), a mandatory nationwide registry of patients undergoing AAA repair in the Netherlands. Patients who underwent elective open surgical (OSR) or endovascular aneurysm repair (EVAR) of an asymptomatic abdominal aortic aneurysm (AAA) between 2013 and 2018 were included. Absolute risk differences (ARDs) with 95% confidence intervals (CIs) in peri-operative mortality between women and men were estimated. Logistic regression analyses were performed to estimate adjusted odds ratios (ORs) for mortality. Confounders included pre-operative cardiac and pulmonary comorbidity, serum haemoglobin, serum creatinine, type of AAA repair, and AAA diameter.

Results: Some 1662 women and 9637 men were included, of whom 507 (30.5%) women and 2056 (21.3%) men underwent OSR ($p < .001$). Crude peri-operative mortality was 3.01% in women and 1.60% in men (ARD = 1.41%, 95% CI 0.64—2.37). This significant difference was also observed for OSR (ARD = 2.63%, 95% CI 0.43—5.36), but not for EVAR (ARD = 0.36%, 95% CI −0.16 to 1.17). Female sex remained associated with peri-operative mortality after adjusting for confounders (OR = 1.79, 95% CI 1.20—2.65, $p = .004$), which was similarly observed for OSR (OR = 1.85, 95% CI 1.16—2.94, $p = .01$), but not for EVAR (OR = 1.46, 95% CI 0.72—2.95, $p = .29$).

Conclusions: Peri-operative mortality after elective repair of an asymptomatic AAA in the Netherlands is higher in women than in men. This disparity might be explained by the higher peri-operative mortality in women undergoing OSR, because no such difference was found in patients undergoing EVAR. Yet, it is likely that there are unaccounted factors at play since female sex remained significantly associated with mortality after adjusting for type of repair.

Keywords: Aortic aneurysm, Abdominal, Elective repair, Mortality, Sex
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INTRODUCTION

Background/rationale

Sex related differences in the natural history and management of patients with an abdominal aortic aneurysm (AAA) have been reported previously. Most significantly, AAAs tend to rupture at smaller diameters in women than men.[1,2] Consequently, the threshold diameter to offer women elective repair is often smaller than for men, which is set at 5.0 cm in the updated AAA guideline of the European

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Society for Vascular Surgery (ESVS).[3] However, this recommendation is based on Class IIb, level C evidence, i.e. consensus of expert opinion and retrospective studies.[3]

Early elective repair is performed to prevent death, and is only effective if the mortality and morbidity risks of the repair itself are very small. Otherwise, the survival benefit will be outweighed by the post-operative mortality. Unfortunately, women may be at a higher risk of losing the survival benefit of AAA repair, as international studies have reported that women have a higher 30 day mortality after elective repair than men.[4–6] A potentially higher mortality rate makes choosing the optimal treatment strategy for women even more challenging. This difficulty is also reflected in the ESVS AAA guideline, as the full recommendation is that only women with *acceptable* surgical risk may be considered for elective repair at a diameter of 5.0 cm. Yet, it is difficult to estimate what acceptable surgical risk should entail in the Netherlands, because no nationwide analyses have separately considered women undergoing elective AAA repair. Therefore, contemporary data regarding potential sex differences in mortality are still needed to optimise the management of women with AAA.

Objectives

The objective was to compare peri-operative mortality (defined as 30 day and/or in hospital deaths) and morbidity after elective repair of an asymptomatic AAA in the Netherlands between women and men up to 2018.

METHODS

Study design

This was a retrospective cohort study that used anonymised data from the Dutch Surgical Aneurysm Audit (DSAA), obviating the need for informed consent for this study. The scientific board of the DSAA approved the study proposal before releasing the data. This report adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[7]

Study setting

The DSAA is a nationwide registry for patients who undergo AAA repair in the Netherlands. It started in 2012 and it is compulsory for medical centres that carry out AAA repairs. From its initiation to 2016, only primary infrarenal or juxtarenal AAAs were registered. Since 2016, aneurysms of the thoracic aorta or aortic arch have also been registered, as have revisions of aneurysm repair.

Patients

Patients were eligible for inclusion in the current study if they underwent a primary open surgical repair (OSR) or endovascular aneurysm repair (EVAR) for an asymptomatic AAA from 1 January 2013 to 1 January 2018. Hybrid procedures were excluded from the current study. Furthermore, cases with missing data for the variables sex, type of AAA procedure, and 30 day or in hospital mortality were excluded.

Variables

The DSAA database registers a number of variables, such as patient and procedural characteristics, post-operative complications, and 30 day and in hospital mortality. Patient characteristics were partly based on the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) score.[8] For the current study, peri-operative mortality was defined as 30 day and/or in hospital mortality. Furthermore, the variables sex, age, pre-operative cardiac and pulmonary comorbidity, pulse rate, systolic blood pressure, serum haemoglobin, serum creatinine, pre-operative electrocardiogram (ECG), AAA diameter and type of AAA repair (OSR or EVAR) were evaluated. Pre-operative cardiac and pulmonary comorbidity were recorded as either no abnormality or abnormality according to the POSSUM score. Specifically, cardiac abnormality was defined as either medication for hypertension or angina, the use of digoxin or diuretics, peripheral oedema, elevated jugular venous pressure, or (borderline) cardiomegaly. Pulmonary abnormality was defined as either dyspnoea on exertion, limiting dyspnoea, or dyspnoea at rest. Definitions for the registration of complications are given in Supplementary material, Appendix 1.

Data sources/measurement

All data were prospectively registered in a centralised database of the DSAA.

Study size

The number of cases in participating centres during the study period determined the sample size for the main analysis. In addition, two separate sample sizes (OSR and EVAR) were calculated based on previous literature to determine what the ideal sample size would be to detect significant differences in peri-operative mortality. Since AAA is more common in men, the sample size calculations had to account for unequal numbers of women and men. These ratios between women and men differed for OSR and EVAR. Both sample size calculations were based on two sided tests with a power of 80% and a significance level of .05. A recent meta-analysis was used for the sample size calculations.[6] For OSR, the meta-analysis estimated a pooled 30 day mortality rate of 5.37% for women and 2.82% for men, with a men to women ratio of 2.995. The required sample size was estimated as 642 women and 1923 men. With regard to EVAR, the meta-analysis estimated a pooled 30 day mortality rate of 2.31% for women and 1.67% for men, with a men to women ratio of 5.541. The required sample size was estimated as 1873 women and 10 375 men. All sample size calculations were done in nQuery Advisor (version 7.0, Statsols, USA).

Statistical methods

Dichotomous or categorical variables were presented as numbers and percentages and compared with the chi-square or Fisher exact test where appropriate. Continuous variables were presented as means with standard deviations (SD) or medians with the interquartile range (IQR), and were compared using either the Student's *t* test or the Mann—Whitney *U* test depending on their distribution. Distribution normality was tested with the Kolmogorov—Smirnov test. Absolute risks (ARs) and the absolute risk difference (ARD) for peri-operative mortality were calculated to compare women with men, for the total cohort and for OSR and EVAR separately. The 95% confidence interval (CI) was estimated for both ARs and ARDs.

Univariable and multivariable logistic regression analyses were carried out to adjust for confounders and to estimate adjusted odds ratios (ORs). The variables sex, age, pre-operative cardiac and pulmonary comorbidity, pulse rate, systolic blood pressure, serum haemoglobin, serum creatinine, pre-operative ECG, AAA diameter, and type of repair (OSR or EVAR) were tested in univariable analysis. Variables with $p < .10$ on univariable analysis were selected for the multivariable analysis. Additionally, potential interactions between sex and any of the variables included in the multivariable analysis were explored. This was evaluated by adding individual interaction terms to the multivariable model to test their statistical significance. If any of the interaction terms were significant, these were kept in the multivariable model. Furthermore, separate subgroup analyses for OSR and EVAR were also done.

Post-operative complications were analysed to see whether there were differences between women and men. All analyses were done with IBM SPSS Statistics (version 25, IBM Corp, USA). A p value $< .05$ was considered statistically significant.

RESULTS

Patients

A total of 12 650 patients with AAA were released by the DSAA for the purpose of this study. However, 1348 cases were excluded for the following reasons: unknown sex ($n = 5$), revision surgery ($n = 408$), unknown type of AAA ($n = 58$), unknown type of AAA repair ($n = 31$), hybrid repair ($n = 14$), unknown mortality status ($n = 18$), and procedures that were primarily done for an iliac artery aneurysm ($n = 817$). Ultimately, 1662 women and 9637 men were included for analysis for a total of 11 299 patients.

Descriptive data

Five hundred and seven of 1662 (30.5%) women underwent OSR compared with 2056 of 9637 (21.3%) men ($p < .001$). Several significant differences in patient characteristics were observed between women and men, which are presented in Table 1. Most importantly, women had a higher median age and a lower median AAA diameter at the time of AAA repair. Type of AAA did not differ between women and men, either in the entire cohort or separately by type of repair.

Main results

Fig. 1 presents the crude peri-operative mortality for women and men in the total cohort and separately for OSR and EVAR. In all comparisons, women had a higher peri-operative mortality than men, which was statistically significant in the total cohort and among patients undergoing OSR.

Table 2 presents the multivariable analysis of the total cohort, and shows that female sex remained significantly associated with peri-operative mortality after adjustment (adjusted OR 1.79, 95% CI 1.20—2.65, $p = .004$). In addition, no statistically significant interactions were found between sex and the variables included in the multivariable model, including type of repair. Separate subgroup analyses for patients undergoing OSR and EVAR were also performed and are presented in Tables 3 and 4. These subgroup analyses showed that female sex was significantly associated with mortality after adjustment for confounders among patients undergoing OSR (adjusted OR 1.85, 95% CI 1.16—2.94), $p = .01$), but not among patients undergoing EVAR (adjusted OR 1.46, 95% CI 0.72—2.95, $p = .29$).

Supplementary material, Appendix 2 presents the complication rate for women and men. Overall, women had a higher rate of any type of complication. More specifically, women had significantly more bleeding and cardiac complications. When analysed separately for type of repair, there were no significant differences in the rate of any complication between women and men following both OSR and EVAR. However, women had significantly more cardiac and graft related complications after OSR, while women had significantly more bleeding and abdominal complications after EVAR.

DISCUSSION

Key results

This retrospective analysis observed that from 2013 to 2018 women had a significantly higher peri-operative mortality than men following elective repair of an asymptomatic AAA in the Netherlands. The association between female sex and peri-operative mortality remained significant after adjusting for confounders in multivariable analysis. Subgroup multivariable analyses further showed that this association was significant among patients undergoing OSR, but not among patients undergoing EVAR. In addition, EVAR demonstrated favourably low rates of peri-operative mortality for both women and men. Furthermore, women had significantly more complications overall, but not when considered separately after OSR and EVAR. Most notably, women had more cardiac and graft related complications after OSR.

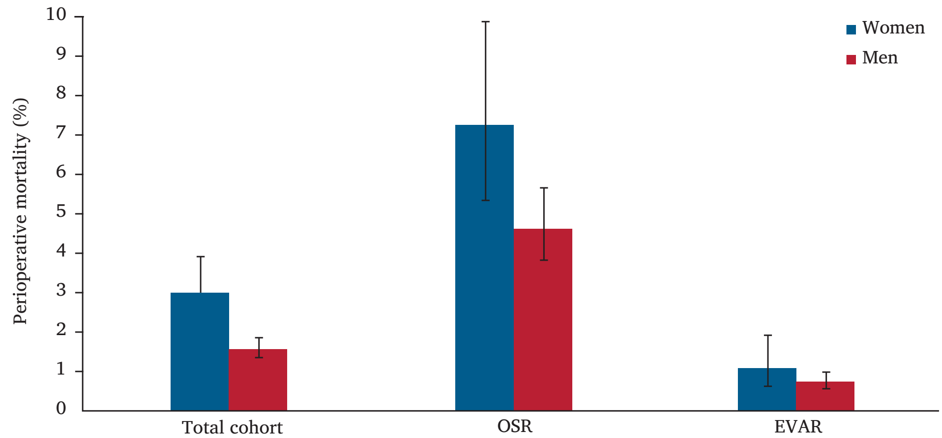
Table 1. Characteristics of patiens undergoing open surgical repair (OSR) or endovascular repair (EVAR) for abdominal aortic aneurysm (AAA) in The Netherlands in 2013-18.

Characteristics	Total cohort			OSR			EVAR		
	Women $n = 1662$	Men $n = 9637$	p value	Women $n = 507$	Men $n = 2056$	p value	Women $n = 1155$	Men $n = 7581$	p value
Median age (IQR) – years	75 (69–80)	73 (68–78)	<.001	72 (67–77)	71 (66–76)	.002	76 (70–81)	74 (68–79)	<.001
Missing – n (%)	1 (<0.1)	7 (<0.1)		0	3 (0.1)		1 (<0.1)	4 (<0.1)	
Pre-operative cardiac comorbidity – n (%)	877 (54.3)	4957 (53.4)	.49	264 (53.5)	1084 (54.5)	.71	613 (54.7)	3873 (53.1)	.32
Missing – n (%)	48 (2.9)	354 (3.7)		14 (2.8)	67 (3.3)		34 (2.9)	287 (3.8)	
Pre-operative pulmonary comorbidity – n (%)	486 (29.7)	2339 (24.6)	<.001	146 (29.3)	486 (24.1)	.02	340 (29.9)	1853 (24.8)	<.001
Missing – n (%)	26 (1.6)	135 (1.4)		8 (1.6)	38 (1.8)		18 (1.6)	97 (1.3)	
Median pulse rate (IQR) – beats/min	74 (65–83)	71 (63–81)	<.001	76 (68–85)	72 (63–82)	<.001	74 (65–82)	71 (63–80)	<.001
Missing – n (%)	93 (5.6)	558 (5.8)		28 (5.5)	127 (6.2)		65 (5.6)	431 (5.7)	
Median systolic blood pressure (IQR) – mmHg	141 (128–157)	139 (126–152)	<.001	142 (129–158)	140 (128–153)	.02	141 (127–157)	139 (126–152)	<.001
Missing – n (%)	82 (4.9)	434 (4.5)		24 (4.7)	105 (5.1)		58 (5.0)	329 (4.3)	
Median serum haemoglobin (IQR) – g/dL	13.4 (12.4–14.3)	14.2 (13.2–15.1)	<.001	13.5 (12.7–14.3)	14.2 (13.1–15.1)	<.001	13.4 (12.2–14.3)	14.3 (13.2–15.1)	<.001
Missing – n (%)	41 (2.5)	213 (2.2)		9 (1.8)	38 (1.8)		32 (2.8)	175 (2.3)	
Median serum creatinine (IQR) – μmol/L	75 (64–92)	92 (79–109)	<.001	74 (63–94)	92 (79–109)	<.001	76 (65–91)	92 (79–109)	<.001
Missing – n (%)	37 (2.2)	293 (3.0)		12 (2.4)	67 (3.3)		25 (2.2)	226 (3.0)	
Pre-operative ECG – n (%)			.001			.005			.07
No abnormality	987 (59.8)	5077 (53.1)		318 (63.3)	1122 (54.9)		669 (58.3)	3955 (52.6)	
Atrial fibrillation	82 (5.0)	701 (7.3)		21 (4.2)	118 (5.8)		61 (5.3)	583 (7.8)	
Ischaemia	36 (2.2)	178 (1.9)		18 (3.6)	44 (2.2)		18 (1.6)	134 (1.8)	
Other abnormality	416 (25.2)	2762 (28.9)		120 (23.9)	631 (30.9)		296 (25.8)	2131 (28.3)	
No pre-operative ECG	129 (7.8)	842 (8.8)		25 (5.0)	128 (6.3)		104 (9.1)	714 (9.5)	
Missing – n (%)	141 (8.5)	919 (9.5)		5 (1.0)	13 (0.6)		7 (0.6)	64 (0.8)	
Median AAA diameter (IQR) – mm	55 (52–60)	59 (55–65)	<.001	56 (52–62)	60 (56–70)	<.001	55 (52–60)	58 (55–64)	<.001
Missing – n (%)	29 (1.7)	120 (1.2)		10 (2.0)	40 (1.9)		19 (1.6)	80 (1.1)	
Type of AAA in 2016–17 – n (%)	721	3861	.06	224	764	.49	497	3096	.92
Infrarenal	616 (85.4)	3408 (88.3)		154 (68.8)	521 (68.2)		462 (93.0)	2887 (93.2)	
Juxtarenal	97 (13.5)	404 (10.5)		69 (30.8)	232 (30.4)		28 (5.6)	172 (5.6)	
Suprarenal	8 (1.1)	48 (1.2)		1 (0.4)	11 (1.4)		7 (1.4)	37 (1.2)	
Missing	0	1		0	0		0	1	
Type of procedure – n (%)			<.001						
OSR	507 (30.5)	2056 (21.3)		n.a.					
EVAR	1155 (69.5)	7581 (78.7)		n.a.					

Data are presented as n (%) or median (interquartile range [IQR]). Percentages for missing data are based on the total sample. Pre-operative cardiac and pulmonary comorbidity are defined as any abnormality according to the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) score. ECG = electrocardiogram; EVAR = endovascular aneurysm repair; n.a. = not applicable; OSR = open surgical repair.

Interpretation

The difference in peri-operative mortality in the entire cohort may be explained by the higher proportion of women undergoing OSR, yet it seems unlikely that this is the only explanation. Female sex remained significantly associated with peri-operative mortality, even after adjusting for type for repair and other confounders. This finding is also in agreement with recent literature.[5,9,10] One explanation may be that female sex itself is the significant risk factor that accounts for the difference in mortality. An alternative explanation may be that female sex has to be considered a surrogate marker for other factors that were not included in the current analysis. The latter seems a more plausible hypothesis, since the current study used data of a quality of care registry, which by design does not exhaustively collect data that might be of particular interest in research. Consequently, multivariable analysis cannot account for all relevant factors, nor identify new risk factors. Limited availability of data such as cause of death, precluded an exploration of drivers of peri-operative mortality in this cohort. Such an exploration is required to determine the risk factors for peri-operative mortality that also could



	Total cohort	OSR	EVAR
Women - *n*/m (%)	50/1662 (3.01)	37/507 (7.30)	13/1155 (1.13)
Men - *n*/m (%)	154/9637 (1.60)	96/2056 (4.67)	58/7581 (0.77)
ARD (95% CI)	1.41% (0.64 - 2.37%)	2.63% (0.43 - 5.36%)	0.36% (–0.16 - 1.17%)

Figure 1. Peri-operative mortality and absolute risk difference (ARD) for women and men after open surgical repair (OSR) or endovascular repair (EVAR) of abdominal aortic aneurysm in the Netherlands in 2013-18. The data are presented as number of events (*n*) per total number of patients (%).

be used as targets for pre- or peri-operative optimisation. An important part of this exploration is to test for possible interactions between sex and potential risk factors. Such interactions should be studied to ensure that identified risk factors are also valid for women. This is important since the majority of study populations of patients with asymptomatic AAA are men. In our analyses, testing the interactions did not reveal effect modification by sex for the various confounders.

Quality of care databases such as the DSAA are likely to be representative of the general population as they often include patients from large areas or even countries. In addition, such databases have contemporary data, which is illustrated by the current analysis of the period 2013—2018. Consequently, observing a high peri-operative mortality rate in the DSAA should serve as a current signal that improvement is necessary. Furthermore, progress can be assessed over time when such databases register additional patients. Quality of care databases can also be used for international comparisons, which can be helpful in judging whether the observed peri-operative mortality rates can be considered acceptable. A recent report of the Vascunet collaboration is especially interesting for the study, as they reported crude peri-operative mortality for women and

Table 2. **Univariable and multivariable logistic regression analyses of 11 299 patients with 204 events, undergoing open surgical or endovascular (EVAR) repair of abdominal aortic aneurysm (AAA)**

Variable	Univariable			Multivariable		
	OR (95% CI)	*p* value	Missing *n* (%)	OR (95% CI)	*p* value	Missing *n* (%)
Female sex reference: male sex	1.910 (1.382—2.639)	<.001	0	1.787 (1.203—2.654)	.004	2403 (21.3)
Age — years	1.041 (1.022—1.062)	<.001	8 (0.1)	1.060 (1.034—1.087)	<.001	
Pre-operative cardiac comorbidity reference: no abnormality	1.432 (1.072—1.914)	.02	402 (3.6)	1.2071 (0.859—1.698)	.28	
Pre-operative pulmonary comorbidity reference: no abnormality	2.426 (1.828—3.219)	<.001	161 (1.4)	2.095 (1.515—2.896)	<.001	
Pulse rate — beat/min	1.013 (1.003—1.023)	.009	651 (5.8)	1.011 (1.000—1.023)	.06	
Systolic blood pressure — mmHg	0.999 (0.992—1.006)	.78	516 (4.6)	—	—	
Serum haemoglobin — g/dL	0.773 (0.714—0.837)	<.001	254 (2.2)	0.889 (0.805—0.983)	.02	
Serum creatinine — μmol/L	1.010 (1.006—1.013)	<.001	330 (2.9)	1.009 (1.005—1.014)	<.001	
Pre-operative ECG reference: no abnormality		.007	1060 (9.4)		.30	
Atrial fibrillation	1.670 (1.012—2.755)	.05		1.289 (0.721—2.304)	.29	
Ischaemia	1.937 (0.838—4.478)	.12		1.609 (0.667—3.882)	.29	
Other abnormality	1.645 (1.207—2.241)	.002		1.369 (0.962—1.950)	.08	
AAA diameter — mm	1.020 (1.008—1.032)	.001	149 (1.3)	1.003 (0.989—1.017)	.67	
Type of procedure reference: EVAR	6.680 (4.990—8.941)	<.001	0	7.774 (5.475—11.0.39)	<.001	

AAA = abdominal aortic aneurysm; CI = confidence interval; ECG = electrocardiogram; EVAR = endovascular aneurysm repair; OR = odds ratio.

Table 3. Logistic regression analyses of 2563 patients with 133 events, undergoing open surgical repair of abdominal aortic aneurysm (AAA)

Variable	Univariable			Multivariable		
	OR (95% CI)	*p* value	Missing *n* (%)	OR (95% CI)	*p* value	Missing *n* (%)
Female sex reference: male sex	1.607 (1.086–2.380)	.02	0	1.846 (1.160–2.938)	.01	453 (17.7)
Age – year	1.076 (1.047–1.105)	<.001	3 (<1)	1.060 (1.027–1.094)	<.001	
Pre-operative cardiac comorbidity reference: no abnormality	1.446 (1.003–2.086)	.05	81 (3.2)	1.229 (0.807–1.871)	.34	
Pre-operative pulmonary comorbidity reference: no abnormality	2.105 (1.463–3.030)	<.001	46 (1.8)	1.785 (1.189–2.679)	.005	
Pulse rate – beat/min	1.011 (0.999–1.024)	.08	155 (6.0)	1.012 (0.998–1.026)	.09	
Systolic blood pressure – mmHg	0.997 (0.988–1.006)	.48	129 (5.0)	–	–	
Serum haemoglobin – g/dL	0.815 (0.734–0.904)	<.001	47 (1.8)	0.936 (0.823–1.064)	.31	
Serum creatinine – μmol/L	1.009 (1.005–1.014)	<.001	79 (3.1)	1.009 (1.004–1.015)	.001	
Pre-operative ECG reference: no abnormality		.05	171 (6.7)		.27	
Atrial fibrillation	1.977 (1.014–3.854)	.05		1.482 (0.705–3.115)	.30	
Ischaemia	2.018 (0.780–5.217)	.15		2.037 (0.754–5.501)	.16	
Other abnormality	1.536 (1.037–2.273)	.03		1.423 (0.918–2.207)	.12	
AAA diameter – mm	1.005 (0.992–1.019)	.47	50 (2.0)	–	–	

AAA = abdominal aortic aneurysm; CI = confidence interval; ECG = electrocardiogram; OR = odds ratio.

men separately based on data from 11 countries.[11] In that report, crude peri-operative mortality was 1.9% for women and 0.9% for men undergoing EVAR, while the rates were respectively 1.13% and 0.77% for women and men in the DSAA. It appears that women underwent EVAR with greater success in the short term in the Netherlands than women in the countries of the Vascunet collaboration. One of several explanations could be the relatively high proportion of women undergoing EVAR; yet it is hard to draw definitive conclusions regarding the nature of this association since the high EVAR proportion in this cohort is not fully understood. Nonetheless, the Vascunet report observed similar findings in their comparison of two different time periods: the more recent time period saw an increased EVAR rate while the corresponding peri-operative mortality decreased.[11] Then again, the EVAR proportion in the DSAA should ideally also be compared with the overall EVAR suitability rate during the study period in order to evaluate the larger population of women with a large asymptomatic AAA. Unfortunately, patients with an asymptomatic AAA who are eligible for – but who do not undergo – elective repair are not registered in the DSAA. Consequently, it is impossible to calculate national EVAR suitability rates in the Netherlands for women and men. Future study of the effect of EVAR volume in combination with the overall EVAR suitability rate might offer further evidence on this issue. By

Table 4. Logistic regression analyses of 8736 patients with 71 events, undergoing endovascular repair (EVAR) of abdominal aortic aneurysm (AAA)

Variable	Univariable			Multivariable		
	OR (95% CI)	*p* value	Missing *n* (%)	OR (95% CI)	*p* value	Missing *n* (%)
Female sex reference: male sex	1.477 (0.807–2.703)	.21	0	1.462 (0.724–2.950)	.29	1391 (15.9)
Age – year	1.080 (1.044–1.118)	<.001	5 (<0.1)	1.056 (1.015–1.098)	.007	
Pre-operative cardiac comorbidity reference: no abnormality	1.366 (0.841–2.219)	.21	321 (3.7)	–	–	
Pre-operative pulmonary comorbidity reference: no abnormality	3.326 (2.075–5.331)	<.001	115 (1.3)	2.675 (1.595–4.487)	<.001	
Pulse rate – beat/min	1.011 (0.994–1.028)	.20	496 (5.7)	–	–	
Systolic blood pressure – mmHg	0.999 (0.988–1.011)	.89	387 (4.4)	–	–	
Serum haemoglobin – g/dL	0.722 (0.634–0.822)	<.001	207 (2.4)	0.800 (0.687–0.932)	.004	
Serum creatinine – μmol/L	1.011 (1.006–1.017)	<.001	251 (2.9)	1.008 (1.002–1.015)	.01	
Pre-operative ECG reference: no abnormality		.07	889 (10.2)		.46	
Atrial fibrillation	1.993 (0.907–4.379)	.09		1.082 (0.434–2.695)	.87	
Ischaemia	1.049 (0.142–7.754)	.96		0.801 (0.106–6.058)	.83	
Other abnormality	1.916 (1.143–3.214)	.01		1.533 (0.884–2.659)	.13	
AAA diameter – mm	1.021 (0.999–1.043)	.06	99 (1.1)	1.016 (0.992–1.041)	.19	

AAA = abdominal aortic aneurysm; CI = confidence interval; ECG = electrocardiogram; OR = odds ratio.

contrast, men appear to have roughly the same peri-operative mortality rate in both the Netherlands and the Vascunet collaboration.

However, women and men undergoing OSR in the Netherlands fared worse than patients included in the Vascunet registries. The mortality rates were 7.30% and 4.67% for women and men in the Netherlands, while the Vascunet collaboration reported crude peri-operative mortality of 6.0% and 4.0% for women and men respectively. These differences between the Netherlands and the Vascunet report might be explained by several factors. The downside of a high proportion of EVAR is a low proportion of patients undergoing OSR. Similar to the trend with EVAR, the Vascunet collaboration observed the reverse for OSR: a decrease in OSR volume and an increase in its peri-operative mortality. Furthermore, with an EVAR first treatment policy more anatomically complex patients will concentrate in the cohort undergoing OSR, thereby representing a different, more challenging patient population.

Yet, the recommendation regarding women in the ESVS 2019 guidelines for AAA must be recalled: “in women with acceptable surgical risk the threshold for considering elective abdominal aortic aneurysm repair may be considered to be $\geq$ 5.0 cm diameter.”[3] Hence, based on the earlier comparisons between the DSAA and the Vascunet report, it can be said that women who underwent EVAR in the current cohort had an acceptable risk, while there was an unacceptable risk for women who underwent OSR. Perhaps the diameter threshold might also depend on the intended type of AAA repair.

Limitations

This study has some limitations. First, the sample sizes for the subgroup analyses for OSR and EVAR were not sufficiently large based on the sample size calculations. Despite this, the subgroup analysis for OSR showed a significant difference in mortality that is in agreement with contemporary literature. With regard to the subgroup analysis for EVAR, a type II error might have occurred, especially since no significant interaction was observed between sex and type of repair in the main analysis. Yet, the possibility that this is a true finding should not be excluded, possibly due to a lower than expected event rate and potential differences in patient selection. It is therefore relevant to repeat this analysis after the DSAA has accrued more patients undergoing EVAR.

Second, not all potentially relevant factors were registered in the DSAA, which is an acknowledged limitation of quality of care databases in general.[12] Relevant factors for the current comparison of women and men are related to AAA morphology, patient selection, comorbidity, and cause of death. Up to 2016, there are no data to distinguish in type of AAA, while it is of relevance to assess whether the proportions in type of AAA differed between women and men. However, based on the data of 2016–2017 it seems unlikely that there were significant differences between women and men. In addition, data regarding suprarenal clamping is unfortunately unavailable for most cases.

Lastly, the variables used were adapted from the POSSUM score.[8] Although the DSAA database registers pre-operative cardiac and pulmonary comorbidity with the original POSSUM categories, some variables were re-coded into dichotomous variables to prevent over fitting of the overall multivariable models due to low frequencies for some of the categories.

CONCLUSION

From 2013 to 2018, there was a significant difference in peri-operative mortality between women and men undergoing elective repair of an asymptomatic AAA. This disparity might be explained by the higher mortality in women undergoing OSR, because no such difference was found in patients undergoing EVAR. Furthermore, EVAR had low peri-operative mortality rates for both women and men. However, the overall difference between women and men persisted after adjusting for several confounders, including type of repair, which suggests that there remain unidentified factors at play that affect post-operative mortality. Future research should explore whether female sex is a surrogate marker for other relevant risk factors that might be of interest for either patient selection or pre-operative optimisation. An evaluation of the underlying reasons for the relatively high EVAR proportion and its effects on peri-operative mortality additionally might help with future patient selection, especially when the favourable peri-operative results persist in mid to long term follow up. As women present themselves only in relatively small numbers to individual hospitals, these efforts need to be undertaken by large multicentre studies.

CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2019.05.017.

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