

SYSTEMATIC REVIEW

## Editor's Choice — Sex Specific Differences in the Management of Descending Thoracic Aortic Aneurysms: Systematic Review with Meta-Analysis

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### WHAT THIS PAPER ADDS

Thirty day mortality after thoracic endovascular aneurysm repair for descending thoracic aortic aneurysm is almost twice as high in women as in men, and women have a slightly longer hospital stay. These facts are similar to previous results from systematic reviews of lower limb revascularisation and abdominal aortic aneurysm repair. The reasons for these sex specific differences need to be identified urgently, with a view to their correction. For open repair, there are insufficient recent data to address sex specific differences in outcomes.

**Objectives:** To assess sex specific differences in 30 day mortality, length of hospital stay, and adverse neurological events following repair of intact degenerative descending thoracic aortic aneurysms (TAAs), by either thoracic endovascular (TEVAR) or open repair.

**Methods:** MEDLINE, Embase, and CENTRAL databases were searched from 2005 to 2019, using ProQuest Dialog. The reviews were registered in PROSPERO (CRD42017020026) and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary outcome was 30 day mortality; secondary outcomes were length of hospital stay and adverse neurological events. Forest plots with random effects meta-analysis to provide odds ratios (OR) were used for primary assessment.

**Results:** For TEVAR, seven studies were identified, including 2758 women and 4674 men; of these studies six were eligible for the primary outcome of 30 day mortality, including 1756 women and 2619 men. There were 94/1756 deaths in women and 82/2619 deaths in men, yielding a pooled 30 day mortality of 5% (95% confidence interval [CI] 3–7) in women and 3% (95% CI 2–4) in men (OR 1.75, 95% CI 1.29–2.38). Length of hospital stay was longer in women, with a standardised mean difference of 0.3 days (95% CI 0.14–0.47; six studies); meta-regression analysis did not identify the slightly older age of women as significant factor in these differences. Stroke rate was not different between the sexes. For open repair only a single study, with national coverage, was identified: this study reported similar 30 day mortality in men and women.

**Conclusions:** In the management of intact degenerative descending TAAs, 30 day mortality after TEVAR appears to be much higher in women than men with no reasons for this difference identified. However, for open repair there is a lack of contemporary evidence owing to insufficient recent data.

**Keywords:** Descending thoracic aortic aneurysm, Length of stay, Operative mortality, Sex, TEVAR

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### INTRODUCTION

Two recent systematic reviews have indicated that women have much higher peri-operative mortality than men

following both lower limb revascularisation and intact abdominal aortic aneurysm (AAA) repair.<sup>1,2</sup> Many surgeons attribute these sex specific differences to the smaller and perhaps more calcified arteries in women, with the more challenging aortic morphology being an additional reason for AAA repair. The thoracic aorta is the largest-diameter artery in the body and therefore the sex specific differences in mortality following thoracic aortic intervention may be less pronounced. Several different aetiologies of

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thoracic aortic disease are subject to aortic repair, including the degenerative conditions of aneurysm, dissection, and penetrating aortic ulcer, as well as genetic syndromes such as Marfan syndrome. The focus of this review is limited to degenerative descending thoracic aortic aneurysm (TAA).

Since the first introduction of thoracic endovascular aneurysm repair (TEVAR) in the late 1990s there has been an accelerating shift from open repair to TEVAR for intact descending TAAs, despite the lack of randomised trial evidence.<sup>3–6</sup> Recent analysis of the Vascular Quality Initiative data of the Society for Vascular Surgery has suggested that women have worse outcomes than men after TEVAR for descending TAAs.<sup>7</sup> However, it is not clear whether these observations either apply to open repair or can be generalised. A recent narrative review of sex differences in mortality after TEVAR was not restricted to descending TAAs, but did note the tendency for women to have a higher 30 day mortality than men.<sup>8</sup>

The first “home made” TEVAR devices were implanted in the 1990s, but the U.S. Food and Drug Administration did not approve the first commercial devices until 2005. During this early period devices developed rapidly, becoming more flexible and available in a wider range of sizes. In the UK endovascular repairs of the thoracic aorta were not identified by separate coding until 2006. During a similar period there have been parallel improvements in anaesthesia, intensive care, and pain management, as well as stabilisation of endovascular techniques and technology, hence the decision to focus on more recent publications for open repair, as well as TEVAR, in the present study.

The aims of this study were to review systematically the recent literature to assess sex specific differences for 30 day mortality, length of hospital stay (LoHS), and neurological events following repair of degenerative descending TAAs, with separate reviews for open repair and TEVAR.

## MATERIALS AND METHODS

### Search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and registered in November 2017 in the PROSPERO database (<http://www.crd.york.ac.uk/PROSPERO/>; registration number CRD42017020026). The aim was systematically to review published and unpublished data of the current (since 2005) influence of sex on the outcomes (principally in hospital or 30 day mortality) of descending TAA repair, both open repair and TEVAR.

MEDLINE, Embase, and CENTRAL databases were searched (by P.U.), using a combination of controlled vocabulary (medical subject heading or Emtree) terms and free text terms in ProQuest Dialog (Ann Arbor, MI, USA), and limiting the search to data published since 1 January 2005. The search was restricted to major European languages, and the following terms were used: “thoracic aortic aneurysm”, “thoracic aorta aneurysm”, “endovascular procedures”, “endovascular aneurysm repair”, “aneurysm

surgery”, “stents/vascular stent”, “vascular surgical procedures”, “vascular surgery”, “blood vessel prosthesis/blood vessel graft”, “endoprosthesis blood vessel prosthesis implantation”, “vascular grafting”, “aortic aneurysm endovascular graft”, “blood vessel transplantation”, “endovascular surgery”, “open surgery”, “mortality”, “surgical mortality”, “mortality rate”, “survival rate”, “treatment outcome”, “length of stay”. The final search date was 30 January 2019.

Other sources, including [ClinicalTrials.gov](http://clinicaltrials.gov) (<http://clinicaltrials.gov>), Current Controlled Trials (<http://www.controlledtrials.com/>), and the National Research Register were also searched for details of ongoing or unpublished trials. This search was complemented by scanning reference lists of relevant articles, and manual searches of *Endovascular Today* and vascular surgery conference proceedings.

### Study selection

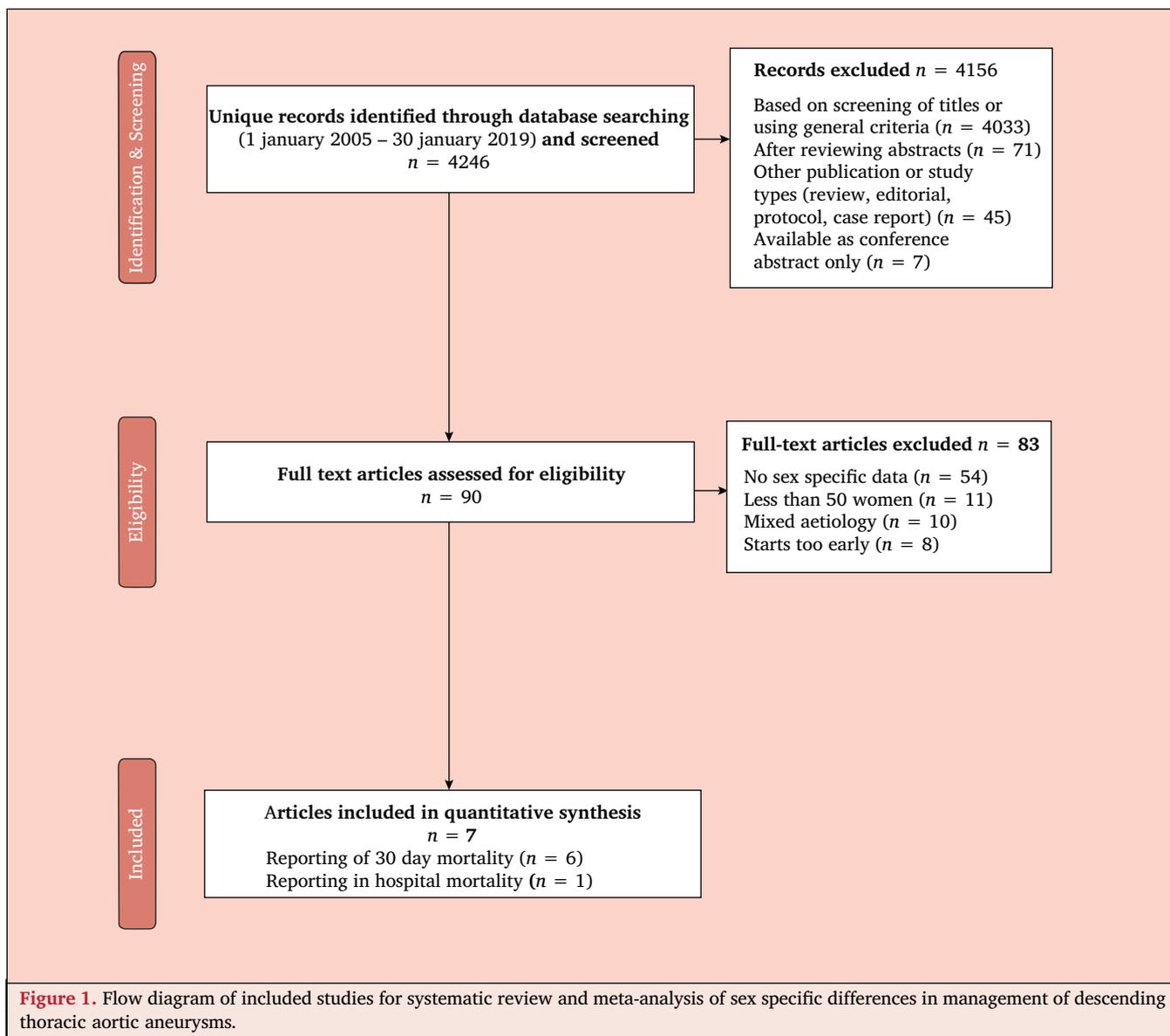
The inclusion and exclusion criteria are given in [Table 1](#). Initial rejection or inclusion was based on assessment of the study title by two reviewers (J.T.P., R.S.v.A.), who retained review articles for examination of their references. Full text versions of the selected studies that met the initial eligibility criteria were obtained. Studies were assessed, included, and extracted (by J.T.P., R.S.v.A., P.U.) if they were of both men and a minimum of 50 women, with data presented for each sex separately, with TAAs being assessed for aneurysm repair by either endovascular aneurysm repair (EVAR) or open repair, and with 30 day all cause mortality available by sex and by type of operation. A PRISMA flow diagram showing the selection process of articles is presented in [Fig. 1](#).

### Data extraction and quality assessment

A data extraction form, which identified demographic and technical details, and potential biases, in the selected studies, was designed, and a preliminary summary checklist was completed for each study. It included data on age, smoking status, aneurysm diameter, operation time, and landing zones/need for iliac conduit. Quality scoring was undertaken (by J.T.P. and R.S.v.A.), using the Newcastle—Ottawa scoring system for cross sectional studies.<sup>9</sup> Criteria

**Table 1. Inclusion and exclusion criteria**

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<i>Inclusion criteria</i>	
Operation date year 2005 or after	
Men and women $\geq 55$ y of age	
Repairs of $\geq 50$ women	
All ethnic groups	
Population described clearly	
For studies reporting duplicated data, the most recent or most comprehensive publication to be included	
<i>Exclusion criteria</i>	
Review articles	
Editorials	
Letters	
Case reports	
Studies of selected subgroups (e.g. people with known cardiovascular disease, etc.)	
Reporting only hazard ratios or in hospital mortality	



for quality assessment included description of population/representativeness of the sample (including sample size) and description of outcomes (including comparability of subjects in different outcome groups and method of assessment of the outcome): the maximum score was nine points. The quality of reporting was independently assessed and disagreements were resolved by consensus (J.T.P., R.S.v.A., P.U.).

### Data synthesis and analysis

Statistical analysis was performed (by R.W.), using the R environment version 3.4.1 ([www.r-project.org](http://www.r-project.org)). All meta-analyses were pooled using a random effects model as the principal analysis, to adjust for possible variation in the effects between studies and sampling variability (selected sample studies vs population based).<sup>10</sup> Fixed effect models also were conducted as secondary analyses. Statistical heterogeneity was quantified using Cochran's Q statistic,<sup>11</sup>

and the  $I^2$  statistic. A funnel plot and the rank correlation test of funnel plot asymmetry were used to examine the possibility of publication bias.<sup>12</sup> To further assess statistical heterogeneity, random effects meta-regressions using the method described by Knapp and Hartung were performed to analyse the potential effect of the studywise mean age difference between female and male patients on the outcomes.<sup>13,14</sup> Pooled mortality was calculated with the inverse variance method using the Freeman–Tukey double arcsine transformation and was based on random effects estimates. The effect of sex on binary outcomes was expressed as odds ratios (ORs) and the effect on continuous outcomes was expressed as standardised mean differences (SMDs).

To increase the sample size, there were two sensitivity analyses. The first was for peri-operative mortality, including both in hospital and 30 day mortality, and the second was for combined neurological deficit outcome (paraparesis, paraplegia, and stroke).

## RESULTS

### Search results

After database searching and evaluation, four papers based on four studies met the inclusion criteria for meta-analysis, which provided data for TEVAR only.<sup>7,15–17</sup> In addition, five further studies with inclusion potential (showing odds or hazard ratios for sex) were identified, of which one reported TEVAR data only,<sup>18</sup> and four reported both TEVAR and open repair data,<sup>19–22</sup> although none had published sex specific data. Therefore, the authors were contacted and three were able to provide further details,<sup>18,19,22</sup> allowing inclusion of these three studies, giving a total number of seven studies for the meta-analysis. However, the additional data received from the nationwide German study revealed that the minority population, who had been

treated by open repair, had a much younger mean age, with wider standard deviation, than other studies, particularly for men, implying that many patients <55 years had been included.<sup>19</sup> Therefore, it must be assumed that this open repair cohort was not limited to degenerative aortic disease and included a variety of other aetiologies, including patients with a connective tissue disease. Therefore, only the TEVAR data from the German nationwide study were included in this review.

Of the 83 studies that were excluded after reviewing the full text, 54 did not meet the inclusion criteria as no sex specific data were provided (including odds or hazard ratios for sex), 11 studies included < 50 women, and the remaining 18 either included patients with mixed thoracic aortic aetiologies or operations were carried out before 2005 (Fig. 1).

**Table 2.** Main characteristics of included studies for systematic review and meta-analysis of sex specific differences in management of descending thoracic aortic aneurysms

Reference	Derivation of cohort	Country	Repair type	Repair date (start)	Repair date (end)	Sex – M or F	Age – y	Peri-operative deaths <sup>a</sup>	Primary hospital stay – d	Stroke <sup>b</sup>	Newcastle–Ottawa score
Jackson <i>et al.</i> , 2011 <sup>16</sup>	VALOR trial, multicentre (n = 38)	USA	TEVAR	2003	2005	F = 80	71.6 ± 10.1	2 (2.5)	9.0 ± 16.2	5 (6.3)	5
						M = 115	69.3 ± 11.7	2 (1.7)	4.7 ± 5.8	2 (1.7)	
Kasirajan <i>et al.</i> , 2011 <sup>17</sup>	TAG thoracic stent graft trials, multicentre (n = 25)	USA	TEVAR	1999	NA	F = 156	72.8 ± 9.5	2 (1.3)	5.5 ± 6.2	2 (1.3)	5
						M = 265	71.0 ± 10.8	3 (1.1)	4.8 ± 13.0	10 (3.8)	
Arnaoutakis <i>et al.</i> , 2014 <sup>15</sup>	Population based ACS-NSQIP database	USA	TEVAR	2005	2011	F = 279	71.3 ± 0.7	18 (6)	7.7 ± 0.5	14 (5)	8
						M = 370	69.9 ± 0.7	11 (3)	7.7 ± 0.5	14 (4)	
von Allmen <i>et al.</i> , 2014 <sup>22</sup>	Population based HES dataset	England	TEVAR	2006	2011	F = 122	73.0 ± 7.7	10 (8.2)	NA	NA	9
			TEVAR			M = 232	71.2 ± 8.7	13 (5.6)		NA	
			OR			F = 127	71.4 ± 7.3	7 (5.5)		NA	
			OR			M = 137	68.0 ± 8.6	13 (9.5)		NA	
Deery <i>et al.</i> , 2017 <sup>7</sup>	Population based VQI database	USA	TEVAR	2011	2015	F = 1038	73 (67–69)	56 (5.4)	5 (3–8)	9 (0.9)	8
						M = 1536	72 (64–78)	51 (3.3)	4 (2–7)	23 (1.5)	
Ranney <i>et al.</i> , 2018 <sup>18</sup>	Single centre	USA	TEVAR	2005	2016	F = 85 <sup>c</sup>	71.5 ± 10.9	6 (7.4)	4 (2–5)	0	6
						M = 107 <sup>d</sup>	70.1 ± 9.9	2 (2)	2 (2–4)	4	
Geisbusch <i>et al.</i> , 2019 <sup>19</sup>	Population based German DRG microdata	Germany	TEVAR	2005	2014	F = 1002	71.7 ± 9.9	44 (4.4)	14.2 ± 12.5	13 (1.3)	8
						M = 2055	69.4 ± 10.2	68 (3.3)	12.8 ± 11.5	49 (2.4)	

Data are given as mean ± standard deviation (SD), median (interquartile range) or n (%).

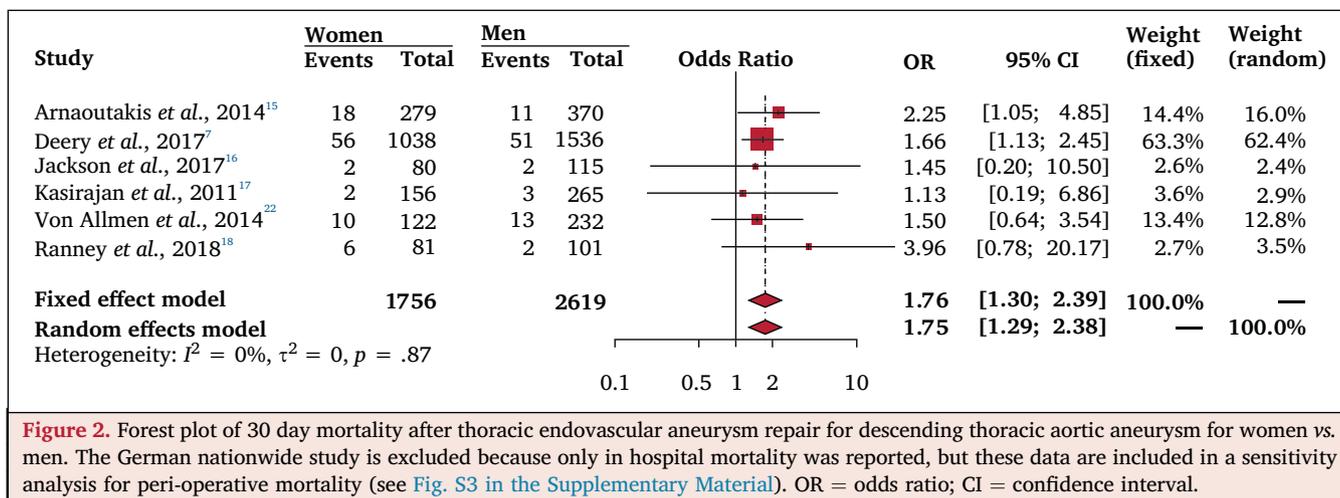
VALOR = The Talent Thoracic Stent Graft System Clinical Study; TEVAR = thoracic endovascular aneurysm repair; F = female; M = male; TAG = W.L. Gore and Associates (Flagstaff, AZ, USA); NA = not available; ACS-NSQIP = American College of Surgeons National Surgical Quality Improvement Program; HES = Hospital Episode Statistics; OR = open repair; VQI = Vascular Quality Initiative; DRG = Diagnosis related Group Statistics.

<sup>a</sup> Peri-operative deaths column indicates 30 day deaths for all studies except Geisbusch, which reports in hospital deaths only.

<sup>b</sup> Geisbusch data reports a combined outcome of stroke, paraplegia, and paraparesis.

<sup>c</sup> Includes four urgent/emergency repairs, but mortality is given for electives only (n = 81).

<sup>d</sup> Includes six urgent/emergency repairs, but mortality is given for electives only (n = 101).



**Figure 2.** Forest plot of 30 day mortality after thoracic endovascular aneurysm repair for descending thoracic aortic aneurysm for women vs. men. The German nationwide study is excluded because only in hospital mortality was reported, but these data are included in a sensitivity analysis for peri-operative mortality (see Fig. S3 in the Supplementary Material). OR = odds ratio; CI = confidence interval.

### Characteristics and quality assessment of studies

The quality score ranged from five to nine with the observational non-population based studies yielding the lowest quality scores,<sup>16–18</sup> while the four population based studies had scores closer to the maximum.<sup>7,15,19,22</sup> The characteristics of all the included studies are summarised in Table 2.

### Thoracic endovascular aneurysm repair studies

There were four population based studies: two from the USA covering different time periods,<sup>7,15</sup> one from the UK,<sup>22</sup> and one from Germany,<sup>19</sup> contributing a total of 2441 women and 4193 men. Other studies from the USA from a single centre and two multicentre clinical trials provided 317 women and 481 men.<sup>16–18</sup> This gave an overall total of 2758 women and 4674 men, operated on in seven separate studies.

**Mortality.** The lowest operative mortality after TEVAR was observed in the early TAG (W.L. Gore and Associates, Flagstaff, AZ, USA) thoracic stent graft trials for both women (1.3%) and men (1.1%),<sup>17</sup> while the highest operative mortality was observed in the English dataset for both women (8.2%) and men (5.6%).<sup>22</sup>

All but one study reported on 30 day mortality after TEVAR.<sup>19</sup> There were 94/1756 deaths in women and 82/2619 deaths in men, yielding a pooled 30 day mortality of 5% (95% confidence interval [CI] 3–7) in women and 3% (95% CI 2–4) in men (OR 1.75 [95%CI 1.29; 2.38]) (Fig. 2), with insignificant heterogeneity ( $I^2 = 0.0\%$ ,  $p = .872$ ). The funnel plot showed no evidence of publication bias ( $p = .851$ ), although with only six data points this may be unreliable (Fig. S1, see Supplementary Material).

In a mixed effects meta-regression model, the sex specific age difference did not appear to mediate the relationship between sex and mortality ( $p = .922$ ) (Fig. S2, see Supplementary Material). There were insufficient consistent data for other parameters, including aneurysm diameter, operation time, and need for iliac conduit to assess their impact on mortality (Table 3), although in every study

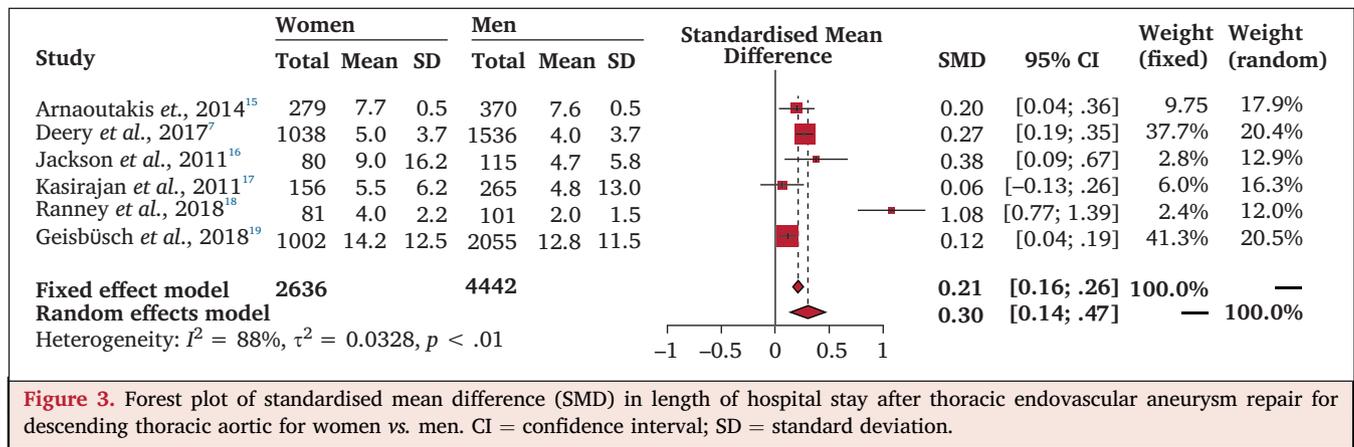
reporting iliac conduit usage, this was always at least twofold higher in women.

The sensitivity analyses assessing peri-operative mortality combining in hospital and 30 day mortality showed similar results, with the risk of post-operative mortality also being higher in women after TEVAR (OR 1.58, 95% CI 1.24–2.01;  $p < .001$ ), with heterogeneity between the studies being low ( $I^2 = 0\%$ ,  $p = .816$ ) (Fig. S3, see Supplementary Material).

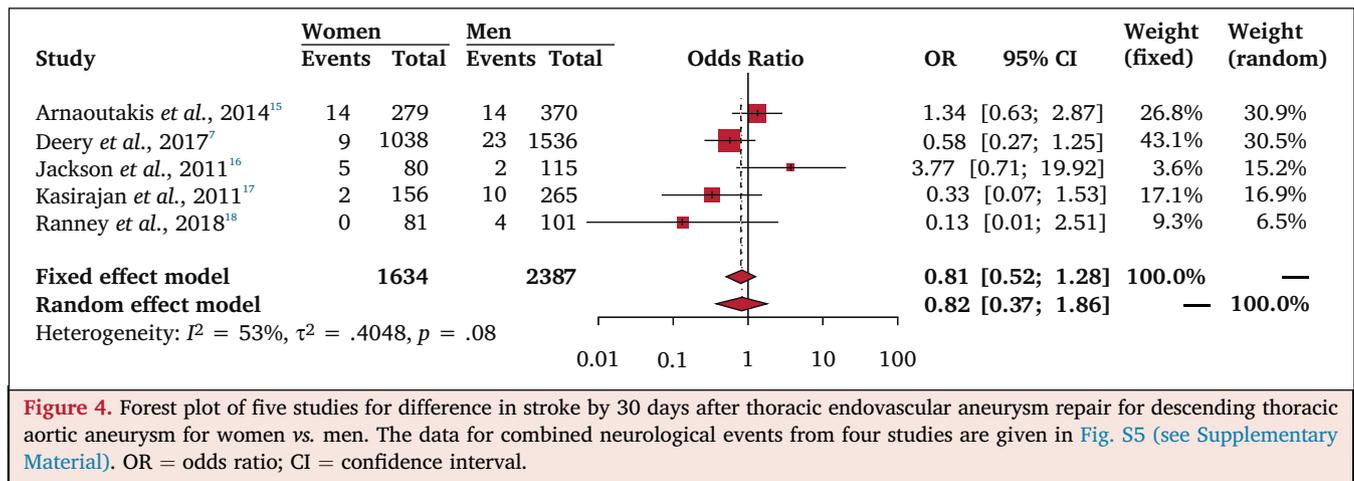
**Length of stay.** All but the English nationwide study reported data on LoHS.<sup>22</sup> Considerable between study differences were revealed, with the longest length of stay in the German population based study,<sup>19</sup> for both women and men ( $14.2 \pm 12.5$  days vs.  $12.8 \pm 11.5$  days), and the shortest in the US single centre study (median 4 days, interquartile range [IQR] 2–5 vs. 2 days, IQR 2–4).<sup>18</sup> Overall, women had a statistically significantly longer LoHS after TEVAR, with a pooled standardised mean difference of 0.3 (95% CI 0.14–0.47) but with significant heterogeneity between studies ( $I^2 = 88\%$ ,  $p < .01$ ) (Fig. 3). In the meta-regression analysis, the sex specific age difference did not explain the effect of sex on LoHS ( $p = .623$ ; data not shown).

**Neurological outcome.** All but one study reported on neurological outcomes.<sup>22</sup> Five of the studies reported separate stroke and/or spinal cord ischaemia rates,<sup>7,15–18</sup> while the German population based study provided only a combined neurological deficit outcome, including both stroke and spinal cord ischaemia events.<sup>19</sup> In the five studies with separate stroke rates, no difference was observed between the sexes (OR 0.82, 95% CI 0.37–1.86) with moderate between study heterogeneity ( $I^2 = 53\%$ ,  $p = .075$ ) (Fig. 4).

Four studies were eligible for sensitivity analysis of a combined outcome, including stroke and spinal cord ischaemia events.<sup>16–19</sup> Two others,<sup>7,15</sup> including the large US study,<sup>7</sup> were excluded owing to missing information on spinal cord ischaemia events. Pooled neurological event rates of these four studies provided similar results, with no sex specific differences following TEVAR (OR 0.80, 95% CI 0.39–



**Figure 3.** Forest plot of standardised mean difference (SMD) in length of hospital stay after thoracic endovascular aneurysm repair for descending thoracic aortic for women vs. men. CI = confidence interval; SD = standard deviation.



**Figure 4.** Forest plot of five studies for difference in stroke by 30 days after thoracic endovascular aneurysm repair for descending thoracic aortic aneurysm for women vs. men. The data for combined neurological events from four studies are given in Fig. S5 (see Supplementary Material). OR = odds ratio; CI = confidence interval.

1.64). Heterogeneity between the studies was moderate ( $I^2 = 56\%$ ,  $p = .08$ ) (Fig. S4, see Supplementary Material).

**Other outcomes.** The other outcomes extracted are shown in Table 3. There were insufficient consistent data for meta-analysis.

**Studies of open repair**

There was only a single eligible study that reported on outcomes after open repair of degenerative descending TAA, covering nationwide English data from 2006 to 2011,

with 127 women and 137 men (mean age 71 years),<sup>22</sup> as the German nationwide study was excluded.<sup>19</sup> Thirty day mortality was not higher in women (5.5% vs. 9.5% in men).

**DISCUSSION**

This meta-analysis confirmed that there are sex specific differences in short term outcomes following endovascular repair of degenerative descending TAAs with an almost 1.8 times higher 30 day mortality and a longer hospital stay in women than in men. There was a similar result for the sensitivity analysis for combined in hospital and 30 day

**Table 3.** Other extracted data from the analysis of sex differences in thoracic endovascular aneurysm repair for descending thoracic aortic due to insufficient consistency

Reference (main paper)	Aneurysm diameter – cm		Mean operation time – min		Iliac conduit usage – %	
	Women	Men	Women	Men	Women	Men
Jackson <i>et al.</i> , 2011 <sup>16</sup>	5.5 (mean)	5.6 (mean)	141	173	39	9
Kasirajan <i>et al.</i> , 2011 <sup>17</sup>	6.0 (NS)	6.2 (NS)	174	160	24	6
Arnaoutakis <i>et al.</i> , 2014 <sup>15</sup>	NA	NA	148 <sup>a</sup>	130 <sup>a</sup>	18	7
von Allmen <i>et al.</i> , 2014 <sup>22</sup>	NA	NA	NA	NA	NA	NA
Deery <i>et al.</i> , 2017 <sup>7</sup>	5.8 (median)	6.0 (median)	150	161	4.3 <sup>b</sup>	2.1 <sup>b</sup>
Ranney <i>et al.</i> , 2018 <sup>18</sup>	NA	NA	NA	NA	NA	NA
Geisbusch <i>et al.</i> , 2019 <sup>19</sup>	NA	NA	NA	NA	NA	NA

<sup>a</sup> From Table II in the paper (different numbers given in text).

<sup>b</sup> Iliac access procedure with iliac conduit not specified. NS = not specified; NA = not available.

mortality, which included the large German nationwide study. The higher operative mortality following TEVAR in women vs. men was not attributable to either their slightly older age or to adverse neurological events. However, for open repair, data are scant and uncertainty remains about whether sex specific differences are present in current practice.

In each separate TEVAR study, as well as overall, the 30 day (or in hospital) mortality was numerically higher in women. The operative mortality rates were lowest in the early Investigational Device Exemption trials in the USA, which specifically looked at patients with very favourable anatomy.<sup>16,17</sup> Subsequently, as the devices continued to improve, TEVAR has been used in a wider range of patients by a wider range of investigators, with an accompanying increase in 30 day mortality rate in population-wide studies.<sup>22,23</sup> Further device improvement and team experience are probably reflected in the reducing operative mortality observed in the most recent studies. However, the sex specific differences in operative mortality do not appear to have changed with time and cannot be explained by the slightly older age of the women included in these studies. Therefore, other underlying factors must be assumed to influence this difference.

Firstly, women have some typical anatomical differences, particularly with regard to smaller access vessel diameters, which prove relevant even for repair of the largest artery in the body. Thoracic aortic endografts require larger iliac access vessels than abdominal aortic endografts and it would appear that iliac conduit usage is much higher in women than men (Table 3). The detailed reporting from the Vascular Quality Initiative (VQI) in the USA reported a twofold increase in iliac and access vessel injuries in women vs. men.<sup>7</sup> This, in turn, may give rise to an increased number of bleeding complications and increased need for blood transfusion in women, which was reported in several of the included studies.<sup>7,15–17</sup> However, the increased need for transfusion in women also may result, at least in part, from pre-operative differences in anaemia between men and women. The large VQI registry dataset reported a significantly higher rate of pre-operative anaemia in women than in men (20% vs. 12%).<sup>7</sup> Pre-operative anaemia has been identified as an independent risk factor for operative 30 day mortality in studies covering a range of different types of surgery and cardiovascular interventions.<sup>24</sup> Moreover, peri-operative transfusion has been shown to be independently associated with 30 day morbidity and mortality (OR 6.9, 95% CI 3.2–15) in patients undergoing major vascular surgery.<sup>25</sup> Other pre-operative differences in morbidities (e.g. cardiac and pulmonary disease) and their management also may contribute to the higher operative mortality in women.<sup>26,27</sup>

It is also noticeable that significantly fewer women than men were identified with coronary artery disease or a prior coronary intervention. Deery *et al.* report a coronary artery disease rate of 19% in women vs. 26% in men.<sup>7</sup> These figures are in contrast to the known high prevalence of cardiovascular disease in patients with small AAAs, which has been assessed in a systematic review by Bath *et al.*,<sup>28</sup> with a weighted mean prevalence of 44.9%

for ischaemic heart disease. The under recognition of coronary artery disease is not uncommon, as prodromal coronary artery ischaemia symptoms are often atypical in women compared with men, and women have higher rates of non-obstructive coronary artery disease.<sup>29–31</sup> Women may also be undertreated for coronary artery disease compared with men. A study assessing physician awareness and adherence to cardiovascular disease prevention guidelines proved a very low level of recognition among physicians that heart disease kills more women every year than men,<sup>32</sup> and the SWEDEHEART registry suggested that women were less likely to receive optimal care compared with men.<sup>33</sup>

The longer hospital stays for women (such as the higher 30 day mortality) were evident in every study, even though the length of stay varied widely. The reasons for this difference are likely to relate to the increased overall rate of complications in women, psychosocial factors such as anxiety, and availability of home care and differences in healthcare systems between the USA and Europe. Notably the study by Deery *et al.* indicated that a much higher proportion of women than men were discharged to a skilled nursing facility rather than to home.<sup>7</sup> Such observations suggest that the costs of the initial hospital stay for TEVAR are likely to be higher for women than men.

This study has several limitations. Firstly, there are few separate outcome data for men and women from medium to large-sized studies for repair of degenerative descending TAAs, a few for TEVAR, and almost none for recent studies of open repair. Secondly, the individual studies did not have systematic reporting of outcome events, particularly neurological events. Thirdly, some of the analyses were dominated by the large VQI study from the USA.<sup>7</sup> However, there was no evidence of publication bias from the funnel plots and sensitivity analyses, and including the large German nationwide study (with in hospital mortality and combined neurological outcomes) did not change the findings. Given the rather lengthy hospital stay in Germany and the reported similarity in hospital and 30 day mortality rates for TEVAR,<sup>34</sup> such sensitivity analyses are justified. Fourthly, the individual studies made little attempt to understand the reasons for the sex specific differences in outcome.

## CONCLUSIONS

For descending TAAs, operative mortality and LoHS for TEVAR are higher in women than men. This difference is not attributable to either age or neurological events and the reasons for the sex differences require further investigation. There are too few recent data to comment on sex specific differences relating to open repair and, with the increasing preference for TEVAR, there may never be sufficient data.

## ACKNOWLEDGEMENTS

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## CONFLICTS 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.2019.04.022>.

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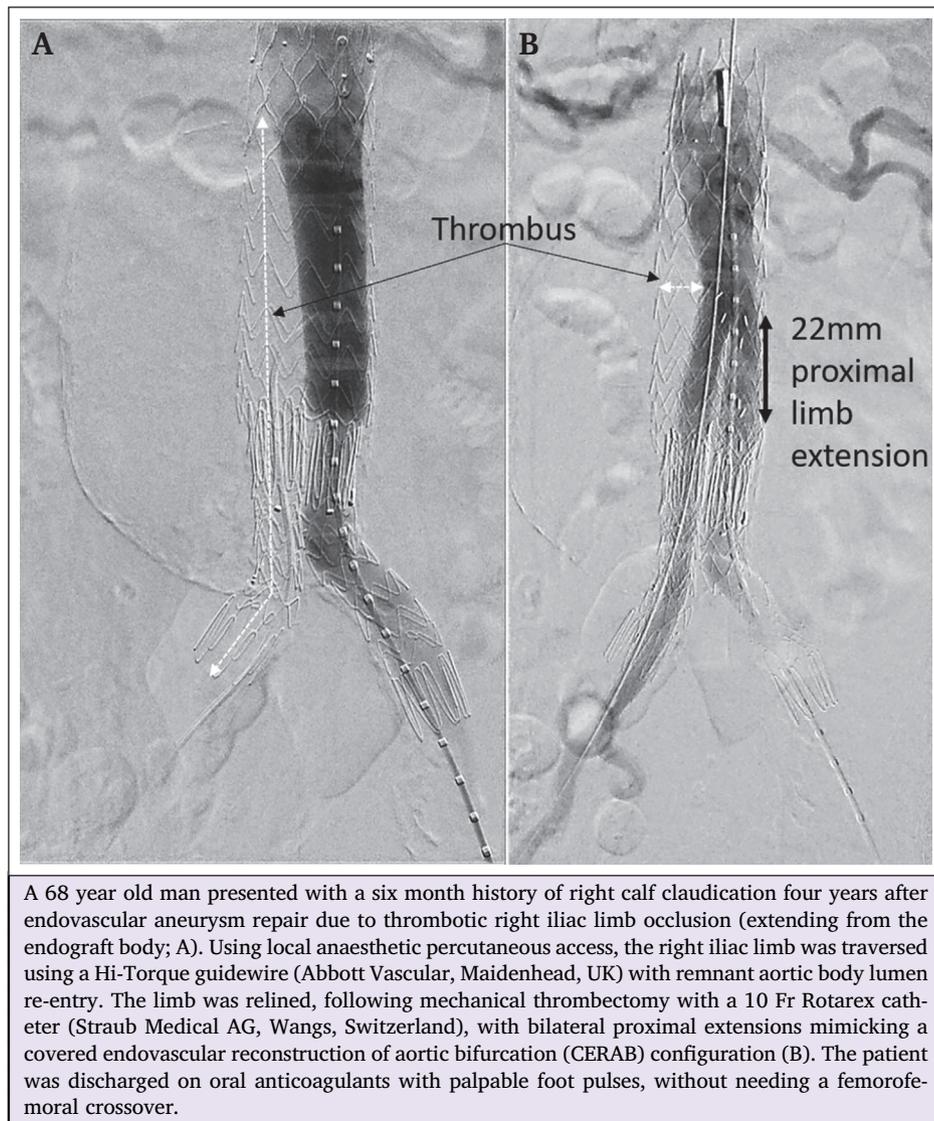
Eur J Vasc Endovasc Surg (2019) 58, 511

## COUP D'OEIL

### “CERAB” After EVAR

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