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OXFORD

BJS Open, 2021, zraa065
DOI: 10.1093/bjsopen/zraa065
Original Article

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Abstract

Background: Increased use of endovascular aneurysm repair (EVAR) and reduced open surgical repair (OSR), has decreased postoperative mortality after elective repair of abdominal aortic aneurysms (AAAs). The choice between EVAR or OSR depends on aneurysm anatomy, and the experience and preference of the vascular surgeon, and therefore differs between hospitals. The aim of this study was to investigate the current mortality risk difference (RD) between EVAR and OSR, and the effect of hospital preference for EVAR on overall mortality.

Methods: Primary elective infrarenal or juxtarenal aneurysm repairs registered in the Dutch Surgical Aneurysm Audit (2013–2017) were analysed. First, mortality in hospitals with a higher preference for EVAR (high-EVAR group) was compared with that in hospitals with a lower EVAR preference (low-EVAR group), divided by the median percentage of EVAR. Second, the mortality RD between EVAR and OSR was determined by unadjusted and adjusted linear regression and propensity-score (PS) analysis and then by instrumental-variable (IV) analysis, adjusting for unobserved confounders; percentage EVAR by hospital was used as the IV.

Results: A total of 11 997 patients were included. The median hospital rate of EVAR was 76.6 per cent. The overall mortality RD between high- and low-EVAR hospitals was 0.1 (95 per cent −0.5 to 0.4) per cent. The OSR mortality rate was significantly higher among high-EVAR hospitals than low-EVAR hospitals: 7.3 *versus* 4.0 per cent (RD 3.3 (1.4 to 5.3) per cent). The EVAR mortality rate was also higher in high-EVAR hospitals: 0.9 *versus* 0.7 per cent (RD 0.2 (−0.0 to 0.6) per cent). The RD following unadjusted, adjusted, and PS analysis was 4.2 (3.7 to 4.8), 4.4 (3.8 to 5.0), and 4.7 (4.1 to 5.3) per cent in favour of EVAR over OSR. However, the RD after IV analysis was not significant: 1.3 (−0.9 to 3.6) per cent.

Conclusion: Even though EVAR has a lower mortality rate than OSR, the overall effect is offset by the high mortality rate after OSR in hospitals with a strong focus on EVAR.

Introduction

Postoperative mortality in elective abdominal aortic aneurysm (AAA) surgery has decreased significantly since the introduction of endovascular aneurysm repair (EVAR)[1]. A meta-analysis[2] of four historical randomized trials reported an odds ratio (OR) as low as 0.40 for mortality following EVAR compared with open surgical repair (OSR). Furthermore, in the mandatory registry, the Dutch Surgical Aneurysm Audit (DSAA), there was a 4.1 per cent risk difference (RD) in mortality between EVAR and OSR (0.9 and 5.0 per cent respectively)[1,3]. For comparison, in the earlier DREAM (Dutch Randomized Endovascular Management) trial in the Netherlands, the RD between EVAR and OSR was 3.4 per cent (EVAR 1.2 per cent, OSR 4.6 per cent)[4].

The question remains whether the RD has truly increased, for example by expanding indications for EVAR, because of hospital preference, and how the mortality difference seen in clinical trials relates to the difference in observational studies reflecting practice in general. Trials include a selected group of patients and therefore might not reflect the real world[5]. However, in observational data from national registries, comparisons may be

Received: March 31, 2020. **Accepted:** November 30, 2020

biased because of both measured and unmeasured confounders[6]. For instance, confounding by indication occurs when the choice of a specific treatment is influenced by characteristics and co-morbidities of the patient, and the preference of both the patient and surgeon[7].

Changes in patient selection, hospital preference, and technical skills over time could explain the increased mortality RD between EVAR and OSR in the DSAA, compared with that in randomized trials. However, the last two factors cannot be risk-adjusted for easily. Standard statistical methods for the adjustment of measured confounders are multivariable regression analysis and propensity score analysis. However, these methods do not adjust for variables that are not or cannot be measured, such as interpretation of the anatomical characteristics of the aneurysm or the preference for one surgical procedure over the other. Possible techniques to adjust for unmeasured confounders are instrumental-variable (IV) analysis or ecological analysis[6,8].

The aim of this study was to compare overall mortality in hospitals with a high preference for EVAR with those with a low preference for EVAR to determine the current mortality RD between OSR and EVAR.

Methods

This observational study was conducted in accordance with the STROBE checklist (https://www.strobe-statement.org). First, the effect of preference for EVAR on elective AAA mortality at hospital level was examined and, second, the RD in postoperative mortality between EVAR and OSR at patient level was calculated.

Data source and participants

Consecutive patients registered in the DSAA, who underwent operation for a primary infrarenal or juxtarenal EAAA between 2013 and 2017, were included in the analysis[3]. The DSAA is a mandatory audit and registers all patients with an AAA undergoing surgical treatment in the Netherlands. Data verification was performed in 2015; 1.7 per cent of the operated patients were not registered in the DSAA, and there were no deaths among these patients[9]. Patients were excluded from the analysis if data on date of birth, date of surgery, survival status, emergency setting, or type of procedure (EVAR or OSR) were missing. Hospitals performing less than 15 procedures in 5 years were excluded from the analysis.

Outcomes

The primary outcome of this study was postoperative mortality, overall, and after OSR and EVAR, in order to determine the mortality RD between OSR and EVAR. Postoperative mortality was defined as death within 30 days of surgery or during the initial admission (30-day/in-hospital mortality).

Statistical analysis

All statistical analyses were done using R statistical software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS® version 23.0 (IBM, Armonk, New York, USA).

Hospital level

To investigate the effect of hospital preference for EVAR on postoperative mortality, hospitals were divided into two groups: The median was set at 76.6% which is a rounded digit that originates from 76.633663%. There was one hospital that had exactly this digit with a percentage of 76.63% which was also a rounded digit from 76.633663%. SPSS has allocated this hospital to the low % EVAR group.

Patient level

The RD in postoperative mortality (expressed as a percentage) between patients treated with EVAR *versus* OSR was determined in four ways: using a linear model unadjusted for confounders, a linear model adjusted for observed confounders, a propensity score analysis, and an IV analysis adjusted for unobserved confounders. Patient characteristics and hospital-related factors were compared using the *t* test and χ^2 test.

Hospitals with high versus *low percentage of endovascular repair*

The percentage of patients with an AAA treated by EVAR per hospital (treatment preference of the hospital) was used as IV for further analysis. The distribution of measured possible confounders between high- and low-EVAR groups was assessed.

Unadjusted linear regression analysis

Crude mortality rates in patients treated with EVAR and OSR were compared using a linear regression model. When considering a binary outcome, it is standard practice to use logistic regression, with the effect size estimated as an OR. Linear regression was used here, however, to estimate the effect as a RD.

Adjusted linear regression analysis

To correct for observed confounders, a linear regression model was used to compare adjusted mortality rates in patients treated with EVAR *versus* OSR. Patient characteristics that influenced mortality were selected by univariable logistic regression. The adjusted RD for mortality was calculated by multivariable linear regression analysis.

Propensity score risk adjustment

This was carried out in two steps. In the first step, a multivariable logistic regression analysis was undertaken, including every variable associated with choice of treatment in univariable analysis. In the second step, the RD was estimated by multivariable linear regression analysis for the primary outcome, postoperative mortality, adjusted for the propensity score obtained in step 1 and the choice of treatment as predictors.

Instrumental-variable analysis

First, a rough calculation was made, on the basis of the distribution in the two hospital groups. Then, for the IV analysis, the proportion of patients treated with EVAR at each centre was used as an IV to adjust for unobserved confounders by the two-stage least squares (2SLS) method. First, the proportion of EVAR in each hospital was computed from the hospital identifier. Next, a model for mortality was fitted with the predicted probability of EVAR as the only co-variable.

An IV analysis can be used to estimate the effect of a treatment in observational data, corrected for unobserved confounders. An IV is a factor that strongly influences the choice of treatment, but which has no independent influence on patient outcome. Thus, an IV is not related to the prognosis of the patient. When carrying out IV analysis, individual patients with differing treatments are not compared, but rather the outcomes of patients with a different chance of receiving a certain treatment. Methods of IV analysis are described in detail elsewhere[6].

When using IV analysis to compare mortality after OSR and EVAR in patients with an AAA, it was necessary to make two

essential assumptions, based on earlier results from the DSAA: that patients with an AAA are divided randomly over all hospitals that perform AAA surgery in the Netherlands[1], and that the quality of AAA-related care is equal in each hospital[1].

The strength of the IV was tested by means of the partial F-statistic. The co-variables used in this model were the same as those in the first step of the propensity score analysis, except that the actual treatment was not in the model. The outcome was reported as an RD between EVAR and OSR.

Results

A total of 12 350 patients were registered. After application of the exclusion criteria, 12 009 patients (97.6 per cent) were analysed. One hospital that registered 12 patients in 5 years was excluded, leaving 11 997 patients who underwent elective AAA repair (*Fig. 1*).

Descriptive data

Of these patients, 9255 (77.1 per cent) were treated with EVAR without conversion, in 24 (0.2 per cent) the procedure was converted from EVAR to OSR and analysed in the EVAR group, and 2718 patients (22.7 per cent) underwent OSR. The percentage of EVAR varied between hospitals (range 53.4–100 per cent), with a mean of 77.3 per cent and median of 76.6 per cent. There were 5961 patients in the high-EVAR group and 6036 in the low-EVAR group. The mean rates of EVAR were 85.7 per cent *versus* 69.1 per cent respectively (mean difference 16.6 per cent). There were 28 high-EVAR hospitals (including 8 university/large teaching hospitals) and 34 low-EVAR hospitals (including 9 university/large teaching hospitals). *Table 1* shows baseline characteristics. Patients who had EVAR were older, more often men, had smaller AAA diameters, and fewer co-morbidities.

The mean overall OSR volume was 52 (range 0–118) patients per hospital: 35 (0–68) in high-EVAR hospitals and 69 (17–118) in low-EVAR hospitals The mean overall EVAR volume was 185 (32–387) patients per hospital: 205 (101–382) in high-EVAR hospitals and 164 (32–387) in low-EVAR hospitals. Information about suprarenal clamping was registered for 1545 consecutive procedures since 2015: 1011 patients in low-EVAR hospitals and 534 patients in high-EVAR hospitals. Of these patients, 256 (25.3 per cent) and 167 (31.3 per cent) respectively underwent suprarenal clamping (OR 1.34, 95 per cent c.i. 1.07 to 1.69; $P = 0.013$).

Outcome data

Outcome by hospital preference: endovascular versus *open repair*

Table 2 shows the postoperative mortality rate in high- and low-EVAR hospitals, with a RD of 0.1 (95 per cent c.i. −0.5 to 0.4) per cent, which was not statistically significant. The mortality rate of 7.3 per cent after OSR in high-EVAR hospitals was significantly higher than the 4.0 per cent in low-EVAR hospitals (RD 3.3 (1.4 to 5.3) per cent). The EVAR mortality rate was also higher in high-EVAR hospitals: 0.9 *versus* 0.7 per cent (RD 0.2 (−0.0 to 0.6) per cent). To understand differences in outcome related to hospital preference for EVAR, confounding variables were analysed for

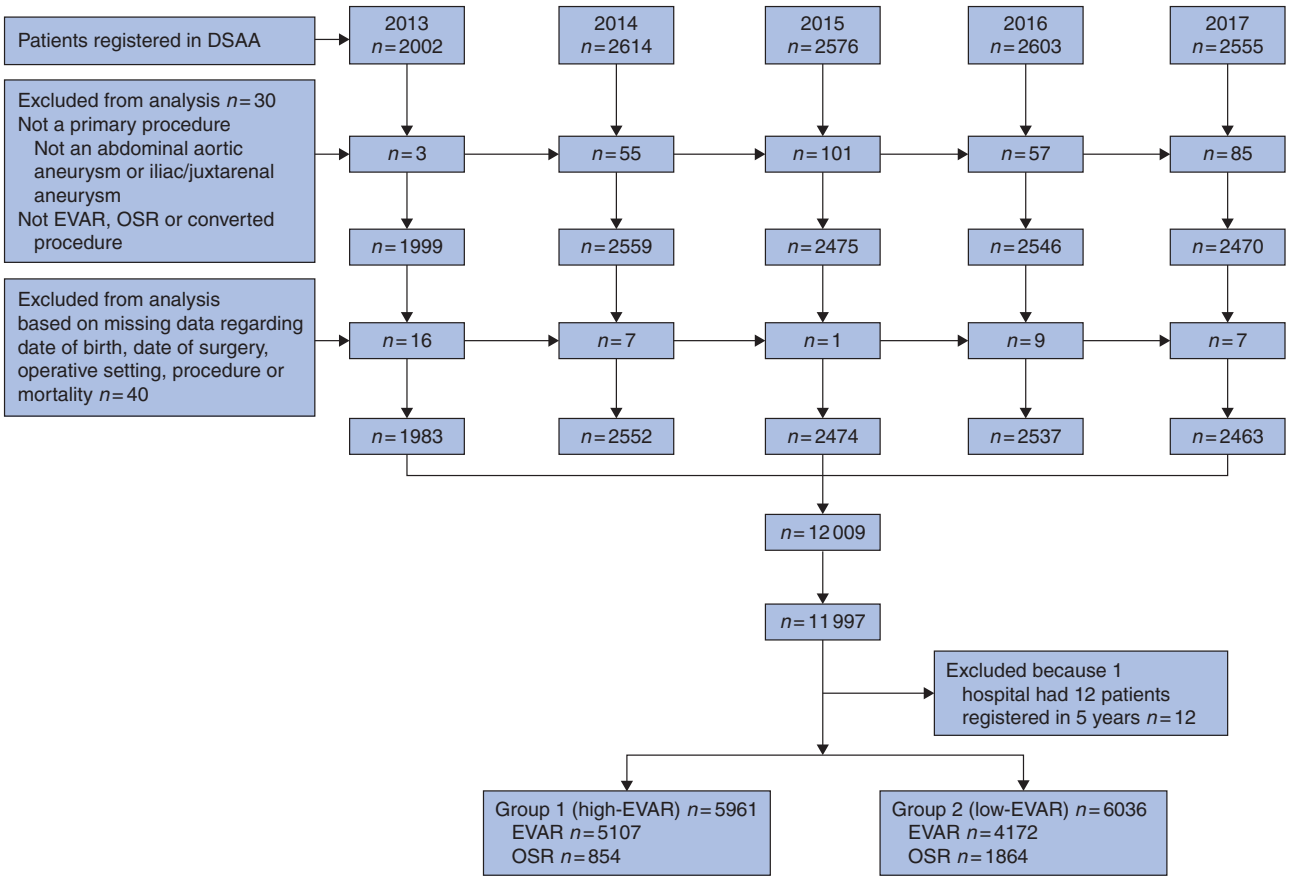

Fig. 1 Study flow diagram

EVAR, endovascular aneurysm repair; OSR, open surgical repair; DSAA, Dutch Surgical Aneurysm Audit.

Table 1 Baseline characteristics by type of procedure and by hospital use of endovacular repair

	Type of procedure		P‡	Hospital use of EVAR		P‡
	EVAR (*n* = 9279)	OSR (*n* = 2718)		High-EVAR group (*n* = 5961)	Low-EVAR group (*n* = 6036)	
Age (years)*	73.8 (7.5)	70.5 (7.6)	<0.001§	73.3 (7.7)	72.8 (7.7)	0.001§
Sex						
M	8086 (87.1)	2186 (80.4)	<0.001	5123 (85.9)	5149 (85.3)	0.567
F	1190 (12.8)	530 (19.5)		836 (14.0)	884 (14.6)	
Missing	3 (0.0)	2 (0.1)		2 (0.0)	3 (0.1)	
Cardiology						
No cardiac problems	4191 (45.2)	1205 (44.3)	0.002	2952 (49.5)	2444 (40.5)	<0.001
Peripheral oedema	811 (8.7)	191 (7.0)		464 (7.8)	538 (8.9)	
Raised CVP	153 (1.6)	35 (1.3)		59 (1.0)	129(2.1)	
Medication†	3797 (40.9)	1205 (44.3)		2250 (37.7)	2752 (45.6)	
Unknown	327 (3.5)	82 (3.0)		236 (4.0)	173 (2.9)	
Pulmonary co-morbidity						
No dyspnoea	6840 (73.7)	2015 (74.1)	0.035	4416 (74.1)	4439 (73.5)	<0.001
Dyspnoea on exercise	1927 (20.8)	573 (21.1)		1265 (21.2)	1235 (20.5)	
Dyspnoea on mild exertion	302 (3.3)	60 (2.2)		188 (3.2)	174 (2.9)	
Dyspnoea at rest	90 (1.0)	24 (0.9)		52 (0.9)	62 (1.0)	
Unknown/missing	120 (1.3)	46 (1.7)		40 (0.7)	126 (2.1)	
Malignancy						
No malignancy	7313 (78.8)	2286 (84.1)	<0.001	4777 (80.1)	4822 (79.9)	0.438
Malignancy	1904 (20.5)	412 (15.2)		1138 (19.1)	1178 (19.5)	
Unknown	62 (0.7)	20 (0.7)		46 (0.8)	36 (0.6)	
Aneurysm diameter (mm)*	59.2 (10.2)	61.7 (13.0)	<0.001§	59.5 (10.8)	60.0 (11.0)	0.012§
ECG						
No abnormalities	4902 (52.8)	1519 (55.9)	<0.001	3314 (55.6)	3107 (51.5)	<0.001
Atrial fibrillation	684 (7.4)	149 (5.5)		399 (6.7)	434 (7.2)	
MI or other	2753 (29.7)	862 (31.7)		1656 (27.8)	1959 (32.5)	
Unknown	940 (10.1)	188 (6.9)		592 (9.9)	536 (8.9)	
Creatinine						
Normal	6070 (65.4)	1766 (65.0)	0.206	3943 (66.1)	3893 (64.5)	<0.001
Abnormal	3007 (32.4)	877 (32.3)		1926 (32.3)	1958 (32.4)	
Unknown	202 (2.2)	75 (2.8)		92 (1.5)	185 (3.1)	
Sodium						
Normal	7903 (85.2)	2371 (87.2)	<0.001	5031 (84.4)	5243 (86.9)	<0.001
Abnormal	464 (5.0)	148 (5.4)		304 (5.1)	308 (5.1)	
Unknown	912 (9.8)	199 (7.3)		626 (10.5)	485 (8.0)	
Potassium						
Normal	8113 (87.4)	2374 (87.3)	0.001	5208 (87.4)	5279 (87.5)	0.983
Abnormal	520 (5.6)	194 (7.1)		355 (6.0)	359 (5.9)	
Unknown	646 (7.0)	150 (5.5)		398 (6.7)	398 (6.6)	
WBC count (× 10^9/l)*	8.3(1.9)	8.6(2.1)	<0.001§	8.4(2.0)	8.4(2.0)	0.501§
Systolic BP (mmHg)*	140(20)	141(20)	0.007§	140(20)	141(20)	<0.001§
Pulse rate (b.p.m)						
60–100	7207 (77.7)	2129 (78.3)	0.478	4724 (79.2)	4612 (76.4)	<0.001
< 60 or >100	1554 (16.7)	430 (15.8)		1013 (17.0)	971 (16.1)	
Unknown	518 (5.6)	159 (5.8)		224 (3.8)	453 (7.5)	
Haemoglobin (mmol/l)*	8.7(1.0)	8.6(1.0)	0.006	8.7(1.0)	8.7(1.0)	0.089

A Values in parentheses are percentages unless indicated otherwise; *values are mean(s.d.). †ntihypertensives, antianginals, diuretics or digoxin. Normal ranges used for blood tests: creatinine 45–100 μmol/l, sodium 135–145 mmol/l, potassium 3.5–5.0 mmol/l. EVAR, endovascular aneurysm repair; OSR, open surgical repair; CVP, central venous pressure; MI, myocardial infarction; WBC, white blood cell count. ‡χ^2 test, except §t test.

Table 2 Crude analysis of mortality by preference of hospital for endovascular aneurysm repair and procedure type

	Mortality rate		
	OSR	EVAR	Overall
High-EVAR group	62 of 854 (7.3)	46 of 5107 (0.9)	108 of 5961 (1.8)
Low-EVAR group	75 of 1864 (4.0)	29 of 4172 (0.7)	104 of 6036 (1.7)
Odds ratio*	1.87 (1.32, 2.64)	1.30 (0.81, 2.07)	1.05 (0.80, 1.38)

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. Rates are those recorded in the Dutch Surgical Aneurysm Audit. OSR, open surgical repair; EVAR, endovascular aneurysm repair.

both OSR and EVAR in high- and low-EVAR hospitals (*Table 3*). In high-EVAR hospitals, patients in both treatment groups had significantly less co-morbidity.

Unadjusted analysis

The overall crude mortality rate was 1.8 per cent (212 patients): 0.8 per cent (75 patients) after EVAR and 5.0 per cent (137 patients) after OSR (RD 4.2 (95 per cent c.i. 3.7 to 4.8) per cent).

Adjusting for observed confounders

Potential confounding variables following univariable analysis for the outcome mortality were sex, age, cardiopulmonary status,

Table 3 Baseline characteristics by type of procedure in relation to hospital use of endovascular aneurysm repair

	OSR		P‡	EVAR		P‡
	Low-EVAR group (*n* = 1864)	High-EVAR group (*n* = 854)		Low-EVAR group (*n* = 4172)	High-EVAR group (*n* = 5107)	
Age (years)*	70.7 (7.7)	70.3 (7.4)	0.225§	73.8 (7.5)	73.8 (7.6)	0.928§
Sex						
M	1510 (81.0)	676 (79.2)	0.314	3639 (87.2)	4447 (87.1)	0.904
F	352 (18.9)	178 (20.8)		532 (12.8)	658 (12.9)	
Missing	2 (0.1)	0 (0.0)		1 (0.0)	2 (0.0)	
Cardiology						
No cardiac problems	765 (41.0)	440 (51.5)	<0.001	1679 (40.2)	2512 (49.2)	<0.001
Peripheral oedema	147 (7.9)	44 (5.2)		391 (9.4)	420 (8.2)	
Raised CVP	31 (1.7)	4 (0.5)		98 (2.3)	55 (1.1)	
Medication†	865 (46.4)	340 (39.8)		1887 (45.2)	1910 (37.4)	
Unknown	56 (3.0)	26 (3.0)		117 (2.8)	210 (4.1)	
Pulmonary co-morbidity						
No dyspnoea	1394 (74.8)	621 (72.7)	0.139	3045 (73.0)	3795 (74.3)	<0.001
Dyspnoea on exercise	385 (20.7)	188 (22.0)		850 (20.4)	1077 (21.1)	
Dyspnoea on mild exertion	35 (1.9)	25 (2.9)		139 (3.3)	163 (3.2)	
Dyspnoea at rest	14 (0.8)	10 (1.2)		48 (1.2)	42 (0.8)	
Unknown/missing	36 (1.9)	10 (1.2)		90 (2.2)	30 (0.6)	
Malignancy						
No malignancy	1572 (84.3)	714 (83.6)	0.862	3250 (77.9)	4063 (79.6)	0.044
Malignancy	279 (15.0)	133 (15.6)		899 (21.5)	1005 (19.7)	
Unknown	13 (0.7)	7 (0.8)		23 (0.6)	39 (0.8)	
Aneurysm diameter (mm)*	61.6(12.7)	61.8(13.7)	0.757§	59.3 (10.1)	59.1 (10.2)	0.449§
ECG						
No abnormalities	994 (53.3)	525 (61.5)	<0.001	2113 (50.6)	2789 (54.6)	<0.001
Atrial fibrillation	115 (6.2)	34 (4.0)		319 (7.6)	365 (7.1)	
MI or other	612 (32.8)	250 (29.3)		1347 (32.3)	1406 (27.5)	
Unknown	143 (7.7)	45 (5.3)		393 (9.4)	547 (10.7)	
Creatinine						
Normal	1200 (64.4)	566 (66.3)	0.140	2693 (64.5)	3377 (66.1)	<0.001
Abnormal	605 (32.5)	272 (31.9)		1353 (32.4)	1654 (32.4)	
Unknown	59 (3.2)	16 (1.9)		126 (3.0)	76 (1.5)	
Sodium						
Normal	1640 (88.0)	731 (85.6)	0.222	3603 (86.4)	4300 (84.2)	0.001
Abnormal	95 (5.1)	53 (6.2)		213 (5.1)	251 (4.9)	
Unknown	129 (6.9)	70 (8.2)		356 (8.5)	556 (10.9)	
Potassium						
Normal	1633 (87.6)	741 (86.8)	0.503	3646 (87.4)	4467 (87.5)	0.977
Abnormal	126 (6.8)	68 (8.0)		233 (5.6)	287 (5.6)	
Unknown	105 (5.6)	45 (5.3)		293 (7.0)	353 (6.9)	
WBC count (× 10^9/l)*	8.5 (2.1)	8.7(2.2)	0.169§	8.3 (1.9)	8.4 (1.9)	0.168§
Systolic BP (mmHg)*	141 (20)	141 (21)	0.291§	141 (20)	139 (20)	0.002§
Pulse rate (b.p.m)						
60–100	1446 (77.6)	683 (80.0)	0.031	3166 (75.9)	4041 (79.1)	<0.001
< 60 or > 100	294 (15.8)	136 (15.9)		677 (16.2)	877 (17.2)	
Unknown	124 (6.7)	35 (4.1)		329 (7.9)	189 (3.7)	
Haemoglobin (mmol/l)*	8.6 (1.0)	8.6 (1.0)	0.879§	8.7 (1.0)	8.7 (1.0)	0.162§

Values in parentheses are percentages unless indicated otherwise; *values are mean(s.d.). †Antihypertensives, antianginals, diuretics or digoxin. Normal ranges used for blood tests: creatinine 45–100 μmol/l, sodium 135–145 mmol/l, potassium 3.5–5.0 mmol/l. EVAR, endovascular aneurysm repair; OSR, open surgical repair; CVP, central venous pressure; MI, myocardial infarction; WBC, white blood cell count. ‡χ^2 test, except §t test.

abnormality on ECG, AAA diameter, sodium, potassium, creatinine, and haemoglobin levels, and year of surgery. Adjusting for these resulted in an RD of 4.4 (95 per cent c.i. 3.8 to 5.0) per cent.

Propensity score risk adjustment

Two models were fitted. The first was a model to estimate the probability of EVAR, given the co-variables selected by univariable analysis: the propensity score (*Table 4*). The second model estimated the EVAR/OSR effect, with adjustment for the propensity score. The RD was estimated at 4.7 (95 per cent c.i. 4.1 to 5.3) per cent in favour of treatment with EVAR.

Adjusting for unobserved confounders

Hospitals were divided into high-EVAR *versus* low-EVAR hospitals, according to the percentage of patients treated by EVAR, and the (dichotomized) percentage used as an IV. The mean difference in EVAR treatment was 16.6 per cent between high- and low-EVAR hospitals. The overall RD in postoperative mortality was 0.1 per cent (*Table 2*). Therefore, the mortality advantage of EVAR compared with OSR was 0.6 per cent (0.1 per cent/0.166). This was a crude number, but much lower than the RDs calculated from unadjusted and adjusted analyses.

On the basis of IV analysis (2SLS with percentage EVAR per hospital as IV), the RD was estimated at 1.3 (95 per cent c.i. –0.9 to 3.6) per cent in favour of EVAR over OSR and the strength of the instrument was good (F-statistic: 1.286 on 1 and 11 995 d.f.; $P = 0.257$).

Table 4 Propensity scores for treatment by endovascular repair

	Odds ratio
Female sex	0.50 (0.44, 0.56)
Age (per year)	1.07 (1.06, 1.08)
Year of surgery	
2013	1.00 (reference)
2014	1.22 (1.05, 1.41)
2015	1.52 (1.31, 1.77)
2016	1.37 (1.18, 1.59)
2017	1.36 (1.17, 1.58)
% **EVAR**	1.06 (1.06, 1.07)
Aneurysm size (per mm)	0.97 (0.97, .98)
Systolic BP	1.00 (0.99, 1.00)
Haemoglobin (mmol/l)	1.01 (1.05, 1.15)
White blood cell count	0.96 (0.94, 0.98)
Sodium	
Normal	1.00 (reference)
High or low	1.01 (0.82, 1.25)
Unknown	1.09 (0.81, 1,47)
Potassium	
Normal	1.00 (reference)
High or low	0.78 (0.64, 0.93)
Unknown	1.26 (0.90, 1.77)
Malignancy	
No malignancy	1.00 (reference)
Any malignancy	1.30 (1.15, 1.47)
Unknown	0.77 (0.44, 1.33)
ECG	
Normal	1.00 (reference)
Atrial fibrillation	1.09 (0.88, 1.34)
MI or any other abnormal result	0.88 (0.79, 0.98)
Unknown	1.35 (1.13, 1.62)
Cardiac co-morbidity	
None	1.00 (reference)
Peripheral oedema	1.15 (0.95, 1.39)
Raised CVP	1.74 (1.16, 2.60)
Medication for hypertension	0.95 (0.86, 1.05)
Unknown	0.87 (0.66, 1.15)
Pulmonary co-morbidity	
None	1.00 (reference)
Dyspnoea on exercise	1.00 (0.89, 1.12)
Dyspnoea on mild exertion	1.57 (1.16, 2.12)
Dyspnoea at rest	1.47 (0.90, 2.39)
Unknown	0.91 (0.62, 1.32)

Values in parentheses are 95 per cent confidence intervals. Normal ranges used for blood tests: sodium 135–145 mmol/l, potassium 3.5–5.0 mmol/l. EVAR, endovascular aneurysm repair; MI, myocardial infarction, CVP, central venous pressure.

Discussion

This study showed that hospitals with a higher preference for EVAR provided no benefit in overall postoperative mortality over hospitals with a lower preference for EVAR. The postoperative mortality rate after OSR in high-EVAR hospitals was 7.3 per cent, with a RD of 3.3 per cent in favour of low-EVAR hospitals. After adjustment for known confounders, the RD was 4.4 per cent. IV analysis resulted in a RD of 1.3 per cent in favour of EVAR, which was not statistically significant.

This apparent paradox requires explanation assuming that IV analysis, by the adjustment for unknown confounders, generates a more reliable outcome estimate. Does this mean that there is really no difference in postoperative mortality between EVAR and OSR, or does a strong preference for EVAR not give better overall results owing to the high mortality rate in the residual group of patients undergoing OSR? What is the reason for the high mortality rate in this group?

Taking the results of the various statistical analyses together, EVAR had a lower postoperative mortality rate than OSR. However, this advantage is likely to be contingent on the procedure being performed by an experienced surgeon in an anatomically favourable patient. The IV analysis attempted to take such caveats into account. However, it did so at the expense of increased uncertainty, which resulted in loss of formal statistical significance. The results of IV analysis are expected to be somewhere between those of RCTs and observational studies[10]. This is because RCTs are optimized by patient selection and tend to overestimate the effect of clinical practice, whereas observational data might be subject to bias because of confounders that need to be adjusted for[10]. When the IV is strong and valid, the RD would ideally approach those presented in RCTs[10]. However, in the Netherlands, after adjustment for non-observed confounders in the IV analysis, EVAR seemed to result in a non-significantly lower postoperative mortality rate compared with OSR.

There may be three reasons for this finding: by correcting for unobserved confounding, bias is removed and the effect is smaller; by replacement of the actual treatment by the expected treatment, there is a major loss of information and therefore a loss of power; and choosing an IV, as explained in the methods section, means that the hospital is a proxy for the choice of treatment and that the outcome depends only on the choice of treatment and not the hospital or practitioner. However, in IV analysis there may still be hidden bias at hospital level with regard to degree of surgical skill and hospital infrastructure[8]. In addition, the applicability of IV analysis can be questioned when there is doubt about the two assumptions described in the methods section[11]. For example, did hospitals with worse results for either treatment affect the IV analysis?

The results of OSR were worse in high-EVAR hospitals even though the patients had less co-morbidity. This could be because a focus on EVAR left only relatively more complex cases being treated with OSR, but this information was not available from the DSAA. The higher mortality rate after OSR in hospitals with a relative preference for EVAR is not in line with published findings. A recent meta-analysis[12] concluded that the postoperative mortality rate after OSR in the pre-EVAR and post-EVAR eras is almost the same at around 2 per cent. Patients who underwent OSR in the post-EVAR era had more complex anatomy, but were shown to be fitter, resulting in an unchanged overall postoperative mortality rate[12,13]. High-EVAR hospitals had a higher percentage of suprarenal clamping than low-EVAR hospitals in the present study, with a difference of 6.0 per cent. However, according to the literature, suprarenal clamping may result in increased morbidity but hardly affects mortality[14]. Where suprarenal clamping is necessary, mortality is comparable to that in patients undergoing OSR and infrarenal clamping[15].

Although it is clear that short-term mortality has decreased since the implementation of EVAR, there are some controversies regarding the results of OSR[1,16]. SWEDVASC reported a decrease in OSR mortality from 4.7 to 2.7 per cent in 17 years, but VASCUNET documented an increase to 4.4 per cent[17]. A recent publication[18] comparing 10-year results in Sweden and the UK described an overall mortality rate of 2.3 and 3.4 per cent respectively. Although the mortality rate after EVAR was slightly higher in both countries (1.5 and 1.4 per cent) than in the present study of patients registered over 5 years in the DSAA, the mortality rate for OSR was lower (3.1 and 4.7 per cent). The percentage of EVAR performed did not exceed 50 per cent in 10 years, but showed a gradual increase in the implementation of EVAR towards 70–80 per cent in 2012[18]. The percentage of EVAR performed in the UK was, however, similar to the mean percentage of EVAR during the 5 years of the DSAA (77.1 per cent) , but the mortality rate after

OSR in the DSAA was also similar to that reported in the UK (4.7 *versus* 5.0 per cent). Although a gradual increase in implementation of EVAR did decrease overall mortality and showed similar results for OSR, high-EVAR hospitals in the DSAA, with a mean percentage EVAR of 85.7 per cent, had a mortality rate of 7.3 per cent after OSR. Interestingly low-EVAR hospitals (mean 69.1 per cent EVAR) had an OSR mortality rate of only 4.0 per cent, which is more in accordance with other results reported for OSR in the literature[17]. Based on IV analysis, applying a low threshold for EVAR did not lead to a definite mortality benefit for the entire patient group. This arises the question whether how or if OSR should be maintained and for what cost.[16] An explanation would be that the low threshold for EVAR may result in EVAR being carried out in relatively more complex cases, more chimneys (ChEVAR) and fenestrations (FEVAR).[12] This strategy leaves the relatively more complex cases in the OSRgroup, but unfortunately this could not be analyzed with the DSAA data. Consequently, these more complex procedures approximate the results of OSR.[15,19] In addition, lower hospital volumes overall or regarding one specific procedure will lead to less experience, and therefore less good results.

A main limitation of this study, in common with other observational studies, is patient selection. The turndown rate for surgery may have differed between hospitals, and there may have been referral selection, meaning that choices of treatment might have been different. However, in this data set, the university and large teaching hospitals were divided equally between high- and low-EVAR groups. High-EVAR centres did not have more co-morbidities registered, but the severity of co-morbidities is difficult to capture, even with the items included in the V-POSSUM[20,21]. It is possible that patients with difficult anatomy were referred selectively to high-volume hospitals, leading to a higher mortality rate in the OSR group in such hospitals. Missing values are another potential limitation, but there were few in this study.

Collaborators*

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Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure. The authors declare no conflict of interest .

References

1. Lijftogt N, Vahl AC, Wilschut ED, Elsman BHP, Amodio S, van Zwet EW *et al.* Adjusted hospital outcomes of abdominal aortic

aneurysm surgery reported in the Dutch Surgical Aneurysm Audit. *Eur J Vasc Endovasc Surg* 2017;**53**:520–532
2. Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin J-P *et al.* Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *Br J Surg* 2017;**104**:166–178
3. Dutch Institute for Clinical Auditing. www.clinicalaudit.nl
4. Prinssen M, Verhoeven EL, Buth J, Cuypers PWM, van Sambeek MRHM, Balm R *et al.* A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;**351**:1607–1618
5. Stansby G, Earnshaw J. Open repair *versus* endovascular stent graft repair of abdominal aortic aneurysms: do we need more randomized clinical trials? *Angiology* 2014;**65**:457–458
6. Baiocchi M, Cheng J, Small DS. Instrumental variable methods for causal inference. *Stat Med* 2014;**33**:2297–2340
7. Steyerberg E. *Clinical Prediction Models; A Practical Approach to Development, Validation, and Updating* (1st edn). Springer-Verlag New York, 2009.
8. Johnston SC. Combining ecological and individual variables to reduce confounding by indication: case study—subarachnoid hemorrhage treatment. *J Clin Epidemiol* 2000;**53**:1236–1241
9. Eindrapport dataverificatie, betreffende de verificatie van de Dutch Surgical Aneurysm Audit (DSAA) over registratiejaar 2015; december 2016 available at http://dica.nl/media/660/Eindrapport_dataverificatie_DSAA_2016.pdf
10. Stukel TA, Fisher ES, Wennberg DE, Alter DA, Gottlieb DJ, Vermeulen MJ. Analysis of observational studies in the presence of treatment selection bias: effects of invasive cardiac management on AMI survival using propensity score and instrumental variable methods. *JAMA* 2007;**297**:278–285
11. Crown WH, Henk HJ, Vanness DJ. Some cautions on the use of instrumental variables estimators in outcomes research: how bias in instrumental variables estimators is affected by instrument strength, instrument contamination, and sample size. *Value Health* 2011;**14**:1078–1084
12. Kontopodis N, Tavlas E, Georgakarakos E, Galanakis N, Chronis C, Tsetis D *et al.* Has anatomic complexity of abdominal aortic aneurysms undergoing open surgical repair changed after the introduction of endovascular treatment? Systematic review and meta-analysis of comparative studies. *Ann Vasc Surg* 2018;**52**:292–301
13. Barshes NR, McPhee J, Ozaki CK, Nguyen LL, Menard MT, Gravereaux E *et al.* Increasing complexity in the open surgical repair of abdominal aortic aneurysms. *Ann Vasc Surg* 2012;**26**:10–17
14. Jongkind V, Yeung KK, Akkersdijk GJ, Heidsieck D, Reitsma JB, Tangelder GJ *et al.* Juxtarenal aortic aneurysm repair. *J Vasc Surg* 2010;**52**:760–767
15. Dubois L, Durant C, Harrington DM, Forbes TL, Derose G, Harris JR. Technical factors are strongest predictors of postoperative renal dysfunction after open transperitoneal juxtarenal abdominal aortic aneurysm repair. *J Vasc Surg* 2013;**57**:648–654
16. Budtz-Lilly J, Venermo M, Debus S, Behrendt C-A, Altreuther M, Beiles B *et al.* Editor's choice—assessment of international outcomes of intact abdominal aortic aneurysm repair over 9 years. *Eur J Vasc Endovasc Surg* 2017;**54**:13–20
17. Mani K, Bjorck M, Wanhainen A. Changes in the management of infrarenal abdominal aortic aneurysm disease in Sweden. *Br J Surg* 2013;**100**:638–644
18. Karthikesalingam A, Grima MJ, Holt PJ, Vidal-Diez A, Thompson MM, Wanhainen A *et al.* Comparative analysis of the outcomes of elective abdominal aortic aneurysm repair in England and Sweden. *Br J Surg* 2018;**105**:520–528
19. de Beaufort HWL, Cellitti E, de Ruiter QMB, Conti M, Trimarchi S, Moll F *et al.* Midterm outcomes and evolution of gutter area after endovascular aneurysm repair with the chimney graft procedure. *J Vasc Surg* 2018;**67**:104.e3–112.e3
20. Prytherch DR, Ridler BM, Beard JD, Earnshaw JJ; Audit and Research Committee, Vascular Surgical Society of Great Britian and Ireland. A model for national outcome audit in vascular surgery. *Eur J Vasc Endovasc Surg* 2001;**21**:477–483
21. Prytherch DR, Sutton GL, Boyle JR. Portsmouth POSSUM models for abdominal aortic aneurysm surgery. *Br J Surg* 2001;**88**:958–963