



ELSEVIER



## REVIEW

# A Meta-analysis and Metaregression Analysis of Factors Influencing Mortality after Endovascular Repair of Ruptured Abdominal Aortic Aneurysms<sup>☆</sup>

C.D. Karkos<sup>a,b,\*</sup>, A.J. Sutton<sup>c</sup>, M.J. Bown<sup>b</sup>, R.D. Sayers<sup>b</sup>

<sup>a</sup> The 5th Department of Surgery, Medical School, Aristotle University of Thessaloniki, Hippocratio Hospital, Thessaloniki, Greece

<sup>b</sup> The Department of Cardiovascular Sciences, Vascular Surgery Group, University of Leicester, Leicester, UK

<sup>c</sup> The Department of Health Sciences, University of Leicester, Leicester, UK

Submitted 9 March 2011; accepted 19 July 2011

**KEYWORDS**

Endovascular repair;  
Ruptured abdominal  
aortic aneurysms;  
Mortality;  
Prognostic risk factors;  
Meta-analysis;  
Metaregression

**Abstract** *Objective:* To determine factors that may influence the perioperative mortality after endovascular repair of ruptured abdominal aortic aneurysms (RAAAs) using metaregression analysis. *Methods:* A meta-analysis of all English-language literature with information on mortality rates after endovascular repair of RAAAs was conducted. A metaregression was subsequently performed to determine the impact on mortality of the following 8 factors: patient age; mid-time study point; anaesthesia; endograft configuration; haemodynamic instability; use of aortic balloon; conversion to open repair; and abdominal compartment syndrome.

*Results:* The pooled perioperative mortality across the 46 studies (1397 patients) was 24.3% (95% CI: 20.7–28.3%). Of the 8 variables, only bifurcated approach was significantly associated with reduced mortality ( $p = 0.005$ ). A moderate negative correlation was observed between bifurcated approach and haemodynamic instability ( $-0.35$ ). There was still a strong association between bifurcated approach and mortality after simultaneously adjusting for haemodynamic instability, indicating that the latter was not a major factor in explaining the observed association.

*Conclusions:* Endovascular repair of RAAAs is associated with acceptable mortality rates. Patients having a bifurcated endograft were less likely to die. This may be due to some surgeons opting for a bifurcated approach in patients with better haemodynamic condition. Further studies will be needed to clarify this.

© 2011 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

<sup>☆</sup> An abstract based on this work was presented at CIRSE 2011, 10-14 September 2011, Munich, Germany.

\* Corresponding author. C.D. Karkos, The 5th Department of Surgery, Medical School, Aristotle University of Thessaloniki, Hippocrateio Hospital, Konstantinoupoleos 49, Thessaloniki 546 42, Greece. Tel.: +30 2310 892162; fax: +30 2310 992886.

E-mail address: ckarkos@hotmail.com (C.D. Karkos).

The introduction of endovascular therapy in the treatment of ruptured abdominal aortic aneurysms (RAAAs) remains a hot topic. Several series, mostly single-centre retrospective reports with small number of patients, have been published to date with some of the results being very promising. Recent meta-analyses estimated the pooled mortality across the published series to be around 24%, but the reported mortality figures of individual studies ranged between 0% and 54%.<sup>1,2</sup> Given this wide variation in the literature results, debate continues whether the outcome of such patients can be improved by endovascular surgery. If the latter goal is to be achieved, elucidation of factors affecting the perioperative results after endovascular repair is needed. Since large original studies on the subject are not yet available, such evidence could be derived by meta-analysing the existing relevant literature. The aim of this meta-analysis was to investigate which factors may influence the operative mortality of endovascular treatment of RAAAs by performing a metaregression analysis of previously published data.

## Methods

An English-language literature review was undertaken through to February 2010 to define the role of endovascular management of RAAAs and identify factors that may influence outcome. This article was prepared according to previously published guidelines for reporting meta-analyses of observational studies.<sup>3</sup>

### Search strategy

The lead author (CDK) performed the literature search. Both the Medline and EMBASE databases were searched using a combination of the terms: 'Endovascular surgery' or 'Endovascular repair' or 'Stents' or 'Stent grafts' and 'Abdominal aortic aneurysm' or 'Aortic aneurysm, abdominal' and 'Rupture' or 'Aortic rupture' or 'Aneurysm rupture'. Both the 'exp' ('explode', i.e., all sub-categorisations are included in the search) and 'mp' ('multipurpose search') tools were used. The electronic search was supplemented by a manual search of the reference lists of relevant articles.

### Study selection

All articles that gave mortality figures following endovascular surgery for RAAA were included in the analysis. Only patients with true ruptures were included. Studies were rejected if they described only selected groups of patients (such as octogenarians), or were single case reports. In case of studies reporting on duplicate clinical material, the most recent study or the larger of the two was selected for analysis.

### Data extraction

Selection of studies and data abstracting were performed by one of the authors (CDK). The primary outcome measure was perioperative mortality, defined as all 'perioperative', 'in-

hospital' and '30-day' mortality. When information on both 'in-hospital' and '30-day' mortality was available, the latter was used for the analysis. Additionally, information on average age of study population (mean or median), mid-time point of the study (the date half-way through the study time period), type of anaesthesia, endograft configuration, haemodynamic instability, use of intra-aortic occlusion balloon, conversion to open repair and the development of abdominal compartment syndrome was sought.

### Statistical analysis

A meta-analysis was performed to calculate the pooled operative mortality after endovascular repair across published series. The degree of within-study heterogeneity was quantified using the  $I^2$  statistic. Meta-analysis was performed on a log odds outcome scale, that is, a log (proportion/(1 - proportion)) transformation. The log odds scale is used because, unlike the probability scale, it is not bounded and, thus, has more desirable statistical properties. Results were transformed to the proportion scale to ease interpretability and were expressed as pooled proportions (%) with 95% confidence intervals (CI). A funnel plot of mortality was constructed in order to assess whether publication bias was likely to be a problem.

Metaregression analyses were subsequently performed on operative mortality in an attempt to explain the observed heterogeneity between study estimates. The effect of age, mid-time study point, anaesthesia, endograft configuration, haemodynamic instability, intra-aortic balloon occlusion, conversion to open repair and abdominal compartment syndrome were all included individually as covariates in the metaregressions. For each metaregression, the slope coefficient (standard error (s.e.)), the  $p$ -value and the  $\tau^2$  are reported along with a metaregression plot of each covariate against operative mortality. The  $p$ -value indicates the strength of association, the graph shows the direction (i.e., positive or negative) and the slope informs how much the outcome changes per unit increase in the covariate. The  $\tau^2$  (the between-study variance) indicates how much residual heterogeneity exists which has not been explained by the covariate. A full meta-analysis random-effect approach to the regression had been used, where studies are weighted by a combination of their within-study variance and the degree of heterogeneity.

Finally, in addition to looking at each covariate individually, correlation between the eight covariates was also investigated and a multivariable model was built. In general, multiple significance testing on exploratory data analysis like this should be avoided, because we already do large numbers of hypothesis tests when model fitting in metaregression. However, it is sound to look at a matrix of correlations to inform the model-building process. Values in matrix are between  $-1$  and  $1$  - values approaching either of these are considered large correlations. It shows not only which metaregression variables are correlated with outcome (and thus likely to be important) but also which of these variables are correlated with each other. To include as much data as possible, missing values had been accounted for during estimation of the pairwise

correlations by using the 'pworth' option of the statistical software. This uses as much data as available rather than excluding all lines of data that have any missing values.

The level of significance was set at  $p < 0.05$ . All statistical analyses were carried out using Stata Statistical Software 10.0 (Stata, College Station, TX, USA).

## Results

Literature search identified 105 relevant articles. Of these, 17 had been excluded because they were series from the same institutions with duplicate clinical material, one was a study on octogenarians and five were single case reports. A further 36 articles had been excluded because they were reviews, meta-analyses and registries or population-based studies from which accurate data could not be extracted. This left 46 studies (1397 patients) for analysis (Table 1).<sup>4–49</sup>

### Mortality after endovascular repair

In-hospital and/or 30-day mortality ranged between 0% and 54% (Fig. 1). The highest mortality was encountered in the single identified randomised trial.<sup>28</sup> There was significant heterogeneity between the included studies (overall  $I^2 = 49.4%$ ,  $p < 0.001$ ). The pooled proportion for the mortality using the random-effect model was 24.3% (95% CI: 20.7–28.3%).

A funnel plot for mortality revealed a large degree of asymmetry (Fig. 2). This is driven primarily by the result in the single largest study in the data set,<sup>26</sup> that is, there could be extreme asymmetry with this large study in the centre of the funnel, or the plot could be reasonably symmetric if this study is considered an outlier. After excluding this study and re-meta-analysing the data, the estimated pooled mortality changed very little (23.9% (95% CI: 20.5–27.7%)). The result of this funnel plot could be described as small study effects, possibly due to publication bias. However, other interpretations should not be ruled out.

### Metaregression analysis

#### Age

Mean age of patients in the study (73.9 years) and mortality demonstrated no strong relationship (slope coefficient (s.e.) = 0.019 (0.041),  $p = 0.65$ ) (Fig. 3). However, this could be due to the relatively similar mean ages of patients across the studies and thus this analysis is probably quite low powered.

#### Mid-time study point

To investigate whether mortality systematically varied over time, mid-time study point was included as a covariate. While there is some suggestion that mortality rate has reduced over time, this is a non-significant association (slope coefficient (s.e.) =  $-0.043$  (0.047),  $p = 0.37$ ) (Fig. 4). This could be due to the relatively short timescale over which all studies have been conducted (~10 years) and the potentially low power of detecting differences given the narrow spread of values for the time-based covariate.

### Local versus general anaesthesia

Information on the type of anaesthesia was available in 33 studies (846 patients). In 306 patients (36%), the procedure had been started and concluded under local anaesthesia. The remaining patients had been operated upon either under general anaesthesia or initially under local anaesthesia, which was later converted to general anaesthesia. Metaregression failed to document a statistically significant association between the use of local anaesthesia and operative mortality (slope coefficient (s.e.) = 0.091 (0.379),  $p = 0.8$ ) (Fig. 5).

### Endograft configuration

Details on the type of endograft implanted were available in 36 studies (909 patients). A bifurcated aortobiliac endograft was employed in 520 (57%) cases and an aortouniiliac/aortounifemoral endograft was used in 373 (41%). A straight tube endograft was employed in 15 patients. Metaregression revealed a strong association between endograft configuration and perioperative outcome. Specifically, the bifurcated approach was associated with a statistically significant reduction in operative mortality (slope coefficient (s.e.) =  $-0.879$  (0.293),  $p = 0.005$ ) (Fig. 6).

### Haemodynamic instability

There was no uniform definition of 'haemodynamic instability' across the endovascular RAAA repair literature.<sup>5</sup> Of the 46 studies, 15 did not provide a definition at all, whereas others used different cut-off levels of systolic blood pressure and/or decreasing level of consciousness, cardiac arrest or severe arrhythmia as criteria for haemodynamic instability (Table 2). As a result, we employed the latter term loosely, accepting the authors' arbitrary definitions even though these were different in the different studies. Taking the above into account, haemodynamic instability was present in 422 out of 1262 patients (33.4%) at time of intervention. Metaregression showed no statistically significant association between haemodynamic instability and mortality (slope coefficient (s.e.) = 0.434 (0.471),  $p = 0.36$ ) (Fig. 7).

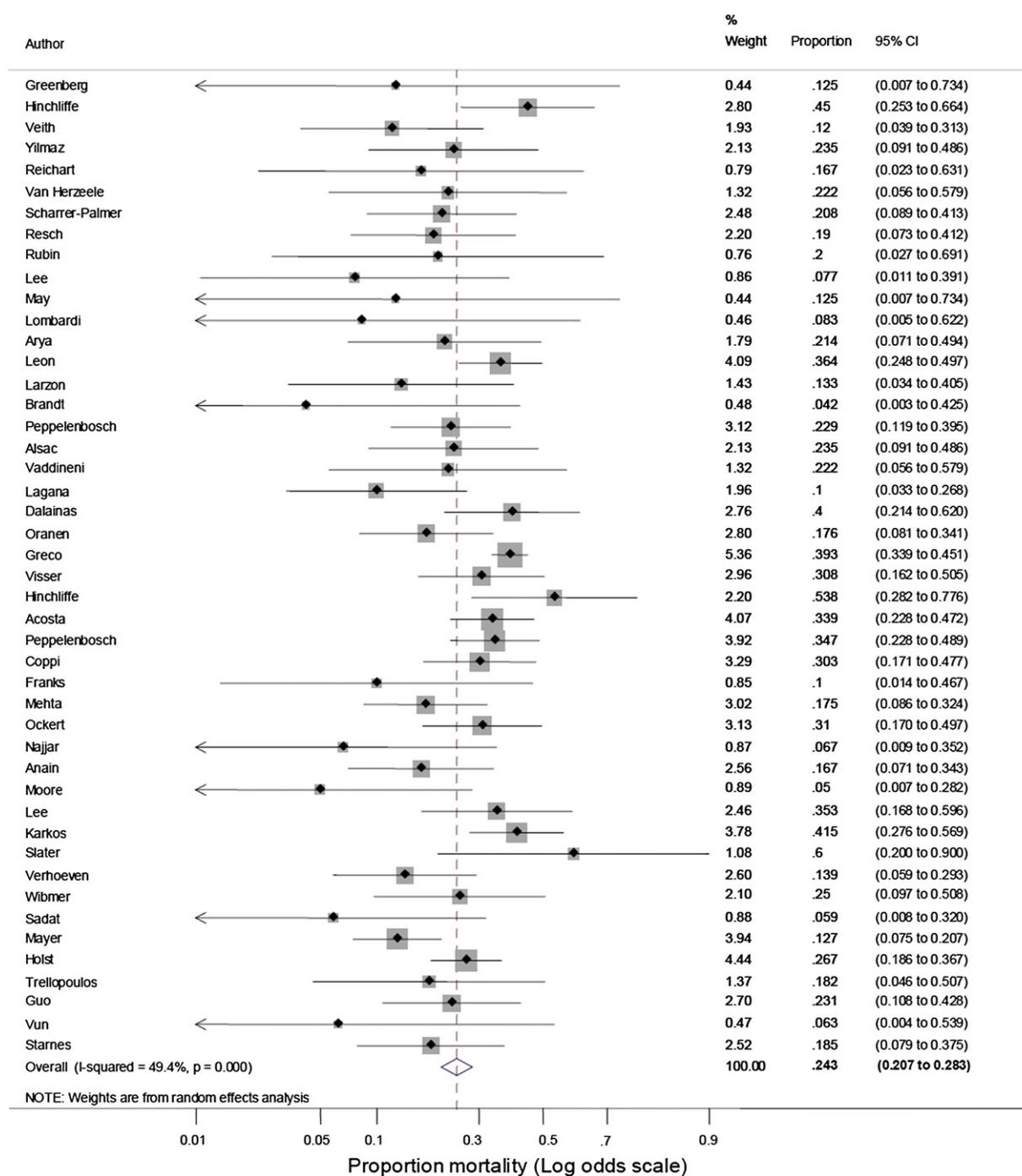
### Use of intra-aortic occlusion balloon

In total, 31 articles provided information on the use of aortic occlusion balloons. In 20, investigators employed balloon occlusion selectively, whereas 10 centres never used a balloon. The utilisation rate was 18% across the total population and ranged from 0% to 100%. Of the 10 studies – centres that did not use a balloon – eight had a policy of selecting (some or all) patients with instability for open repair. One centre had a policy of selective balloon occlusion, but did not use it in any of their patients.<sup>35</sup> Finally, one centre had a policy of not using a balloon because the authors felt that this represented an additional endovascular manoeuvre which led to delays and which may be associated with complications, such as visceral embolisation. Instead, this centre preferred the quick deployment of an aortouniiliac endograft.<sup>7</sup> Metaregression revealed no significant association between the use of balloon and mortality (slope coefficient (s.e.) =  $-0.064$  (0.577),  $p = 0.91$ ) (Fig. 8). To investigate whether the lack of balloon occlusion could influence outcome, subgroup

**Table 1** Study details. ER: number of patients undergoing endovascular repair in each study; LA: local anaesthesia; pts: patients; OR: open repair; NA: not available. \* 90-day mortality figure quoted.

First author	Year of publication	Country of origin	Mid-date of study	ER	Operative mortality	Age	Anaesthesia (LA)	Bifurcated approach	Unstable pts	Balloon occlusion	Primary conversion to OR	Abdominal compartment syndrome
Greenberg	2000	USA, Sweden	NA	3	0	82	0	0	2	2	0	0
Hinchliffe	2001	UK	15 Jan 97	20	9	75	0	0	4	2	3	NA
Veith	2002	USA	15 Jan 98	25	3	NA	0	0	8	8	0	2
Yilmaz	2002	The Netherlands	1 Sep 00	17	4	NA	NA	NA	12	0	0	NA
Reichart	2003	The Netherlands	15 Jul 01	6	1	NA	4	0	2	NA	NA	2
Van Herzeele	2003	Belgium	15 Dec 99	9	2	70	0	3	6	NA	0	1
Scharrer-Palmer	2003	Germany	15 Jan 98	24	5	69	NA	19	4	0	1	0
Resch	2003	Sweden	15 Oct 99	21	4	78	12	9	5	5	NA	1
Rubin	2004	USA	1 Dec 00	5	1	72	4	5	0	0	1	0
Lee	2004	USA	15 Aug 00	13	1	NA	1	13	0	0	0	NA
May	2004	Australia	1 Jan 98	3	0	NA	NA	3	NA	NA	NA	NA
Lombardi	2004	USA	1 Jan 02	5	0	NA	1	4	0	0	0	0
Arya	2004	UK	15 Jan 01	14	3	74	NA	3	0	NA	1	0
Leon	2005	USA	1 Jun 99	55	20	NA	NA	NA	NA	NA	NA	NA
Larzon	2005	Sweden	15 Sep 02	15	2	73	2	15	11	11	1	1
Brandt	2005	Germany	15 Nov 02	11	0	NA	0	3	NA	NA	0	NA
Peppelenbosch	2005	The Netherlands, Belgium	15 Aug 00	35	8	73	0	3	20	NA	NA	NA
Alsac	2005	France	15 Sep 02	17	4	72.9	1	8	1	1	3	1
Vaddineni	2005	USA	1 Mar 02	9	2	70.8	0	9	0	0	0	NA
Lagana	2006	Italy	1 Nov 02	30	3	76	0	25	9	3	0	0
Dalainas	2006	Italy	1 July 02	20	8	NA	20	11	NA	20	0	1
Oranen	2006	The Netherlands	1 Jan 02	34	6	73	27	NA	NA	NA	1	1
Greco	2006	USA	1 Jan 02	290	114	NA	NA	NA	36	NA	20	NA
Visser	2006	The Netherlands, USA	1 Jul 03	26	8	72.5	0	24	2	NA	2	1
Hinchliffe	2006	UK	1 Nov 03	13	7	74	0	0	5	0	2	NA
Acosta	2006	Sweden	1 Jan 02	56	19	75.5	NA	23	47	NA	NA	3
Peppelenbosch	2006	International multicentre	1 Dec 03	49	17	75.1	16	0	21	3	3	NA
Coppi	2006	Italy	15 Feb 03	33	10	81	12	7	15	4	3	1
Franks	2006	UK	1 Dec 99	10	1	NA	NA	NA	3	NA	1	0
Mehta	2006	USA	1 Jul 03	40	7	74	0	34	10	7	2	7
Ockert	2007	Germany	1 Jan 03	29	9	71	9	10	14	1	1	5
Najjar	2007	USA	1 Jan 03	15	1	73	0	15	3	0	0	1
Anain	2007	USA	1 Nov 03	30	5	NA	0	29	15	10	2	0
Moore	2007	USA	1 Aug 03	20	1	NA	2	6	7	7	0	NA
Lee	2008	USA	15 Apr 04	17	6	NA	NA	NA	8	3	0	0
Karkos	2008	Greece	1 Jun 02	41	17	73	27	27	21	2	0	1



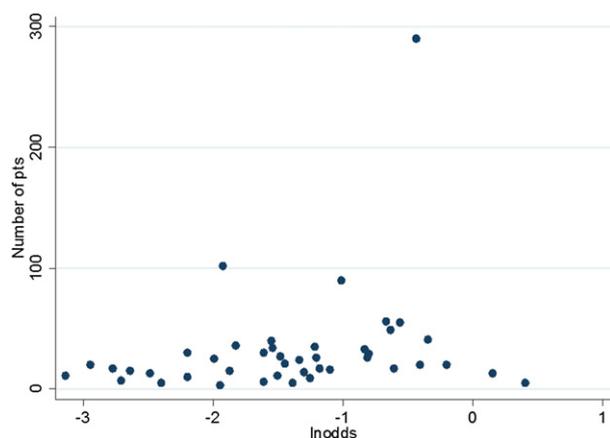


**Figure 1** Forest plot (random-effects meta-analysis) for the mortality figures after endovascular repair in the 46 studies. The point estimate (black dot) and the 95% CI (horizontal line) for the mortality are plotted for each study. Each black dot is surrounded by a grey box whose area represents the weight of the study in the overall meta-analysis. The relative weight given to each study is provided to the right of the plot as a percentage. The pooled estimate for the meta-analysis is presented directly below the estimates from the 46 studies and is represented as a 'diamond' with the centre corresponding to the point estimate and the extreme tips spanning the 95% CI.

a surrogate measure for centre experience. There was still a strong association between the 'bifurcated approach' and the outcome after simultaneously adjusting for sample size of the study. Hence, it would appear that experience was not a major factor in explaining the observed association.

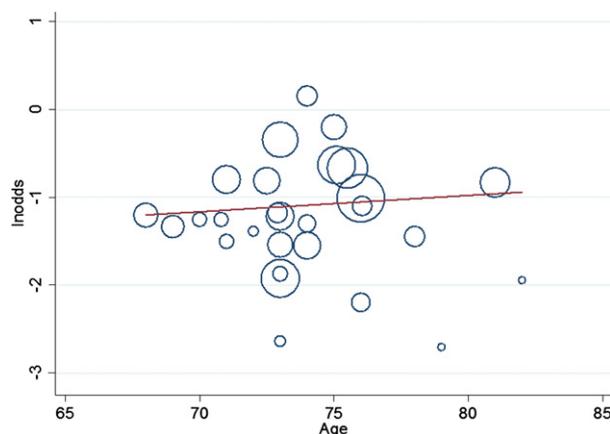
## Discussion

The advent of endovascular therapy has revolutionised elective aneurysm surgery and several large trials have shown multiple benefits with endovascular repair compared

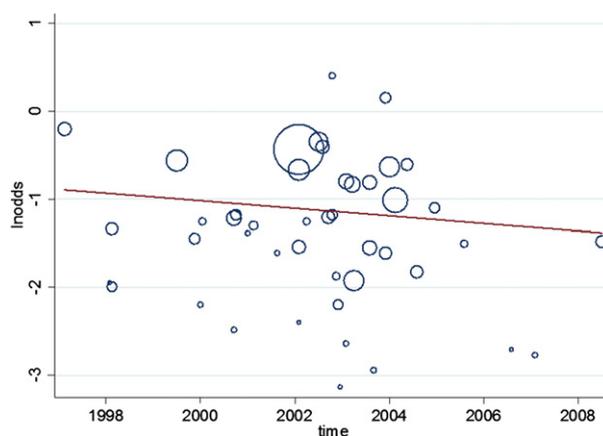


**Figure 2** Funnel plot of the 46 studies included in the meta-analysis with log odds of mortality (lnodds) on the x-axis and sample size (patient number/study) on y-axis. The plot is highly asymmetric, possibly indicating publication bias. The asymmetry could largely be due to the outlying study which is much larger than the rest. Excluding the top study, the funnel appears to be much more symmetric.

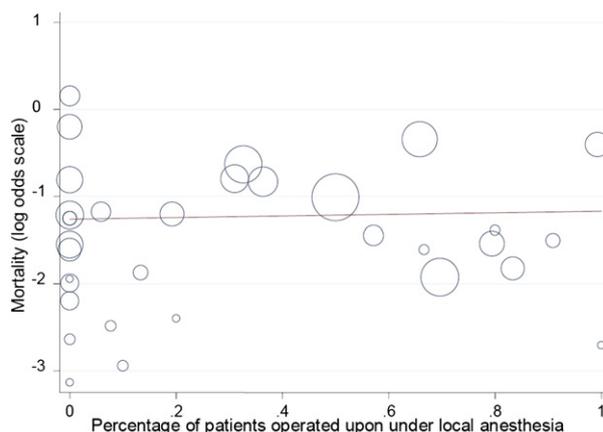
to elective open AAA repair. This has raised hope that endovascular repair may similarly benefit RAAA patients. However, level I evidence is lacking and apart from a single randomised controlled trial of 32 people, the rest of the evidence is observational.<sup>28</sup> Useful data about the true status of endovascular RAAA repair can also be derived from multicentre registries and meta-analyses of published series (Table 4). Although the figures from these registries and meta-analyses are much better than those traditionally reported in the literature for open repair, they should be interpreted with caution. Comparison of endovascular with open RAAA repair is misleading because endovascular repair cannot be performed on all patients. Additionally, these



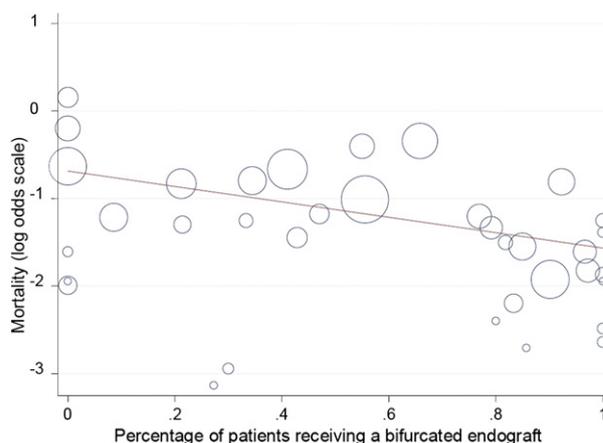
**Figure 3** Metaregression plot of age against operative mortality (log odds scale on y-axis) ( $n = 28$  studies,  $p = 0.65$ ,  $\tau^2 = 0.1225$ ). Circles represent individual studies; the size of the circle is proportional to the inverse of the variance of the mortality estimate for that study, indicating the relative influence in the meta-analysis. lnodds: mortality (log odds scale).



**Figure 4** Metaregression plot of mid-time study point against mortality (log odds scale on y-axis) ( $n = 45$  studies,  $p = 0.37$ ,  $\tau^2 = 0.1692$ ). lnodds: mortality (log odds scale).



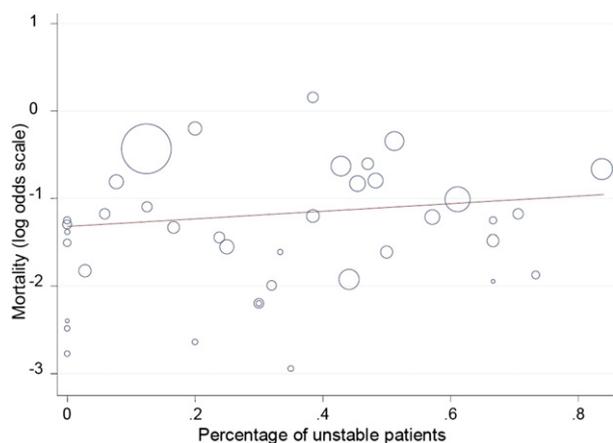
**Figure 5** Metaregression plot of the use of local anaesthesia against operative mortality (33 studies,  $p = 0.8$ ,  $\tau^2 = 0.1961$ ).



**Figure 6** Metaregression plot of bifurcated endograft configuration against operative mortality (36 studies,  $p = 0.005$ ,  $\tau^2 = 0.07518$ ).

**Table 2** Definition of haemodynamic instability across the 46 studies. Abbreviations: CT, computed tomography; NA, not available; SBP, systolic blood pressure.

	First author	Unstable pts/total	Defining Criteria for Haemodynamic Instability
1	Greenberg	2/3	NA
2	Hinchliffe	4/20	SBP <90 mm Hg
3	Veith and Ohki	8/25	SBP < 50–70 mm Hg (all patients were taken directly to the operating room for angiography)
4	Yilmaz	12/17	SBP < 100 mm Hg
5	Reichart	2/6	NA (“serious intraoperative haemodynamic problems”)
6	Van Herzeele	6/9	SBP < 70 mm Hg
7	Scharrer-Palmer	4/24	NA
8	Resch	5/21	NA
9	Rubin	0/5	NA
10	Lee	0/13	SBP <80 mm Hg or reduced mentation
11	May	NA/3	NA
12	Lombardi	0/5	NA
13	Arya	0/14	NA
14	Leon	NA/55	NA
15	Larzon	11/15	SBP <80 mm Hg at any time from arrival until induction to anaesthesia
16	Brandt	NA/11	NA but excluded all “unstable” patients
17	Peppelenbosch	20/35	SBP <90 mm Hg
18	Alsac	1/17	Excluded patients with profound hypovolaemic shock (SBP <80 mm Hg and/or cardiac arrest) but included those with moderate instability, i.e., SBP >80 mm Hg and no severe cardiac arrhythmia
19	Vaddineni	0/9	SBP <80 mm Hg and/or reduced mentation
20	Lagana	9/30	SBP <80 mm Hg
21	Dalainas	NA/20	NA (“profound haemorrhagic shock”)
22	Oranen	NA/34	NA
23	Greco	36/290	NA
24	Visser	2/26	SBP <90 mm Hg. Those who were “haemodynamically too unstable” (i.e., SBP <70 mm Hg with no adequate verbal reply) were excluded and underwent open repair
25	Hinchliffe	5/13	SBP <100 mm Hg
26	Acosta	47/56	Circulatory instability: loss of consciousness, either transient or permanent, prior to operation
27	Peppelenbosch	21/49	Patients with moderate instability (SBP 60–100 mm Hg, without cardiac arrhythmia) underwent preoperative CT to determine suitability for endovascular repair; patients with severe instability (SBP <60 mm Hg, with cardiac arrhythmia) were transferred directly to the operating room for angiography
28	Coppi	15/33	Loss of consciousness with or without a SBP <80 mm Hg after fluid resuscitation
29	Franks	3/10	SBP <100 mm Hg
30	Mehta	10/40	SBP <80 mm Hg
31	Ockert	14/29	A shock index (pulse rate/systolic blood pressure) $\geq 1.0$
32	Najjar	3/15	SBP < 80 mm Hg
33	Anain	15/30	SBP <80 mm Hg and/or loss of consciousness
34	Moore	7/20	SBP <80 mm Hg and/or loss of consciousness
35	Lee	8/17	2 or more of the following: SBP < 120 mm Hg, heart rate > 100, and respiratory rate > 20
36	Karkos	21/41	SBP < 80 mm Hg and/or reduced mentation
37	Slater	NA/5	NA
38	Verhoeven	1/36	SBP < 70 mm Hg
39	Wibmer	2/16	1) SBP <80 mm Hg or 2) loss of consciousness or cardiac arrest due to exsanguination
40	Sadat	0/17	SBP < 60 mm Hg and/or loss of consciousness
41	Mayer	45/102	SBP < 50 mm Hg despite adequate resuscitation
42	Holst	55/90	Loss of consciousness or SBP < 80 mm Hg before induction of anaesthesia
43	Trellopoulos	0/11	SBP < 60 mm Hg
44	Guo	10/26	SBP < 80 mm Hg
45	Vun	NA/7	NA
46	Starnes	18/27	SBP < 80 mm Hg or with lack of neurocognitive ability

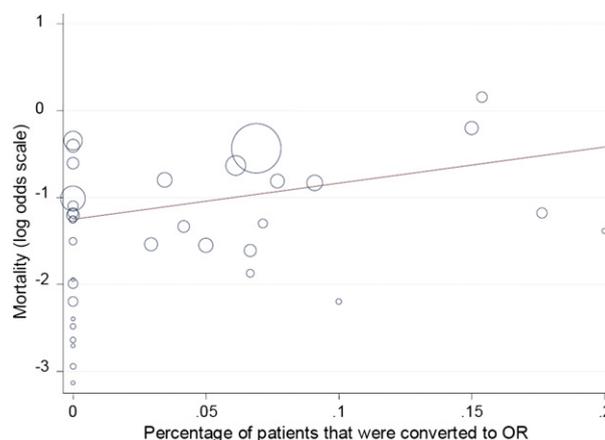


**Figure 7** Metaregression plot of haemodynamic instability against operative mortality (39 studies,  $p = 0.362$ ,  $\tau^2 = 0.1829$ ).

results may reflect increasing experience and seem to be influenced by both publication and selection bias.

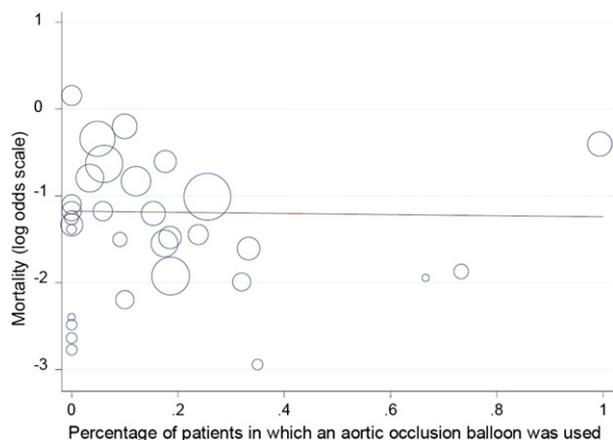
If these results are to be improved, identification of factors influencing the perioperative mortality is a crucial first step. In the absence of large series addressing the issue, we attempted to identify significant prognostic factors using previously published data and employing meta-analytical tools. The eight variables, which had been tested here, had been selected because they were frequently reported across the endovascular RAAA repair literature. We initially intended to investigate many other parameters, such as history of cardiorespiratory disease, renal impairment, time delay to presentation, adverse anatomy, speed of aneurysm exclusion, blood loss, the presence of endoleaks, the need for re-interventions and the occurrence of complications in the postoperative period. However, this was not possible, because these details were either not reported or not presented uniformly enough to allow meaningful pooling of the data.

The main finding of this metaregression was that a bifurcated approach was associated with a statistically

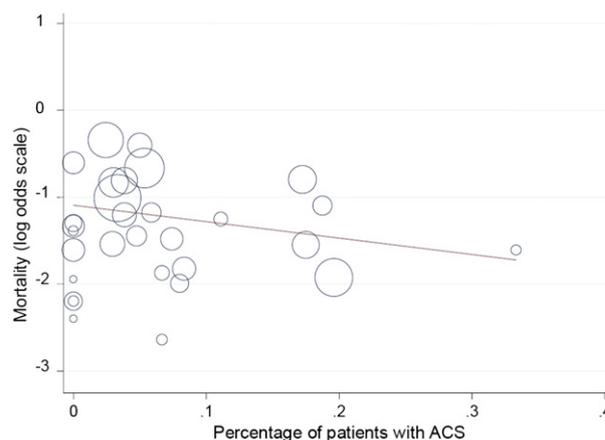


**Figure 9** Metaregression plot of intraoperative conversion to open repair (OR) against operative mortality (35 studies,  $p = 0.066$ ,  $\tau^2 = 0.1275$ ).

significant reduction in mortality. Glancing through the original papers, one would see that, in the RAAA setting, the choice of a bifurcated over an aortouniiliac endograft depends on several factors, such as the expertise and preference of the operator, endograft availability at the time of presentation, aneurysm anatomy and haemodynamic status of the patient. A bifurcated option is more anatomical and avoids a femorofemoral bypass, but a drawback is the time taken to cannulate the contralateral stump. The latter is a crucial factor in RAAA patients and any delay in excluding the aneurysm may make the difference between life and death. The aortouniiliac approach is easier and quicker, has higher eligibility rate, requires fewer endografts in stock and also requires a femorofemoral graft with all the disadvantages of an extra-anatomic bypass. As a result, many surgeons would exclusively use aortouniiliac endografts, whereas others would adopt a selective policy, opting for a bifurcated approach only in haemodynamically stable, anatomically suitable patients. Finally, few surgeons would rely on anatomical-only criteria without taking into account the haemodynamic status of



**Figure 8** Metaregression plot of intra-aortic balloon occlusion against operative mortality (31 studies,  $p = 0.913$ ,  $\tau^2 = 0.1875$ ).



**Figure 10** Metaregression plot of the development of post-operative abdominal compartment syndrome (ACS) against operative mortality (30 studies,  $p = 0.249$ ,  $\tau^2 = 0.08408$ ).

**Table 3** Matrix of correlations between the 8 metaregression covariates. Values in matrix range between  $-1$  and  $1$  with those approaching either of these being considered large correlations. The two most highly correlated variables are “unstable patients” and “balloon occlusion”. Pts: patients; OR: open repair; ACS: abdominal compartment syndrome.

	Age	Mid-time point	Anaesthesia	Bifurcated approach	Unstable pts	Balloon occlusion	Conversion to OR	ACS
Age	1.00							
Mid-time point	0.26	1.00						
Anaesthesia	0.09	0.33	1.00					
Bifurcated approach	-0.39	0.24	0.21	1.00				
Unstable pts	0.26	0.05	-0.18	-0.35	1.00			
Balloon occlusion	0.41	0.01	0.18	-0.13	0.58	1.00		
Conversion to OR	-0.01	-0.22	-0.07	-0.16	-0.24	-0.18	1.00	
ACS	-0.15	0.14	0.15	-0.24	0.05	-0.10	-0.16	1.00

the patient. Therefore, one possible explanation for the improved survival in the ‘bifurcated’ group is that a bifurcated endograft was usually employed in patients who were considered haemodynamically stable enough to tolerate the inevitable delay occurring during contralateral stump cannulation. This implies that patients receiving a bifurcated endograft were in better haemodynamic condition than the aortouniiliac group, and, hence, less likely to die. In the present meta-analysis, there was, indeed, a moderate (negative) correlation between the ‘bifurcated endograft’ and the ‘unstable patients’ groups. However, there was still a strong association between bifurcated approach and mortality after adjusting for haemodynamic instability, indicating that the latter was not a major factor in explaining this.

Haemodynamic instability is, perhaps, the single most important determinant of survival in RAAA patients undergoing endovascular repair. However, we were unable to demonstrate any statistically significant association between haemodynamic instability and mortality. A possible explanation is that the definition of ‘haemodynamic instability’ differed widely across the pooled studies based upon differing criteria of blood pressure and level of consciousness.<sup>2</sup> These differences may also explain the

observed within-study heterogeneity and have an impact on reported mortality figures. Furthermore, lack of statistical power is another possible explanation.

This study also suggested a trend for a higher mortality when immediate conversion to open repair was necessary, albeit not a statistically significant one. This is hardly surprising, since conversion usually occurs intraoperatively because of access difficulties, type I endoleak and/or stent-graft migration, continued blood loss, the inability to catheterise the contralateral limb and inadvertent coverage of the renal arteries, all problems which may render a difficult open repair to an even more complicated one. Although available information on outcome of patients undergoing immediate conversion was limited, this scenario appears to be extremely ominous with more than two-thirds of patients eventually dying.

Finally, this meta-analysis has certain limitations. Many clinically significant markers of perioperative outcome, in particular haemodynamic instability and the use of aortic balloon, had not been found as being statistically significant in the present data set. This is potentially because the quality of a meta-analysis depends on the quality of the original studies. Unfortunately, there were many inconsistencies in the reporting, which is a weakness. Also,

**Table 4** Multicentre registries and meta-analyses of series reporting patients undergoing endovascular repair of RAAA. Of particular note are the exceptionally low operative mortality rates in the VASCUNET and the Swedish vascular registry.

First author	Country	Year	Number of pts	Overall mortality
<i>Registries</i>				
Veith <sup>50</sup>	World experience	2009	1037	21.2%
Richards <sup>51</sup>	UK National Vascular Database	2007	51	29%
Gibbons <sup>52</sup>	VASCUNET (Europe, Australia, New Zealand)	2008	474	15%
Mani <sup>53</sup>	Swedish Vascular Registry	2009	91	14.3%
<i>Meta-analyses</i>				
Harkin <sup>54</sup>	Belfast, UK	2007	891 (34) <sup>a</sup>	18%
Visser <sup>55</sup>	The Netherlands	2007	148 (10) <sup>a</sup>	22%
Mastracci <sup>56</sup>	Hamilton, Ontario, Canada	2008	436 (18) <sup>a</sup>	21%
Sadat <sup>57</sup>	Cambridge, UK	2008	730 (23) <sup>a</sup>	30%
Azizzadeh <sup>58</sup>	Houston, USA	2008	531 (26) <sup>a</sup>	30%
Rayt <sup>1</sup>	Leicester, UK	2008	981 (31) <sup>a</sup>	24%
Karkos <sup>2</sup>	Thessaloniki, Greece	2009	897 (29) <sup>a</sup>	24%

<sup>a</sup> Number of studies included in the meta-analysis.

covariates were not available for a proportion of studies, and, as a result, the eligible sample size was considerably reduced. Additionally, a multivariable metaregression model investigating the correlation between several covariates is associated with a large degree of uncertainty because large numbers of hypothesis tests are being done. Therefore, caution is always needed in drawing conclusions based on such a multivariable model.

The definitive level I evidence about the role of endovascular RAAA repair requires good-quality randomised control trials. Three such trials are underway. The French ECAR and the Dutch AJAX trial have been designed to recruit only stable patients, all of whom will be anatomically suitable for endovascular repair. By contrast, the UK IMPROVE trial would randomise patients at diagnosis, that is, before computed tomography (CT) scanning, in an attempt to define the role of an endovascular-first strategy versus open repair on an intention-to-treat basis. Their results are awaited with interest. In the meantime, there are many enthusiastic endovascular specialists who argue that such trials are simply not needed because of the exceptional results that have been achieved in many published reports of single-centre or collected experience.<sup>44,50</sup> Finally, all these may have important implications for training. With more and more centres offering endovascular repair for RAAA patients and with more than half of all elective AAAs being treated by endovascular means in most European countries, it can be foreseen that accumulating enough experience and surgical skills to perform an open RAAA repair is becoming an issue.

In conclusion, this meta-analysis confirms that the mortality from endovascular repair of RAAAs seems to be lower than the one usually reported after open repair. Metaregression analysis identified the bifurcated endograft approach as being the only perioperative variable significantly associated with a better chance of survival after endovascular repair. This observation could not be fully explained by the haemodynamic status of the patients or the experience of the centre. Immediate conversion to open repair showed a trend for a higher mortality, but no statistically significant association. Finally, none, that is, type of anaesthesia, haemodynamic instability, intra-aortic balloon occlusion and development of abdominal compartment syndrome postoperatively, appeared to significantly influence the perioperative mortality.

## Conflict of Interest

None.

## Funding

None.

## References

- 1 Rayt HS, Sutton AJ, London NJM, Sayers RD, Bown MJ. A systematic review and meta-analysis of endovascular repair (EVAR) for ruptured abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2008;**36**:536–44.
- 2 Karkos CD, Harkin DW, Giannakou A, Gerassimidis TS. Mortality after endovascular repair of ruptured abdominal aortic aneurysms: a systematic review and meta-analysis. *Arch Surg* 2009;**144**:770–8.
- 3 Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology. A proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *J Am Med Assoc* 2000;**283**:2008–12.
- 4 Greenberg RK, Ouriel K, Shortell C, et al. An endoluminal method of hemorrhage control and repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther* 2000;**7**:1–7.
- 5 Hinchliffe RJ, Yusuf SW, Macierewicz JA, MacSweeney STR, Wenham PW, Hopkinson BR. Endovascular repair of ruptured abdominal aortic aneurysm—a challenge to open repair: results of a single centre experience in 20 patients. *Eur J Vasc Endovasc Surg* 2001;**22**:528–34.
- 6 Veith FJ, Ohki T. Endovascular approaches to ruptured infrarenal aortoiliac aneurysms. *J Cardiovasc Surg* 2002;**43**:369–78.
- 7 Yilmaz N, Peppelenbosch N, Cuypers PW, Tielbeek AV, Duijm LEM, Buth J. Emergency treatment of symptomatic or ruptured abdominal aortic aneurysms: the role of endovascular repair. *J Endovasc Ther* 2002;**9**:449–57.
- 8 Reichart M, Geelkerken RH, Huisman AB, van Det RJ, de Smit P, Volker EP. Ruptured abdominal aortic aneurysm: endovascular repair is feasible in 40% of patients. *Eur J Vasc Endovasc Surg* 2003;**26**:479–86.
- 9 Van Herzeele I, Vermassen F, Durieux C, et al. Endovascular repair of aortic rupture. *Eur J Vasc Endovasc Surg* 2003;**26**:311–6.
- 10 Scharrer-Pamler R, Kotsis T, Kapfer X, Gorich J, Sunder-Plassmann L. Endovascular stent-graft repair of ruptured aortic aneurysms. *J Endovasc Ther* 2003;**10**:447–52.
- 11 Resch T, Malina M, Lindbland B, Dias NV, Sonesson B, Ivancev K. Endovascular repair of ruptured abdominal aortic aneurysms: logistics and short-term results. *J Endovasc Ther* 2003;**10**:440–6.
- 12 Rubin BG, Sanchez LA, Choi ET, Sicard GA. Endoluminal repair of ruptured abdominal aortic aneurysms under local anaesthesia: initial experience. *Vasc Endovascular Surg* 2004;**38**:203–7.
- 13 Lee WA, Hirneise CM, Tayyarah M, Huber TS, Seeger JM. Impact of endovascular repair on early outcomes of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2004;**40**:211–5.
- 14 May J, White GH, Stephen MS, Harris JP. Rupture of abdominal aortic aneurysm: concurrent comparison of outcome of those occurring after endovascular repair versus those occurring without previous treatment in an 11-year single-center experience. *J Vasc Surg* 2004;**40**:860–6.
- 15 Lombardi JV, Fairman RM, Golden MA, et al. The utility of commercially available endografts in the treatment of ruptured abdominal aortic aneurysm with hemodynamic stability. *J Vasc Surg* 2004;**40**:154–60.
- 16 Arya N, Lee B, Loan W, et al. Change in aneurysm diameter after stent-graft repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther* 2004;**11**:319–22.
- 17 Leon LR, Labropoulos N, Laredo J, Rodriguez HE, Kalman PG. To what extent has endovascular aneurysm repair influenced abdominal aortic aneurysm management in the state of Illinois? *J Vasc Surg* 2005;**41**:568–74.
- 18 Larzon T, Lindgren R, Norgren L. Endovascular treatment of ruptured abdominal aortic aneurysms: a shift of the paradigm? *J Endovasc Ther* 2005;**12**:548–55.
- 19 Brandt M, Walluscheck KP, Jahnke T, Graw K, Cremer J, Muller-Hulsbeck S. Endovascular repair of ruptured abdominal aortic aneurysm: feasibility and impact on early outcome. *J Vasc Interv Radiol* 2005;**16**:1309–12.
- 20 Peppelenbosch N, Cuypers PWM, Vahl AC, Vermassen F, Buth J. Emergency endovascular treatment for ruptured abdominal

- aortic aneurysm and the risk of spinal cord ischemia. *J Vasc Surg* 2005;**42**:608–14.
- 21 Alsac JM, Desgranges P, Kobeiter H, Becquemin JP. Emergency endovascular repair for ruptured abdominal aortic aneurysms: feasibility and comparison of early results with conventional open repair. *Eur J Vasc Endovasc Surg* 2005;**30**:632–9.
  - 22 Vaddineni SK, Russo GC, Patterson MA, Taylor SM, Jordan Jr WD. Ruptured abdominal aortic aneurysm: a retrospective assessment of open versus endovascular repair. *Ann Vasc Surg* 2005;**19**:782–6.
  - 23 Lagana D, Carrafiello G, Mangini M, et al. Emergency endovascular treatment of abdominal aortic aneurysms: feasibility and results. *Cardiovasc Intervent Radiol* 2006;**29**:241–8.
  - 24 Dalainas I, Nano G, Bianchi P, et al. Endovascular techniques for the treatment of ruptured abdominal aortic aneurysms: 7-year intention-to-treat results. *World J Surg* 2006;**30**:1809–14.
  - 25 Oranen BI, Bos WTGJ, Verhoeven ELG, et al. Is emergency endovascular aneurysm repair associated with higher secondary intervention risk at mid-term follow-up? *J Vasc Surg* 2006;**44**:1156–61.
  - 26 Greco G, Egorova N, Anderson PL, et al. Outcomes of endovascular treatment of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2006;**43**:453–9.
  - 27 Visser JJ, Bosch JL, Hunink MGM, et al. Endovascular repair versus open surgery in patients with ruptured abdominal aortic aneurysms: clinical outcomes with 1-year follow-up. *J Vasc Surg* 2006;**44**:1148–55.
  - 28 Hinchliffe RJ, Bruijstens L, MacSweeney STR, Braithwaite BD. A randomised trial of endovascular and open surgery for ruptured abdominal aortic aneurysm – results of a pilot study and lessons learned for future studies. *Eur J Vasc Endovasc Surg* 2006;**32**:506–13.
  - 29 Acosta S, Lindblad B, Zdanowski Z. Predictors for outcome after open and endovascular repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2007;**33**:277–84.
  - 30 Peppelenbosch N, Geelkerken RH, Soong C, et al. Endograft treatment of ruptured abdominal aortic aneurysms using the Talent aortouniliac system: an international multicenter study. *J Vasc Surg* 2006;**43**:1111–22.
  - 31 Coppi G, Silingardi R, Gennai S, Saitta G, Ciardullo AV. A single-center experience in open and endovascular treatment of hemodynamically unstable and stable patients with ruptured abdominal aortic aneurysms. *J Vasc Surg* 2006;**44**:1140–7.
  - 32 Franks S, Lloyd G, Fishwick G, Bown M, Sayers R. Endovascular treatment of ruptured and symptomatic abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2006;**31**:345–50.
  - 33 Mehta M, Taggart J, Darling III C, et al. Establishing a protocol for endovascular treatment of ruptured abdominal aortic aneurysms: outcomes of a prospective analysis. *J Vasc Surg* 2006;**44**:1–8.
  - 34 Ockert S, Schumacher H, Bockler D, Megges I, Allenberg JR. Early and midterm results after open and endovascular repair of ruptured abdominal aortic aneurysms in a comparative analysis. *J Endovasc Ther*; 2007;**32**:4–32.
  - 35 Najjar SF, Mueller KH, Ujiki MB, Morasch MD, Matsumura JS, Eskandari MK. Percutaneous endovascular repair of ruptured abdominal aortic aneurysms. *Arch Surg* 2007;**142**:1049–52.
  - 36 Anain PM, Anain Sr JM, Tiso M, Nader ND, Dosluoglu HH. Early and mid-term results of ruptured abdominal aortic aneurysms in the endovascular era in a community hospital. *J Vasc Surg* 2007;**46**:898–905.
  - 37 Moore R, Nutley M, Cina CS, Motamedi M, Faris P, Abuznadah W. Improved survival after introduction of an emergency endovascular therapy protocol for ruptured abdominal aortic aneurysms. *J Vasc Surg* 2007;**45**:443–50.
  - 38 Lee RW, Rhodes JM, Singh MJ, et al. Is there a selection bias in applying endovascular aneurysm repair for rupture? *Ann Vasc Surg* 2008;**22**:215–20.
  - 39 Karkos CD, Karamanos D, Papazoglou KO, et al. Usefulness of the Hardman index in predicting outcome after endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2008;**48**:788–94.
  - 40 Slater BJ, Harris EJ, Lee JT. Anatomic suitability of ruptured abdominal aortic aneurysms for endovascular repair. *Ann Vasc Surg* 2008;**22**:716–22.
  - 41 Verhoeven EL, Kapma MR, Groen H, et al. Mortality of ruptured abdominal aortic aneurysm treated with open or endovascular repair. *J Vasc Surg* 2008;**48**:1396–400.
  - 42 Wibmer A, Schoder M, Wolff KS, et al. Improved survival after abdominal aortic aneurysm rupture by offering both open and endovascular repair. *Arch Surg* 2008;**143**:544–9.
  - 43 Sadat U, Hayes PD, Kullar PJ, Cousins C, Varty K, Boyle JR. An emergency EVAR service reduces mortality in ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2009;**37**:189–93.
  - 44 Mayer D, Pfammatter T, Rancic Z, et al. 10 years of emergency endovascular aneurysm repair for ruptured abdominal aortic aneurysms: lessons learned. *Ann Surg* 2009;**249**:510–5.
  - 45 Holst J, Resch T, Ivancev K, et al. Early and intermediate outcome of emergency endovascular aneurysm repair of ruptured infrarenal aortic aneurysm: a single-centre experience of 90 consecutive patients. *Eur J Vasc Endovasc Surg* 2009;**37**:413–9.
  - 46 Trellopoulos G, Megalopoulos A, Sfyroeras GS, Arambatzakos S, Ampatzidou F. Endovascular treatment of symptomatic and ruptured abdominal aortic aneurysms. *Acta Chir Belg* 2009;**109**:327–32.
  - 47 Guo W, Zhang HP, Liu XP, et al. Endovascular repair: alternative treatment of ruptured abdominal aortic aneurysm. *Chin Med J* 2009;**122**:1728–31.
  - 48 Yun S, Walker SR. Endovascular repair of ruptured abdominal aortic aneurysms in a rural center is both feasible and associated with reduced blood product requirements. *Vascular* 2009;**17**:303–8.
  - 49 Starnes BW, Quiroga E, Hutter C, et al. Management of ruptured abdominal aortic aneurysm in the endovascular era. *J Vasc Surg* 2010;**51**:9–17.
  - 50 Veith FJ, Lachat M, Mayer D, et al. Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. *Ann Surg* 2009;**250**:818–24.
  - 51 Richards T, Goode S, Kuhan G, et al. EVAR for emergency AAA: not an easier option. Annual Meeting of the Vascular Society of Great Britain & Ireland, 28–30 November 2007, Manchester, UK [abstract presentation].
  - 52 Gibbons C, Björck M, Jensen LP, et al. *The second vascular surgery database report*. European Society for Vascular Surgery, ISBN 1-903968-21-6; 2008.
  - 53 Mani K, Björck M, Lundkvist J, Wanhainen A. Improved long-term survival after abdominal aortic aneurysm repair. *Circulation* 2009;**120**:201–11.
  - 54 Harkin DW, Dillon M, Blair PH, Ellis PK, Kee F. Endovascular ruptured abdominal aortic aneurysm repair: a systematic review. *Eur J Vasc Endovasc Surg* 2007;**34**:673–81.
  - 55 Visser JJ, van Sambeek MRHM, Hamza TH, Hunink MGM, Bosch JL. Ruptured abdominal aortic aneurysms: endovascular repair versus open surgery – systematic review. *Radiology* 2007;**245**:122–9.
  - 56 Mastracci TM, Garrido-Olivares L, Cinà CS, Clase CM. Endovascular repair of ruptured abdominal aortic aneurysms: a systematic review and meta-analysis. *J Vasc Surg* 2008;**47**:214–21.
  - 57 Sadat U, Boyle JR, Walsh SR, Tang T, Varty K, Hayes PD. Endovascular vs open repair of acute abdominal aortic aneurysms – a systematic review and meta-analysis. *J Vasc Surg* 2008;**48**:227–36.
  - 58 Azizzadeh A, Villa MA, Miller CC, Estrera AL, Coogan SM, Safi HJ. Endovascular repair of ruptured abdominal aortic aneurysms: systematic literature review. *Vascular* 2008;**16**:219–24.