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RESEARCH

Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial


OPEN ACCESS

IMPROVE trial investigators

Abstract

Objective To assess whether a strategy of endovascular repair (if aortic morphology is suitable, open repair if not) versus open repair reduces early mortality for patients with suspected ruptured abdominal aortic aneurysm.

Design Randomised controlled trial.

Setting 30 vascular centres (29 UK, 1 Canadian), 2009-13.

Participants 613 eligible patients (480 men) with a clinical diagnosis of ruptured aneurysm.

Interventions 316 patients were randomised to the endovascular strategy (275 confirmed ruptures, 174 anatomically suitable for endovascular repair) and 297 to open repair (261 confirmed ruptures).

Main outcome measures 30 day mortality, with 24 hour and in-hospital mortality, costs, and time and place of discharge as secondary outcomes.

Results 30 day mortality was 35.4% (112/316) in the endovascular strategy group and 37.4% (111/297) in the open repair group: odds ratio 0.92 (95% confidence interval 0.66 to 1.28; P=0.62); odds ratio after adjustment for age, sex, and Hardman index 0.94 (0.67 to 1.33). Women may benefit more than men (interaction test P=0.02) from the endovascular strategy: odds ratio 0.44 (0.22 to 0.91) versus 1.18 (0.80 to 1.75). 30 day mortality for patients with confirmed rupture was 36.4% (100/275) in the endovascular strategy group and 40.6% (106/261) in the open repair group (P=0.31). More patients in the endovascular strategy than in the open repair group were discharged directly to home (189/201 (94%) *v* 141/183 (77%); P<0.001). Average 30 day costs were similar between the randomised groups, with an incremental cost saving for the endovascular strategy versus open repair of £1186 (€1420; $1939) (95% confidence interval –£625 to £2997).

Conclusions A strategy of endovascular repair was not associated with significant reduction in either 30 day mortality or cost. Longer term cost effectiveness evaluations are needed to assess the full effects of the endovascular strategy in both men and women.

Trial registration Current Controlled Trials ISRCTN48334791.

Introduction

Ruptured abdominal aortic aneurysm remains one of the most common vascular emergencies, even though mortality from ruptured aneurysm has been declining at the population level.[1] Without repair, ruptured aneurysm is nearly always fatal.[2] The 30 day mortality from emergency open repair has remained at nearly 50% for many years,[3 4] but findings from national datasets suggest that emergency endovascular aneurysm repair (EVAR) may be associated with a lower 30 day mortality rate of about 30%.[4-6] Such data may be subject to major confounding bias. Many patients with ruptured aneurysm have aortic morphology that is unsuitable for conventional EVAR. Observational studies do not consider centres' expertise, which potentially influences selection of patients and diagnostic criteria.

Two small randomised trials of EVAR versus open repair for ruptured abdominal aortic aneurysm have reported on 30 day mortality. The first of these was a pilot, single centre trial in 32 patients in Nottingham, England, in which the overall mortality was over 50%.[7] A three centre trial in 116 patients in the Netherlands reported recently.[8] This trial randomised patients only after local confirmation of both rupture of aneurysm and anatomical suitability for EVAR and therefore excluded haemodynamically unstable patients. Neither trial has published economic evaluations nor shown any difference in 30 day mortality between the EVAR and open repair groups (21% and 25% respectively in the Dutch trial).[8] The low mortality rates in the Dutch trial have been attributed to the presence of specialist teams and patients' characteristics (relative haemodynamic stability and anatomy favouring repair by both open and endovascular methods).

Debate is ongoing about how to configure hospital services to ensure equitable access to complex emergency surgery. Improving the variable outcomes for ruptured aneurysm repair, seen in several countries,[5-10] typifies the challenge in providing 24/7 access to high quality emergency surgery based on robust evidence. The logistics of providing an endovascular service for ruptured abdominal aortic aneurysm are formidable with

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regard to the availability of appropriate personnel, facilities, and consumables. Whether patients with clinical suspicion of rupture should be referred to a centre providing a comprehensive endovascular service and how widely such services should be available, to optimise both patients' outcomes and organisation of services, are therefore unclear. The Immediate Management of Patients with Rupture: Open Versus Endovascular Repair (IMPROVE) trial aims to answer this question and tests the hypothesis that a strategy of endovascular repair, if anatomically feasible, reduces the 30 day mortality of patients with a clinical diagnosis of ruptured abdominal aortic aneurysm, compared with treatment by open repair.

Methods

Study design

IMPROVE is a multicentre trial that randomised patients with a clinical diagnosis of ruptured abdominal aortic aneurysm to either an endovascular strategy of immediate computed tomography and emergency EVAR, with open repair for patients anatomically unsuitable for EVAR (endovascular strategy group), or to the standard treatment of emergency open repair (open repair group). This trial was conducted in 29 eligible centres in the United Kingdom and one in Canada. The eligibility of each centre to participate in the trial was determined by their clinical credentials, including audited volumes of elective EVAR of more than 20 cases a year out of at least 50 cases of aortic surgery, evidence of good interdisciplinary team working, availability of the team for at least 66% of the week, rapid access to emergency computed tomography (target 20 minutes), and audited experience of emergency EVAR (minimum of five cases). The trial protocol, guidelines, and statistical analysis plan are available on the trial websites (www.imperial.ac.uk/medicine/improvetrial or www.improvetrial.org).

All patients aged over 50 years with a clinical diagnosis of ruptured abdominal aortic aneurysm or ruptured aorto-iliac aneurysm, made by a senior trial hospital clinician (either in emergency medicine or vascular surgery), were recorded and were eligible for inclusion. The first brief consent process could be written, verbal, or (if necessary, in England) by using the Mental Capacity Act 2005. Patients were re-consented, for continued participation in the trial, during the recovery period.

We excluded patients if they had a previous aneurysm repair, rupture of an isolated internal iliac aneurysm, aorto-caval or aorto-enteric fistulae, recent anatomical assessment of the aorta (for example, awaiting elective EVAR), or a connective tissue disorder or if intervention was considered futile (patient moribund).

Randomisation

An independent contractor provided telephone randomisation, with computer generated assignation of patients in a 1:1 ratio, using variable block size and stratified by centre. Date and time of randomisation together with type of initial consent (written/verbal/other) were recorded automatically. The randomisation was confirmed by email to the trial manager, the principal investigator at the site, and the trial coordinator. Patients were randomised either to an endovascular strategy (immediate computed tomography followed by EVAR if locally determined as anatomically suitable and open repair when not suitable) or to immediate open repair with computed tomography being optional. As this was a surgical trial, neither investigators nor patients could be masked to the treatment allocated. Adherence to the allocated treatment group was reinforced wherever possible by onsite training and newsletters.

Data verification, computed tomography core laboratory, and diagnosis

All consents were audited, and a minimum of 15% of patients at each centre had source data verified. Computed tomography scans on admission were sent for analysis in the trial core laboratory (St George's Hospital, London) and were subject to expert review for the presence of rupture. Rupture of aneurysm was defined according to protocol. Briefly, evidence on computed tomography of the presence of blood or haematoma outside the aneurysm wall (abdominal aorta, common iliac artery, or both) constituted a diagnosis of ruptured aneurysm. In patients without computed tomography, the diagnosis of rupture was made intraoperatively. In those without either computed tomography or laparotomy, diagnosis was from the underlying cause of death provided. All patients randomised in the UK were registered to obtain automatic reporting of the date and cause of death from the national Data Linkage Service.

Patients admitted with symptoms referable to an abdominal aortic aneurysm but no proven evidence of aorto-iliac rupture (core laboratory diagnosis or laparotomy findings) who underwent repair semi-electively in the same admission were categorised as symptomatic, non-ruptured aneurysm. Other patients had primary hospital discharge diagnoses unrelated to abdominal aortic aneurysm.

Outcomes and oversight

The primary outcome was survival at 30 days after randomisation. The trial, comparing the groups as randomised, had more than 90% power to detect (as significant at 5%) a difference in 30 day mortality of 14% with 600 patients enrolled. This was based on estimated 30 day mortalities of 47% for patients receiving open repair and 21% for those receiving EVAR,[3 11] an estimate of 55% of patients being anatomically suitable for EVAR after computed tomography, and that 5% of both randomised groups would not have a proven diagnosis of ruptured abdominal aortic aneurysm.[7] Hence, estimated 30 day mortality was 44.7% in the open repair group and 30.4% in the endovascular strategy group.

Secondary outcomes reported here include 24 hour mortality, in-hospital mortality, costs of primary admission, re-interventions during the primary admission, and time and place to which discharged from the trial hospital. Mortality and cost effectiveness at 12 months are secondary outcomes scheduled for future reporting.

An independent data monitoring committee reviewed the data, with interim analyses after enrolment of 50, 200, and 400 patients, and agreed that continuing the trial was safe.

Statistical analysis

We analysed data according to a pre-specified analysis plan (available on trial websites), and all analyses, except the causal analysis, were by intention to treat. The primary analysis assessed the difference in the proportion surviving 30 days between the randomised groups, following an intention to treat policy and using a Pearson's χ^2 test without continuity correction. We then adjusted the primary outcome for sex, age, and Hardman index by using logistic regression (with the last two variables considered as continuous), providing an adjusted odds ratio. The Hardman index is a validated risk scoring system for ruptured aneurysms.[12 13] We multiply imputed missing baseline data by using chained equations to increase the precision of the estimates (see web supplement for details).[14] We did sensitivity analyses including centre as a random effect in a generalised linear mixed model and restricting analysis to

patients with a confirmed diagnosis of rupture only. We also fitted a complier average causal effects model to obtain an unbiased estimate of the potential effect if patients had adhered to trial allocation.[15] Specifically, patients who were randomised to the endovascular strategy, found to be not anatomically suitable, and treated by open repair had adhered to trial allocation. Otherwise, we classified reasons for crossover as non-adherence (see supplement for further details).

We assessed a limited number of pre-specified subgroups (age, sex, and Hardman index) for differences in effect of the endovascular and open strategies by using logistic regression with a test of interaction. Because of the number of statistical tests, we required a P value below 0.01 to claim strong evidence of differences between subgroups.

We did secondary endpoint analyses to assess time to in-hospital mortality and time to discharge by using competing risks methodology, with in-hospital mortality and discharge as the two competing risks. We used Gray's non-parametric test to compare cumulative incidence curves.[16]

The cost analysis took a hospital perspective and reported costs (£GBP, 2011-12) within 30 days of randomisation (web supplement). We recorded individual resource use data for each primary hospital admission and readmissions (including re-interventions) prospectively.

Results

Study population

Between September 2009 and July 2013, 1275 patients (78% male) were admitted with a diagnosis of ruptured aorto-iliac aneurysm across the 30 trial centres, and 623 (49%) patients were randomly assigned to the two study groups. Of the 354 patients who met exclusion criteria, 263 were not considered for repair, 74 were awaiting elective repair with recent anatomical assessment of their aneurysm, five had previous aortic aneurysm repair, and 12 had isolated iliac, thoracoabdominal, or other complex aneurysms. Ten randomised patients were excluded from the analysis after review by the Data Monitoring Committee for breach of inclusion criteria: two patients had a secondary rupture with previous aneurysm repair, one patient was admitted electively for aneurysm repair, three patients were randomised before reaching the trial centre and the in-hospital clinical diagnosis was not ruptured aneurysm, and four patients could not be identified in any hospital records. We assumed that these four patients were randomised before reaching hospital and did not arrive alive. The consent processes used for initial consents for the remaining 613 patients were 396 written, 113 verbal with witness, 44 relative/guardian/carer, and 60 Mental Capacity Act. Figure 1⇓ shows the flow of patients through the trial. Baseline variables including age, sex, and Hardman index were balanced between the groups as randomised (table 1⇓).

Interventions

Of 316 patients randomised to the endovascular strategy, the diagnosis of rupture was confirmed in 275 (87%), 8 (3%) had repair of a symptomatic non-ruptured aneurysm in the same admission, and 33 (10%) had other discharge diagnoses. Table 2⇓ shows operative details, with reasons for open repair. Of the patients with ruptured or symptomatic aneurysm, 272 had computed tomography assessed and 174 (64%) were considered anatomically suitable for EVAR; local reporting of unfavourable anatomy at the aneurysm neck was the most common reason for lack of suitability for EVAR (75/84 cases). EVAR was attempted in 154 patients (four were converted to open repair), open repair was attempted in 112 other patients (84 anatomically unsuitable for EVAR, 28 crossovers who were anatomically suitable for EVAR), 16 patients died before aneurysm repair, and one patient with a symptomatic aneurysm refused repair and was discharged.

Of the 297 patients randomised to open repair, the diagnosis of rupture was confirmed in 261 (88%), 14 (5%) had repair of a symptomatic intact aneurysm in the same admission, and 22 (7%) had other discharge diagnoses. Table 2⇓ shows operative details with reasons for crossover to EVAR. EVAR was attempted in 36 (13%) patients and open repair in 220 (80%) patients, and 19 patients died before aneurysm repair.

The 55 patients (33 in the endovascular strategy group and 22 in the open repair group) with a final diagnosis unrelated to abdominal aortic aneurysm had a wide range of other conditions (ranging from ruptured thoracic aortic aneurysm to urinary tract infection), and 45/55 had incidental, usually small, abdominal aortic aneurysms.

Primary outcome

Overall 30 day mortality was 35.4% (112/316) in the endovascular strategy group and 37.4% (111/297) in the open repair group (unadjusted odds ratio 0.92, 95% confidence interval 0.66 to 1.28; P=0.62) (fig 2⇓). Figure 1⇓ shows mortality for each group by treatment received. After adjustment for age, sex, and Hardman index, no difference in 30 day mortality existed between the endovascular strategy and open repair groups (odds ratio 0.94, 0.67 to 1.33; P=0.73); Hardman index was strongly predictive of mortality (table C in web supplement). Inclusion of trial centre in the model did not change the results, and a separate cohort analysis showed no significant effects of centre or volume.[17] The subgroup analyses showed no evidence of an interaction with age or Hardman index. However, the endovascular strategy seemed to be more effective in women than in men (P=0.02) (fig 2⇓). For women, 30 day mortality was 26/70 (37%) in the endovascular strategy group and 36/63 (57%) in the open repair group, compared with 86/246 (35%) and 75/234 (32%) for men. The 30 day mortality rates in patients with confirmed aneurysm rupture were 100/275 (36.4%) in the endovascular strategy group and 106/261 (40.6%) in the open repair group (P=0.31). In a sensitivity analysis for 623 patients (including the post-randomisation exclusions), 30 day mortality rates were 36% (114/319) in the endovascular strategy group and 38% (115/304) in the open repair group (unadjusted odds ratio 0.91, 0.66 to 1.27).

Overall, 549/613 (90%) patients adhered to the trial protocol. Among 501 patients with ruptured aneurysm who received aneurysm repair, the 30 day mortality was 84/259 (32%) in the endovascular strategy group and 87/242 (36%) in the open repair group (odds ratio 0.86, 0.59 to 1.24). The estimated unbiased causal odds ratio for a trial in which everyone adhered to the randomised policy was slightly lower (0.82, 0.51 to 1.32).

Secondary outcomes

Twenty four hour mortality was 22% (68/316) in the endovascular strategy group and 19% (57/297) in the open repair group (unadjusted odds ratio 1.15, 0.78 to 1.71) (fig 3⇓). Results for in-hospital mortality (odds ratio 0.92, 0.66 to 1.27) were similar to those for 30 day mortality (table 3⇓); the risk differences for all three mortality outcomes are given in the supplement. The number and type of re-interventions within 30 days was similar between the randomised groups (table 2⇓), but the average lengths of stay in critical care and in hospital were

shorter in the endovascular strategy group (table 4⇓). Ninety four per cent of discharges within 30 days were directly to home in the endovascular strategy group compared with only 77% in the open repair group (P<0.001) (table 3⇓; fig 4⇓). The average hospital costs within the first 30 days of randomisation were similar between the randomised groups overall (table 4⇓) and for pre-specified subgroups or when using alternative assumptions (web supplement figure A and tables D-F).

Discussion

In this multicentre, pragmatic, randomised trial of patients with a clinical diagnosis of ruptured abdominal aortic aneurysm, an endovascular strategy did not reduce either 30 day mortality or costs overall (30 day mortality 35.4% for endovascular strategy and 37.4% for open repair) or in those with confirmed rupture (36.4% and 40.6%). Although 10% of patients crossed over to the non-allocated treatment group, causal analysis focusing on compliers showed similar results. However, patients were discharged earlier and more often to home, and women may have better survival, with an endovascular strategy.

The observation that women may benefit from an endovascular strategy could be of particular importance, as the effectiveness of EVAR for ruptured aneurysm in women has been questioned, owing to a paucity of evidence.[18] Similar proportions of men and women were included in and excluded from the trial, so our results are not attributable to selection bias. Moreover, women may form an increasing proportion of patients presenting with ruptured aneurysm in future years, as national screening programmes for aneurysm usually focus on men.

Analysis of secondary endpoints suggested that patients randomised to an endovascular strategy had reduced stay in critical care and were discharged home earlier than were patients randomised to open repair. An endovascular strategy was associated with a similar cost to open repair, as the shorter critical care stay and the greater proportion discharged directly to home offset the additional cost of the endovascular device and consumables. Unlike in previous trials of elective repair,[19] patients in the endovascular strategy group had a similar number of re-interventions to the open repair group

Comparison with other studies

The IMPROVE trial had a real world design and hence was fundamentally different from the recent Dutch trial.[8] All patients with clinically diagnosed ruptured aneurysm, in whom aneurysm repair was considered, were eligible for randomisation before knowledge of aortic anatomy, definitive imaging, or laparotomy, with a brief consent process, to permit inclusion of haemodynamically unstable patients (in half, systolic blood pressures of <90 mm Hg were recorded). The trial randomised half of all patients presenting with ruptured aneurysm; of those not randomised, 57% did not undergo repair and a further 17% had operational reasons for non-randomisation (either staff or facilities for EVAR unavailable). A core laboratory reviewed computed tomography scans to verify the diagnosis of rupture, and although the aneurysms were large (mean diameter >8 cm), the proportion of patients judged to be anatomically suitable for endovascular repair was 64%, in keeping with previous studies of ruptured aneurysm.[20 21] As the risk of aneurysm rupture escalates with increasing aortic diameter, the high mean aneurysm diameter was perhaps not surprising. The escalating use of statins in this age group also may offer protection from rupture,[1] and may lead to rupture at higher diameters than previously. That aneurysms of 10 cm or more in diameter did not cause symptoms and had escaped detection is more surprising.

Strengths and limitations

The strength of this trial is its size and "real world" design, starting with the suspicion of ruptured abdominal aortic aneurysm. In the trial, the clinical diagnosis of rupture was incorrect in 13% of patients (compared with the 5% predicted in the power calculation), which illustrates the difficulty in making a clinical diagnosis of ruptured aneurysm, particularly when patients had a small aneurysm identified by screening and presented with classic symptoms of rupture. Although the mortality in patients who received EVAR (25%) was lower than that in those who received open surgery (38%), this did not translate into a lower overall mortality for the patients randomised to an endovascular strategy. Several factors may have contributed to this finding, including the post-randomisation selection of patients to receive EVAR or open repair, the mortality of patients with non-aortic pathology, and unstable patients dying before they underwent aneurysm repair. The subgroup analyses show a direction in favour of lower mortality with the endovascular strategy in patients with the highest Hardman index and age. Misjudgement, leading to conversion from endovascular to open repair, was uncommon but was associated with a very high mortality (100%). The suitability of ruptured aneurysm for EVAR is subjective and will be defined by the aortic morphology, the experience of the operator, and the range of resuscitation, endovascular, and anaesthetic techniques available. The importance of resuscitation and anaesthetic techniques is highlighted in a cohort analysis of the patients with proven rupture.[17] Overall, our findings suggest that identifying realistic candidates for endovascular repair is crucial to improving clinical outcomes.

The appropriate time to subject new technologies to a randomised controlled trial is controversial. The IDEAL recommendations suggest that a randomised trial should be considered when an intervention is sufficiently well evolved to warrant evaluation, but with the expectation that the intervention will continue to develop.[22] Before the IMPROVE trial, uptake of endovascular repair for ruptured abdominal aortic aneurysm in the UK was geographically patchy, with a low uptake, and the procedure was recommended for evaluation purposes only.[23] The IMPROVE trial acted as a focus for widespread evaluation of aneurysm rupture in centres experienced in using EVAR electively but relatively immature with respect to emergency EVAR.

Conclusions and policy implications

The question the trial aimed to answer (to which hospital should patients with suspected ruptured aneurysm be sent?) cannot be answered robustly until longer term survival estimates and cost effectiveness evaluations become available. For the moment, it would seem prudent to send all patients to centres that can offer both emergency endovascular and open repair, with audited results. Patients, particularly women, will favour this approach, as the endovascular strategy offers the potential advantages of earlier discharge directly to home.

In conclusion, a disparity remains between evidence from well equipped, highly specialised single centres, systematic reviews, national datasets, and small randomised clinical trials.[4-27] In IMPROVE, the largest pragmatic randomised trial, 30 day mortality and costs were similar in the endovascular strategy and open repair groups. Evaluation of whether the early fringe benefits of an endovascular strategy translate into longer term

survival benefit and cost effectiveness is needed before definitive conclusions can be drawn about the relative merits of the endovascular strategy (versus open repair) for ruptured aneurysm.

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Transparency statement: JTP as corresponding author confirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: Patient level data can be made available from the corresponding author after authorisation by the Trial Management Committee. Consent from participants for data sharing was not obtained, but any shared data will be anonymised.

1 Anjum A, von Allmen R, Greenhalgh R, Powell JT. Explaining the decrease in mortality from abdominal aortic aneurysm rupture. *Br J Surg* 2012;99:637-45.
2 Lindholt JS, Sogaard R, Laustsen J. Prognosis of ruptured abdominal aortic aneurysms in Denmark from 1994-2008. *Clin Epidemiol* 2012;4:111-3.
3 Bown MJ, Sutton AJ, Bell PR, Sayers RD. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg* 2002;89:714-30.
4 Egorova N, Giacovelli J, Greco G, Gelijns A, Kent CK, McKinsey JF. National outcomes for the treatment of ruptured abdominal aortic aneurysm: comparison of open versus endovascular repairs. *J Vasc Surg* 2008;48:1092-100.
5 Holt PJ, Karthikesalingam A, Poloniecki JD, Hinchliffe RJ, Loftus IM, Thompson MM. Propensity scored analysis of outcomes after ruptured abdominal aortic aneurysm. *Br J Surg* 2010;97:496-503.
6 Schermerhorn ML, Bensley RP, Giles KA, Hurks R, O□Malley AJ, Cotterill P, et al. Changes in abdominal aortic aneurysm rupture and short-term mortality, 1995-2008: a retrospective observational study. *Ann Surg* 2012;256:651-8.
7 Hinchliffe RJ, Bruijstens L, MacSweeney ST, 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.
8 Reimerink JJ, Hoornweg LL, Vahl AC, Wisselink W, van den Broek TA, Legemate DA, et al. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: a multicenter randomized controlled trial. *Ann Surg* 2013;258:248-56.
9 Mell MW, Callcut RA, Bech F, Delgado MK, Staudenmayer K, Spain DA, et al. Predictors of emergency department death for patients presenting with ruptured abdominal aortic aneurysm. *J Vasc Surg* 2012;56:651-5.

What is already known on this topic

For selected patients with ruptured abdominal aortic aneurysm, national datasets and single centre series suggest that endovascular repair is associated with a lower operative mortality than open surgical repair

However, two small randomised trials have failed to show any difference in operative mortality between the two types of repair

Many vascular centres cannot offer emergency endovascular repair at all times

What this study adds?

Similar overall 30 day mortality was seen with an endovascular strategy (35%) and open surgical repair (37%)

However, the study starts to identify patients who may benefit from an endovascular strategy (such as women) and shows that, after 30 days, the endovascular strategy did not cost more than open repair and offers the patient earlier discharge home

10 Brattheim BJ, Eikemo TA, Altreuther M, Landmark AD, Faxvaag A. Regional disparities in incidence, handling and outcomes of patients with symptomatic and ruptured abdominal aortic aneurysms in Norway. *Eur J Vasc Endovasc Surg* 2012;44:267-72.
11 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.
12 Hardman DT, Fisher CM, Patel MI, Neale M, Chambers J, Lane R, et al. Ruptured abdominal aortic aneurysms: who should be offered surgery? *J Vasc Surg* 1996;23:123-9.
13 Acosta S, Ogren M, Bergqvist D, Lindblad B, Dencker M, Zdanowski Z. The Hardman index in patients operated on for ruptured abdominal aortic aneurysm: a systematic review. *J Vasc Surg* 2006;44:949-54.
14 White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011;30:377-99.
15 Cuzick J, Edwards R, Segnan N. Adjusting for non-compliance and contamination in randomized clinical trials. *Stat Med* 1997;16:1017-29.
16 Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk, *Ann Stat* 1988;16:1141-54.
17 IMPROVE trial investigators. Observations from the IMPROVE trial concerning improving the clinical care of patients with ruptured abdominal aortic aneurysm. *Br J Surg* [forthcoming].
18 De Rango P, Lenti M, Cieri E, Simonte G, Cao P, Richards T, et al. Association between sex and perioperative mortality following endovascular repair for ruptured abdominal aortic aneurysms. *J Vasc Surg* 2013;57:1684-92.
19 Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;364:843-8.
20 Hoornweg LL, Wisselink W, Vahl A, Balm R. The Amsterdam Acute Aneurysm Trial: suitability and application rate for endovascular repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2007;33:679-83.
21 Dick F, Diehm N, Opfermann P, von Allmen R, Tevaearai H, Schmidli J. Endovascular suitability and outcome after open surgery for ruptured abdominal aortic aneurysm. *Br J Surg* 2012;99:940-7.
22 McCulloch P, Altman DG, Campbell WB, Flum DR, Glasziou P, Marshall JC. No surgical innovation without evaluation: the IDEAL recommendations. *Lancet* 2009;374:1105-13.
23 National Institute for Health and Clinical Excellence. Endovascular stent-grafts for the treatment of abdominal aortic aneurysms. NICE, 2009 (available at http://guidance.nice.org.uk/TA167).
24 Mayer D, Aeschbacher S, Pfammatter T, Veith FJ, Norgren L, Magnuson A, et al. Complete replacement of open repair for ruptured abdominal aortic aneurysms by endovascular aneurysm repair: a two-center 14-year experience. *Ann Surg* 2012;256:688-95.
25 Karkos CD, Sutton AJ, Bown MJ, Sayers RD. A meta-analysis and metaregression analysis of factors influencing mortality after endovascular repair of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2011;42:775-86.
26 Mayer D, Pfammatter T, Rancic Z, Hechelhammer L, Wilhelm M, Veith FJ, et al. 10 years of emergency endovascular aneurysm repair for ruptured abdominal aortoiliac aneurysms: lessons learned. *Ann Surg* 2009;249:510-5.
27 Mehta M, Byrne J, Darling RC III, Roddy SP, Taggert JB, Sternbach Y, et al. Endovascular repair of ruptured infrarenal abdominal aortic aneurysm is associated with lower 30-day mortality and better 5-year survival rates than open surgical repair. *J Vasc Surg* 2013;57:368-75.

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Tables

Table 1| Baseline characteristics of patients by randomised group. Values are numbers (percentages) unless stated otherwise

Variable	Missing	Endovascular strategy (n=316)	Open repair (n=297)
Mean (SD) age, years	0	76.7 (7.4)	76.7 (7.8)
Male sex	0	246/316 (78)	234/297 (79)
Mean (SD) admission blood pressure, mm Hg:	12	(n=306)	(n=295)
Systolic		110.3 (32.9)	110.4 (31.2)
Diastolic		65.3 (21.4)	66.8 (22.5)
Mean (SD) admission haemoglobin (g/dL)	6	11.2 (2.5); (n=312)	11.1 (2.3); (n=295)
Median (interquartile range) admission creatinine, μM/L	13	117 (94-152); (n=312)	115 (93-151); (n=288)
Acute myocardial ischaemia on electrocardiogram	52	22/291 (8)	23/270 (8)
Loss of consciousness	27	29/305 (10)	21/281 (7)
Hardman index* (0-5):	74	(n=282)	(n=257)
0		93 (33)	69 (27)
1		130 (46)	126 (49)
2		46 (16)	48 (19)
3		11 (4)	12 (5)
4		2 (1)	2 (1)
5		0 (0)	0 (0)
Computed tomography scan performed	0	305/316 (97)	266/297 (90)
Mean (SD) maximum aortic diameter, mm	86	84 (19); (n=263)	81 (18); (n=264)

*Scores 1 point each for age >76 years, acute myocardial ischaemia on electrocardiogram, haemoglobin <9.0 g/dL, creatinine >190 μM/L, and loss of consciousness after admission.

Table 2| Operative details for patients with ruptured and symptomatic abdominal aortic aneurysm by randomised group, including reasons for not receiving allocated treatment. Values are numbers (percentages) unless stated otherwise

Variable	Missing	Endovascular strategy (n=283)	Open repair (n=275)
Median (interquartile range) time from randomisation to theatre admission*:			
Rupture (minutes)	5	47 (28-73); (n=259)	37 (22-62); (n=240)
Symptomatic (hours)	2	3.6 (3.1-15.6); (n=6)	3.0 (1.5-17.6); (n=13)
Lowest systolic pressure before arrival in operating suite:	35	(n=267)	(n=256)
<70 mm Hg		54 (20)	41 (16)
70-89 mm Hg		83 (31)	73 (29)
≥90 mm Hg		130 (49)	142 (55)
Complied with allocated treatment:		254/283 (90)	239/275 (87)
EVAR		150† (54)	—
EVAR converted to open		4 (1)	—
Open repair because unsuitable for EVAR		84 (30)	—
Open repair		—	220 (80)
Died before repair		16 (6)	19 (7)
Refused repair of symptomatic aneurysm		1 (0)	0 (0)
Reasons for not complying with allocated treatment:		Open repair in 28/283 (10)	EVAR in 36/275 (13)
Operational reason‡		4	1
Rapid clinical deterioration		20	0
Medical comorbidities		0	16
Anaesthetist's decision		0	9
Patient's or clinician's preference		2	2
Other		2	8
Type of anaesthesia:	6	(n=262)	(n=254)
General		176 (67)	237 (93)
Local to general		32 (12)	2 (1)
Local		54 (21)	15 (6)
Re-interventions in 30 days§:	8	(n=238)	(n=235)
0		195 (82)	187 (80)
1		28 (12)	33 (14)
≥2		15 (6)	15 (6)
Reasons for re-intervention:	9		
Control of bleeding		9 (4)	11 (5)
Limb ischaemia		19 (8)	17 (7)
Mesenteric ischaemia		14 (6)	19 (8)
Abdominal compartment syndrome		14 (6)	12 (5)
Other		8 (3)	26 (11)
Unknown		2 (1)	1 (0)

EVAR=emergency endovascular aneurysm repair.

*For 525 patients who arrived alive for aneurysm repair.

†Graft configurations used were 35 aorto-uni-iliacs, 104 bifurcated, 2 tube, 9 missing.

‡Essential staff or facilities unavailable.

§For 481 patients who left theatre alive after aneurysm repair.

Table 3| **Place of discharge by randomised group and in-hospital mortality. Values are numbers (percentages)**

Outcome	Endovascular strategy group (n=316)	Open repair group (n=297)
Discharged alive from trial hospital	201 (64)	183 (62)
Place of discharge:		
Home	189 (94)	141 (77)
Another hospital—routine bed	7 (3)	28 (15)
Another hospital—intensive care	0 (0)	1 (1)
Nursing home	0 (0)	3 (2)
Residential home	1 (1)	3 (2)
Sheltered accommodation	1 (1)	0 (0)
Other	3 (1)	7 (4)

Table 4| **Resource use and costs to 30 days by randomised group. Values are mean (SD) unless stated otherwise**

Cost component	Endovascular strategy (n=316)	Open repair (n=297)
Primary admission:		
Time in emergency room (mins)*	93 (370)	73 (157)
Cost (£)	136 (138)	119 (51)
Devices and consumables	4337 (2915)	2523 (2036)
Time in theatre (mins)†	156 (100)	180 (107)
Cost (£)	2050 (1290)	2101 (1264)
Days in critical care	4.2 (5.9)	6.3 (7.7)
Cost (£)	5249 (8779)	8100 (11 020)
Days on routine ward‡	5.2 (5.0)	5.7 (6.7)
Cost (£)	1425 (1591)	1518 (1814)
No (%) re-interventions	44 (14)	48 (16)
Cost (£)	172 (581)	224 (1042)
Readmissions:		
No (%) readmissions	6 (1.7)	5 (1.9)
Cost (£)	64 (554)	34 (290)
Total hospital stay (days)	9.8 (9.0)	12.2 (10.2)
Total cost (£)	13 433 (10 354)	14 619 (12 353)
Incremental cost (£) (95% CI)	−1186 (−2997 to 625)	

For approximately 8% of patients, resource use data were missing; results reported are following multiple imputations. Unit costs are reported in table D in web supplement.

*Includes costs of computed tomography and contrast agent.

†Unit costs of theatre time were £885/hour for patients who actually received emergency endovascular aneurysm repair (EVAR) procedure and £675/hour for those who actually received open repair and reflected the additional staff required for EVAR procedure (for further details see supplement on IMPROVE website).

‡Patients who did not undergo aneurysm repair (8.9%) were assumed to stay on routine ward throughout hospital admission (further details of subgroup and sensitivity analyses are available in web supplement figure A and tables E and F).

Figures

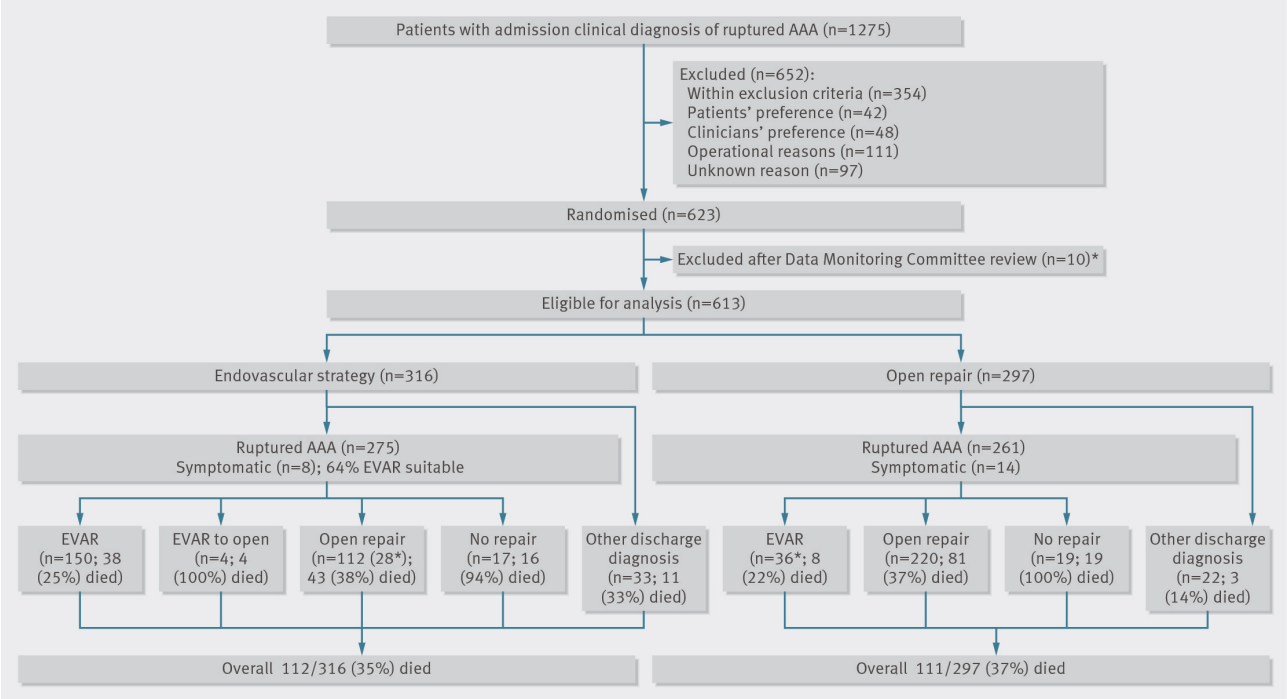

Fig 1 CONSORT diagram showing flow of patients through trial, with 30 day mortality for each group. AAA=abdominal aortic aneurysm; EVAR=endovascular aneurysm repair. *Patients breaching trial protocol

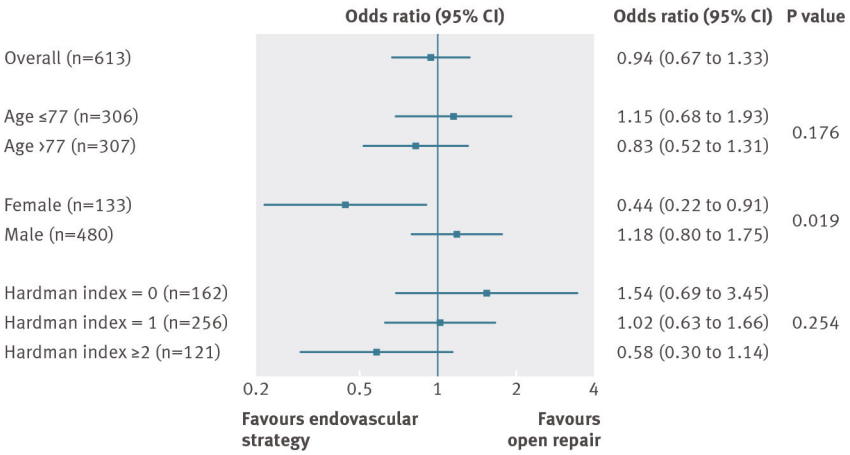

Fig 2 30 day mortality by randomised group with subgroup analyses for age, sex, and Hardman index. Interaction P values consider age and Hardman index as continuous variables

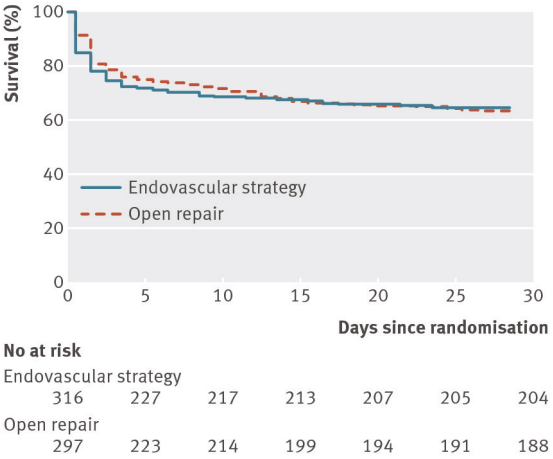

Fig 3 Time to 30 day death by randomised group

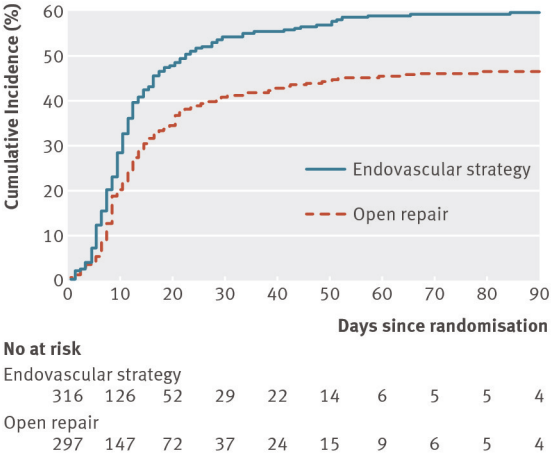

Fig 4 Cumulative incidence of being discharged directly to home by randomised group