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REVIEW

Ruptured Aneurysm Trials: The Importance of Longer-term Outcomes and Meta-analysis for 1-year Mortality

M.J. Sweeting [a], P. Ulug [b], J.T. Powell [b,*], P. Desgranges [c], R. Balm [d], for the Ruptured Aneurysm Trialists [e]

[a] Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK
[b] Vascular Surgery Research Group, Imperial College, Charing Cross Hospital, Fulham Palace Road, London, UK
[c] Vascular Surgery Unit, Hospital Henri Mondor, Creteil, France
[d] Department of Vascular Surgery, Academic Medical Centre, Amsterdam, Netherlands

Objective: To assess current knowledge for the management of ruptured abdominal aortic aneurysm (AAA), based on the 1-year outcomes of 3 recent randomised trials.
Methods: An individual patient data meta-analysis of three recent randomised trials of endovascular versus open repair, including 817 patients, was conducted according to a pre-specified analysis plan, report all-cause mortality and re-interventions at 1 year after the index event.
Results: Mortality across the 3 trials at 1-year was 38.6% for the EVAR or endovascular strategy patient groups and 42.8% for the open repair groups, pooled odds ratio 0.84 (95% CI 0.63–1.11), $p = .209$. There was no evidence of heterogeneity in the odds ratios between trials. When the patients in the endovascular strategy group of the IMPROVE trial were restricted to those with proven rupture who were anatomically suitable for endovascular repair, the pooled odds ratio reduced slightly to 0.80 (95% CI 0.56–1.16), $p = .240$.
Conclusions: After 1 year there is a consistent but non-significant trend for lower mortality for EVAR or an endovascular strategy. Taken together with the recent gains in health economic outcomes demonstrated at 1 year in the IMPROVE trial, the evidence suggests that endovascular repair should be used more widely for ruptured aneurysms.

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INTRODUCTION

The gold standard for surgical reporting standard is 30-day mortality. The French ECAR trial, which reports in this issue again shows that for ruptured abdominal aortic aneurysm (AAA) 30-day mortality is similar after either endovascular or open repair, echoing the recent AJAX and IMPROVE trials and confirmed in an individual patient meta-analysis.[1,2] For patients and health economies a longer-term perspective is needed.[3] Earlier this year the IMPROVE trial reported outcomes to 1 year.[4] There was no statistically significant difference in either overall mortality or AAA-related mortality between the randomised groups, although the estimate of overall mortality was numerically slightly lower for the endovascular strategy group: 41% versus 45% for open repair. ECAR also reports results to 1-year, again with a survival estimate that is numerically lower for the endovascular repair group albeit with no statistically significant difference in survival.[1]

Collaboration between the AJAX, ECAR, and IMPROVE trials (the Ruptured Aneurysm Trialists) also means that we can investigate the hypothesis that the numerically higher mortality in the open repair group of each trial would summate to a significant overall difference at 1 year after randomisation. The results of this individual patient meta-analysis are then discussed in the context of the total information available from the three trials.

METHODS

The methods for the three trials included in this meta-analysis have been published previously.[6–8] The AJAX trial (ISRCTN 66212637) randomised 116 patients, with a computed tomography (CT) scan showing probable rupture and patients being eligible for both open and endovascular aneurysm repair (EVAR), in three centres between 2004 and 2011, using a software-generated randomisation sequence provided by an independent clinical research unit, concealed in sealed envelopes for a 1:1 randomisation to either open or endovascular repair (aorto-uni-iliac grafts for endovascular repair). The ECAR trial (NCT 0057716)

[e] Full list in Appendix 1.

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* Corresponding author. Vascular Surgery Research Group, Imperial College, Charing Cross Hospital, Fulham Palace Road, London W6 8RP, UK.
E-mail address: j.powell@imperial.ac.uk (J.T. Powell).

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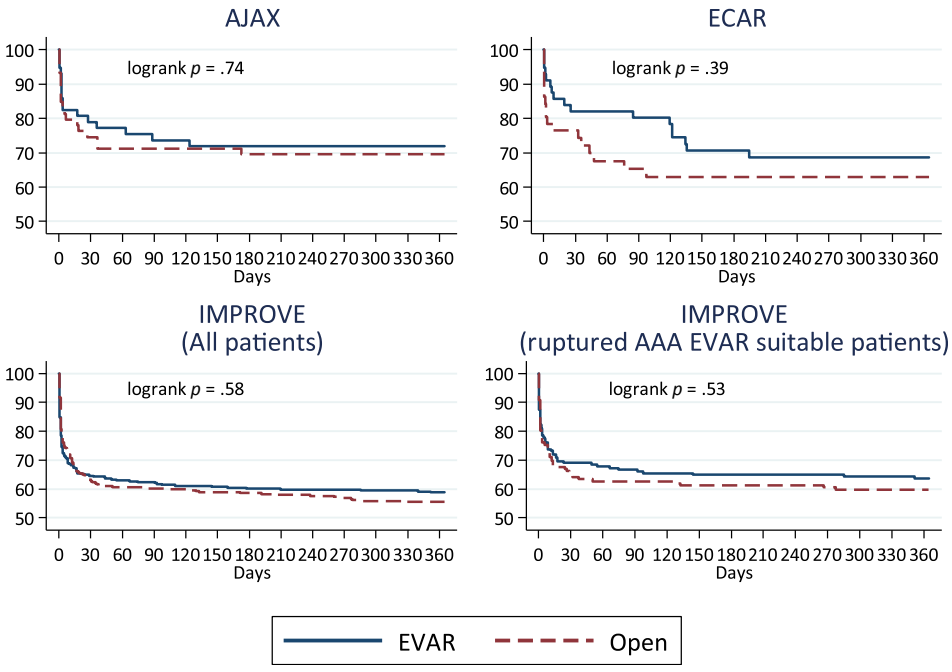

Figure 1. Survival to 1 year in the AJAX, ECAR, and IMPROVE randomised trials. The bottom right hand panel also shows data for the 308 IMPROVE trial patients with ruptured aorto-iliac aneurysm who were anatomically suitable for EVAR.

randomised 107 patients, with a CT scan showing confirmed rupture and an aortic anatomy suitable for endovascular repair and a systolic pressure of >80 mmHg, with treatment allocation by weekly rotation, in 14 centres between 2008 and 2012. The IMPROVE trial (ISRCTN 48334791) randomised 613 eligible patients with an in-hospital clinical diagnosis of ruptured aneurysm in 29 centres between 2009 and 2013, using an independent contractor providing telephone randomisation, with computer-generated assignation of patients in a 1:1 ratio, using variable block size and stratified by centre. For IMPROVE, patients were randomised before CT scan, and randomised to either an endovascular strategy (with open repair if endovascular repair was not anatomically feasible) or to open repair. All three trials were conducted with appropriate ethical approvals; information about these have been reported previously.[6–8] The three data sets were merged based on fields available in the case record forms of the largest trial (IMPROVE), range checks were conducted and queries resolved with the individual trial coordinating centres.

Unfortunately the data from the pilot Nottingham trial[9] could not be retrieved for the meta-analysis.

Statistical analysis

The primary analyses considered the groups "as randomised" within each trial, irrespective of the different trial designs and assessed mortality at 1 year after randomisation (for IMPROVE) and after admission (for AJAX and ECAR). The odds ratio of mortality for the endovascular strategy or EVAR versus open repair was estimated using logistic regression adjusting for trial as described previously.[2] Analyses were then repeated for odds ratios estimated from logistic regression models adjusted for age, sex, and Hardman index, a validated risk scoring system for ruptured aneurysms.[10] Patients lost to follow-up before 1-year were excluded from these analyses. Secondary analyses were conducted with the purpose of making the groups in the different trials more homogeneous. Only those patients with a ruptured AAA final diagnosis and considered suitable for EVAR were retained in the analyses. For AJAX and ECAR, suitability for EVAR was a prerequisite for inclusion in the trial. For the IMPROVE trial suitability for EVAR was defined as either local CT assessment of suitability or, if not assessed locally, a "within liberal Instructions For Use" definition from a core laboratory CT analysis was used.

RESULTS

Summary Kaplan—Meier curves for survival to 1 year for all three trials are shown in Fig. 1. All trials show a small non-significant numerically higher mortality estimate after open repair. The lower right-hand panel of Fig. 1 also shows the summary survival by randomised group for those patients from IMPROVE who had a confirmed rupture and were anatomically suitable for EVAR, a cohort more similar to the AJAX and ECAR cohorts. At 1 year the pooled mortality was 38.6% for EVAR/endovascular strategy and 42.8% for open repair.

For survival at 1-year after admission or randomisation, some patients had been lost to follow-up (AJAX 0, ECAR 17, IMPROVE 2). The remaining 817 patients have been included in an individual patient meta-analysis (Fig. 2A). The evidence from all three trials is homogeneous and hints at a slightly lower 1-year mortality after either EVAR or an endovascular strategy, although the pooled odds ratio is not