Editors’ Introduction

Trans-Atlantic Debate: Whether Endovascular Repair Offers a Survival Advantage over Open Repair for Ruptured Abdominal Aortic Aneurysms

T.L. Forbes, Associate Editor, Journal of Vascular Surgery
Division of Vascular Surgery, London Health Sciences Centre & Western University, 800 Commissioners Road East, Room E2-119, London, ON N6A 5W9, Canada

A.R. Naylor, Editor-in-Chief, European Journal of Vascular and Endovascular Surgery
Vascular Research Group, Division of Cardiovascular Sciences, Clinical Sciences Building, Leicester Royal Infirmary, Leicester LE2 7LX, UK

During the last decade new information and reports have been published regularly describing endovascular and open repair of ruptured abdominal aortic aneurysms; despite this, however, disagreement persists over which therapy is best. At the root of the problem is the discrepancy between the findings of multiple, well-performed observational studies and a smaller number of randomized controlled trials. Our debaters do an excellent job of summarizing the current status of the world literature and describing their conflicting interpretations.

*Corresponding author.
Email-address: ross.naylor@uhl-tr.nhs.uk (A.R. Naylor)
1078-5884/$ — see front matter
http://dx.doi.org/10.1016/j.ejvs.2014.11.013

Part One: For the Motion. EVAR Offers No Survival Benefit over Open Repair for the Treatment of Ruptured Abdominal Aortic Aneurysms

L. Dubois
Division of Vascular Surgery, London Health Sciences Centre & Western University, Department of Epidemiology & Biostatistics, Western University, London, ON N6A 5W9, Canada

Introduction

There is no doubt that endovascular aortic aneurysm repair (EVAR) results in lower perioperative mortality when compared with open aneurysm repair in elective, nonruptured, patients. Multiple well-designed, large, randomized controlled trials (RCTs) have consistently shown a roughly 50% reduction in the risk of 30-day mortality in favor of endovascular repair for elective abdominal aortic aneurysms (AAAs).1–3 Given the increased mortality associated with open repair of ruptured AAAs (rAAAs), many surgeons and investigators expected to see a similar improvement in mortality when EVAR was compared with open repair (OR) in this high-risk patient group. The observational literature has indeed shown such an improvement, with reported mortality rates following EVAR ranging from 16% to 35% compared with 37–63% following OR.4–14 This difference in mortality has been further substantiated by large administrative database studies,15–17 the largest of which included data on >42,000 patients and reported a reduced in-hospital mortality rate associated with EVAR in ruptured patients (26% vs. 39%; p < .001).17 With the sheer volume of observational and administrative data available indicating a reduction in perioperative mortality, some authors have argued that randomized trials comparing EVAR and OR are unnecessary and may even be unethical.11,18

Many of the benefits touted for EVAR in a patient with a ruptured AAA seem self-evident: reduced physiologic stress with avoidance of aortic cross clamping and ischemia-reperfusion injury, the ability to carry out the procedure under local anesthetic, reduced hypothermia, and reduced blood loss. Yet despite these considerations and the weight of the previous observational data, RCTs to date have shown no difference in early mortality between EVAR and OR in ruptured patients. Certainly, these results would seem surprising to many surgeons; however, one cannot ignore the evidence.

Two of the trials are smaller, and may be criticized for being underpowered. The first trial, from the UK, included
just 32 patients and found that the 30-day mortality rate was similar between OR and EVAR (53% in both groups).\textsuperscript{19} Similarly, in the Dutch trial that included the results of 116 patients, there was no difference in 30-day mortality between EVAR and OR (21% vs. 25%).\textsuperscript{20} The latter trial has been criticized for being too selective as it excluded patients who were either too unstable for computed tomography (CT) scan or had anatomy unsuitable for EVAR. These criticisms were addressed by the recent publication of early results from the IMPROVE trial. This trial was not only larger and more appropriately powered but was designed in a pragmatic style that strove to include all patients who presented to hospital with a suspected diagnosis of rAAA. In doing so, the investigators ensured generalizability of their results. The IMPROVE trial clearly demonstrated, based on the analysis of 613 patients, that a nonselective approach to EVAR in patients with rAAA resulted in equivalent 30-day mortality when compared with OR (35.4% vs. 37.4%; \( p = .620 \)).\textsuperscript{21} Some may criticize this trial for its pragmatic design, where patients were randomized to a therapeutic approach as opposed to a specific procedure. Patients were randomized once a clinical diagnosis of suspected rAAA was made, without knowledge of their anatomic suitability for EVAR. If randomized to the EVAR strategy arm, patients would undergo a CT scan to determine anatomic suitability and, if suitable, would undergo EVAR; otherwise, they would undergo open repair. This method of allocation resulted in only 64% of those in the EVAR group being anatomically suitable, and 13% of patients had a diagnosis other than rAAA. These limitations where necessary consequences of the pragmatic trial design, ultimately ensuring that both treatment strategies were comparable and free of selection bias and confounding.

All RCTs to date have shown no difference in mortality between OR and EVAR in ruptured patients. How can there be such a discrepancy between the RCT literature and observational data?

**WHY OBSERVATIONAL STUDIES ARE MISLEADING**

Regardless of the number of observational studies showing improved mortality with an EVAR, they all suffer from the same inherent biases that tend to favor EVAR. The most recent and complete meta-analysis of the observational literature comparing EVAR and OR in ruptured patients found that most studies suffered from severe selection bias.\textsuperscript{22} The key factors determining why many surgeons in these studies offer EVAR to ruptured patients (stable enough to have imaging and favorable anatomy) are also both strong independent predictors of postoperative mortality. The effect of preoperative hemodynamic instability on mortality from ruptured aneurysms is well known.\textsuperscript{23} This inherently favors the EVAR group by restricting EVAR to those patients that at baseline have stable blood pressure and an improved survival. Similarly, in observational studies patients with short aortic necks (<10 mm) and challenging iliac anatomy (tortuosity, calcification) tended to have OR. These same anatomic factors that make EVAR unfavorable also make OR more complex and increase perioperative mortality. In a recent abstract using the IMPROVE data, investigators noted that mortality was associated with the aortic neck length in both the EVAR and OR groups. In those patients with aortic necks between 5 and 9 mm the 30-day mortality for EVAR was 63% (vs. 44% for OR), while in those with aortic neck lengths >30 mm, mortality in both groups was ~25%.\textsuperscript{24} Other authors have also shown EVAR anatomic suitability to be a strong independent predictor of mortality following open repair of rAAA.\textsuperscript{25} In addition to the effect of selection bias, the observational studies also suffer from a lack of blinded outcome assessments, selective reporting of results, and publication bias.\textsuperscript{22} Publication bias may be particularly important as centers with poor results following EVAR for ruptured patients would be unlikely to publish those results. Even those authors that are strong advocates for an aggressive “EVAR-first” policy for rAAA have admitted that many of the centers reporting their results for rAAA limit the procedure to hemodynamically stable patients or those with “contained” ruptures and that “it is totally invalid to compare the lower procedural EVAR mortality rates with those for open repair.”\textsuperscript{26} I would agree, and state that the only valid comparison comes from properly designed, powered, and reported RCTs like IMPROVE.

Not only do administrative and clinical database studies suffer from the same limitations, they are also compounded by errors in diagnostic coding, missing data on key confounders (hypotension, level of consciousness, anatomy), and lack of information on the volume and experience of the surgeons performing the interventions.\textsuperscript{17,27} These limitations further compromise the comparison between EVAR and OR for rAAA.

Observational studies often overestimate the benefit of new interventions when compared with RCTs.\textsuperscript{28} The literature is filled with examples where RCTs have contradicted the results of observational studies and tempered early enthusiasm for new procedures. Classic examples from the vascular literature include the disappointing results of prosthetic bypasses for leg ischemia when compared with vein grafts, as reported by Veith et al. in the 1980s,\textsuperscript{29} the harmful effects of extracranial—intracranial arterial bypass in patients with cerebrovascular disease,\textsuperscript{30} and the lack of benefit to preoperative coronary artery revascularization prior to vascular surgery.\textsuperscript{21} Similar to these examples, the mortality benefit ascribed to EVAR in rAAA patients by observational studies has not been confirmed by RCTs. Despite all of EVAR’s theoretical advantages and presumed effectiveness based on uncontrolled data, it seems that favorable anatomy, hemodynamic instability, and overall patient health status exert a greater influence on postoperative mortality in ruptured patients than the method of repair.

It is evident that surgeons expected to find a mortality benefit to EVAR in ruptured patients. The language used in
Conclusions

Although most observational and administrative database studies suggest a reduction in mortality with EVAR for patients with a rAAA, RCTs have found equivalent early mortality when compared with OR. The observational literature suffers from selection bias, with EVAR generally reserved for those with favorable anatomy and hemodynamic stability. The IMPROVE trial has shown that EVAR results in a reduced length of hospital stay and a higher proportion of home discharges. These benefits should be acknowledged but a misinterpretation of the literature resulting in an aggressive “EVAR-only” policy may lead to increased short- and long-term morbidity and mortality if the procedure is attempted in those with unfavorable anatomy. The level I evidence suggests that the same care and attention that goes into selecting anatomically and physiologically suitable candidates for EVAR in the elective setting should also be applied to the ruptured patient. If patients are found to be poor anatomic candidates for EVAR, then they are likely best served with an expeditious OR.

References

Part Two: Against the Motion. EVAR Offers No Survival Benefit over Open Repair for the Treatment of Ruptured Abdominal Aortic Aneurysms

D. Mayer *, Z. Rancic, F.J. Veith, M. Lachat

Division of Vascular Surgery, University Hospital of Zurich, Raemistrasse 100, 8091 Zurich, Switzerland

Email-address: Luc.Dubois@lhsc.on.ca

1078-5884/$ — see front matter © 2014 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejvs.2014.11.015