TRANS-ATLANTIC DEBATE

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Debate: Whether endovascular repair offers a survival advantage over open repair for ruptured abdominal aortic aneurysms

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During the last decade, new information and reports have been published regularly describing endovascular and open repair of ruptured abdominal aortic aneurysms, but despite this, 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. (J Vasc Surg 2015;61:546-55.)

PART I: ENDOVASCULAR ANEURYSM REPAIR OFFERS NO SURVIVAL BENEFIT OVER OPEN REPAIR FOR THE TREATMENT OF RUPTURED ABDOMINAL AORTIC ANEURYSMS + FOR THE ARGUMENT

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There is no doubt that endovascular aneurysm repair (EVAR) results in lower perioperative mortality compared with open aneurysm repair in elective, nonruptured, patients. Multiple well-designed, large, randomized controlled trials (RCTs) have consistently shown an ~50% reduction in the risk of 30-day mortality in favor of EVAR 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 in this high-risk patient group. The observational literature has indeed shown such an improvement, with reported mortality rates after EVAR ranging from 16% to 35% compared with 37% to 63% after open repair.[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 RAAA patients of 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 open repair are unnecessary and may even be unethical.[11,18]

Many of the benefits touted for EVAR in an RAAA patient seem self-evident: reduced physiologic stress with avoidance of aortic cross-clamping and ischemia-reperfusion injury, ability to perform 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 endovascular and open repair in RAAA 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 United Kingdom, included just 32 patients and found the 30-day mortality rate was similar between open and EVAR (53% in both groups).[19] Similarly, in the Dutch trial, which included results for 116 patients, there was no difference in 30-day mortality between EVAR and open repair (21% vs 25%).[20] The latter trial has been criticized for being too selective because it excluded patients who were too

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unstable for a computed tomography (CT) scan or had anatomy unsuitable for endovascular repair.

These criticisms were addressed by the recent publication of early results from the Immediate Management of the Patient With Rupture: Open vs Endovascular Repair (IMPROVE) trial. This trial was not only larger and appropriately powered but was also designed in a pragmatic style that strove to include all patients who presented to the 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 endovascular aneurysm repair in RAAA patients resulted in equivalent 30-day mortality compared with open repair (35.4% vs 37.4%, $P = .62$).[21] Some may criticize this trial for its pragmatic design, where patients were randomized to a therapeutic approach rather than to a specific procedure. Patients were randomized once a clinical diagnosis of suspected RAAA was made, without knowledge of their anatomic suitability for EVAR. Patients randomized to the EVAR strategy arm underwent a CT scan to determine anatomic suitability and, if suitable, underwent EVAR; otherwise, they underwent 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 were 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 open and endovascular repair in ruptured patients. How can there be such a discrepancy between the randomized controlled literature and observational data?

Why observational studies are misleading. Regardless of the number of observational studies showing improved mortality with 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 open repair in ruptured patients found most studies suffered from severe selection bias.[22] The key factors determining why many surgeons in these studies offer EVAR to ruptured patients (stability 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 RAAAs is well known.[23] This inherently favors the EVAR group by restricting EVAR to those patients who have stable blood pressure at baseline and an improved survival. Similarly, patients in observational studies with short aortic necks (<10 mm) and challenging iliac anatomy (tortuosity, calcification) tended to have open repair. These same anatomic factors that make EVAR unfavorable also make open repair 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 the EVAR and open treatment groups. In those patients with aortic necks between 5 and 9 mm, the 30-day mortality was 63% for EVAR and 44% for open repair, whereas in those with aortic neck lengths >30 mm, mortality in both groups was ~25%.[24] Other authors have also shown EVAR anatomic suitability is a strong independent predictor of mortality after open repair of RAAA.[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.[22] Publication bias may be particularly important because centers with poor results after EVAR for ruptured patients would be unlikely to publish those results. Even those authors who 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."[26] I would agree and state that the only valid comparison comes from properly designed, powered, and reported RCTs such as IMPROVE.

Administrative and clinical database studies not only suffer from the same limitations but 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.[17,27] These limitations further compromise the comparison between EVAR and open repair for RAAA.

Observational studies often overestimate the benefit of new interventions compared with RCTs.[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 compared with vein grafts as reported by Veith et al[29] in the 1980s, the harmful effects of extracranial-intracranial arterial bypass in patients with cerebrovascular disease,[30] and the lack of benefit to preoperative coronary artery revascularization before vascular surgery.[31] 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 patients with RAAA 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 some of the publications surrounding the topic speaks toward this investigator bias: "The finding that mortality rates were comparable in open and endovascular groups was disappointing…"[19]; however, the existing level I evidence quite clearly shows that EVAR does not confer a survival advantage to patients with RAAA. Misinterpreting this literature could lead to troubling consequences for patient care.