

# EVAR Versus Open Repair: Do We Need Another Trial?

Exploring the AAA data landscape and the options for the next generation of data.

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**A** bdominal aortic aneurysm (AAA) rupture is a frequent cause of cardiovascular death in industrialized countries, particularly among older men. In patients with infrarenal AAAs, open surgical repair and endovascular aortic repair (EVAR) are treatment options. For more than 50 years, open surgical repair has been the gold standard practice,<sup>1</sup> whereas EVAR was first reported in 1986.<sup>2</sup> However, EVAR is now the most common procedure for treating AAAs. Nevertheless, controversy still exists as to the relative efficacy of the two techniques in short, mid, and long term.

## THE DATA: WHERE DO WE STAND TODAY?

A meta-analysis of retrospective studies and three prospective randomized controlled trials (RCTs) have all shown a marked benefit of endovascular repair with respect to 30-day postoperative mortality,<sup>3-6</sup> and these results have been supported by data from large registries.<sup>7,8</sup> Conversely, investigating relatively low-risk patients, the ACE trial did not find a benefit with EVAR.<sup>9</sup> Study design, population studied, selection of centers (low volume vs high volume), surgical techniques, type of stent graft, specialists performing the procedure (vascular, cardiac, or general surgeons), postoperative care, national standards of care, and date of publication are among numerous factors potentially accounting for differences in mortality rates.

As reported in RCTs and defined in practice guidelines,<sup>10</sup> EVAR typically resulted in a significantly shorter duration of procedure, less blood loss and blood replacement, a lower rate of use of postoperative mechanical ventilation, a shorter stay in the intensive care unit, and a shorter hospital stay, but required substantial exposure to x-rays and contrast medium.

At midterm (2–4 years) and long-term (6–8 years) follow-up in patients with low to intermediate risk factors, all-cause mortality and aneurysm-related mortality did not differ between the two treatment groups, as shown by four RCTs<sup>3,4,6,9</sup> and a large registry.<sup>8</sup> As reported in EVAR-1, the early benefit was completely lost in the longer term, with slightly higher aneurysm-related mortality after 4 years in the endovascular repair group. In other words, low- and intermediate-risk patients had better results with the more aggressive treatment (open surgery) in these studies.

These findings have implications for the selection of patients for endovascular repair, and issues such as patient preference, need for and burden of surveillance after endovascular repair, and costs have to be addressed. After 8 years, the continuing occurrence of graft-related complications and reinterventions underscores the need for continued surveillance, and these clinical episodes contribute to the increase in the lifetime cost of aneurysm-related events after endovascular repair as compared with open repair.<sup>3</sup> The results also confirm that careful long-term follow-up of surgical innovations is essential, as highlighted in recent recommendations.<sup>11</sup>

In EVAR-1, DREAM, ACE, and the Medicare database, EVAR was associated with more vascular reinterventions and complications. The OVER trial, which investigated all reinterventions, including those that were nonvascular, did not confirm these findings. As a matter of fact, indications for reinterventions are subjects of discussion; rupture, thrombosis, or type I endoleaks are clear indications for reintervention, whereas the need for reintervention in type II endoleaks is less certain. For example, the EVAR-1 and ACE trials have counted reinterventions only as procedures directly related to graft placement,

whereas OVER included any secondary therapeutic procedures resulting from the original procedure, such as incisional hernia repairs.

Incisional hernia repairs were the most common secondary therapeutic procedures in the open repair group in the OVER study, occurring in 4.9% of patients at 2 years. This is comparable with the 5.8% rate reported in a Medicare population within 4 years after open repair.<sup>8</sup> A meta-analysis found that open AAA repair carries a fivefold greater risk of incisional hernia than surgery for aortoiliac occlusive disease, possibly reflecting an underlying collagen defect in patients with AAAs.<sup>12</sup>

In EVAR groups, as reported in the ACE and OVER trials, buttock claudication appears as a well-known complication of overlapping hypogastric arteries by the limb of a stent graft when the aneurysm extends close to or involves the hypogastric bifurcation. In the other studies, this complication was not specifically studied.

Health-related quality of life decreased in the early postoperative period in the European trials, particularly following open repair, but these changes resolved before 6 months.<sup>13</sup> In the DREAM trial, quality of life at 6 months and 1 year was lower in the endovascular group.<sup>4</sup> OVER focused on later postoperative quality of life and found no differences between the two treatment groups at 1 and 2 years.

## WHERE DO WE GO NEXT?

Despite the extensive clinical trials conducted to date, uncertainties remain regarding the comparative effectiveness of these two techniques in the medium and long term. It therefore seems necessary to conduct further studies to try to answer those uncertainties, especially since several new stent grafts have become available. These stent grafts have been developed to overcome limitations due to anatomical conditions such as small, diseased, or tortuous iliac arteries and challenging necks (ie, short, angulated, calcified, or thrombotic). They are promoted as more durable by preventing material fatigue, component disconnection, fabric tears, and metallic frame rupture. Basically, they may decrease the need for reintervention and therefore improve the overall results of EVAR.

How can we prove this expectation? RCTs are major enterprises and cannot answer all of the questions arising about new technologies. Strict entry criteria limit the conclusions to a small subset of patients. The cost and energy spent are considerable. Long-term results are awaited to draw firm conclusions, but in the meantime, the technologies improve, rendering conclusions obsolete sometimes even before the study publication. Another weakness of RCTs is the slow pace of enrollment and the general fail-

ure to reach the expected number of patients. This clearly affects the power of the analysis.

The question of which parties should pay to meet the need for medical evidence is open. Industry-sponsored trials are to be taken with caution, knowing that 70% of negative trials are never published. Independent trials, such as the four RCTs on this topic, are to be commended; however, public money is currently scarce. Patient choice is also a major issue. When patients are told that there is one treatment with no incision, rapid recovery, but long-term uncertainty versus a more aggressive approach that is a definitive AAA cure but one that comes with a higher rate of complications including risk of hernia, the large majority choose the former. For all of those reasons, it is very doubtful that a new RCT will ever be organized to test the latest stent graft generation.

## ALTERNATIVES TO TRADITIONAL RCTs

A seemingly easier and more realistic way to obtain this information would be a large cohort study by propensity score methods. Propensity score is the conditional probability of having an exposure to risk given a set of measured baseline covariates.<sup>14,15</sup> The propensity score models used are adjusted for differences among patients in terms of demographic characteristics and coexisting conditions, with the use of claims data, in both inpatient and outpatient settings and accumulated over a period of time. The Medicare reports on AAA treatments found no clinically or statistically significant differences between the two treatments.<sup>8</sup> The weakness of propensity analyses is that they cannot account for selection bias related to unmeasured characteristics. Secondly, the administrative data can be subject to coding errors and the difficulty of differentiating postoperative complications from pre-existing conditions.

Nevertheless, the advantage of this type of study is that it is based on large cohorts representing the real world. These studies can be carried out quickly, are cost effective, and can be repeated. Can we trust them? I believe the answer is yes. This methodology has been used for the comparison of carotid stenting and carotid endarterectomy procedures among more than 68,000 patients who were enrolled in the REACH registry.<sup>16</sup> In terms of late outcomes, they found similar results to the CREST, EVA-3S, and SPACE RCTs. Similarly, with EVAR, the Medicare<sup>8</sup> and EUROSTAR<sup>7</sup> registries showed similar results to RCTs.

We owe our patients the answers to questions of safety and efficacy of new devices. More and more, national health care providers, such as in France, for example, oblige companies to set up postmarket registries. If a

company does not comply with the rules, it is put out of the market, and the use of these grafts is no longer reimbursed. The physician and the company must declare adverse events linked to any device to the Haute Autorité de Santé. Although this system is not perfect, at least surveillance is established, and graft malfunction can be detected early.

## CONCLUSION

In summary, new RCTs comparing EVAR and open surgery for infrarenal AAA treatment, even if believed to be necessary, will not be the answer for the foreseeable future. Large, prospective, postmarket registries are a safer bet to answer the remaining questions. ■

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