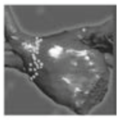

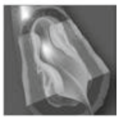

The benefits of treating abdominal aortic aneurysms with minimally invasive endovascular repair

"The apparent shift in burden of disease to older age groups calls for increasingly less invasive treatment options and will provide real challenges to the future management of this condition."

Sherif Sultan
Author for correspondence:
Western Vascular Institute, Department of Vascular & Endovascular Surgery, University College Hospital Galway, Newcastle Road, Galway, Ireland
and
Department of Vascular & Endovascular Surgery, Galway Clinic, Dublin Road, Galway, Ireland
Tel.: +353 9172 0121
Fax: +353 9172 0122
sherif.sultan@hse.ie

Niamh Hynes
Department of Vascular & Endovascular Surgery, Galway Clinic, Dublin Road, Galway, Ireland

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Open repair, endovascular repair (EVAR) and optimal medical therapy each have a role to play in the management of abdominal aortic aneurysms (AAAs); however, the latter has proven to be ineffective in preventing the expansion and rupture of AAAs.

The benefits of EVAR over open repair of AAAs have been repeatedly demonstrated in the short- to medium-term and, as a result, EVAR is the treatment of choice in most vascular centers. In 2006, the number of EVAR procedures performed in the USA exceeded that of open repair and this paradigm shift toward EVAR continues. However, despite global dissemination of endovascular technology, unproven benefits continue to cause controversy, such as long-term durability, surveillance, emergency repair, the use of endografts outside of the instructions for use (IFU), costs, patient age and screening. These unresolved issues will strongly influence technical developments and future configuration of vascular services.

Durability of EVAR

Several randomized controlled trials (RCTs) have highlighted a significant reduction in 30-day operative mortality and length of hospital stay in favor of EVAR compared with open repair. These trials have been established with the intent to determine long-term outcomes after EVAR compared with open surgical repair, but the trials remain incomplete. However, medium-term follow-up suggests that the early survival benefit of EVAR may be lost over time [1,2]. In addition, data from registries have indicated that complication rates post-EVAR can be as high as 25–40%, necessitating close lifelong surveillance [3]. These concerns have led some authors to believe that they may negate the initial survival advantage associated with EVAR.

However, when evaluating the data on the long-term outcome of EVAR, it must be taken into consideration that long-term data are also limited on mortality and reintervention after open surgical repair.

A number of meta-analyses have been published that confirm the suggested short-term benefits of EVAR, but fail to confirm the long-term advantages, compared with open repair [4]. They found that EVAR and open repair were equivalent with respect to all-cause mortality at both 2-year and 4-year or greater follow-up, and late aneurysm-related mortality [4].

Meta-analyses results challenge the durability of EVAR, reporting significantly higher reintervention rates with EVAR [4]. On the other hand, the OVER trial identified equivalent reintervention rates after EVAR and open repair [5]. This calls into question the accuracy of reports, suggesting an underestimation of complications following open repair.

However, it is only with the inclusion of data from the OVER trial [5] and two unconfirmed ruptures from the DREAM trial [2] that the meta-analysis determines the rate of rupture to remain significantly higher after EVAR. In this context, it is worth noting that the OVER trial used a significant proportion (20%) of Medtronic AneurX® (Medtronic, MN, USA) endografts, which were shown to be associated with a worse survival rate; these were used in six out of the ten aneurysm-related deaths, and two out of the three who experienced nonfatal rupture. The rate of rupture in the EVAR 1 trial is exceptionally high (4%) compared with the other RCTs (1.4%). When the RCTs are analyzed with the exclusion of the EVAR 1 trial, the likelihood of rupture significantly decreases from 7.20 to 3.37% and results in a nonsignificant rupture risk between EVAR and open repair ($p = 0.16$). The reason for the higher rate of rupture after EVAR 1 remains unknown, with neither endograft selection nor operator experience being blamed. Recruitment into EVAR 1 began in 1999 and was completed in 2003. Much progress has since been made in terms of endograft design and operator experience. However, all six published RCTs comparing EVAR with open surgical repair are similarly limited by their questionable application to contemporary practice and, consequently, the 10-year data that we are waiting for with great expectations may actually fail to deliver an accurate estimation of long-term durability.

EVAR surveillance

There is debate regarding whether current surveillance protocols are clinically efficacious and cost effective. Meta-analysis by Karthikesalingam *et al*. confirms that duplex ultrasound (DUS) detects types 1 and 3 endoleak with sufficient accuracy for surveillance after EVAR [6]. DUS reduces the long-term burden of nephrotoxicity, cost and radiation exposure incurred by computed tomography and it also provides additional data regarding in-stent flow characteristics, which are of use in detecting limb stenosis and kinking. Beeman *et al*. calculated a 29% reduction in surveillance costs by changing from computed tomography to DUS-only surveillance, amounting to a saving of US$1595 per patient per year, without compromising safety [7].

"...when evaluating the data on the long-term outcome of endovascular repair it must be taken into consideration that long-term data are also limited on mortality and reintervention after open surgical repair."

In addition to the controversy surrounding imaging modality, surveillance time intervals are also controversial. The majority of reinterventions after EVAR occur in patients who present symptomatically between normal surveillance scans [8]. Furthermore, the risk of reintervention after EVAR is not homogenous; a minority of patients are at greater risk and constitute a high-risk group in need of closer surveillance. Studies reveal that hostile aneurysm morphology is prognostic of later endograft complications [8,9]. There is ongoing research into the development of a preoperative morphological scoring system to determine those at highest risk of reintervention who would benefit from intensive surveillance, with rationalization of surveillance in those at lowest risk.

DUS is cost effective and has proven accuracy in the measurement of sac expansion and type 1 and 3 endoleaks, with the extra benefit of being nontoxic for high-risk patients requiring frequent imaging.

Use of endografts outside of IFU/pararenal EVAR

The IFU specify anatomic characteristics including aortic neck diameter, aortic neck length, aortic neck angle and iliac artery morphology, which are recommended to guide patient selection for suitability for EVAR. Patients enrolled in RCTs were treated in accordance with IFU. However, as EVAR has dispersed globally into everyday clinical practice and operators have become more experienced, many have pushed the envelope and treated patients who did not strictly conform to IFU, especially in cases where patients are too high risk for open repair. Schanzer *et al*. published their analysis of the M2S, Inc. (NH, USA) imaging database on 10,228 patients. They determined that compliance with EVAR device guidelines across the USA was poor and that liberalization in anatomic criteria deemed appropriate for EVAR was associated with worse outcomes and an increased risk of rupture [9]. However, this study represented a very heterogeneous data set, encompassing multiple centers with variable experience.

"The common factor in studies reporting successful outcomes in the use of endografts outside of instructions for use is the experience of the center and individual operators."

We reported a comparative study on pararenal AAA repair using open versus endovascular approaches outside of the manufacturer's IFU, and demonstrated a 3-year survival benefit in the EVAR group compared with those treated by open surgery [10]. It is important to note that in our study only 57% of patients undergoing pararenal repair were still alive at 3 years, demonstrating, as has been shown in multiple studies, that those with complex aortic aneurysms are more likely to have a poor comorbid status, rendering repair palliative in the hope that it will prevent aneurysm rupture for long enough, so that they end up dying from their comorbid disease conditions.

We found that using EVAR did not increase the risk of secondary intervention and was actually associated with an improved quality of life, and that the incremental cost–effectiveness was significantly improved in the EVAR group. Other authors have had similarly encouraging results.

Donas *et al*. reported a 24-month computed tomography follow-up of high-risk patients with pararenal AAA treated outside of IFU, using chimney and/or periscope endografts, and found that 90% maintained successful aneurysm exclusion at 2 years [11]. The common factor in studies reporting successful outcomes in the use of endografts outside of IFU is the experience of the center and individual operators.

EVAR for emergency repair of ruptured AAA/EVAR of ruptured aortic aneurysm

Death rates from open ruptured AAA (RAAA) repair are unacceptably high and little has changed in recent years. Bown *et al.* showed a gradual reduction in operative mortality by 3.5% per decade, with estimated operative mortality rate from open repair for RAAA in 2000 at 41% [12]. This figure remains high despite advances in intensive care medicine and the development of specialist vascular centers with separate on-call services. This study also concluded that this constant improvement in survival would not be continued, but instead would level off at a maximum beneficial level [12]. The major contributing factors to mortality following open repair of RAAA are multiple organ failure and shock, both of which can be minimized by using EVAR. Furthermore, EVAR can be performed quicker, under local anesthetic and with less blood loss to improve chances of survival.

> "*...high-volume elective endovascular repair centers had a fivefold increase in the use of endovascular repair in a ruptured aortic aneurysm setting...*"

Although RCTs are being attempted, in the context of acute rupture recruitment and randomization of dying patients raises a major ethical dilemma. Can one really enroll or randomize a moribund patient, especially when there is ample and consistent evidence to justify an EVAR-first policy?

Several meta-analyses have been published that demonstrate significantly reduced mortality with the use of EVAR. Rayt *et al.*, in a meta-analysis of 31 studies, demonstrated an operative mortality rate of 24% after treatment with EVAR of ruptured aortic aneurysm [13]. Visser *et al.* conducted a systematic review of ten studies comparing EVAR with open repair in RAAA and quoted a mortality rate of 22% for EVAR of ruptured aortic aneurysm [14]. Harkin *et al.* quoted a mortality rate of 17% [15]. Similar rates of mortality were found by Mastracci *et al.* at 21% [16].

The benefits of EVAR for RAAA are far reaching, as long as experienced operators undertake the procedure. In a nationwide study, McPhee *et al.* showed that while the incidence of RAAA between 2001 and 2006 remained fairly constant, EVAR was used to treat RAAA in an increasing proportion of patients [17].

Establishment of a multidisciplinary ruptured AAA protocol maximizes the ability to perform EVAR in an emergent fashion in both hemodynamically stable and unstable patients [18]. Mehta *et al.* found that following the implementation of a protocol for EVAR for RAAA, the mean time to the operating room from a presumptive diagnosis of RAAA was 20 min, with an overall mortality rate of 24% [18]. The authors attributed their success to maintaining an adequate inventory of available stent grafts and a diverse array of endograft options, thereby facilitating emergency usage, surgeon comfort with EVAR in the elective setting and the practice of 'hypotensive hemostasis' (minimizing volume resuscitation and only tolerating hypotension as long as the patient maintained a detectable blood pressure, in an effort to minimize ongoing hemorrhage). This is why high-volume elective EVAR centers had a fivefold increase in the use of EVAR in a ruptured AAA setting, with mortality rate as low as 20%.

Decrease in AAA death rate & shift toward treatment of patients aged 75 years & older

From 1979 to 1999, a steady increase in the incidence of death from AAA was observed [19]. During this time period, population screening studies suggested that the prevalence of AAA in elderly men was approximately 5%. However since 1999, evidence suggests that both the prevalence and incidence of AAA has been declining [19]. The reasons for the rise and fall of AAA are likely to be complex, including safer elective surgery, particularly since the introduction of EVAR, improved aneurysm screening and diagnosis, and the increasing longevity of populations in developed countries. In addition, during the past 40 years there have been considerable changes in public attitudes to health, ranging from a reduction in the prevalence of smoking to more aggressive cardiovascular risk protection strategies. These changes in public health measures are likely to positively impact on the reduced rate of AAA rupture, as previous studies have shown that current smoking and higher mean arterial pressure increase rupture rates, whereas antihypertensive use decreases ruptures rates.

The benefit in RAAA reduction from increasing numbers of elective repairs appears to be limited to those aged 75 years and over [19], whereas the sharpest decline in admissions for ruptured aneurysm has occurred in those younger than 75 years. This is possibly because of the increasing availability of endovascular repair. Nevertheless, the highest percentage change in mortality from AAA has occurred in those aged under 75 years, pointing towards changes in both the epidemiology and management of AAA. The apparent shift in burden of disease to older age groups calls for increasingly less invasive treatment options and will provide real challenges to the future management of this condition.

AAA screening

There is no doubt that screening is cost effective, and will become even more cost effective with the advent of EVAR. Important lessons can be learned from the most recent publication from the MASS group, who found that AAA ruptures in those with a normal aorta who were formerly screened, diminished the degree of benefit seen in earlier years of follow-up. Approximately half of those ruptured had a baseline aortic diameter in the range 2.5–2.9 cm, emphasizing the need for rescreening all men with a normal aortic diameter after 5 years [20]. Furthermore, considering that the octogenarian survival rate is highest following elective repair [21,22] and that this age group is at the highest risk of death once ruptured [18], screening should be offered to this population cohort, especially those with favorable life expectancy.

Cost analysis

Initial trials on EVAR suggested that the cost associated with EVAR was significantly higher than that for open repair [1,2]. However, technology has become cheaper, such as in most commercial entities, and operators have become more skilled. More contemporary series have shown that EVAR is cost effective, even in high-risk patients or those with considerable anatomical complexity [10,21].

In financial terms, hospitals have profited from EVAR programs. High patient turnover rates and low use of ICU facilities have certainly contributed to its profitability and overall benefit to the individual, health economy and the community as a whole.

Furthermore, the cost per quality-of-life year gained is considerably higher, a factor that is all the more pertinent for elderly comorbid laden patients in whom the line between intervention and best medical treatment may be thinner. The caveat with the cost–effectiveness benefit is that this can only be achieved in high-volume centers, where operative success is high and length of stays are short. Results from the OVER trial provide level 1 evidence for cost benefits, a factor that can only improve with time [23].

Reconfiguration of services

There is ample evidence from both sides of the Atlantic that confirms the need for centralization of vascular services to high-volume centers [17,24]. This volume–outcome relationship can not be accredited to surgeon volume alone; it is also a result of improved anesthetic experience, enhanced intensive care facilities, infrastructure and staffing.

Technological advancements

There have been no major advancements or disruptive technologies since the first EVAR was performed in Russia in 1986 [25]. Experience has taught us that it is the physicians themselves who are most likely to invent game-changing innovation, which calls for a strengthening of the physician–industry relationship that needs to occur in high-volume academic centers.

> *"In financial terms, hospitals have profited from endovascular repair programs."*

Future developments will continue to focus on reducing invasiveness, driven by our aging population. Current endograft designs, such as the multilayer stent, promise simplicity and a steep learning curve even for complex anatomies. Developments in the worlds of stem cell and nanotechnology offer exciting prospects, and although the treatment may be more complex, the mode of delivery will be even more simplistic.

Conclusion

In experienced hands, both EVAR and OR options are plausible and both can be tailored to the specific patient. There are certain instances in which OR is still the most favorable option, but these instances are becoming increasingly rare. An EVAR-first policy reduces both aneurysm-related and all-cause mortality, with minimal operative mortality risk and a low secondary intervention rate.

The future success of AAA management will depend on centralization of services to high deliberate practice volume centers, procedural innovation, AAA screening, low threshold for intervention with minimally invasive technologies and enhanced understanding of the management of high-risk patients. The evolution of endovascular technology has led to substantial gains in aneurysm survival rates and has had a profoundly positive impact on both quality of life and cost–effectiveness.

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