

Endovascular Repair of Abdominal Aortic Aneurysm

An Evidence-Based Analysis

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The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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ABBREVIATIONS/ACRONYMS

AAA	Abdominal aortic aneurysm
EVAR	Endovascular repair of abdominal aortic aneurysm
OSR	Open surgical repair
PTFE	Polytetrafluoroethylene
RCT	Randomized controlled trial

EXECUTIVE SUMMARY

The Medical Advisory Secretariat conducted a systematic review of the evidence on the effectiveness and cost-effectiveness of endovascular repair of abdominal aortic aneurysm in comparison to open surgical repair. An abdominal aortic aneurysm [AAA] is the enlargement and weakening of the aorta (major blood artery) that may rupture and result in stroke and death. Endovascular abdominal aortic aneurysm repair [EVAR] is a procedure for repairing abdominal aortic aneurysms from within the blood vessel without open surgery. In this procedure, an aneurysm is excluded from blood circulation by an endograft (a device) delivered to the site of the aneurysm via a catheter inserted into an artery in the groin. The Medical Advisory Secretariat conducted a review of the evidence on the effectiveness and cost-effectiveness of this technology. The review included 44 eligible articles out of 489 citations identified through a systematic literature search. Most of the research evidence is based on non-randomized comparative studies and case series. In the short-term, EVAR appears to be safe and comparable to open surgical repair in terms of survival. It is associated with less severe hemodynamic changes, less blood transfusion and shorter stay in the intensive care and hospital. However, there is concern about a high incidence of endoleak, requiring secondary interventions, and in some cases, conversion to open surgical repair. Current evidence does not support the use of EVAR in all patients. EVAR might benefit individuals who are not fit for surgical repair of abdominal aortic aneurysm and whose risk of rupture of the aneurysm outweighs the risk of death from EVAR. The long-term effectiveness and cost-effectiveness of EVAR cannot be determined at this time. Further evaluation of this technology is required.

OBJECTIVE

The objective of this health technology policy assessment was to determine the effectiveness and cost-effectiveness of endovascular repair of abdominal aortic aneurysms (EVAR) in comparison to open surgical repair (OSR).

BACKGROUND

Clinical Need

An abdominal aortic aneurysm (AAA) is a localized, abnormal dilatation of the aorta greater than 3 cm or 50% of the aortic diameter at the diaphragm. (1) A true AAA involves all 3 layers of the vessel wall. If left untreated, the continuing extension and thinning of the vessel wall may eventually result in rupture of the AAA. The risk of death from ruptured AAA is 80% to 90%. (61) Heller et al. (44) analyzed information from a national hospital database in the United States. They found no significant change in the incidence rate of elective AAA repair or ruptured AAA presented to the nation's hospitals. The investigators concluded that technologic and treatment advances over the past 19 years have not affected the outcomes of patients with AAAs, and the ability to identify and to treat patients with AAAs has not improved.

Classification of Abdominal Aortic Aneurysms

At least 90% of the AAAs are affected by atherosclerosis, and most of these aneurysms are below the level of the renal arteries.(1)

An abdominal aortic aneurysm may be symptomatic or asymptomatic. An AAA may be classified according to their sizes:(7)

- Small aneurysms: less than 5 cm in diameter.
- Medium aneurysms: 5-7cm.
- Large aneurysms: more than 7 cm in diameter.

Small aneurysms account for approximately 50% of all clinically recognized aneurysms.(7)

Aortic aneurysms may be classified according to their gross appearance as follows (1):

- Fusiform aneurysms affect the entire circumference of a vessel, resulting in a diffusely dilated lesion
- Saccular aneurysms involve only a portion of the circumference, resulting in an outpouching (protrusion) in the vessel wall.

Prevalence of Abdominal Aortic Aneurysms

In community surveys, the prevalence of AAA is reported to be between 1% and 5.4%. (61) The prevalence is related to age and vascular risk factors. It is more common in men and in those with a positive family history.

In Canada, Abdominal aortic aneurysms are the 10th leading cause of death in men 65 years of age or older. (60) Naylor (60) reported that the rate of AAA repair in Ontario has increased from 38 per 100,000 population in 1981/1982 to 54 per 100,000 population in 1991/1992. For the period of 1989/90 to 1991/92, the rate of AAA repair in Ontarians age 45 years and over was 53 per 100,000. (60) In the United States, about 200,000 new cases are diagnosed each year, and 50,000 to 60,000 surgical AAA repairs are performed. (2) Ruptured AAAs are responsible for about 15,000 deaths in the United States annually. One in 10 men older than 80 years has some aneurysmal change in his aorta. (2)

Symptoms of Abdominal Aortic Aneurysms

AAAs usually do not produce symptoms. However, as they expand, they may become painful. Compression or erosion of adjacent tissue by aneurysms also may cause symptoms. The formation of mural thrombi, a type of blood clots, within the aneurysm may predispose people to peripheral embolization, where blood vessels become blocked. Occasionally, an aneurysm may leak into the vessel wall and the periadventitial area, causing pain and local tenderness. More often, acute rupture occurs without any prior warning, causing acute pain and hypotension. This complication is always life-threatening and requires an emergency operation.

Diagnosis of Abdominal Aortic Aneurysms

An AAA is usually detected on routine examination as a palpable, pulsatile, and non-tender mass. (1)

Abdominal radiography may show the calcified outline of the aneurysms; however, about 25% of aneurysms are not calcified and cannot be visualized by plain x-ray. (1) An abdominal ultrasound provides more accurate detection, can delineate the traverse and longitudinal dimensions of the aneurysm, and is useful for serial documentation of aneurysm size. Computed tomography and magnetic resonance have also been used for follow-up of aortic aneurysms. These technologies, particularly contrast-enhanced computer tomography, provide higher resolution than ultrasound.

Abdominal aortography remains the gold standard to evaluate patients with aneurysms for surgery. This technique helps document the extent of the aneurysms, especially their upper and lower limits. It also

helps show the extent of associated atherosclerotic vascular disease. However, the procedure carries a small risk of complications, such as bleeding, allergic reactions, and atheroembolism. (1)

Prognosis of Abdominal Aortic Aneurysms

The risk of rupture of an untreated AAA is a continuous function of aneurysm size as represented by the maximal diameter of the AAA. The annual rupture rate is near zero for aneurysms less than 4 cm in diameter. The risk is about 1% per year for aneurysms 4 to 4.9 cm, 11% per year for aneurysms 5 to 5.9 cm, and 25% per year or more for aneurysms greater than 6 cm. (7)

The 1-year mortality rate of patients with AAAs who do not undergo surgical treatment is about 25% if the aneurysms are 4 to 6 cm in diameter. This increases to 50% for aneurysms exceeding 6 cm. Other major causes of mortality for people with AAAs include coronary heart disease and stroke.

Treatment of Abdominal Aortic Aneurysms

Treatment of an aneurysm is indicated under any one of the following conditions:

- The AAA is greater than 6 cm in diameter.
- The patient is symptomatic.
- The AAA is rapidly expanding irrespective of the absolute diameter.

Open surgical repair of AAA is still the gold standard. It is a major operation involving the excision of dilated area and placement of a sutured woven graft. The surgery may be performed under emergent situation following the rupture of an AAA, or it may be performed electively.

Elective OSR is generally considered appropriate for healthy patients with aneurysms 5 to 6 cm in diameter. (7) Coronary artery disease is the major underlying illness contributing to morbidity and mortality in OSR. Other medical comorbidities, such as chronic renal failure, chronic lung disease, and liver cirrhosis with portal hypertension, may double or triple the usual risk of OSR.

Serial noninvasive follow-up of small aneurysms (less than 5 cm) is an alternative to immediate surgery.

Endovascular repair of AAA is the third treatment option and is the topic of this review.

Technology

Endovascular Abdominal Aortic Aneurysm Repair

Endovascular abdominal aortic aneurysm repair (EVAR) is a procedure to treat AAAs with an endograft (a device) without the need for open surgery.

In this procedure, a single or bilateral incision is made in the groin, and a stent graft is passed into the aneurysm from a catheter inserted via the femoral artery. The graft seals the aneurysm from circulating blood, thus preventing its expansion and rupture (See Appendix 1, Figure 1). Most surgical teams for EVAR include a surgeon, an interventional radiologist, and a cardiologist.

Endovascular Stent Systems for Repair of Abdominal Aortic Aneurysms

Endovascular stents (endografts) are used to repair AAAs within the blood vessel without open surgery. They are generally composed of a metal frame covered with a woven polyester material that is similar to the standard surgical grafts. The endografts may be manufactured in a tubular, bifurcated, or aortoiliac configuration. The proximal and distal ends of the endografts contain hooks to attach to the inner wall of the blood vessels. The endografts may be self-expanding or may be deployed by a balloon system.

Since 1991, numerous stent graft systems have been developed and enhanced. Some of the second-generation endografts available at the time of the review are described in Table 1.

Regulatory Status of Endograft Systems in Canada

As of March 2002, only Ancure® (Guidant Corp., Indianapolis, USA) has been licensed by Health Canada as a Class 4 medical device.

Table 1: Second-Generation Endograft Systems

Name of Stent Graft	Manufacturer (Location)	Description	Licensed by Health Canada?
Ancure®	Guidant Corp. (Indianapolis, IN)	Composed of a polyester graft (tubular, bifurcated, and aorto-uni-iliac) with self-expanding Elgiloy hooks at proximal and distal ends for anchoring.	Yes Class 4 medical device
AneuRx®	Medtronic Inc. (Minneapolis/St. Paul's, MN)	A self-expanding, modular, bifurcated device consisting of a thin-walled, non-crimped, woven polyester graft that is joined to an exoskeleton constructed with 1-cm stent rings throughout its length.	Not at the time of the review
Excluder®	W. L. Gore & Associates, Inc. (Newark, DE)	A stent graft with a spiral frame of nitinol covered in and out with PTFE sealed by heat. The device is wrapped around the delivery system and tied with dental-floss-like thread.	Not at the time of the review
Vanguard®	Boston Scientific Corp. (Natick, MA)	A 2-piece self-expanding modular graft consisting of a nitinol frame covered by a polyester graft. Six small barbs are sewn onto the top stent for additional fixation and the stent graft is placed infrarenally.	Not at the time of the review
Talent®	World Medical Inc. (A division of Medtronic Vascular, Sunrise, FL)	A modular system in which the individual components are assembled inside the patient to form the desired graft (bifurcated and aorto-uni-iliac systems). Each module consists of a polyester fabric supported by a Z-shaped nitinol framework. The uncovered proximal portion can be designed with wide openings of bare spring that allow suprarenal fixation of the graft.	Not at the time of the review
Zenith®	Cook Inc. (Bloomington, IN)	A fully supported modular system with sophisticated mechanisms that allow for fine-positioning adjustment and controlled release of a series of suprarenal barbs to mimic a surgical anastomosis.	Not at the time of the review

Illustrations of the Ancure®, AneuRx®, and Excluder® endografts are shown in Appendix 1, Figures 2 to 4.

Recall of Stent Grafts and United States Food and Drug Administration Letter

In March 2001, Guidant Corporation suspended production of its Ancure® stent graft and recalled all Ancure inventory. According to a April 27, 2001 Public Health Notification (62) from the United States Food and Drug Administration (USFDA), Guidant told USFDA that it had failed to report many device malfunctions and adverse events, including severe vessel damage associated with problems relating to the deployment of the device. It also did not properly report manufacturing changes to the USFDA. Guidant's internal audit revealed problems with its complaint handling system, manufacturing quality system, documentation procedures, and training. In July 2001, the USFDA gave Guidant approval to resume producing Ancure.

In the April 27, 2001 notification letter (62), the USFDA also alerted physicians to its concerns about reports of adverse events in patients who have received AneuRx® stent grafts. These events included about 25 aneurysm ruptures, suboptimal placements of the grafts, endoleaks, migration of the main bodies of the devices and cuffs, and problems with device integrity due to metal frame fractures, suture breaks, or fabric tears. The letter recommended that physicians stay informed, ensure all implanted patients are carefully followed-up and undergo periodic follow-up imaging, and report problems associated with the devices to the manufacturer and to the USFDA.

LITERATURE REVIEW

Objective

To assess the safety, effectiveness, and cost-effectiveness of EVAR compared to OSR in the treatment of abdominal aortic aneurysm.

Questions

- What is the success rate of EVAR compared to OSR?
- What are the mortality rates of EVAR compared to OSR?
- What are the types and frequency of adverse events in EVAR compared to OSR?
- What are the indications for EVAR?
- What are the costs and cost-effectiveness of EVAR compared with OSR?

Methods

Search for Systematic Reviews

A search of Cochrane and other health technology databases yielded two English language systematic reviews; one prepared for the United States Department of Veterans Affairs (5), and a 1999 review by the Medical Services Advisory Committee in Australia. (6) Both reviews determined that no definitive conclusions could be drawn from the studies and that the effectiveness and durability of EVAR were not established.

The Medical Advisory Secretariat conducted an updated search of the literature.

Follow-up Literature Search

Databases Searched

- MEDLINE
- Manufacturers' Web sites
- Health Canada's Web sites (to obtain a listing of licensed medical devices)

Search Strategy

- MEDLINE
- Search terms: abdominal aortic aneurysm, endovascular repair, endoluminal repair)
- Search period: January 1998– January 28, 2002, updated February 13, 2002
- The period for the search begins in 1998 because the last systematic review on this technology was conducted by the Medical Secretariat Advisory Committee in Australia and included studies published in mid 1998.
- Websites of regulatory agencies and endograft manufacturers were also searched.

Inclusion Criteria

- English language journal publications reporting primary data on the effectiveness or cost-effectiveness of EVAR in a clinical setting.
- The study design and methods were clearly described.
- Randomized controlled trials (RCTs), non-randomized comparative studies, registries, or case series with 50 patients or more.
- The studies were not superseded by later publications with the same purpose by the same group or by later publications that included the data from multiple centres involved in the same multicenter study.
- The studies were published in 1998 or later to reflect the status of EVAR since the Cochrane-assessed review published in 1998 and the Australian review in 1999.

Results of Literature Search and Quality of Evidence

The search yielded 489 citations. One researcher reviewed the abstracts to determine whether the inclusion criteria were met. The citations included multiple articles by the same study groups reporting findings at different phases of their studies. In these situations, due to the time constraint, only the most recent report was included. Forty-four articles were included in this review. The levels of evidence of these studies are shown in Table 2.

Table 2: Level of Evidence

Study Design	Level of Evidence	No. of Eligible Studies
Large RCT,* systematic review of RCTs	1	
Small RCT	2	1
Non-randomized controlled studies with contemporaneous controls	3 a	7
Non-randomized controlled studies with historical controls	3 b	1
Surveillance (database or register)	4 a	5
Case series, multisite	4 b	4
Case series, single site	4 c	26
Total		44

*RCT indicates randomized controlled trials

In addition to these 44 studies, other references (comprising reviews, texts, and expert opinions) were used to complement the research findings.

As shown in Table 2, with the exception of 1 small RCT and 7 non-randomized comparative studies, the studies were mostly case series. Hence, the evidence on effectiveness, particularly long-term effectiveness, is weak.

Data Extraction and Synthesis

One researcher extracted data from the selected publications and summarized in Table 2 to Table 5. The studies are summarized in Table 5. Studies that focused on a specific aspect of EVAR were not included in the appendices, but were summarized in the text of this report. These are included in the reference list.

This report is a descriptive synthesis of the available evidence. No meta-analysis was conducted.

Summary of Systematic Reviews

Medical Services Advisory Committee MSAC (Australia 1999)

The MSAC review (6) included 13 studies published in 1995 to 1997, consisting mainly of case series. The sample size of the studies ranged from 18 to 133 subjects with a follow-up period of 12 to 133 days. No meta-analysis was performed. The studies reported technical success rates of 48% to 95%. Mean mortality rate was 2.5% in low risk patients and 8% in high-risk patients. Endoleak ranged from 6% to 33%. About 50% of the endoleak sealed spontaneously.

The review concluded that:

- EVAR appears to be safe in the short term based on level IV evidence with mortality similar to OSR.
- Persistent endoleaks are a serious problem.
- The long-term effectiveness and durability of EVAR are still unknown.
- There is a lack of rigorous Australian cost comparisons of EVAR to OSR. The studies available did not cover outpatient costs. (6)

Bertram et al, 1998 (Health Services Research and Development Services, US)

This 1998 systematic review examines the evidence on the effectiveness of EVAR for the repair of infrarenal abdominal aortic aneurysms. (5) The review is based on a qualitative analysis of 14 case series on EVAR published in the period of 1995 to 1997. The sample size of the studies ranged from 10 to 154 with a follow-up period of 153 days to 23 months. Immediate technical success ranged from 48% to 95%, but improved to 60%–97% with additional endovascular interventions or spontaneous healing. By follow-up, 0% to 30% had a conversion to standard open surgical procedure. The length of hospital stay ranged from 3.8 to 11.5 days. Mean perioperative mortality rates following EVAR ranged from 0% to 36% and the mean overall mortality rate was 10% (range 0.6%-23%). About 10% to 31% of total patients across the studies experienced complications after EVAR with the incidence of individual complications ranging from 0.6% to 20%. Endoleaks were associated with bigger increases in aneurysm expansion. There has been little systematic study of variables related to health care costs. (5)

Based on the above evidence, Bertram et al (5) concluded that:

- There were very few comparative studies of EVAR to alternative interventions. The available studies had significant methodological limitations.

- The literature available for the review represents studies that are methodologically inadequate to definitively answer the questions addressed in the report.
- A critical issue relates to the question: "The authors also raised the questions whether the availability of a minimally invasive treatment option lead to over-utilization of that procedure in patients with marginal indications for surgery."

Summary of a Randomized Controlled Trial

There is only one randomized controlled trial reported by Cuypers et al (19) with a small sample size (57 EVAR and 19 OSR). The purpose of this study was to compare the cardiac response and the incidence of adverse cardiac events during and after EVAR and OSR of AAA. The results showed that at one month, there were no differences in mortality rates, myocardial infarction (MI), congestive heart failure and combined clinical cardiac outcome events (combined cardiac deaths, MI and episodes of heart failure) following EVAR or OSR. Patients that underwent EVAR had significantly lower incidence of myocardial ischemia during EVAR than OSR.

Eight comparative studies including the RCT are summarized in Table 2 (Appendix 3). The other studies and their outcomes are summarized in Tables 3 to Table 5.

SUMMARY OF FINDINGS

Key findings of the studies are summarized.

Success Rates

The rates of successful deployment of the endografts in 17 clinical studies were high, ranging from 81% to 100% (median, 97%). These rates are consistent with those reported in a review by Hallet (7) and are comparable to those of OSR. However, primary technical success rates (defined as successful deployment with graft patency, no conversion to OSR, and no endoleak) ranged from 62% to 98% (median, 83.5%), mainly because of the presence of endoleaks (Figure 5). These values are lower than the technical success rates reported for OSR.

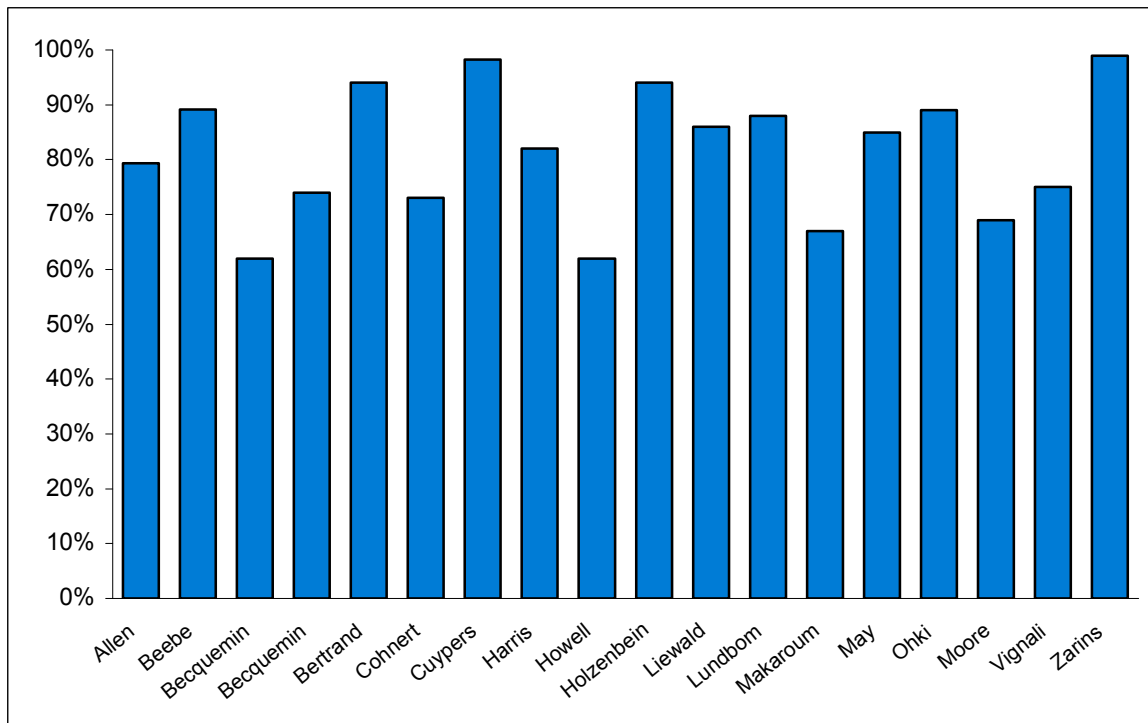


Figure 5: Primary technical success rates of endovascular repair of abdominal aortic aneurysms across studies

Shorter length of stay in the hospital and intensive care unit, and less blood loss/transfusion have been reported for EVAR compared to OSR (Appendix 2, Table 2). (14; 16; 8; 17; 21). Length of hospital stay for EVAR ranged from 2 to 10 days (median 3.6 days), and for OSR 6.1-14 days (median 9 days). Zarins et al reported a 63% reduction in hospital stay for EVAR compared to OSR (36).

Perioperative Mortality Rates and Complication Rates

One randomized controlled study and 7 comparative studies reported similar perioperative mortality rates for EVAR and OSR (Appendix 2, Table 2).

The perioperative mortality rates of EVAR ranged from 0% to 8.4% (median, 2%) (Figure 6). This is consistent with a report from the United Kingdom prospective Registry of Endovascular Treatment of Abdominal Aortic Aneurysm (RETA) (8), that found a 30-day mortality rate of 4% for patients fit for surgery. The perioperative EVAR mortality rate of patients at high surgical risks has been shown to be as high as 18%. (8) Overall mortality rates for EVAR ranged from 2.2% to 22% (median, 7.6%).

The perioperative mortality rates for EVAR appear to be comparable to the mortality rates reported for OSR of AAA. The probability of perioperative death in OSR was 5% to 7% in 2 population-based studies (9; 10) and 1% to 5% in a large case series. (11) A review by Cruz et al. (12) reported mortality rates of 0% to 5.6% for elective surgical repair. Akkersdijk et al. (13) reported an in-hospital mortality rate of 4.1% in a multicenter study of 291 patients who had undergone OSR of AAA. The 8 comparative studies included in this review showed perioperative mortality rates for elective OSR that ranged from 0% to 6% (median 4%). (14; 15; 16; 17; 18; 19; 20; 21) However, the mortality rate of OSR of ruptured AAA has been reported to be as high as 50%.

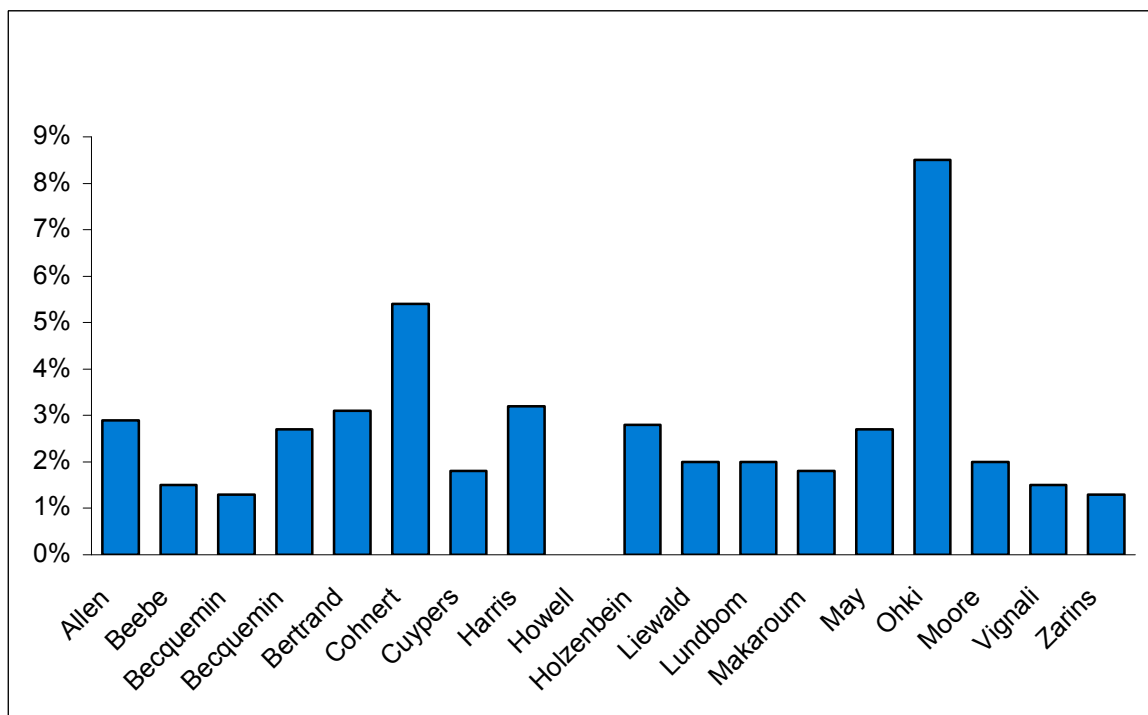


Figure 6: 30-Day mortality rates after endovascular repair across studies

Reported perioperative complication rates ranged from 9% to 26% (Appendix 2). Of the early complications, the major systemic complications included cardiac problems, stroke, and renal failure.

A randomized study (19) that compared 57 EVARs with 19 OSRs showed that the incidence of combined clinical cardiac complications (including cardiac death, myocardial infarction, and congestive heart failure) was 5% after EVAR and 11% after OSR. This difference was not statistically significant; however, the sample may not have been large enough to detect a difference if one had existed. The study did show that hemodynamic changes were less severe, and there was a lower incidence of ischemia (deficiency of blood supply) during EVAR than during OSR.

Bertrand et al. (17) prospectively compared 193 EVARs with 193 OSRs in a non-randomized study and concluded that despite an absence of statistically significant differences in cardiac complications and mortality, there was a lower incidence of pneumonia, acute respiratory failure, and acute renal failure in the EVAR group.

Conversion Rates

When EVAR fails, the patient must be converted to OSR, usually at the time of the EVAR attempt. Seventeen studies reported primary conversion rates ranging from 0% to 10% (median, 3%). While two of the studies reported primary conversion rates of 8% and 10%, the other studies reported rates that ranged from 0% to 5%. Secondary or late conversions were reported in 0.5% to 2.7% of patients.

Based on a 5-year experience (1992 to 1997) with 156 patients, May et al. (22) reported that the incidence and indications for conversions from EVAR to OSR are changing. Primary conversion was required in 20% of patients in the first half of the study, whereas the primary conversion rate dropped to 2% in the second half.

The main reasons for primary conversion were access problems, balloon-related problems, endograft migration, endograft thrombosis, and failed deployment of the endograft. The current indications for primary conversion include rupture of the aorta; complete endograft migration, resulting in obstruction of the iliac arteries; and irreversible twisting of a nonmodular bifurcated endograft. The current indications for secondary conversion include persistent endoleak, sealed endoleak with continued AAA expansion, apparently successful endoluminal repair with continued AAA expansion, and infected endograft.

The authors attributed the change in incidence and indications to improvements in technology and to interventional techniques for overcoming obstacles.

Endoleak Rates

Endoleak is a complication that is unique to EVAR. It is defined as the incomplete exclusion of the aneurysmal sac from the circulation with persistent perfusion of the aneurysm. (24)

Leaks may be classified as follows: (4)

- Type I: from the proximal or distal attachment sites of the graft
- Type II: from side-branch vessels that continue to feed the excluded aneurysm sac
- Type III: due to fabric tear, modular or graft disconnection, or graft disintegration
- Type IV: transgraft flow caused by the high porosity of the graft, most likely created by the numerous suture holes holding the graft material to the stent
- Type V: growth of the aneurysm sac but reperfusion of the sac could not be demonstrated(30)

Endoleaks can occur and be detected early after implantation, or they may be discovered during routine postoperative follow-up studies. Initial endoleaks occur within 30 days following EVAR. Initial endoleaks that fail to seal 30 days after EVAR are called persistent endoleaks.

Rates of initial endoleaks reported by 16 studies included in this review ranged from 0% to 42% (median, 21%) (Appendix 2). Schurink et al. (25) conducted a meta-analysis of 23 publications in which 1,118 patients with successful implantation of AAA endografts were described. The analysis yielded an endoleak rate of 24%. Of these endoleaks, 66% were present immediately after stent graft placement and 37% were persistent over time. Many (36%) occurred at the distal stent attachment site. The analysis also showed that self-expandable stent grafts were more frequently associated with endoleaks than were balloon-expandable grafts.

In a review of major studies, Hallett (7) reported that endoleaks were observed in one-third of the cases. The review also showed that 40% to 50% of initial endoleaks closed spontaneously and 8% to 10% were sealed by secondary procedures, usually coiling embolization. Makaroun et al. (29) reported an initial endoleak rate of 38% and a persistent endoleak rate of 14% at 6 months after EVAR.

In this review, rates of persistent endoleaks ranged from 1% to 24% (median, 9%). (See Figure 7.) Late endoleaks are new endoleaks that develop during the follow-up period. Moore et al(21), Ohki et al (26), Vignali et al(27), and Liewald et al(28) reported rates of late endoleaks that ranged from 5% to 16% among patients who had undergone EVAR.

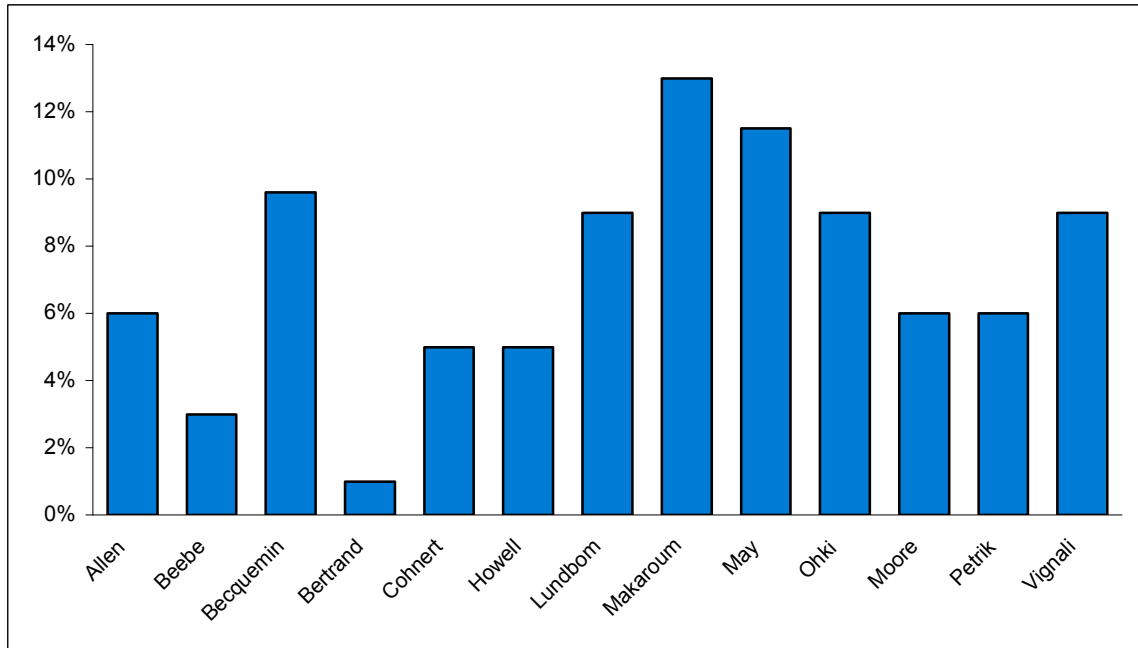


Figure 7: Rates of persistent endoleak in endovascular repair of abdominal aortic aneurysms across studies

The natural history of endoleaks is poorly understood. The sites of origin and behaviour of such leaks might be different among the various systems being investigated in the treatment of AAA. The proper management also remains unclear. Conversion to standard OSR is the only certain cure. (29)

Holzenbein et al. (30) followed 166 patients that had received EVAR for a median of 18 months. They reported an endoleak rate of 24% requiring 49 interventions. The report showed the following breakdown in occurrence and treatment of the endoleaks:

- Type I: 42.5%. Proximal endoleaks were treated with extension only. Distal endoleaks were treated by conversion of tubular to bifurcated one.
- Type II: 12.5%. These endoleaks were treated mainly by coil embolization.
- Type III: 30%. These endoleaks were treated mainly by separating and reconnecting the graft segments.
- Type IV: 10%. These were treated by overstenting with a covered stent alone.
- Type V: 5%. No intervention was taken for these endoleaks because the patients' condition did not allow for open repair.

The authors hypothesized that inherent anatomic factors such as aortic thrombus, calcification, excessive angulation, patent lumbar or inferior mesenteric arteries, and vessel-graft size discrepancies might predispose patients to the development of endoleaks.

Petrik et al. (24) conducted a retrospective review of 100 cases of EVAR, but failed to find a predictive value associated with any of the above-listed anatomic factors.

In a case series of 73 patients treated by EVAR, Gorich et al. (31) identified patency of 4 or more lumbar arteries visualized preoperatively by computed tomography scans as the single correlating risk factor for

initial endoleaks. In a case series of 55 patients who were followed-up for at least 6 months, Makaroun et al. (29) identified a strong association between neck angulation and proximal endoleaks and between endoleaks around the distal bifurcated attachment systems and ectatic common iliac arteries. The latter seems to indicate that a certain distance of apposition of the graft is important for a seal to develop.

Zarins et al. (3) found no difference in the rates of patient survival, aneurysm ruptures, surgical conversions, new endoleaks, or stent graft migrations between patients with and without endoleaks at 1 month. However, the same study showed that patients with persistent endoleaks were more likely to have enlarged aneurysms at 1 year.

Becquemin et al. (23) also reported in the French Vanguard Trial that persistent endoleak was associated with an increase in diameter of the aneurysm. However, Brewster et al (2) believe that endoleak status is overemphasized in evaluating the efficacy of EVAR.

Rhee et al. (32) reported that in a case series of 123 EVARs, the group of patients with initial endoleaks had similar regressions of sac size (5 mm or more) at 24 months when compared to the group of patients without endoleaks. Moreover, the study showed no difference in sac shrinkage between the treated endoleak group and the untreated endoleak group whose endoleaks spontaneously sealed.

The clinical significance of endoleaks and their impact on the natural history of aneurysms is uncertain and poorly understood. Brewster (2) suggested that until actual pressure inside the AAA sac can be measured accurately after endograft repair, changes in AAA maximal diameter, instead of rates of endoleaks, may be a better measure of treatment efficacy.

Change in Mean Aneurysm Diameter

The report on the French Vanguard Trial (23) reported a 2.3 mm mean reduction in aneurysm diameter at 6 months following EVAR. After a mean follow-up of 18 months, the aneurysm diameter remained unchanged in 13% of the patients, decreased in 75% of the patients, and increased in 11% of the patients. Allen et al. (14) reported that the mean aneurysm diameter of 33 patients decreased by 5.8% (3 mm) over a mean follow-up of 6 months following EVAR.

Rates of Late Adverse Events

Several investigators have reported mixed midterm results. May et al. (20) reported higher survival rates for EVAR compared with OSR in a 5-year RCT. Zarins et al. (3) reported a rupture-free rate of 99.5% at 3 years. However, other studies have raised concerns about the midterm durability of EVAR.

Harris (33) reported the outcomes of 2,464 patients who had undergone EVAR and were registered with EUROSTAR, the European endovascular therapy registry. These patients were followed-up for up to 4 years (mean, 12.19 months) after being treated with EVAR. Rupture of aneurysm occurred in 14 patients 0 to 24 months after EVAR. There were 9 deaths. The report showed a cumulative risk of rupture of 1% per year. Eighty-six percent of patients with ruptured AAAs required emergency surgery, and there was a mortality rate of 58.4%.

Factors for rupture were proximal (type I) endoleak, midgraft (type III) endoleak, graft migration, and postoperative kinking of the endograft. Of the patients with successful deployments of endografts, 1.7% underwent late conversion to OSR with a perioperative mortality rate of 24.4%. The cumulative risk of late conversion was about 2.1% per year.

Harris et al. concluded that EVAR of infrarenal AAAs with the first- and second-generation devices that predominated in this study was associated with a risk of late failure according to an analysis of observed hard end points of 3% per year. They also concluded that until the long-term efficacy of EVAR has been established through further analysis of reliable hard end points, caution should be exercised with respect to its application in routine clinical practice.

Zarins et al. (36) reported 7 unexpected AAA ruptures that caused 5 deaths among 149 patients after EVAR. Holzenbein et al. (30) reported that 26% of patients had late complications requiring secondary interventions.

The Need for Secondary Intervention

Nine studies (14; 16; 15; 4; 30; 28; 26; 21; 36) reported secondary intervention rates that ranged from 6% to 32%. (See Figure 8.) The median secondary intervention rate was 12%.

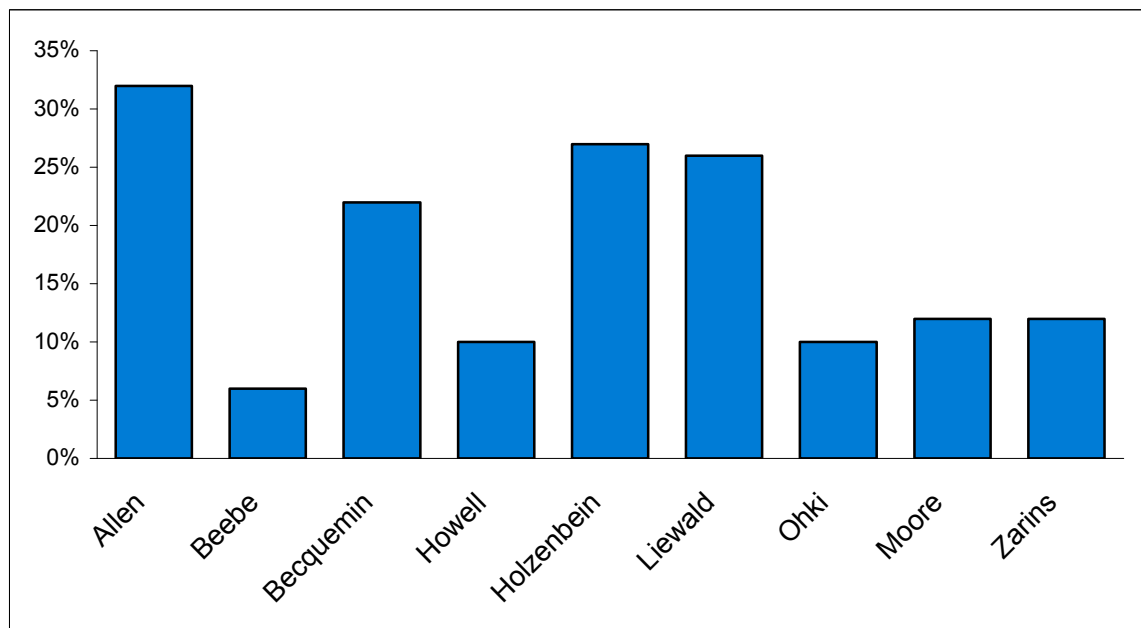


Figure 8: Secondary intervention rates after endovascular repair of abdominal aortic aneurysms across studies

Laheij et al. (34) reviewed the data for 1,023 patients in the EUROSTAR registry who had a mean follow-up period of 14 months following EVAR. They found that 18% of the patients required secondary intervention. Analysis of the interventions showed that 12% were transabdominal, 11% consisted of extra-anatomic bypasses, and 76% involved transfemoral procedures. Eleven percent of patients required secondary intervention by the first year, 32% by the third year, and 38% by the fourth year. Graft migration and aneurysm rupture were the most frequent causes of transabdominal interventions. Graft limb thrombosis was the principal indication for extra-anatomic bypass. Endoleak, graft kinking, stenosis or thrombosis, and device migration were the main reasons for secondary transfemoral interventions.

First-Generation Versus Second-Generation Stent Grafts

Resch et al. (35) studied 158 patients who had received either a first-generation or second-generation stent graft and found that immediate and late conversion and 30-day mortality were reduced for second-generation devices.

Specifically, the mean early conversion rates were 12% and 7% for the first-generation stent grafts and 0% for the second-generation stent grafts. Late conversions were required in 14% to 40% of the first-generation stent grafts and in 0% of the second-generation stent grafts. The perioperative mortality rate was 11% for one of the second-generation stent grafts, 7% for another second-generation graft, and 0% for the other devices. Type I endoleaks were statistically significantly more common in first-generation stent grafts (7%–17%) when compared with the second-generation stent grafts (0%–12%). First-generation stent grafts also required significantly more secondary interventions up to 20 months postoperatively. However, the number of unplanned intraoperative adjunctive procedures was higher with second-generation stent grafts (43%–87% compared with 20–34% for first-generation stent grafts). (35)

Suitability and Indications for Endovascular Repair of AAAs

The selection of candidates for EVAR is based mainly on the morphology of the aneurysm. (36)

Woodburn (37) identified the following as absolute contraindications for EVAR:

- Proximal neck < 15 mm
- Infrarenal aortic diameter > 26mm
- Thoracoabdominal aortic aneurysm
- External iliac diameter < 9mm or > 16 mm
- Bilateral internal and external iliac aneurysms
- Prosthetic graft material in both groins
- Evidence of retroperitoneal leak on CT.

The following were identified as relative contraindications for EVAR:

- Iliac tortuosity
- Proximal neck angulation > 60°
- Bilateral common and internal iliac aneurysms
- Iliac artery occlusive disease

What Percentage of AAAs Would Be Suitable for Endovascular Repair?

Woodburn reviewed all AAA referrals (115 patients) in a geographically isolated population of 400,000, among whom the confounding effects of a tertiary referral practice were excluded. The authors found no more than 30% of AAAs were entirely suitable for EVAR despite the versatility offered by the modular stent grafts. The inclusion of patients with suboptimal AAA morphology but no absolute contraindication to EVAR increased suitability to 41% of referrals.

Triesman et al. (38) reported as few as 15% of AAAs were suitable for EVAR using the EVT Endovascular Technologies Menlo Park device in tube or aorto-bi-iliac alone.

Carpenter et al. (53) evaluated 307 patients for suitability for EVAR. Reasons for exclusion included short aneurysm neck, inadequate access, wide aneurysm neck, presence of bilateral common iliac

aneurysms extending to the hypogastric artery, excessive neck angulation, extensive mural thrombus in the aneurysm neck, extreme tortuosity of the iliac arteries, accessory renal arteries originating from the AAA, and malignancy. The authors found 66% of patients were eligible for EVAR, but only 49% of patients at high risk for surgery qualified for EVAR in this study. Men were more likely than women to meet the anatomic criteria for EVAR (70% versus 40%). This gender difference has also been reported by Mathison et al. (54)

Is Endovascular Repair of AAAs Suitable for High-Risk Patients?

Chuter et al. (39) studied 116 high-risk patients who underwent elective EVAR. The diagnosis of high risk is based on various clinical and laboratory criteria. All patients had serious comorbidities. EVAR was considered feasible in 67% of the patients. The mean age was 75 years and mean aneurysm diameter was 6.3 cm. The preoperative status of the patients according to The American Society of Anesthesiologists Physical Status Classification System ranged from grade II (a patient with mild systemic disease) to grade IV (a patient with severe systemic disease that is a constant threat to life), out of a total of 6 grades. (Higher grades indicate higher morbidity.). About one-third of the patients had a grade of IV. The technical success rate at 2 weeks was 86.2%, and the continuing success rate was 87.9%. The rate of late mortality was 14.7%, and the projected 5-year mortality rate was 25%. These mortality rates are higher than those reported for low-risk patients. Of the patients deemed unsuitable for EVAR because of anatomic reasons, less than one half subsequently underwent OSR despite a mean aneurysm diameter of more than 6 cm. The mortality rate of OSR for these patients was 17%.

Cuypers et al. (40) demonstrated in a case series of 64 EVAR cases that older and medical comorbidity were associated with increased risk for perioperative complications.

Based on a case series of 307 patients, Carpenter et al. (53) reported that patients who are at high surgical risks and who might benefit most from EVAR are less likely to qualify for the procedure. Of the patients who were found to be unfit for EVAR, 67% were also deemed to be unfit for OSR.

Is Endovascular Repair of AAAs Safe for Patients Who Are Unfit for Surgery?

Riambau et al., (41) as part of the EUROSTAR registry, studied 862 patients who underwent EVAR. Of these patients, 272 were unfit for surgery, and 109 were unfit for general anesthesia. In patients fit for OSR and anesthesia, the rates of early and late mortality were 2.7% and 5.2%, respectively. In patients unfit only for OSR, the rates of early and late mortality were 5.1% and 11.4%, respectively. In patients unfit only for anesthesia, the rates of early and late mortality were 3.7% and 11%, respectively. The authors concluded that patients with poor medical conditions have higher mortality rates after EVAR compared with patients fit for surgery. Consequently, EVAR seems to have a limited benefit for patients ineligible for OSR.

Thomas et al. (8) reported similar findings in the Prospective Registry of Endovascular Treatment of Abdominal Aortic Aneurysm (RETA) in the United Kingdom. They reported that the mortality rate of EVAR for patients eligible for OSR was 4% (comparable to OSR), whereas the mortality rate of EVAR among patients unfit for surgical repair (i.e., those at high risk) was 18%. The authors noted that offering EVAR when its long-term effectiveness is unproven, and when it has high rates of complication and mortality in unfit patients, raises important implications for ethics and consent. Also, conversion to OSR is occasionally required for these patients due to complications during the procedure. Furthermore, the mortality rate of OSR in these patients could be as high as 66%.

Studies show that patients with AAAs in whom OSR is contraindicated because of problems such as hostile abdomens, inflammatory aneurysms, horseshoe kidneys, or gross obesity, but who are otherwise

fit, are particularly well suited to EVAR. Nonetheless, the potential need for conversion to OSR remains a concern.

Should Endovascular Repair of AAAs Lower the Threshold for Elective Repair of AAAs?

Finlayson et al. (42) used a Markov decision analysis model to address the question of whether the threshold for elective repair of AAAs should be lowered. The assumptions for this model included annual risk rupture is a continuous function of AAA diameter, operative mortality is 1% for EVAR and 3.5% for OSR, and immediate endovascular to open conversion rate is 1% per year for a 70-year-old patient. With these assumptions, this model did not justify changing the indications for AAA repair in most patients. EVAR would substantially lower the optimal threshold diameter for elective AAA repair, but the authors noted that the benefit of repair in this population is small.

The randomized United Kingdom Small Aneurysm Trial (43) compared the outcomes of early elective surgery (n=563) to those of ultrasonographic surveillance (n=527) for small AAAs (4–5.5 cm in diameter). The authors found that early surgery provided no long-term survival advantage over ultrasonographic surveillance at a 6-month interval, unless the aneurysm exceeded 5.5 cm. Over a 5-year follow-up, 64% of observed patients underwent elective surgical repair. There are no studies that compare the outcomes of EVAR to those of surveillance in small aneurysms.

ECONOMIC ANALYSIS

Cost comparisons between EVAR and OSR are summarized in Table 6 in Appendix 4.

Sternberg et al. (45) retrospectively analyzed hospital costs for 131 patients undergoing EVAR compared with 49 patients undergoing OSR as a part of a USFDA phase II prospective multicenter clinical investigation. The results showed that EVAR requires higher diagnostic costs before and after the procedure, lower room and board costs, lower intensive care unit (ICU) and total bed costs, comparable recovery room costs, and lower pharmacy and blood costs, but higher device costs. The total in-hospital cost for EVAR was about \$21,250 (US) versus \$12,342 for OSR. The device cost \$10,200. The authors concluded that the total in-hospital cost for EVAR is significantly greater than that for OSR when the cost of the device greatly exceeds \$5,000.

Seiwert et al. (46) recorded the use of hospital resources, actual costs, clinical descriptors, and treatment outcomes for 2 contemporaneous groups, each having 16 consecutive patients who underwent either EVAR or OSR. Patients in the 2 groups were similar in age, gender, AAA size, smoking status, diabetes, ischemic heart disease, history of coronary artery bypass grafts, previous vascular surgery, or other comorbidities. EVAR significantly lowered the length of hospital stay and length of ICU stay, but the cost of an endograft prosthesis was 10 to 14 times higher than the cost of a standard graft. The total in-hospital cost (in US funds) was not different between the 2 treatments (\$12,905+/-495 for EVAR versus \$12,714+/-1,116 for OSR).

Patel et al. (47) constructed a decision analysis model using important clinical descriptors of patients. Clinical characteristics were matched to those of 22,460 patients undergoing AAA repair from a large national database (Medicare Provider Analysis and Review). The estimated costs from modeling closely matched actual costs from analysis and were similar to other studies. The model included costs of morbidity/mortality, follow-up monitoring, and reinterventions.

Results showed higher total costs for EVAR (\$28,901US) versus OSR (\$19,314 US). However, the authors estimated that EVAR provided an additional 0.42 quality-adjusted life years (QALY), and hence yielded a cost-effectiveness ratio of \$22,826 per QALY. Patel et al (47) concluded that EVAR is cost-effective because society is usually willing to pay for interventions with cost-effectiveness ratios of less than \$60,000. They also found that the cost-effectiveness of EVAR was critically dependent on EVAR producing a large reduction in the combined mortality and long-term morbidity rates compared with OSR. The investigators noted EVAR might not be cost-effective in medical centres where OSR could be performed with low risk.

Registries for Endovascular Repair of Aortic Abdominal Aneurysms

Lifeline Registry of Endovascular Aneurysm Repair

This registry (48) was set up to collect and analyze long-term outcome data on the safety and effectiveness of endovascular grafts used in AAA repair in the United States and Canada. Its aim is to help define appropriate patients for endograft therapy and to evaluate long-term device performance and patient outcome.

EUROSTAR

This large database (33) collects data on EVAR from 18 countries. Contributors are required to follow the EUROSTAR Protocol.

Registry of Endovascular Treatment of Abdominal Aortic Aneurysms

The Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA) (8) was started January 1996 in the United Kingdom. This registry is co-ordinated by the Sheffield Vascular Institute on behalf of the Joint Working Party of the Vascular Surgical Society of Great Britain and Ireland and the British Society of Interventional Radiology. Data submission is voluntary with all United Kingdom members of these two societies. Members may submit their cases using a simple registration form.

Other New Technologies for the Treatment of Abdominal Aortic Aneurysms

- Current clinical trials (7) are investigating if beta-blockers retard growth of small aneurysms.
- Upcoming clinical trials will investigate if tetracycline-related drugs can impede proteolytic enzyme activity in AAAs and slow or stabilize their growth.

SYNOPSIS OF FINDINGS

Safety and Effectiveness

- The success rates of performing EVAR in eligible patients are high (81%–100%, median 97%) and comparable to those of OSR.
- Technical success (complete exclusion of the aneurysm from blood circulation) rates of EVAR (62%–98%, median 83.5%) is reduced because of high rates of initial endoleak (failure of the graft to exclude blood flow into the aneurysm) in EVAR.
- Mortality rates within 30 days following EVAR (0–8.5%, median 2%) are comparable to those of elective open surgical repairs (0–6%, median 4%). Patients with high surgical risks may have higher mortality (up to 18%) and morbidity rates.
- Fluctuations in blood flow are less severe and there is a lower incidence of myocardial ischemia during EVAR than during OSR.
- EVAR has been associated with less blood transfusion and shorter stay in the intensive care unit and hospital compared to OSR.

Concerns

- A median of 3% of patients that underwent EVAR was required to convert to open surgical repair because of failure of EVAR. The risk of death from conversion to open surgical repair in patients unfit for open surgery could be as high as 66%.
- Endoleaks occurred in 0% to 42% (median 21%) of patients following EVAR. Although more than 50% of endoleaks seal spontaneously, up to 37% may remain and require additional interventions.
- Secondary interventions were required in 6% to 32% (median 12%) of patients following EVAR to correct persistent endoleaks, graft migrations, device failures, and occlusions of iliac or renal arteries. Most of the secondary interventions did not require open surgical procedures.
- Adverse events such as late endoleaks, late ruptures and device failures were reported with longer follow-up.
- The importance of persistent and late endoleaks is not well understood. While some evidence point to late endoleak as a potential cause of continuing aneurysm sac expansion, a case series has demonstrated continuing aneurysm sac reduction in patients with endoleaks requiring treatment and in those that sealed spontaneously.

Cost-effectiveness

- Despite a significant reduction in the need for ICU stay, hospital stay, and blood transfusion, the costs of EVAR were similar to or higher than the costs of OSR due to the considerable cost of the stent graft.
- The concern is: “Does the availability of a minimally invasive treatment option lead to over-utilization of that procedure in patients with marginal indications [e.g., aneurysms less than 4 to 5 cm in diameter] for surgery?” (5)
- Analyses of the cost-effectiveness of EVAR have not been extensive, and several reports suggest that the evidence is still too inconclusive. (5)
- One US study estimated the cost-effectiveness ratio of EVAR compared to OSR to be \$22,826 (US) per quality adjusted life year. There is indication that EVAR might not be cost-effective in medical centres where OSR can be performed with low risk.
- Canadian-based economic analyses were not found.

Indications

- Although EVAR is being touted as the treatment of choice for older patients and patients who are unfit for OSR, studies have shown higher rates of mortality and morbidity for these patients. Ethical concerns have also been expressed about the potential need for these patients to be converted to OSR, which may not be feasible.
- Benefits of aneurysm repair depend on the operative mortality, the risk of aneurysm rupture, and the life expectancy of the patient. Mortality rates of EVAR for patients who are unfit for surgical AAA repair have been reported to be as high as 18%. In addition, there is a 3% risk (median value) of conversion to surgical procedure that carries a mortality risk of 66% for high-risk patients. (8) Hence, the combined mortality risks of EVAR outweigh the risk of rupture in aneurysms with a diameter up to 5.9 cm (estimated to be up to 11% per year). However, for aneurysms that are 6 cm in diameter or bigger, the risk of rupture is at least 25%. For these patients, the risk of rupture outweighs the mortality risks of EVAR.
- Although EVAR has reduced the risk of AAA repair compared to OSR, the limited life expectancy of high-risk patients may undermine its value.
- Evidence does not support lowering the threshold (based on maximum diameter of the aneurysm sac) for elective aneurysm repair using endovascular means.

- EVAR has good potential, but there is need for long-term RCTs. Two RCTs are in progress. The results are due in 2005.

CONCLUSIONS

- Endovascular aneurysm repair is an adjunctive technology rather than a replacement technology to open surgical repair.
- Although perioperative mortality rates and conversion rates have improved with second-generation devices, no definitive conclusion about the long-term effectiveness of EVAR can be drawn because of the poor quality of the available evidence.
- There is insufficient quality evidence to support the use of EVAR in patients with small aneurysms or in those who are fit for open surgical aneurysm repair.
- EVAR may be appropriate for treating AAAs in a small subset of patients who are unfit for surgical repair (high risk) and whose risk of aneurysm rupture outweighs the risk of dying from EVAR.
- Long-term follow-up is required following EVAR.

APPENDIX 1

Figure 1: Examples of Endografts¹

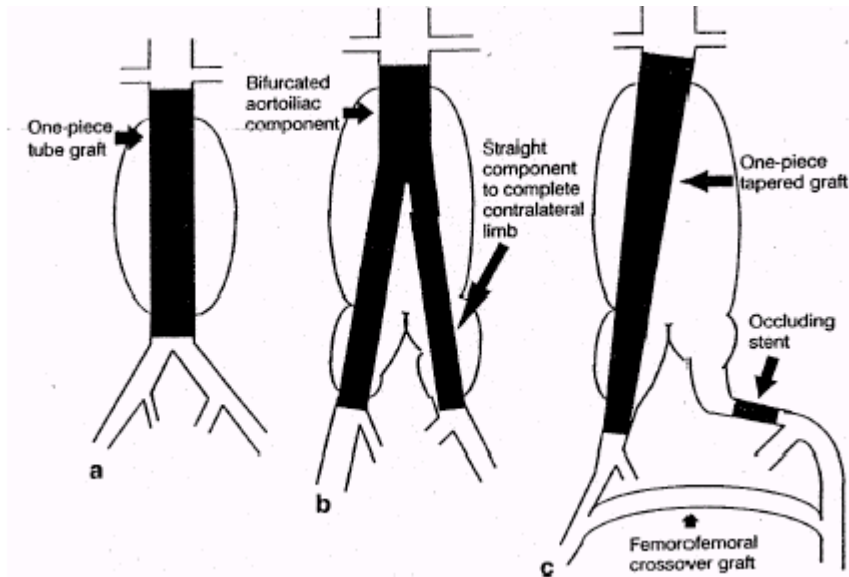


Figure 1 The three main categories of grafts for endoluminal repair of abdominal aortic aneurysm: (a) aorto-aortic tube graft; (b) aorto-bi-iliac graft; (c) aorto-uni-iliac graft with occlusion of contralateral iliac artery and femorofemoral crossover graft.

¹ Endoluminal Grafting for abdominal aortic aneurysm, Systematic Review, MASC, 1999 (6)

APPENDIX 2

Table 3: Summary of Studies Comparing Endovascular Repair of AAAs* With Open Surgical Repair

		Allen et al., 1998 ¹⁴	Becquemin et al., 2000 ¹⁵	Beebe et al., 2001 ¹⁶	Bertrand et al., 2001 ¹⁷	Moore et al., 1999 ²¹	Cohnert et al., 2000 ¹⁸	Cuypers et al., 2001 ¹⁹	May et al., 2001 ²⁰
Level of Evidence		3a	3a	3a	3a	3a	3a	2 [†]	3a
Sample size	EVAR	34	73	268	193	100	37	57	148
	OSR	9	107	98	193	100	37	19	135
Primary success rate, %	EVAR	97	96	98	97	90	100	98	99
	OSR	100	94	97	100	100	100	95	100
Technical success	EVAR	79	74	89	94	69	73	98	85
30-day mortality rate, %	EVAR	2.9	2.7	1.5	3.0	2.0 [‡]	5.4 [‡]	2.0 [‡]	2.7 [‡]
	OSR	0	2.8	3.1 [‡]	6	3	0	5	5.9
Mean ICU stay, days	EVAR			0.34	0.9	0	1.5+/-0.9	NA	NA
	OSR			1.3 (p<0.001)	1.1	2 (p<0.005)	1.4+/-0.6 (p=0.81)		
Mean Hospital stay, days	EVAR	3	7	3.6	10	2	10+/-4.4	NA	NA
	OSR	6.1 (p=0.002)	13	9 (p=<.001)	14	7 (P<0.005)	10.4+/-2.8		
Blood loss, ml or Transfusion, units	EVAR	458	96	457	90 postop	4 units	NA	NA	NA
	OSR	983 (p=0.03)	985	1367 (p<0.001)	400	1.6 units (p<0.005)			
Perioperative complication rate, %	EVAR	9	NA	NA	NA	NA	NA	NA	NA
	OSR	11							
Second intervention rate, %	EVAR	32.4	22	14.2	NA	13	NA	NA	NA
	OSR	NA	7.5	0		NA			
Overall mortality rate, %	EVAR	NA	NA	1 yr: 15.1	NA	NA	13.5	NA	NA
	OSR			19.7			0		
Cumulative survival rate or survival probability rate, %	EVAR	NA	1 yr: 82.2	2yr: 84.9	NA	5 yr: 65	NA	NA	3 yr: 96
	OSR		96	2 yr: 80.3 (p=0.48)		72 [‡]			3 yr: 85 (p=0.004)
Combined CV events rate, %	EVAR	NA	6.9	NA	NA	NA	NA	5	NA
	OSR		19.6					11 [‡]	
Late death rate, %	EVAR	NA	NA	NA	NA	NA	NA	NA	0.7
	OSR								8
3-year survival with functioning graft %	EVAR	NA	NA	NA	NA	NA	NA	NA	82
	OSR								85 [‡]

*AAA represents abdominal aortic aneurysm; CV cardiovascular

[†]This was a randomized controlled trial

[‡] Not significant

[^] Hospital stay for EVAR patients as a percentage of hospital stay for open surgical patients

NA: Not available NS Not significant

APPENDIX 3

Table 4: Outcomes of Studies on Endovascular Repair of Abdominal Aortic Aneurysm

	Allen et al. (14)	Beebe et al. (16)	Becquemin et al. (23)	Becquemin et al. (15)	Bertrand et al. (5)	Cohnert et al. (18)	Cuyper et al. (19)	Harris et al. (33)	Howell et al. (4)	Holzenbein et al. (30)	Liewald et al. (28)	Lundbom et al. (55)	Makaroum et al. (29)	May et al. (20)	Ohki et al. (26)	Moore et al. (21)	Petrik Et al (24)	Vignali et al. (27)	Zarins et al. (36)
Year of publication	1998	2001	1999	2000	2001	2000	2001	2000	2001	2001	2001	1999	1999	2001	2001	1999	2001	2001	2000
Level of evidence	3a	3a	4b	3a	3a	3b	2	4c	4c	4c	4c	4c	4c	3a	4c	3a	4c	4c	4c
Sample size	34	268	75	73	193	37	57	2464	215	173	130	100	55	148	239	100	100	64	149
Successful deployment rate, %	97	98	100	96	97	100	98.2	97.6	99.5	99	96	96	96	99		90		95	81
Technical success rate, %	79.4	89.2%	62.0	74	94	73	98.2	82	62	94	86	88	67	85	89	69		75	99
30-day conversion rate, %	3	2	8	4	3	0	1.8	1	0	1	4	4	4	1		10		5	1.3
30-day mortality rate, %	2.9	1.5	1.3	2.7	3.1	5.4	1.8	3.2	0	2.8	2	2.0	1.8	2.7	8.5	2.0		1.5	1.3
ICU stay, days (mean)	3.09	0.9			0.9											0			
Hospital stay, days (mean)	6.1	3.6		7	10				2						4.1	2			
Blood loss, ml	458			96			90								468				
Blood transfusion, units					0.9		0.8									4			
Perioperative complication rate, %	9			7			26		16		20				17.6				10
Initial endoleak rate, %		6	30%	23		22	0	17.4	42	26.5	8.	8	29	7		29	39	20	18
Persistent endoleak rate, %	6	3		9.6	1	5			5			9	13	11.5	9	6	6	9	
Late endoleak rate, %										24	16			5	9.6	5		6	
Second intervention rate, %	32	6		22					10	27	26				10	12			12
Late complication rate, %		6										17							
Late conversion rate, %				1.4					0.5			1.0		2.7		2.0		1.6	
Overall mortality rate, %	5.9	2.2		9				6.2	5.6	11.6	11				22				
Late death rate, %								0	5.6	0.6	10.3			0.7					10

APPENDIX 4

Table 5: Summary of Studies in Literature Review*

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
MSAC, 1999 (6)	Systematic review of 13 studies, mainly case series from 1995–1997	N=18–133 Follow-up 12–133 days	48–95	EVAR low risk, 2.5 EVAR high risk, 8	PC: 50% of initial endoleaks seal spontaneously	NA	Endoleak: 6–33%	NA	Long-term effectiveness & cost-effectiveness unknown
Bertram and Flynn, 1998 (5)	Systematic review of 14 studies, mainly case series from 1995–1997	N=10–154 Follow-up 153 days –23 months	NA	EVAR, 0–36	NA	NA	Endoleaks associated with bigger increase in aneurysm expansion Patients with complications: 10–31%. Incidence of individual complications: 0.6–20%	Mean, 10 (0.6–23)	Studies were methodologically inadequate to definitively answer questions on effectiveness & cost-effectiveness
Cuypers et al., 2001 (19)	RCT Stentor Vanguard Lifepath AneuRx	EVAR, n=57 OSR, n=19 Mean follow-up: 1 month	EVAR, 98	EVAR, 2 (n=1) OSR, 5 (n=) NS	PC: MI EVAR, 4% MI OSR, 5% CHF EVAR, 4% CHF OSR, 5% (not significant) Combined EVAR, 5% OSR, 11% (p=0.6)	NA	Other: Decrease in systemic vascular resistance greater in EVAR (p=0.03) Hemodynamic changes less severe in EVAR	NA	NA
Allen et al., 1998 (14)	Non-RCT Ancure	EVAR, n=34 OSR, n=9 Mean follow-up EVAR 6.2 months (1–24)	EVAR, 79.4 (n=27/33) OSR, 100 (n=9/9)	EVAR, 2.9 OSR, 0	Conversion: EVAR, 2.9% (n=1) PC: EVAR, 8.8% (n=3) CHF, lymphocele & ileus OSR, 11.1% (n=1) MI Periprosthetic leak, 18.2% (n=6) 66.7% resolved spontaneously	Hospital stay: (mean \pm SD) EVAR, 3.09 \pm 0.3 days OSR, 6.1 \pm 0.8 days Blood loss: EVAR, 458.1 \pm 76.5 ml OSR, 983.3 \pm	Endoleaks: 5.8% (n=2) Other: Additional intervention required in 32% of EVAR patients for stenosis and endoleaks	EVAR, 5.8 (n=2) OSR, 0	EVAR has potential Further device modifications needed to reduce periprosthetic leaks and limb stenosis

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						230.1 ml			
Beebe et al., 2001 (16)	Non-RCT 17-centre double cohort trial Vanguard	EVAR, n=268 OSR, n=98		EVAR, 1.5 OSR, 3.1 (p=0.59)	Conv: 1.9% (n=5) PC: 30 day endoleak EVAR, 5.7%	ICU:EVAR, 20.6 hr OSR, 78 hr Hospital stay: EVAR, 3.6 +/- 4.6 (SD) days OSR, 9 +/- 7.4(SD) Days (p<0.001) Mean blood transfusion: EVAR, 457.2 +/- 827 ml OSR, 1367.5+/- 1306.5 ml (p<0.001)	Other: 24 months EVAR, 14.2%	24 months EVAR, 15.1 OSR, 19.7 NS	EVAR: 6% device failure mostly after 12 months due to dislocation, migration, fabric erosion
Becquemin et al., 2000 (23)	Non-RCT comparative study Endografts: Mixed	EVAR, n=73 OSR, n=107 All suitable for OSR Mean follow-up: 1 y		EVAR, 2.7 OSR, 2.8	PC: Cardiac-pulmonary complications EVAR, 6.9% OSR, 19.6% Endoleak EVAR, 23.3%	Hospital stay EVAR, 7 days OSR, 13 days Blood loss: EVAR, 96 ml OSR, 985 ml	Endoleak: 1y, EVAR, 9.6% Other: At 1 y, reintervention EVAR, 22% OSR, 7.5%	1 y Cumulative survival rate EVAR, 82.2 OSR, 96	Primary success rate EVAR, 74% OSR, 94%
Bertrand et al., 2001 (17)	Non-RCT Endograft: made to measure stainless steel auto-expandable	EVAR, n=193 OSR, n=193 Ended at discharge		EVAR, 3 OSR, 6 Not significant Surgical time: EVAR 2.5+/- 1.1 hour OSR 3.1+/-1.3 hour (p<0.001) Bleeding: EVAR 650+/- 1100 ml	Endoleak: 1.1% (n=6) PC: Reoperation EVAR=6% OSR=11% Cardiac complications NS Lesser incidence of pneumonia, and acute respiratory and renal failure in EVAR	ICU EVAR, 21 hrs (0-140) OSR, 27 hrs (2.5-144) (p<0.001) Hospital stay: EVAR, 10 days OSR, 14 days Need any blood: EVAR, 18% OSR, 57%	Had at least 1 reoperation: EVAR 6% OSR 11% (p<0.05) Pneumonia EVAR 3% OSR 17% (p<0.001) Acute renal failure EVAR 5% OSR 10% (p<0.02)		

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				OSR 1800+/-1600 ml (p<0.001)		Autologous Packed cells EVAR, 0.3+/-0.8 U OSR, 0.6+/-1.2 U (p<0.001)	Acute Respiratory failure EVAR 2% OSR 10% (p<0.001)		
Moore et al., 1999 (21)	Non-RCT with contemporaneous controls Endografts: Endovascular Technologies EVT (Menlo Park)	EVAR, n=100 OSR, n=100 No significant difference in age or comorbidity Study period 1992-1998	EVAR, 90 OSR, 100	EVAR, 2 (was converted to OSR) OSR, 3	Conv: EVAR 10% - (9/10 converted during surgery due to technical difficulties) PC: Initial endoleak 29% (29/100) At 12 months, 79% (23/29) have sealed spontaneously	ICU(median): EVAR, 0 days OSR, 2 days Hospital stay: EVAR, 2 days OSR, 7 days Blood loss: EVAR 326 ml OSR 1010 ml (p<0.005) Blood replacement: EVAR, 0.4+/-1.1 units OSR, 1.6+/-0.2 units	At 12 months 6% + 5% new endoleaks (n=11/100) Other: Late conversion EVAR, 2% 16 secondary interventions 13% (n=12/90) Balloon Angioplasty, dilatation and stenting, coil embolization, endovascular repair Causes of late deaths: MI & CV arrests, no rupture	5-year cumulative survival rate EVAR, 65 OSR, 72	
Zarins et al., 2001 (36)	United States AneuRx trial Phase II Prospective non-RCT (1999) AneuRx	EVAR 1192 in all phases of the trial EVAR, n=416 OSR, n=66	EVAR, 98	EVAR, 2 OSR, 0 NS Primary graft patency 98%	Conv: 1.5% PC: EVAR has 50% reduction in major morbidity versus OSR Initial endoleak, 38% 1 month, 13% 1 rupture	EVAR has a 63% reduction in hospital stay EVAR has a 66% reduction in blood loss	Endoleaks: Rupture 0.8% 3.4% with early stiff bifurcated SG; 0.4% with current flexible SG. 6 month=16% 12 month=1% Other: Freedom from conversion Year 1, 98% Year 2, 97% Year 3, 93% 1 rupture	Patient survival rate: Year 1, 93 Year 2, 88 Year 3, 86	

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
							Secondary intervention 5% for endoleaks, 2% for graft patency Secondary graft patency 99%		
Cohnert et al., 2000 (18)	Non-RCT with matched historical controls Mean=12+/-6 months Vanguard or Talent bifurcated	EVAR, n=37 OSR, n=37 Minimum 18 months	EVAR 100 OSR 100 Mean surgical time: EVAR 221min OSR 256 min (p<0.005)	EVAR, 5.4 OSR, 0 (p=0.15)	PC: Endoleak, 21.6% Type I, 2 Type II, 6 3 required secondary intervention PC: Excluding endoleak EVAR 18.9% OSR 10.9% (p=0.33)		Endoleaks: 5.4% (n=2) persisted despite coil embolization		2.7% (n=1) late conversion to OSR Mortality during follow-up: EVAR 8.1% OSR 0% Morbidity & mortality higher in EVAR group and required reoperation in follow-up
May et al., 2001 (22)	Non-RCT Second- Generation endograft Median follow-up 29 months EVAR 24 months OSR 37 months	EVAR, n=148 OSR, n=135 Minimum 18 months	EVAR, 99	EVAR, 2.7 OSR, 5.9 Not significant Significant	Conversion: total 3.4% (n=5)		Graft failure EVAR 22/148 OSR 0/135 (p<0.0001)		3-year survival probability EVAR, 96% OSR, 85% (P=0.004) 3-year survival with functioning graft similar (82% vs 85%)
Zarins et al., 2000 (36)	Retrospective review of 2 cohorts over 2 40-month periods Median follow-up 11.5 months	EVAR, n=149 OSR, n=578 Only 190/353 patients eligible for EVAR Morphology	EVAR, 98.7 Primary graft patency 99%	EVAR, 1.3 (n=2) due to acute MI NS	Conversion: EVAR=1.3% PC: Major 10% (MI, CHF, early major endoleak, femoral pseudoaneurysm,	EVAR has significantly shorter ICU stay (p<0.5) and hospital stay (P<0.5)	Endoleak at discharge, 36% 1 month, 18% Other: 21 secondary interventions 11% at follow-up, 20 for	Late deaths 10% of patients (n=15) at 1 y Cardiac Total mortality, 11.4	Secondary graft patency rate, 100%

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
	[Query: Range?]	matched EVAR, n=79 OSR, n=70			colon ischemia, transient renal failure, hemispheric transient ischemic attack) Minor complications 9% NS difference in rate Severity greater in OSR group	EVAR has less blood loss (p<0.05)	endoleaks 1 for graft limb occlusion		
Petrik and Moore, 2001 (24)	Retrospective radiogr review of 100 EVARs by 1 surgeon	EVAR, n=100	90		Conv: 10% PC: Initial endoleak, 39%		At 12 months 6% had residual endoleaks (no anatomic factor found to be predictive)		
Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
Harris et al., 2000 (33)	Surveillance-EUROSTAR Registry	EVAR, n=3464	98.7	3.2	Conv: 1.3% PC: Initial endoleak, 17.4% (n=140/1688)		Other: Accumulated risk of fatal adverse events, 3% y Late rupture peaks at 18 months	At 48 months, 8.7 (n=215/2464)	Proven rupture of AAA at 24 months=13, Death due to late rupture=9
Fairman et al., 2001 (51)	Case Series Ancure Talent	EVAR, n=74 Divided into 3 groups	100	0	Conv: 0% PC: Intraoperative critical event: 1 event, 89% 2 events, 51% Difficult access, 28% Graft foreshortening, 44% Graft limb twist/kinks, 12% General incidents, 6% Endoleak, 44% 30-day rate of endoleak, 20%	NA	NA	NA	NA

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
Treiman et al., 1999 (38)	3-centre case series	162 patients screened; 22 underwent EVAR	86		Conversion: 14%	NA	NA	NA	
Cuypers et al., 1999 (40)	Case series	EVAR N=64 Follow-up Mean=9.3 months (1-24 months)	Successful exclusion of AAA, 95%. Needed additional procedure, 59	5	Conversion: 3% (n=2) PC: 30-day endoleak rate, 14.5% (n=9)		Total endoleak, 19% (13 in 12 patients) Other: 28 pts had complications: mild, 24% moderate, 55% Severe (fatal), 21%		
Howell et al., 2001 (4)	Non-RCT case series AneuRx	EVAR, n=215 Follow up n=132 at 6 months n=84 at 1 y n=22 at 2 y	99.5	0	Conv: 0% PC: At discharge endoleaks in 42%	Mean hospital stay 1.9 days	Endoleaks: 6 months, 11.3% 1y, 11.9% Other: 10.2% (n=22) for endoleak repair 3 converted to OSR	5.6% (n=12) late deaths not related to device failure or rupture	
Becquemini et al., 1999 (23)	Prospective case series Bifurcated Vanguard	EVAR, n=75 Follow-up Mean 18.35 months	100	0	Conv: 0 PC: Significant complications needing surgery, 8% Systemic complications, 8% Total endoleaks, 30.7%		Other: At 18.35 months reintervention EVAR, 23% of patients for occlusion stenosis or endoleak	18.35 months EVAR, 9 2-year cumulative survival rate, 86+/-5.9	
Velazquez et	Non-RCT	EVAR		Male, 3.7	Conversion:		Male, 2 late endoleaks		

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
al., 2001 (50)	comparative study on gender differences Ancure Talent	Male, n= 81/122 (86.5%) Female, n= 7/19 (13.5%)		Female, 14 NS between gender	Male, 1.2% (n=1) Female, 14% (n=1) PC: NS difference Iliac artery rupture Male, 2.5% (n=2) Female, 0 30-day endoleak Male, 18.5% (n=15) Female, 28.6% (n=2)		(2.5%) Female, 0 Other: Female: significantly fewer suitable for EVAR because more likely to have significantly reduced iliac artery size, shorter, more dilated, more angulated proximal aortic neck		
Liewald et al., 2001 (28)	Non-RCT case series Vanguard Talent Gore Excluder Corvia Stenford AneuRx Baxter	EVAR, n=130 Male, n=117 Female, n=13 Mean follow-up in 108 cases = 20 months	86	2	Conversion : total, 4% PC: 20% (including renal insufficiency, CVA, perforated gastric ulcer, and ischemic colon		Late problems in 26%, including endoleaks 16% Type I, 5% Type II, 10% Type III, 1% Limb occlusion 3% Other: Rate of freedom from intervention First 85 patients 1 y, 86% 3 y, 65% Last 65 patients 1y, 90%	Late mortality, n=11/108 Total success including intervention, 93	Intervention rate comparable to EUROSTAR EVAR is associated with higher complication rate than OSR
Riambau et al., 2001 (41)	Part of multicentre study EUROSTAR registry	EVAR N=2,862 Unfit for surgery 9.5 Unfit for anesthesia 3.8		Fit for surgery 2.7 Unfit for surgery 5.1 Unfit for anesthesia 3.7	PC: Coexisting diseases did not affect mortality in patients unfit for surgery or anaesthesia	Diabetes M and pulmonary Diseases increase mortality rate in patients eligible for OSR	Late mortality Fit for surgery 5.2% Unfit for surgery 11.4% Unfit for anesthesia 11.0%		

Study	Type of Study and Type of Graft	Sample Size/ Follow-up time	Primary Technical Success Rate, %	Perioperative 30-day Mortality Rate, %	Conversion to OSR (Conv) and Perioperative Complication (PC) Rates	ICU/Hospital Stay and Blood Transfusion Rates	Persistent Endoleak and Other Complications	Overall Mortality Rate, %	Conclusion
Resch et al., 2001 (35)	Prospective non-RCT case series Median Radiol follow-up, 638 days (301—1105 days) First- and second-generation Ivancev-Malmo (IM), Chuter Vanguard Zenith	<u>EVAR</u> 158 IM-I, 58 IM-II, 17 Chuter, 15 Vanguard, 15 Zenith, 53		IM-I = 11 Vanguard 7 Other grafts, 0	Conversion: IM-I, 12% Chuter, 7% Second- generation grafts, 0%		Type I endoleak IM-I, 31% (n=13/42) Chuter, 21.4% (n=3/14) IM-II, 11.7% (n=2/17) Vanguard, 0% Zenith, 3.8% (n=2/53) Type II no significant difference (11–24%) Other: Secondary interventions IM-I, 49/56 Chuter, 18/15 IM-2, 15/17 Vanguard, 9/15 Zenith, 5/53 Device migration: IM-I, 52% Chuter, 64% Other grafts, 0%	Size of aneurysm: Excluded aneurysms decreased in size at 1 y, increase in size with type I endoleak, stable or decrease with type II endoleak	Enhanced stent graft design has improved the probability of SG success after EVAR Better technical skills may also have contributed to improved results

*OSR indicates open surgical repair; AAA abdominal aortic aneurysm; EVAR endovascular repair of AAA; RCT randomized controlled study; NS not significant; MI myocardial infarction; CHF Congestive heart failure; y year; SG stent graft.

APPENDIX 5

Table 6: Summary of Studies Comparing Cost of Endovascular Repair AAAs with Open Surgical Repair*

Study	Procedure	Pre-op Diagnostic US\$	Post-op Diagnostic US\$	Room and Board US\$	ICU US\$	Recovery Room US\$	OR cost excluding graft US\$	OR cost excluding graft US\$	Device US\$	Anesthesia US\$	Medical and Surgical Supplies US\$	Pharmacy and Blood Supplies US\$	Total US\$
Sternbergh et al., 2000 (45)	OSR EVAR	644 1,100	698 1,760	1,099 752	1,210 639	1,898 1,225	2,642 2,577		653 10,200	940 1,038	972 1,094	1,588 865	12,342 21,250
Seiwert et al., 1999 (46)	OSR	^					2,934^ +/-158	3,459^ +/-218		1,414^ +/-260		536 +/-131	12,714 +/-1,116
	EVAR	1,370 +/-67					2512 +/-144	7512 +/-143		8.5 +/-8.5		131 +/-18	12,905 +/-495
Oriel et al., 1999	OSR 93 EVAR 33								EVAR= 8,898				EVAR costs \$5,985 more than OSR
Patel et al., 1999 (47)	Markov model 70 yr pt with a 5cm- AAA&			In. Hospital OSR \$16,016 EVAR \$20,083 Lifetime cost included estimated cost for mortality, long term- morbidity ,& re-intervention									Lifetime cost OSR=19,314 EVAR=28,905 QALYs OSR=7.53 EVAR=7.95 Cost- effectiveness ratio of EVAR= \$22,826 Cost-effective

*AAA indicates abdominal aortic aneurysm; EVAR endovascular repair of AAA; OSR open surgical repair; Costs in US dollars

^ Mean plus standard deviation

Patel et al: cost-effectiveness ratio critically dependent on mortality & morbidity rates

GLOSSARY

Aorta	The main trunk of the major blood vessel carrying blood from the heart to other parts of the body
Aortoiliac	Pertaining to the aorta and the iliac artery
Aneurysm	An expansion and weakening of a segment of a blood vessel that may lead to rupture
Abdominal aortic aneurysm	The expansion and weakening of a section of the aorta in the abdominal area.
Atherosclerosis	A buildup of plaque in the arteries
Endovascular aneurysm repair	Repair of an aneurysm done from within the blood vessel by inserting an endograft using a catheter. No open surgery is required.
Endograft	A device designed for repairing the aneurysm from within the blood vessel
Endoleak	Continued blood flow into the aneurysm after repair from within using an endograft.
Ischemia	An insufficient supply of blood to an organ, usually due to a blocked artery
Lumen	The cavity or channel within a tube or tubular organ
Mortality rate	Rate of death
Nitinol	Any of several alloys of nickel and titanium that are resistant to fatigue, have low moduli of elasticity, and return to their original shape after deformation if they are heated
Outpouching	The obtusion of a layer or part to form a pouch
Periadventitial	Outside the adventitia, the outermost connective tissue covering of an organ, vessel, or other structure
PTFE	Polytetrafluoroethylene: a high performance polymer that is resistant to most chemicals and corrosive environment

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