The term "evidence-based medicine" was first coined by Sackett and colleagues[1] as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." The key to practicing evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding and it is impossible for an individual clinician to read all of the medical literature. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility and utility of individual articles. These skills are known as critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis and economics as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsors a program entitled "Evidence-Based Reviews in Surgery (EBRS)," supported by an educational grant from Ethicon Inc and Ethicon Endo Surgery Inc. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. During the academic year, 8 clinical articles are chosen for review and discussion. They are selected not only for their clinical relevance to general surgeons but also because they cover a spectrum of issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, how to quantify disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodologic and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS website. Also, a listserve discussion is held where participants can discuss the monthly article. Fellows and candidates of the College can access Evidence Based Reviews in Surgery through the American College of Surgeons website (www.facs.org). All journal articles and reviews are available electronically through the website. Currently we have a library of 40 articles and reviews which can be accessed at any time. Each October a new set of articles will be available each month until May. Surgeons who participate in the current (modules) packages can receive CME credits by completing a series of MCQ. For further information about EBRS the reader is directed to the ACS website or should email the administrator, Marg McKenzie (email: mmckenzie@mtsinai.on.ca).

In addition to making the reviews available through the ACS and CAGS websites, 4 of the reviews are published in condensed versions in the Canadian *Journal of Surgery* and the other four will be published in the *Journal of the American College of Surgeons* each year.

REFERENCE

1. Evidence Based Medicine Working Group. Evidence-based medicine. JAMA 1992;268:2420–2425.

SELECTED ARTICLE

Endovascular Aneurysm Repair versus Open Repair in Patients with Abdominal Aortic Aneurysm (EVAR trial 1): Randomized Controlled Trial

Evar Trial Participants. Lancet 2005;365:2179–2186.

Reviewed by

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ABSTRACT

Question: What is the long term all cause mortality of endovascular aneurysm repair (EVAR) compared with conventional open repair?

Design: Randomized controlled trial.

Setting: Thirty four hospitals in the United Kingdom proficient in EVAR technique.

Patients: One thousand eighty two patients aged 60 years or older, who had aneurysms of at least 5.5cm in diameter and were suitable candidates for EVAR or open repair.

Intervention: EVAR (n = 543) or open repair (n = 539).

Main Outcomes Measure: All cause mortality. Secondary outcomes were aneurysm-related mortality, rate of postoperative complications, need for re-intervention, HRQL and hospital costs.

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Results: Ninety four percent (1017/1082) patients complied with their allocated treatment and 209 died by the end of the 4 year follow-up (53 of aneurysm related causes). The all cause mortality was similar in both groups (about 28%, hazard ratio 0.90, 95% CI 0.69–1.18 P = 0.46), however there was a reduction in aneurysm related deaths in the EVAR group 4% vs. 7%; (hazard ratio 0.55, 0.31–0.96, P = 0.04). Postoperative complications were observed in 41% in the EVAR group vs. 9% of the open repair group (hazard ratio 4.9, 3.5–6.8, P < 0.0001). After 12 months there was no significant difference in the HRQL between the two groups. The mean hospital costs were £3311 higher in the EVAR group.

Conclusions: The EVAR offers no advantage with respect to all cause mortality and HRQL is more expensive and leads to greater number of complications and re-interventions. There is, however, a 3% decrease in aneurysm-related mortality.

Commentary: Endovascular aneurysm repair was first described by Parodi in 1991 and has gained acceptance as an alternative treatment for elective aneurysm repair. The procedure prevents aneurysm rupture by placing a fabric-covered metal stent through an aneurysm, attaching it to the normal caliber aorta above and the iliac arteries below the dilated segment. The aneurysm is left in place, but sealed from hemodynamic stresses by the stent graft. Because the stent is placed by femoral artery cut-down, EVAR avoids laparotomy so there are no sudden changes in cardiac afterload (the aorta is never clamped) and blood loss is minimal (the aorta is never opened). Because EVAR leaves an aneurysm in place, the procedure can fail if there is persistent blood flow and pressure in the aneurysm around the stent. Such blood flow, termed "endoleak," is the primary mechanism of stent graft failure and can occur if there is inadequate seal of the stent to the native circulation, back-bleeding through branch arteries arising from an aneurysm or disconnection of modular segments of the multi-piece stent graft. Critical aortic dimensions, including length, diameter, and angulation of the aneurysm neck and iliac arteries and the diameter at the aortic bifurcation has been studied to provide guidance to surgeons who must decide if an aneurysm is anatomically eligible for EVAR. After implementation, long term surveillance is necessary to detect endoleak and potential complications such as stent fracture component separation or fatigue or stent migration. The anatomic criteria specified by each endovascular device manufacturer allow a surgeon to decide if an aneurysm is suitable for EVAR with a low probability of early endoleak. Long-term post-operative surveillance of all EVAR patients is required to watch for late endoleak. Late post-operative imaging will show diminishment of AAA diameter in most cases of successful EVAR. Progressive AAA enlargement after EVAR or visible contrast in an aneurysm sac, however, indicates an endoleak, and the risk of a future aneurysm rupture is high. Most endoleaks can be corrected by secondary interventions including implantation of further sealing stents or coil embolization of branch arteries back bleeding into an AAA sac.

The EVAR trial 1 was designed to compare mortality, durability, health related quality of life, and costs after open AAA repair and EVAR. The authors conducted a randomized controlled trial where 1082 patients were randomized to either of the two treatments. Patients were included if they were over 60 years of age and had a AAA greater than 5.5cm, were deemed suitable for endovascular treatment, and medically fit for conventional, open surgery. Interventions were performed at one of 34 hospitals in the United Kingdom that met minimum criteria for expertise in endovascular repair. Regular follow up was scheduled for patients in both groups. After 4 years follow-up, the authors found that all cause mortality was similar in both groups although there was a persistent reduction in aneurysm-related deaths in the EVAR group due to a decreased risk of death post procedure. The proportion of patients having complications was higher in the EVAR group compared to the open repair group (41% vs. 9%). There was a negligible difference in HRQL between the two groups but mean hospital costs were higher in the EVAR group.

Overall, the methodologic quality of this trial is quite good. The inclusion criteria were appropriate; generally most vascular surgeons would use endograft placement in older patients only because of the increased number of postoperative interventions needed over time. The table of baseline characteristics is included in an earlier publication, and revealed no differences in average aneurysm diameter, cardiovascular risk factors, or preoperative parameters in the two groups. Those under 60 theoretically would need more interventions if they survived a longer period of time. The sample size was based on all cause mortality rate of 7.5% per year of follow-up, and an assumption that a 2.5% reduction in all cause mortality would be clinically important. In fact, mortality at 4

years was 29% in the open vs. 26% in the EVAR group. Randomization was performed using a permuted block sequence and stratified by centre, but details of allocation concealment were not well described. Data collation was centralized, but trained trial coordinators oversaw data collection at each included centre. Mortality outcomes were collected through the Office for National Statistics: patients who were included in the trial were flagged at the time of randomization so that their mortality status would be captured. An outcomes assessment committee, to whom patient allocation was not revealed, also reviewed outcomes. The loss to follow up was minimal: 5 patients in total, 3 in the open group and 2 in the endovascular group. All cause mortality and aneurysm-related mortality were reported using an intention to treat analysis; complications and secondary interventions were reported using a per protocol analysis, and no intention to treat analysis was provided. The choice of a general, rather that disease-specific health related quality of life scale was used, which was justified by the lack of validated instruments in the AAA population. Cost assumptions, specific to the health care system in the United Kingdom, are described in detail.

The authors of this study concluded that because of equivocal results, all cause mortality, and health-related quality of life (HRQL), EVAR offers no advantage over open AAA repair because of it being more expensive and associated with more complications and a need for more interventions. Based on these results, EVAR may offer little advantage over open repair for the fit patient with a low perioperative risk. But there are some limitations to this study. First, the primary outcome measure was all cause mortality. Most patients with AAA have cardiac and respiratory co-morbidities that shorten their lifespans independent of their aneurysmal disease. It is not unexpected that beyond the perioperative period, the mortality of AAA patients was similar in both groups. This is supported by the fact that more than 92% of deaths after 30 days in both groups were not aneurysm related. Even after four years, AAA-related mortality was lower in the EVAR group and while this event rate is lower than all cause mortality and therefore, if it were the primary outcome a larger study would have been required, it is probably the more meaningful outcome measure.

A second limitation of the study relates to the description and ascertainment of complications after both procedures. The complication rate may have been higher in the EVAR group at least in part because some of the complications listed in Table 3 are EVAR specific and not pertinent to open surgery. As well, the EVAR group had more intense follow-up which, by itself, may have resulted in the detection of more complications. On the other hand, however, the follow-up imaging protocol for the EVAR group in this study was less vigilant than that followed by most surgeons currently and recommended by graft manufacturers. For example, a CT scan was not performed before hospital discharge nor was one performed between 3 and 12 months. This less intensive follow-up regimen may account for some of the early graft related complications. Overall there was a high rate of reintervention in the EVAR patients, compared with the rates reported in other studies. Approximately 30% of patients required reintervention for complications at 2 years post EVAR in this study, more than double the rate of reintervention reported in the DREAM trial,[1] a contemporary large randomized controlled trial comparing EVAR to open repair where the reintervention rate was less than 5% per year. Although only centers that had experience with at least 20 EVAR procedures were eligible for participation, this threshold of experience may have been inadequate.

The literature now suggests that an endovascular specialist must perform a minimum of 60 procedures before the rate of peri-procedural complications falls below 10% and the interval between procedures should not exceed 10 days in order to maintain expertise.[2] Not only could the threshold of 20 procedures, specified before a centre could participate in the trial, be inadequate but if one averages the number of EVAR procedures performed in patients in the trial in the 34 participating centers, it is approximately 15 cases over the four year trial enrollment.

These problems are often those seen in surgical trials performed to compare a new technology to a standard treatment. By definition, experience with the new technology will be limited and almost always individual experience with the procedure increases over time. Additionally, modifications in the technology and the technique are made over time so that the results obtained in the trial might not be relevant by the time the trial is completed. This is a quandary faced by surgeons who want to evaluate a new technique-performing a study early in its development may bias the results against the

new technology; a delay in performing a trial may result in widespread acceptance of the new technique or technology and eliminate the possibility of performing a trial. Thus, in this trial, it is not surprising that the complication rates are higher than those observed currently and that patient selection, follow-up regimens, and indications for reintervention differ from those that are accepted currently.

While there are limitations to this trial, it is one of only two that attempt to compare the outcome of EVAR to open surgery in a rigorous manner. It suggests that EVAR provides perioperative benefit compared with conventional open repair.[3] Ongoing follow-up of this cohort of patient will provide information about the durability of EVAR and the results of the trial will also assists in planning future trials.

REFERENCES

1. Prinssen M, Verheoven ELG, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med 2004;351(16):1607–1618.
2. Forbes TL, DeRose G, Kribs SW, Harris KA. Cumulative sum failure analysis of the learning curve with endovascular abdominal aortic aneurysm repair. J Vasc Surg 2004;39:102–108.
3. Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR), 30 day operative mortality results: randomized control trial. Lancet 2004;364:843–848.

The Evidence-Based Reviews in Surgery Group is comprised of: