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EDITORIAL

Registries *versus* Trials for the Evaluation of the Endovascular Treatment of Abdominal Aortic Aneurysms

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Introduction

Since the introduction of aortic stent grafting to repair abdominal aortic aneurysm (EVAR),[1] much of the data concerning this new technology has been derived from registries rather than trials. The two most important registries have been the UK registry for Endovascular Treatment of Aneurysms (RETA) based in Sheffield[2] and the European Collaborators on Stent-Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) registry based in Holland.[3] These registries, although voluntary, have provided important information on EVAR and data from the RETA registry was used in the design of the UK EVAR trials and as an audit tool to assess centres for trial entry.

The 5-year RETA registry results are published in this issue of the European Journal of Vascular and Endovascular Surgery.[2] Nevertheless, such registry data, especially that related to follow up, is often incomplete and may present a biased view of the overall performance of new technologies. It is, therefore, essential that data derived from these registries is interpreted with caution and, more importantly, that definitive clinical practice does not change until the on-going randomised controlled clinical trails have had an opportunity to report their data.

RETA Registry

The RETA registry was set up in 1996 to audit EVAR deployments within the UK. It contains both retrospective and prospective data on 1823 procedures. Annual audit reports are produced on behalf of the Vascular Society of Great Britain and Ireland and the British Society of Interventional Radiology. The database has been an invaluable source of data on the performance of EVAR devices over the last 8 years, but as with all registries suffers in that it is voluntary and audited in an 'open' fashion, possibly leading to selection bias.

The mid-term results from the RETA registry show that at 30 days, 90.4% of aneurysms were successfully excluded and 5.8% of patients had died. The conversion rate to open repair was 3.3%, but this rate has been falling with time (9.1% in 1996 and 0.3% in 1999). Post-procedural complications within 30 days occurred in 27.8% of cases and 6.1% had persistent endoleaks. The data shows significantly more deaths in unfit (ASA IV) patients (14.8 *versus* 3.3%), and a higher mortality rate for aorto-uni-iliac devices (12.5 *versus* 3.3%) and in women (5.7 *versus* 1.9%).

Mortality in the first year was 11% (mostly cardiac disease and malignancy) and 10% per year thereafter up to 5 years. Most of these deaths were not graft related, the cumulative 5-year risk of rupture being only 2%.

Complications related to the device and aneurysm were reported at a rate of approximately 15% per year. These included secondary endoleaks, graft migration, kinking, and limb occlusions. Treatment was by further interventional radiology or surgery, with only 38% of patients surviving with no secondary intervention at 5 years.

EUROSTAR Registry

The EUROSTAR registry shows similar results.[3]

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Launched in 1996, it is a prospective audit of EVAR performance across 135 centres in 18 European countries. This registry is also voluntary, but is the largest registry of devices in Europe with a total of 5466 cases of EVAR on record by July 2003. Results from first generation devices were characterised by excellent early performance, but poor durability. The latest data from newer devices show significant improvements in all outcome measures, most importantly durability. One hundred and eighty seven patients have been followed up for more than 5 years. Life table analysis shows a 5-year cumulative results as follows; survival 79.2% and freedom from all endoleaks 71.9%, persistent endoleaks 91.4%, secondary intervention 76.3% and rupture 98.6%.

The main conclusions from analysis of the EUROSTAR database are that the incidence of rupture increases progressively with time at least up to 5 years, but that serious adverse events occur less often with newer devices, EVAR in high-risk patients is probably justified if they are not expected to die within 1 year from the effects of their co-morbid conditions, and the medium-term outcome is significantly better in patients with small aneurysms.

The above data clearly shows that open audit, in the form of voluntary registries, is an essential tool for the clinical evaluation of new technologies, but they do not replace randomised controlled trials in that they are incomplete and open to data interpretation bias. They do provide data as to the long term performance of EVAR, but in a 'selected' group of patients. Such registry data is considered useful in the evaluation of new technologies and organisations such as the UK National Institute of Clinical Excellence (NICE) now specifically recommend that, for EVAR, patients are either entered into a registry or treated within the confines of a randomised controlled trial.

Randomised Controlled Trials

To date, registries provide the only evidence we have as to the long term durability of EVAR, and no level 1 evidence exists to support the use of aortic stent grafts for the repair of abdominal aortic aneurysm. Nevertheless, the uncertainty about how EVAR compares to conventional open repair has led to the instigation of several randomised controlled multi-centred trials. The UK EVAR trials were initiated in 1999.[4] EVAR 1 randomises suitable patients to either endovascular stent graft repair or conventional open repair. Patients who are unfit to undergo open repair due to significant co-morbidity are entered into the EVAR 2 trial. This randomises patients to either EVAR and best medical treatment or best medical treatment alone. Three other randomised controlled trials have also been initiated. These are the Dutch DREAM, the French ACE and the American OVER trials.

EVAR 1 trial 30-day results

Early results of the EVAR 1 and Dream trials were published in 2004 and appear to support the use of EVAR. The EVAR 1 trial[5] randomised 1082 patients over 60 years of age with an aneurysm of 5.5 cm or greater to either open repair or EVAR. The 30-day mortality for EVAR was 1.7% compared to 4.7% for open repair ($p=0.007$). This mortality was lower than that reported by the RETA and EUROSTAR registries, perhaps because the patients randomised in EVAR 1 were those deemed fit to have an open repair compared to the registry data which includes 'unfit' patients treated with primary stent grafts. In addition, the EVAR 1 trial 30-day results report that secondary procedures were necessary in 9.8% of EVAR patients compared to 5.8% in the open repair group. Endoleaks needed treatment in 3.4% of EVAR patients and 10 patients required conversion to open repair intraoperatively.

DREAM trial 30-day results

The Dutch DREAM trial[6] has also published its 30-day mortality results for endovascular *versus* open repair. Despite only 345 patients being randomised, representing a 12% under recruitment, operative mortality was similar to the UK EVAR trial at 1.2% in the EVAR group *versus* 4.6% in the open repair group. Nevertheless, these results did not reach significance. Intervention for endoleak occurred in 1.2% and the combined rate of operative mortality and severe complication was 4.7% for the endovascular group *versus* 9.8% for the open group.

Conclusions

It is essential that, as for registry data, the 30-day randomised controlled trial data are interpreted with caution, since the long term benefit of EVAR has yet to be proven. At the time of writing, the 30-day EVAR 1 and DREAM randomised trial data should not be used to advocate the widespread use of EVAR over open repair. The authors of the EVAR 1 trial conclude that the results of 30-day mortality serve only as evidence to continue investigating the use of EVAR and stress the importance of obtaining the long-term data. The

DREAM study authors state that, taken together, these results indicate that EVAR is preferable over open repair in those who are suitable despite the results not reaching significance. This conclusion is later muted, suggesting that further long term data are required to determine if the early benefit is sustained in favour of EVAR.

The EVAR 1 and 2 trials are due to report their medium term results in June 2005. Professor Roger Greenhalgh will present these results at an extraordinary meeting of the Endovascular Forum to be held at the Belfry, Warwickshire, England on June 16th 2005. On the same day the Lancet will publish the scientific paper. By this time, one third of EVAR 1 patients will have been followed for 4 years and these results will give us the first robust evidence of the medium term durability of EVAR. Funding has also recently been secured to enable this cohort of patients to be followed up for a further 5 years. The Dutch DREAM trial patients are also to be followed for longer and the French ACE and American OVER trials are continuing.

In summary, the early and mid-term registry data appears promising for the use of EVAR. The early EVAR 1 and Dream trial data supports the use of EVAR in fit patients, but concerns still exist regarding stent graft durability and the need for continued intervention. The registries show us that newer generation devices appear to be performing better, but it will require the positive reporting of the mid term data from the randomised controlled trials before we have sufficient evidence to allow EVAR to be fully integrated into everyday surgical practice.

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