

Eur J Vasc Endovasc Surg 31, 1–2 (2006)

doi:10.1016/j.ejvs.2005.10.015, available online at <http://www.sciencedirect.com> on  SCIENCE @ DIRECT®

EDITORIAL

How Much Evidence is Needed for the Introduction of New Technologies Into Clinical Practice in Vascular Surgery?

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The introduction of new technologies into the market place proceeds at an accelerating pace. Medicine is no exception. How much evidence is needed before a new technology can be recommended for routine clinical practice?

The introduction of new technologies into vascular surgery follows the Technology Hype Cycle described by Gartner.¹ First the emerging technology is developed and tested in a limited environment. Second there is an inflated peak of expectation of the application for the new technology, often fuelled by an excited press and manufacturers (over-hype). Third there is a descent into a trough of disillusionment as the technology fails to meet all expectations and problems are identified, often compounded by adverse press comments. Products that pull through this stage are likely to be successful and after further development and new definition of application move up the slope of enlightenment to establish the appropriate range of application allowing the final stability for marketing the technology. Much later, in turn, newer technologies will replace the new technology.

This cycle almost has been completed for endovascular repair of abdominal aortic aneurysm (EVAR). The possibility of endovascular repair of aortic aneurysms was demonstrated first by Volodos and Parodi in 1986–91.^{2,3} Five years later, there was an inflated peak of expectation about the role of EVAR, as the first phase I trials reached the public domain; level 3 or 4 evidence.⁴ The companies developing endografts worked to ensure the visibility of the new technology and develop their market place. Later still,

in 1999–2000 long term follow up from registries such as EUROSTAR illustrated the prevalence of problems, re-interventions and even rupture at long-term follow up.^{5,6} There was a trough of disillusionment, with editorial content sometimes indicating that there would be no place for EVAR.⁷ However, between 1994 and 1999, the endografts underwent a process of continued technological improvement and the 1999 endografts were considered much superior to those used in 1994. Now, with the technology becoming stabilized it was time to start randomised controlled trials, to compare EVAR with the contemporary gold standard, open surgical repair of abdominal aortic aneurysm (AAA). The first to start were EVAR 1 in September 1999 and DREAM in November 1999 enrolling patients with large AAA.^{8,9} Both these trials were supported by not-for-profit organizations and this is important, since industry sponsored trials often overestimate treatment effect (by about 30%) and negative trials may not get reported.¹⁰ So up the slope of enlightenment, although it was not until 2004 that the first results, showing that EVAR reduced 30-day operative mortality by three-fold, were published. One year later in 2005, mid-term results became available, showing a persistent reduction in aneurysm-related mortality but no difference in all-cause mortality. After 16 years, there is clear evidence that EVAR matches the previous gold standard, open surgery, and offers benefits with respect to early recovery and aneurysm-related mortality. Each randomised controlled trial provides level 1b evidence, synthesis of their similar findings in a meta-analysis provides the highest level of evidence. However, for patients unfit for open surgery, the EVAR 2 trial showed little benefit for EVAR.¹¹ The indications for the use of EVAR and the potential commercial market for endografts have been clarified by these randomised controlled trials. For now the stable market

Precis of a lecture given at European Society of Vascular Surgery, Helsinki, 19th September 2005.

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should be limited to the treatment of large AAA in fit patients, since currently there is no level 1 evidence to support the endovascular treatment of either large AAA in patients unfit for open surgery or AAA smaller than 5.5 cm in diameter.

The final step in the Hype Cycle is the approval of EVAR by the regulatory authorities in the different European countries. Some may not respond with an immediate answer about the use of EVAR in routine clinical practice but await longer-term results to the ascertain more robustly the cost-effectiveness of EVAR. In this context, it is disconcerting that the Belgian Health Technology Assessment group already have decided that financial incentives should be given to open surgery and that any added costs of EVAR should be carried by research budgets. The conclusion is likely to be different in other countries.

Although evidence from randomised clinical trials, preferably at least two with similar outcome measures, should be the minimum evidence required before new technologies are translated into routine clinical practice, this is far from reality. In 1998, a Dutch trial showed that routine stenting at iliac angioplasty was unnecessary and not cost-effective.¹² No one has taken any notice, with the ongoing development of newer covered stents and drug eluting stents being tested and marketed. No one has taken up the challenge of running a trial of endolaser therapy for varicose veins against the gold standard of surgical stripping.¹³ High risk (and high reimbursement) areas appear to be more likely to reach a randomised controlled trial. These randomised controlled trials should be open access, to all qualified practitioners, and can be started before the technology has fully stabilised. In this way, recruitment can be maximised and trials will be started before it is too late (with new technology introduced without being compared robustly to the contemporary gold standard), hoping to achieve results rapidly. Randomised controlled trials have quite a rigid structure, which makes it difficult to introduce assessment of new technologies into ongoing trial collaborations. For carotid disease, endarterectomy under general anaesthesia is the gold standard. A trial comparing general and local anaesthesia for carotid endarterectomy cannot be modified to include a carotid artery stenting arm. If the benefits of new technologies are to be passed on to patients rapidly, we need to reconsider how current trial management and steering committees can be diverted to investigate new technologies as they evolve. Also patients whom these technologies will benefit should have a more important role in decision making.

It has taken over 16 years to improve the technology and obtain the evidence for EVAR. We owe it to patients to speed up the process of evidence. Such an approach is likely to be welcomed by industry. Flexibility needs to be introduced into the design of randomised clinical trials, which should have 'not-for-profit support', open access for participants, an early start before technology is fully stabilised and more patient involvement. Could there be a European Vascular Surgical Clinical Trials Centre whose principal role was to horizon scan and start the important trials of emerging technology relevant to vascular surgery?

References

- 1 www.gartner.com
- 2 VOLODOS NL, SHEKHANIN VE, KARPOVICH IP, TROIAN VI, GUR'EV IA. A self-fixing synthetic blood vessel endoprosthesis. *Vestn Khir Im I I Grek* 1986;**137**:123–125.
- 3 PARODI JC, PALMA JC, BARONE HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysm. *Ann Vasc Surg* 1991;**5**:491–497.
- 4 MOORE WS, RUTHERFORD RB. Transfemoral endovascular repair of abdominal aortic aneurysm: results of the North American EVT phase 1 trial. EVT Investigators. *J Vasc Surg* 1996;**23**:543–553.
- 5 CUYPERS P, BUTH J, HARRIS PL, GEVERS E, LAHEY R. Realistic expectations for patients with stent-graft treatment of abdominal aortic aneurysms. Results of a European multicentre registry. *Eur J Vasc Endovasc Surg* 1999;**17**:507–516.
- 6 HARRIS PL, VALLABHANENI SR, DESGRANGES P, BECQUEMIN JP, VAN MARREWIKK C, LAHEIJ RJ. Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: the EUROSTAR experience. European Collaborators on stent/graft techniques for aortic aneurysm repair. *J Vasc Surg* 2000;**32**:739–749.
- 7 COLLIN J, MURIE JA. Endovascular treatment of abdominal aortic aneurysm: a failed experiment. *Br J Surg* 2001;**88**:1281–1282.
- 8 EVAR Trial Participants. Endovascular aneurysm repair *versus* open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;**365**:2179–2186.
- 9 Blankensteijn JD, de Jong SE, Prinssen M, *et al.* For Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2005;**352**:2398–2405.
- 10 DJULBEGOVIC B, LACEVIC M, CANTOR A, FIELDS KK, BENNETT CL, ADAMS JR *et al.* The uncertainty principle and industry-sponsored research. *Lancet* 2000;**356**:635–638.
- 11 EVAR Trial Participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. *Lancet* 2005;**365**:2187–2192.
- 12 TETTEROO E, VAN DER GRAAF Y, BOSCH JL, VAN ENGELEN AD, HUNINK MG, EIKELBOOM BC *et al.* Randomised comparison of primary stent placement *versus* primary angioplasty followed by selective stent placement in patients with iliac-artery occlusive disease. Dutch Iliac Stent Trial Study Group. *Lancet* 1998;**351**:1153–1159.
- 13 MUNDY L, MERLIN TL, FITRIDGE RA, HILLER JE. Systematic review of endovenous laser treatment for varicose veins. *Br J Surg* 2005;**92**:1189–1194.