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Expert Reviews on Current Research

Vascular and Endovascular Surgery Highlights 2010–11

Edited by Alun H Davies

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Fast Facts

Fast Facts: Vascular Surgery Highlights 2010–11

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Declaration of Independence
This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com

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Introduction

Welcome to this 13th edition of *Fast Facts: Vascular and Endovascular Surgery Highlights*.

The purpose of this book is to give a brief update to medical professionals on certain key areas of interest in the field of vascular disease. The authors have been chosen for their expertise in specific areas. This year's book covers topics ranging from advice on best medical therapy for asymptomatic carotid intervention to the treatment of aortic dissection.

A key chapter for all clinicians is the one on cost-effectiveness; this is an area in which vascular surgeons need to become more aware as 'financial rationing' will become a feature of many healthcare systems.

Again I would like to thank the authors for their support, and hope that you, the reader, enjoy this edition.

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Symptomatic carotid artery stenosis is best treated by carotid endarterectomy

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Ask a patient with dysphasia following carotid artery stenting (CAS) if he or she would instead have rather had a troponin enzyme leak or minor myocardial infarction (MI). Although the answer is clear to most of us, there are many interventionalists and clinicians who have inappropriately interpreted recent data from the Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) to conclude that CAS is equivalent to carotid endarterectomy (CEA).

Almost 30 years ago, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) indicated that symptomatic high-grade carotid artery stenosis results in stroke rates > 20% at 1 year if not treated by CEA.[1] Although a great debate currently exists as to whether or not most asymptomatic carotid artery stenoses warrant intervention, most physicians still believe that symptomatic disease should be treated by some invasive intervention. However, there is presently considerable controversy centering on whether CAS should replace CEA in a few or many patients. Ethics, economics, skill levels, and physician and patient preference all play a role in deciding between CEA and CAS for the treatment of symptomatic carotid stenosis.

Today, there exists a great deal of information relating to the treatment of carotid disease. Robust evidence from properly conducted prospective randomized trials helps to guide us in the treatment of our patients. Endarterectomy Versus Angioplasty in Patients with Severe Symptomatic Stenosis (EVA-3S), Stent Protected Angioplasty Versus Carotid Endarterectomy (SPACE) and the International Carotid Stenting Study (ICSS) have all exclusively recruited symptomatic patients.[2–4]

Trials

EVA-3S was stopped prematurely because of safety concerns regarding CAS after enrolling 527 patients. The peri-procedural stroke rate was 8.8% after CAS versus 2.7% after CEA (relative risk [RR] 3.3, 95% confidence interval [CI] 1.4–7.5, $p = 0.004$). This represented more than a threefold increase in stroke incidence in the stenting group.

SPACE. After randomization and treatment, the SPACE trial reported on 573 CAS patients and 563 CEA patients. The major stroke rate was 4.2% for CAS and 2.5% for CEA (RR 1.68, 95% CI 0.89–3.19).

ICSS randomized 855 patients to CAS and 858 patients to CEA. The interim 120-day stroke rate was 7.7% for CAS and 4.1% for CEA (hazard ratio 1.92, 95% CI 1.27–2.89, $p = 0.002$). A substudy of ICSS was recently published that looked at MRI to assess for new diffusion-weighted lesions. Compared with pre-procedure imaging, CAS was found to have a threefold increase in new cerebral lesions based on diffusion-weighted MRI compared with CEA.[5] Although some have questioned the skill levels of the CAS operators in each of these trials, all of them favor CEA when considering the incidence of peri-procedural stroke, the very endpoint that the procedure in question is supposed to prevent.

CREST was deemed a very important and well-conducted trial. It randomized both asymptomatic and symptomatic patients into CAS and CEA groups of patients (CAS: $n = 1262$; CEA: $n = 1240$).[6] Many interventionalists and others have expressed the opinion that CREST has finally answered the over decade long debate regarding the safety and efficacy of CAS and its equivalence to CEA in the treatment of both symptomatic and asymptomatic carotid stenosis. Unfortunately, this is just not true.

Just as with the previously mentioned randomized trials, there are several intrinsic limitations to CREST.[7] The interpretation of the CREST data is further compounded by physicians bringing their own set of biases to the analysis of the data. With a non-significant p value of 0.51, CREST concluded that the composite primary endpoint of

Why asymptomatic carotid stenosis is now a medical condition

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Historical trials and standards

There have been three major randomized trials of carotid surgery (carotid endarterectomy [CEA]) for moderate-to-severe (> 50–60%) asymptomatic proximal internal carotid artery stenosis:

- the Veterans Affairs Cooperative Study (VACS)
- the Asymptomatic Carotid Atherosclerosis Study (ACAS)
- the Asymptomatic Carotid Surgery Trial (ACST).[1–4]

In these trials, in which a total of 5226 patients were randomized from 1983 to 2003, patients who were allocated to CEA and medical intervention had a reduction in the average annual risk of stroke of 0.5–1% compared with patients who were allocated medical intervention alone.[4,5]

These randomized trials are often referred to as landmark trials, and awarded the best level of evidence (level A, class 1) on which to base routine practice. Accordingly, best-practice guidelines were produced around the world,[6] many still holding today,[7,8] recommending or supporting CEA for asymptomatic carotid stenosis if patients are reasonably fit and the operation can be performed with a 30-day perioperative stroke or death rate ≤ 3%. Rates of CEA for asymptomatic cases grew notably and such patients now comprise the dominant indication for CEA in many series.

Also in the wake of these randomized surgical trials, new randomized trials have flourished of CEA versus stenting (without a medical-intervention-only arm) for asymptomatic carotid stenosis. The debate, by many, has now turned to which of these interventions is preferable to the other. However, of the three randomized trials of stenting versus CEA for asymptomatic carotid stenosis,[9–11] only two had a sample size greater than 100. In these two larger trials, the

30-day stroke and death rate from stenting were 4.6%[10] and 2.5%,[11] higher than or similar to rates in the original randomized surgical trials.

At the same time, many have questioned the relevance of the randomized surgical trial results for routine clinical practice. There are several reasons for this. First, even under the carefully controlled conditions of the randomized trials, CEA caused almost as many strokes as it prevented. ACAS, for instance, was the only randomized trial demonstrating a stroke-prevention benefit with respect to ipsilateral stroke. In this trial, the 30-day perioperative stroke/death rate was 2.3%. The projected Kaplan–Meier estimate for the 5-year rate of ipsilateral ischemic stroke was 11.0% for the group receiving medical intervention only and 5.1% for the surgical group. This is equal to a 1.2% reduction in the overall average annual risk of ipsilateral stroke with surgery. Therefore, the number needed to treat to be ahead by (or 'prevent') one ipsilateral stroke per year was about 83 (100/1.2). So, for every 83 patients with asymptomatic carotid stenosis randomized to surgery in ACAS, about 3 patients had a stroke prevented by surgery at the expense of 2 who had an immediate stroke caused by surgery, while the stroke risk in the remaining 78 patients was not altered. Further, all patients were subject to other immediate complications including heart attack, ischemic legs, neck hematoma and cranial nerve damage.

Second, in the randomized surgical trials of moderate-to-severe asymptomatic carotid stenosis all patients faced an immediate risk of stroke/death. The 30-day perioperative rate of stroke/death was 4.3% in VACS (about 4.7% if angiographic risk is included), 2.3% in ACAS and 3.1% (or 3.0%) in ACST.[1–4]

Third, in routine practice surgical complication rates are not usually known. Where perioperative stroke and death rates have been estimated they are often higher than those in randomized trials.

A final major limitation for routine practice is that a surgical approach for stroke prevention, based on the results of these randomized trials, is very expensive. For instance, the cost of 83 carotid endarterectomies to be ahead by one stroke using ACAS results would be over about 600 000 AUD (> £375 000).[12]