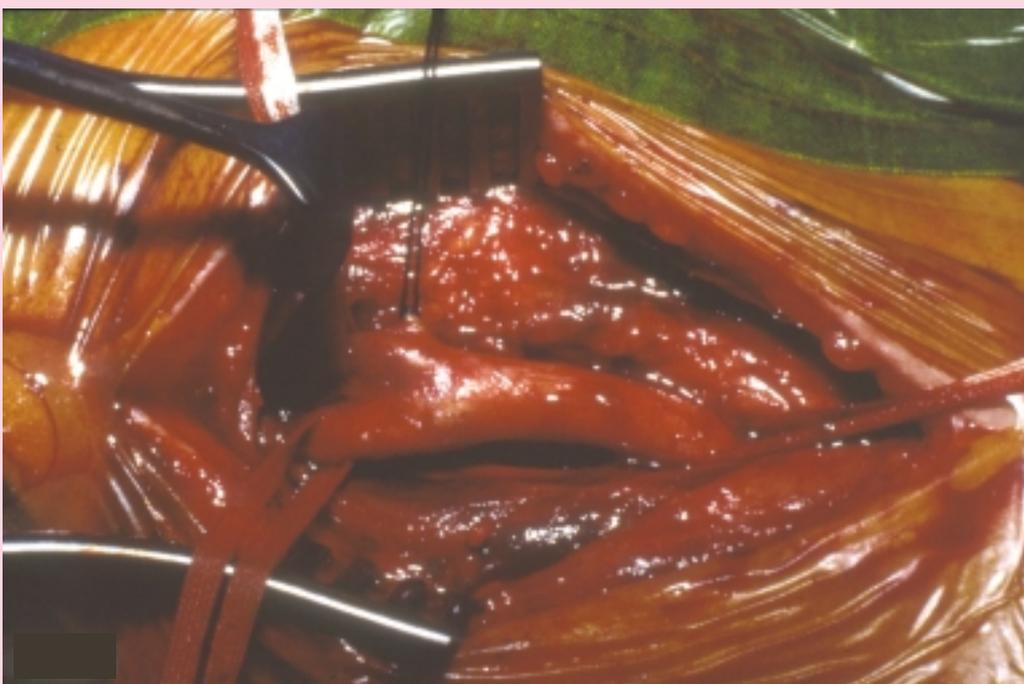


EDITORIAL

Carotid endarterectomy for asymptomatic stenosis – firm on the uncertainty



The carotid bifurcation is exposed and the surgeon is about to do the endarterectomy (courtesy of Alison Halliday).

Carotid endarterectomy Asymptomatic Picking up Faintly

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People with asymptomatic carotid stenosis, which is almost always due to atheroma, are seldom asymptomatic. After all, atheroma is generally a widespread disease – if it affects one artery it probably affects others. So although carotid stenosis may be asymptomatic in the sense that there have been no downstream symptomatic ischaemic events in the brain or eye, the patient will often have had symptoms in the distribution of the contralateral carotid artery, or the vertebro-basilar system, or symptoms of coronary heart or peripheral vascular disease. Sometimes, the so-called asymptomatic carotid artery *has* in fact

been the cause of symptoms, but many months or years previously, so it is not *recently* symptomatic – the meaning of asymptomatic varies, a point to be watched when reading the literature.

Occasionally an asymptomatic stenosis is picked up by a doctor hearing a bruit in the neck during the course of an examination for some completely unrelated problem. Rather more often the stenosis comes to light when patients are being worked up for symptomatic carotid stenosis on the other side, or for major surgery below the neck, in particular coronary artery surgery.

So what to do when an asymptomatic stenosis is discovered? The patient may well, and probably should, be taking antiplatelet, cholesterol lowering and blood pressure lowering drugs for symptoms in other arterial territories, getting some exercise and a decent diet, and hopefully not smoking

So what to do when an asymptomatic stenosis is discovered? The patient may well, and probably should, be taking antiplatelet, cholesterol lowering and blood pressure lowering drugs for symptoms in other arterial territories, getting some exercise and a decent diet, and hopefully not smoking. The additional option of carotid endarterectomy is tempting. After all, the artery is only just under the skin, and the operation is fairly trivial in these days of sophisticated general or regional anaesthesia. But, on the other hand, asymptomatic stenosis, unlike recently symptomatic stenosis, has a rather benign prognosis unoperated, even when > 70%; looking across several studies the risk of *ipsilateral* ischaemic stroke (i.e. the sort of stroke likely to be a consequence of the stenosis) is probably only about 2% per annum, on average. And, given the all but inevitable widespread atheromatous disease, the patient is more likely to die of a heart attack in the next few years than of an ipsilateral ischaemic stroke (Warlow *et al.* 2001).

As usual with any intervention, there is therefore a potential benefit (prevent ipsilateral ischaemic stroke over the next few years by operating) and a potential risk (cause stroke, or myocardial infection by operating, and occasionally death). What is the balance of benefit and risk, in general and in an individual patient? As usual, the best way to answer the 'in general' question is by looking for the results of a randomised controlled trial (RCT), and if there is more than one, a meta-analysis of all the available RCTs. Unusually for a surgical intervention, there is now quite a lot of randomised evidence available, at least when no other surgery is being contemplated in the very near future (where there remains extreme uncertainty what to do, and when, about any asymptomatic carotid stenosis).

The Cochrane review estimated that surgery, including the early risk, for severe stenosis reduced the *relative* risk of perioperative stroke or death or subsequent ipsilateral stroke by about one-quarter (Chambers *et al.* 2004) and another review put the figure at about one-half (Benavente *et al.* 1998). But, given the low risk in the no surgery group, the number-needed-to-operate to prevent one stroke over five years is about 20. Rounding the numbers and given the risk of stroke without surgery at say 10% in five years, and the stroke risk of surgery at about 5%, that is an absolute risk reduction of 5%. Furthermore, an individual does have to expect to live for a few years to make any advantage of surgery worthwhile. That doesn't sound a particularly good buy for the funders of health care, or a particularly good bet for the patient: a 1 in 10 chance of being in the benefited group (i.e. was going to have a stroke but it is prevented) rather than in the harmed group (1 in 20 chance of a surgical stroke) or in the group that was never going to have a stroke even without surgery. Not surprisingly most of us wanted better evidence of overall benefit before recommending surgery, and in particular better 'cost-effectiveness' in the sense of a much smaller 'number-needed-to-operate'. So, everyone was eagerly awaiting the results of the only ongoing RCT in the area – the Asymptomatic Carotid Surgery Trial (ACST) (MRC Asymptomatic Carotid Surgery Trial Collaborative Group 2004).

Although it was well conducted and the largest ever trial of carotid endarterectomy, it has not, irritatingly, got us very much further:

- the relative risk reduction of stroke over about five years was much the same as anticipated from the meta-analyses, but at least we now

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know this applies to preventing bad strokes as well as mild strokes;

- the risk of stroke in the unoperated group was much the same (about 12%);
- the risk of surgery was much the same (about 3%);
- and, adding in the few strokes that did occur after successful surgery, the absolute risk reduction was much the same too (about 6%).

This leaves us with a number-needed-to-operate of almost 20 – back to square one! And, for disabling or fatal strokes the number is an even more depressing 40. The situation may even be worse than that if the future unoperated risk is lower than it is now due to more widespread blood pressure and cholesterol lowering. We are therefore just more certain about what the operation does, but no more certain about what to do for an individual patient.

The problem of course is that the trials simply did not contain enough patients at such high risk of stroke to infer that even the small early surgical risk is worth taking in an individual patient. There are two ways round this. To try and select out those asymptomatic carotid stenosis patients who are at much higher unoperated risk than the average, but so far we have no way of doing this. Or, to follow up all the ACST patients for another five years because if the unoperated risk doubles to say about 24%, and the operated patients still have rather few strokes, then the number-needed-to-operate will come down. However this latter strategy will be wrecked if the surgeons in the ACST decide to recommend (completely inappropriately in my view) surgery to those originally allocated no surgery. And it will never happen at all unless the researchers can get funding for further follow up, a fraction of what the trial cost so far. Amazingly, the UK MRC who funded the origi-

nal trial declined to fund further follow up, so the future for understanding carotid surgery for asymptomatic stenosis does not look too bright. Plus, it will get a whole lot worse if the stenters are let loose on the patients way ahead of any decent evidence at all that stenting is as safe or as durable as carotid endarterectomy.

In the meantime what to do for the individual patient? The paternalistic answer is to try and talk him or her out of surgery unless for some reason the patient is thought to be at much higher than the average risk of stroke without surgery, but it is very difficult to think of a good way of knowing this (perhaps a fit middle-aged patient with no clinical evidence of coronary heart disease and likely to live for another 20 years?). The politically correct answer is to provide the patient with the information in this editorial, and any other information available, and share the responsibility for the decision with the patient. Uncomfortable.

COMPETING INTEREST

I was Chairman of the ACST Data Monitoring Committee.

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