

Carotid endarterectomy

Bias may affect outcome of trials

EDITOR,—Roger N Baird and Mark Lambert—and Peter C Rubin in his commentary—draw varying conclusions about the usefulness of carotid endarterectomy in the prevention of stroke.¹ None, however, mention the likelihood of bias in assessments of the outcomes of the two quoted trials of the procedure.^{2,3} No placebo operations were done in the control groups, so the neurologists assessing the outcomes were almost certainly aware of whether each patient had been operated on. It is unfortunate that their preferred outcome measure, severe ipsilateral ischaemic stroke, is so clearly liable to unconscious bias in its assessment; classic cases are easy to diagnose but there are many on the borderline, which could be included or excluded according to the hopes of the clinician. Noseworthy *et al* document an instance in which such unblinded assessments by neurologists would have led to a false conclusion of benefit from a trial.⁴

The likely direction of bias is made clear by the fact that the North American investigators, on their own figures, recruited less than 1% of all patients considered (because of clinical uncertainty) to be suitable for endarterectomy into their trial. If clinicians had no bias towards finding endarterectomy effective the proportion with clinical uncertainty of effectiveness might be expected to be considerably higher. It is therefore inadequate, although it may be necessary, to show an apparent reduction in severe ipsilateral ischaemic stroke or other such end points. The only published outcome measure that is likely to be reasonably unbiased is rate of death from all causes. The table gives the relevant figures. The typical odds ratio estimate of death calculated from these figures according to the method of Chalmers *et al*⁵ is 0.74 (95% confidence interval 1.08 to 0.51). This analysis does not take into account the likelihood that deaths in the treated group are more likely to occur early, soon after surgery. Nor does it incorporate the point, made by Lambert,¹ that

Results of carotid endarterectomy for severe stenosis (70-99%) in two trials. Figures are numbers of deaths/numbers of patients entered

	Treated	Controls
European carotid surgery trial ²	45/455	41/364
North American symptomatic carotid endarterectomy trial ³	15/328	21/331
Total	60/783	62/695

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the screening and diagnostic procedures before surgery (and, in the trials, before randomisation) are potentially risky. This analysis is therefore biased towards finding effectiveness. Nevertheless, it fails to give reasonable confidence of benefit.

Placebo surgical procedures are unlikely to be ethically acceptable. If trials of this issue are to be valid they should therefore use primary outcome measures less likely to be biased by the hopes of professionals, and their conclusions should include the implications of diagnosis as well as those of treatment in the strict sense.

I agree with Lambert that other services are likely to prove a better investment of scarce resources. I suggest further that a programme of carotid endarterectomy has not been shown to offer net benefit to any group of patients.

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- 1 Baird RN, Lambert M. Should carotid endarterectomy be purchased? *BMJ* 1995;310:316-8. (4 February.)
- 2 European Carotid Surgery Trialists Collaborative Group. MRC European carotid surgery trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. *Lancet* 1991;337:1235-43.
- 3 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445-53.
- 4 Noseworthy JH, Ebers GC, Vandervoort MK, Farquhar RE, Yetisir E, Roberts R. The impact of blinding on the results of a randomized, placebo-controlled multiple sclerosis clinical trial. *Neurology* 1994;44:16-20.
- 5 Chalmers I, Hetherington J, Elbourne D, Keirse MJNC, Enkin M. Materials and methods used in synthesizing evidence to evaluate the effects of care during pregnancy and childbirth. Appendix 2.3: statistical methods used to derive typical odds ratio. In: Chalmers I, Enkin M, Keirse MJNC, eds. *Effective care in pregnancy and childbirth*. Vol 1. Oxford: Oxford University Press, 1991: 62-4. (Reprinted with corrections.)

Is cost effective

EDITOR,—Roger N Baird and Mark Lambert are correct in stating that prevention of stroke is an important public health issue.¹ There is now good evidence that treating hypertension in older patients, giving anticoagulants to patients with atrial fibrillation, and prescribing aspirin to patients with minor ischaemic stroke and transient ischaemic attacks reduces rates of stroke and costs. Lambert suggests, however, that only 154 strokes are preventable by carotid surgery among the 20 500 patients presenting to their general practitioners with transient ischaemic attacks each year. He ignores a similar number of patients with minor ischaemic strokes due to carotid disease. The Association of British Neurologists estimates that 500 strokes are preventable by carotid surgery.²

Lambert is right to highlight the cost and risk of carotid angiography. Use of this invasive and expensive technique as the primary investigation of carotid disease must be discouraged. Our stroke prevention clinic uses colour flow duplex Doppler ultrasonography performed by experienced vascular technicians, which is at least as reliable as angiography except in differentiating extreme stenosis from complete occlusion.

Although carotid endarterectomy is a specialised operation, it is minor surgery for the patients, requiring only four to five days in hospital. Rather than argue that carotid surgery should be abandoned because of bad practices, surely Lambert should encourage purchasing of carotid services

from specialist centres that use non-invasive investigation and quick, appropriate, and safe surgery.

The vascular studies unit in south Manchester investigates 1800 patients with transient ischaemic attacks each year; this results in over 200 carotid endarterectomies for severe carotid stenosis. The cost of investigation, operation, and inpatient care is £2600 per patient—a total of £520 000 a year. The total cost of one stroke is £45 000,³ so if we prevent 22 strokes⁴ we save £990 000. Hence the net economic saving is £470 000. The additional cost of investigating patients who do not require surgery is small: the annual cost of our vascular studies unit with two colour duplex Doppler machines, three technicians, and one secretary is only £90 000 a year, which leaves nearly £400 000 to be spent on other improvements in the quality of health care.

If carotid endarterectomy is done well it is well worth doing. The risk of stroke is reduced, and the procedure is cost effective.

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- 1 Baird RN, Lambert M. Should carotid endarterectomy be purchased? *BMJ* 1995;310:316-8. (4 February.)
- 2 Brown MM, Humphrey PRD, on behalf of the Association of British Neurologists. Carotid endarterectomy: recommendations for the management of transient ischaemic attacks and ischaemic stroke. *BMJ* 1992;305:1071-4.
- 3 Bamford J. *The cost of care. Seminar on district stroke services*. London: Stroke Association, 1993:5.
- 4 North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effects of carotid endarterectomy in symptomatic patients with high grade carotid stenosis. *N Engl J Med* 1991;325:445-53.

Evidence is available for selected patients in selected units

EDITOR,—The art of debate is to develop a persuasive argument however inadequate the data. Mark Lambert is to be congratulated on his adroit confusion of different problems (a time honoured politician's ploy).¹ The problems of poor selection, poor investigation, and poor surgery are not to be confused with an ineffective operation.

Carotid endarterectomy is not appropriate for all patients with transient ischaemic attacks any more than appendicectomy is appropriate for all patients with pain in the right iliac fossa. We know that carotid endarterectomy reduces stroke after a transient ischaemic attack by a factor of six to eight in appropriate patients operated on in appropriate units: this is proved beyond reasonable doubt. The role of the operation is proved, however, only for patients with symptoms suggesting that the carotid territory is affected and with a stenosis of >70% who are operated on by surgeons whose patients have a risk of having a stroke during the operation of <6%. Occasional carotid surgery is to be deplored, and the current training guidelines should help to avoid this.² Duplex ultrasonographic assessment need not be 20% inaccurate, and a policy of using duplex ultrasonography plus intravenous digital subtraction angiography (advocated by my unit and others for more than a decade) prevents any complications of stroke from angiography. Best practice should and can be achieved.