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 necesssary, 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 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.

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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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.
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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 strokes[4] 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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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.

Purchasers need clear evidence of efficacy before they buy services from their inadequate resources. For 40 years the evidence for carotid endarterectomy relied on prolific but inadequate data, so that too many operations were performed in the United States and too few in Britian. We now have the evidence for a selected group of patients in selected units and should not deny any person a sixfold to tenfold improvement in his or her prognosis. No treatment is effective if applied inappropriately, and if an inappropriate denominator is used the benefits of carotid endarterectomy are spuriously shown to be "vanishingly small." A similarly Luddite argument could be applied to appendicectomy for appendicitis if the denominator is taken as pain in the right iliac fossa and account is taken of the fact that appendicitis may resolve spontaneously or with antibiotics.

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Should be offered to appropriately selected patients

EDITOR,—Roger N Baird and Mark Lambert debate whether carotid endarterectomy should be purchased.[1] There is no doubt that carotid endarterectomy works.[2] Starting another trial in symptomatic patients with tight stenoses would be unethical as the two large trials in Europe and North America have proved beyond doubt that this operation is highly successful.[3] It is medically indefensible not to offer this operation to appropriate patients; if these patients are denied surgery then before long they will seek compensation in the courts and will undoubtedly win. The question becomes, can the NHS afford the quality service that the treatment of such patients requires?

Firstly, a prompt clinical assessment is required to make sure that only the right patients come to surgery. This requires a careful history so that only those with appropriate symptoms are offered surgery.[4] We run three cerebrovascular clinics a week. About two patients in every 25 seen come to carotid surgery; most patients do not even have transient ischaemic attacks.

Secondly, patients require careful investigation with minimal risk. In our unit we operate after a non-invasive work up with ultrasound scanning and magnetic resonance angiography in most cases.[5] Both these tests depend on the operator but in skilled hands are highly accurate.[5]

Finally, the operation should be performed by someone whose patients have a complication rate of less than 5% and preferably less than 3%.[3] A national survey by the Vascular Society of Great Britain and Ireland showed a rate of death or stroke after carotid endarterectomy of 3·4% (personal communication). Regular independent audit needs to be performed.

The above considerations, however, do not challenge the validity of the operation.

Carotid endarterectomy will not make a big difference to the overall incidence of first stroke: a 0·5% reduction. Lambert fails to point out, however, that aspirin reduces the overall incidence of stroke by only 1-2%, and we all give aspirin.[6] There will be no single cure for stroke, which is a multifactorial disease. Treating high blood pressure confers the greatest benefit.[6]

Carotid endarterectomy in an individual symptomatic patient who is fit with a tight (70-99%) stenosis reduces the risk of stroke by 75%.[2]

We know more about the efficacy of carotid endarterectomy than about the efficacy of almost any other operation because large, properly controlled trials have been performed. We have no choice but to purchase it or patients will force our hand. It should not be an operation for an elite few. The question is, how do we purchase quality?

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Preoperative angiography is outdated

EDITOR,—I am surprised that Mark Lambert should minimise the impact of carotid endarterectomy[1] as its benefits have been more than proved in randomised controlled studies. Much of his criticism seems to hinge on his contention that angiography causes stroke in 1% of patients and that if this figure is added to the surgical morbidity and mortality the whole thing becomes worthless. He does not seem to accept or understand that most centres these days do not perform angiography before carotid endarterectomy. In my centre, for example, we have performed angiography in few cases in the past seven years and operate on many patients with carotid stenosis. Duplex scanning is all that is required in most cases and has no mortality.

Lambert mentions that, of over 97 000 strokes each year, only 154 can be prevented by carotid endarterectomy. He fails to mention that the remaining cases (>96 000) cannot be prevented, even if the usual preventive measures are undertaken. What he seems to be saying is that good results cannot be achieved by most people and that we should therefore ignore this operation, which has an excellent record of saving people from strokes. What he should be saying is that we should try to increase the number of centres offering an excellent service and reap the benefits of prevention of stroke.

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Efficacy is proved

EDITOR,—We are surprised by the negative attitude of Mark Lambert, who suggests that more than 5000 symptomatic patients with stenosis of >70% each year should be denied the benefit of carotid surgery.[1] The efficacy of carotid surgery in symptomatic patients with stenosis of >70% has been proved in both European and Northern American trials.[2,3] In addition to giving an inadequate and selective review of the literature, Lambert fails to realise the possible difference in the prevalence of the disease between different communities. For example, he mentions that 40% of patients with a transient ischaemic attack are not fit for investigations. He quotes this figure from an article by Hankey *et al*, who studied 485 consecutive patients with transient ischaemic attacks between 1977 and 1986.[4] They did not have non-invasive ultrasonography for screening, and angiography was performed only in patients who were potential candidates for carotid endarterectomy on clinical grounds.

In our experience under a tenth of patients are unfit for surgery, which, although technically demanding for the surgeon, is relatively stress free for the patient and can even be performed under local anaesthesia. Hankey *et al* stated clearly in their article that their findings should not be applied to other medical centres without consideration of the possible differences in the prevalence of carotid artery disease, the efficacy and reliability of duplex ultrasonography, the local rate of complications of cerebral angiography, and the local cost of the imaging procedures.

We also dispute the correctness of the statement that 20% of patients are missed by non-invasive tests. In Bristol we performed duplex scanning two days before triplanar selective carotid arteriography in 103 symptomatic patients.[5] The results were independently scored and classified as normal, <25% stenosis, >25% stenosis, >50% stenosis, >75% stenosis, and occlusion. Twenty eight arteries had >50% stenosis (sensitivity 92%, specificity 91%), 21 had >75% stenosis (sensitivity 95%, specificity 96%), and 10 were occluded (sensitivity 100%, specificity 95%). For all grades of stenoses ultrasound examination showed good correlation with arteriography ($\kappa = 0{\cdot}854 \pm 0{\cdot}026$ (perfect agreement gives a maximum value of 1; inverse correlation gives $\kappa < 0$)). A similar audit of more than 200 colour Doppler scans performed by the vascular studies unit in Sheffield has shown that only 1% of carotid stenoses >70% (that is, those requiring operation) were missed. In addition, the rate of stroke from non-selective digital subtraction arch arteriography is much less than 1%, and many centres now proceed to surgery on the basis of duplex scanning and computed tomography alone.

The debate about whether resources should be diverted from treatment to prevention applies to many diseases: no one would suggest that coronary artery bypass surgery prevents many myocardial infarctions in the population as a whole. We agree with Lambert about the benefits of primary preventive measures for stroke. We believe strongly, however, that carotid endarterectomy should be purchased for symptomatic patients.

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Continuous ambulatory electrocardiography in elderly people

EDITOR,—Mayer Bassan[1] did not read our article carefully.[2] We did not recommend routine Holter monitoring for elderly people to stratify their risk