Carotid endarterectomy for asymptomatic carotid stenosis

Better data, but the case is still not convincing

Eleven years ago, before any randomised trials were published, a *BMJ* editorial came down against endarterectomy for asymptomatic carotid stenosis.[1] In 1995, based on what now would be regarded as a less than rigorous review of the trials then available, I thought surgery was still not worthwhile. Too many operations would have to be done to prevent one patient having a stroke.[2] Today the *BMJ* publishes the first systematic review of the evidence (p 1477).[3] Should the earlier conclusions be modified, and what should we do now?

The present review is far more rigorous: there was an extensive search strategy (which didn't reveal any previously unknown trials); only randomised controlled trials were included; publication bias was considered; sensible outcomes were defined, although some might want to see the outcome of stroke combined with all rather than just with surgical deaths; trial quality was taken into account; the relevant data were extracted independently by two people; appropriate sensitivity analyses were done; and the patients were reasonably well described. On the other hand, with only 222 outcome events among just 2440 patients, estimates of treatment effect were bound to be imprecise; there were differences between the trials in their design, but there were no definite differences in the effect of treatment (for example, stenosis was variably defined); it was not clear that randomisation was always secure enough to prevent foreknowledge of the treatment to be allocated; some information on outcomes was not available even when requested from the authors; and—unavoidably—the outcome assessment could not be completely "blinded" to treatment allocation.

The bottom line is fairly clear: over about three years surgery reduces the odds of stroke by around 30%, but with a wide 95% confidence interval from 10% to 50%. Of course, account has to be taken of the inevitable fact that the risk of treatment is all early (surgical strokes occur within days) whereas the benefit accrues gradually (in unoperated patients the strokes occur over the years). Also, although this relative reduction in stroke risk seems impressive, the absolute benefit is small because the risk of stroke without surgery for asymptomatic stenosis is so low. Therefore, it is necessary to operate on about 50 patients to prevent one stroke in the next three years—or even more to prevent just disabling and fatal strokes. On the other hand, if even a low unoperated annual risk of ipsilateral ischaemic stroke persists for many years, it is then conceivable that the benefit of surgery may go on accruing for more than just three years and this would reduce the numbers needed to treat.

But, all this is an "on average" treatment estimate, which illustrates the problem of applying the results of randomised trials and meta-analyses in routine practice. Clinicians want to know what to do in a particular case.[4] Ideally, surgery should be offered to just the small number of patients who *will* have what it can prevent, an ipsilateral ischaemic stroke, and not to the much larger number who *might* have a stroke. But how can we identify the patient with a particularly high risk?

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It is hardly the fault of the meta-analyst if the original trials do not provide enough information on such potentially important variables as age, sex, and severity of stenosis that treatment effect can be analysed in possibly relevant subgroups (bearing in mind the dangers of making incorrect inferences from subgroup analysis, particularly when the number of patients and outcome events is so small). Better would be an analysis based on baseline risk of stroke derived from a robust and validated mathematical model, but this would require individual patient data from a very much larger number of people. In practice we need two models, as has been suggested for surgery for symptomatic stenosis[5]: one to predict the risk of what surgery can prevent (ipsilateral ischaemic stroke)—which has been attempted for symptomatic stenosis,[6] and another to predict the risk of stroke as a consequence of surgery, which on balance is lower for asymptomatic than for symptomatic stenosis.[7] Surgery could then be targeted on those who have most to gain and avoided in those likely to be harmed. To this end, the collaborators from the trials and some of the large observational studies are pooling their data from about 10 000 patients (asymptomatic carotid stenosis collaborative study, P Rothwell, personal communication).

In the meantime, clinicians must base their advice to individual patients using the on average treatment effect, along with the myriad of other factors that are so hard to define in clinical decision making (is the patient a risk taker, for example?). In most patients this assessment must surely argue against surgery for asymptomatic carotid stenosis. Far better energetically to wield the knife where it is more cost effective: at the neck of patients with recently symptomatic and severe carotid stenosis, who are not all reaching surgery and who are far more likely to have a stroke unless they do.[8]

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