Editorial

Risk stratification and carotid surgery: new technology but old trials

It is now nearly a decade since evidence from the European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) began to replace anecdote as the basis on which patients with high-grade symptomatic carotid stenosis could be advised about the risks and benefits of carotid endarterectomy (CEA). One remembers a certain sense of euphoria immediately after the interim results of these ‘positive’ trials were published and it is striking how the calls to identify subgroups of patients for whom surgery might be particularly beneficial were much less strident than after the earlier ‘negative’ Extracranial-Intracranial (EC-IC) Bypass Study (The EC/IC Bypass Study Group, 1985). Indeed, the impetus to identify such subgroups for CEA has come largely from the study investigators themselves following the publication of the final results of both studies (European Carotid Surgery Trialists’ Collaborative Group, 1998; North American Symptomatic Carotid Endarterectomy Trialists’ Collaborative Group, 1998).

Ideally, in order to recommend any treatment, the clinician should be able to compare the risks and benefits for the individual patient of the proposed intervention with those of non-intervention. Whilst large trials and meta-analyses allow the overall results to be more generalizable within populations, within any group result there will be a spectrum of individual outcomes. Both the ECST and NASCET collaborators individually have made important observations about certain subgroups such as the higher surgical risk, but nevertheless, greater overall benefit for surgery in patients with contralateral ICA stenosis or occlusion; the lower background risk and more questionable surgical benefit in those with collapse of the ICA distal to an extremely severe stenosis; and the possibility that CEA is of less value in patients with lacunar stroke. Hopefully, when the individual patient data from the various endarterectomy trials are combined, even more robust analyses of certain pre-specified subgroups will be possible (Rothwell et al., 2000).

Having all this information, however, does not necessarily make the counselling of the individual patient any easier and certainly clinicians should be extremely cautious about how they use the pieces of data that may be available to them. Useful prediction models based on easily identified factors such as sex, systolic blood pressure, peripheral vascular disease, degree of stenosis, plaque surface irregularity and time and site of last event have been published. But further validation is needed before we would be justified or, perhaps more importantly, willing to use them to counsel individual patients, particularly if this results in advice against surgery in the face of the overall ‘positive’ results from the trials. Nevertheless, if the figures derived from the ECST are confirmed, even within the symptomatic high-grade stenosis group, the number of CEA needed to be performed to prevent one stroke over the subsequent 5 years may vary between three and 100 (Rothwell et al., 1999).

Not surprisingly because of the ‘negative’ EC-IC Bypass Study, the pressure to find potentially responsive subgroups has been much greater for patients with either ICA occlusion or with an asymptomatic high grade carotid stenosis. A recent overview of CEA in the latter group, whilst supporting the view that the operation can reduce the risk of subsequent ipsilateral stroke in those with the tightest stenoses, noted that ‘the effect is at best barely significant, and extremely small in terms of absolute risk reduction’ (Chambers et al., 2000). To many patients and physicians the number needed to treat remains unacceptably high. It has been known for many years that there are subgroups of patients who have ongoing haemodynamic compromise in the cerebral hemisphere distal to either an ICA occlusion or high-grade stenosis. However, until recently, the technologies that were able to demonstrate such areas (such as PET or xenon) were only available in relatively few centres. Consequently, they were not used for stratification in the large treatment trials. The paper by Markus and Cullinane highlights the potential role of trans-cranial doppler ultrasound (TCD) in these patients (Markus and Cullinane, 2001) and there are also evolving MR techniques which may give similar information. Thus, there is a real possibility that routine information about cerebral haemodynamics will become available to many more clinicians. Of course, this then raises the question about how (or even should) such information be factored into our current practice? Ever since the failure of the EC-IC Bypass Trial to show any reduction of stroke rate in the surgical group...
despite a patent bypass being created in 96% of the patients and prior evidence that the procedure could reverse haemodynamic abnormalities, there have been calls for another trial confined to this subset of haemodynamically compromised patients, Klijn and colleagues, in a detailed review of haemodynamic factors associated with symptomatic carotid occlusion, noted rather heterogeneous results from case series of variable quality, although overall the annual ipsilateral ischaemic stroke rate was more than four times greater (9.5% versus 2.1%) in patients with demonstrable haemodynamic compromise (Klijn et al., 1997). However, Henry Barnett argued forcibly that ‘a succession of uncontrolled case-series reports may raise hopes but prove nothing’ and that further epidemiology was required (Barnett, 1997), whilst Derdeyn and colleagues have reviewed in detail the potential methodological problems of measuring cerebral haemodynamic impairment (Derdeyn et al., 1999). Markus and Cullinane’s study does address many of their concerns about methodology, but in order to establish a causal link between haemodynamic compromise and subsequent stroke risk there needs to be a positive result from a randomized trial. Although the paper makes a significant contribution to the overall debate, I do not believe that it should be viewed as a green light to expose patients once again to the risks of EC-IC bypass, even if they can be shown to have haemodynamic compromise. However, if these results can be replicated in other centres and further data are published which support the attractive hypothesis that links hypoperfusion and embolism to the occurrence of stroke in such patients (Caplan and Hennerici, 1998), then a niche trial may soon be back on the cerebrovascular research agenda.

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References


