There are 3 major asymptomatic cerebrovascular diseases that challenge the stroke clinician at the bedside. These are asymptomatic carotid disease, unruptured cerebral aneurysms and unruptured brain arteriovenous malformations (AVMs). In all 3 conditions, there are uncertainties about natural history, risks and benefits of intervention. While controversy remains, there have been 2 trials that have provided useful information concerning the risk-benefit ratio for carotid endarterectomy in patients with asymptomatic stenosis.1,2 Although no single randomized clinical trial removes all uncertainty, there is no doubt that the endarterectomy trials have provided an evidence base to assist in making clinical decisions.

There are common themes with these 3 cerebrovascular diseases. First, there is a striking difference between the symptomatic and asymptomatic natural history. Symptoms substantially elevate risk. Second, within the asymptomatic groups, there are real uncertainties about the lifetime risk and prognostic determinants. Third, there are uncertainties concerning the risks and benefits of intervention. We have trial evidence to help guide management in only 1 of these 3 conditions. Obviously, this needs to be rectified.

When planning any trial of an intervention, there are several important principles that should be considered. The clinical problem should be significant, the intervention should be biologically plausible, there should be real uncertainty concerning the risks and benefits of the procedure and hence ethical equipoise, and that the trial is feasible, well-designed and has a substantial likelihood of success. Cockroft particularly addresses this last issue (low annual risk versus high lifetime risk of unruptured AVMs) when expressing reservations about the planned duration of follow-up in the ARUBA trial. Indeed, the same issue is relevant for interventional management for either asymptomatic carotid stenosis or unruptured cerebral aneurysms. However, despite the relatively short period of follow-up, the results generated by the asymptomatic carotid trials were clinically useful. In contrast, the management of unruptured cerebral aneurysms is unresolved.3

Where does this place the unruptured AVM story? In our view, the important criteria for a large randomized clinical trial have been met. As with previous clinical trials of a procedural intervention, questions have been raised about selection bias. We believe that this would be counterbalanced by the “uncertainty principle.”4 In other words, a representative cohort of unruptured AVMs would be entered, given different levels of uncertainty by different investigators. Whatever the limitations of the ARUBA trial, we consider that the results will reduce uncertainty and benefit clinicians. Let the trial begin!

Disclosures

None.

References


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