The current status of carotid endarterectomy—part 2

Carotid endarterectomy is a surgical procedure in which an atherosclerotic plaque is removed from the carotid artery to avoid future stroke. A small proportion of patients will have adverse effects from surgery and need emergency blood-pressure management to avoid intracranial haemorrhage. This paradoxical risk of operation-related stroke leads to continuing controversy about this procedure. Data for carotid endarterectomy in asymptomatic patients are less conclusive than those for symptomatic patients. Trials are underway to determine the benefits of carotid angioplasty with stenting.

The rationale underlying carotid endarterectomy is simple; removal of an atherosclerotic plaque from the internal carotid artery removes a source of thromboembolism and so reduces the long-term risk of stroke. However, in the 50 years since its introduction, carotid endarterectomy has remained one of the most enduringly controversial and scientifically scrutinised procedures. Part 1 of this review, dealing with the current status of carotid endarterectomy in symptomatic patients was published in the May 2009 issue of GM. Part 2 looks at evidence in asymptomatic patients and how endarterectomy compares with stenting.

The asymptomatic trials

The Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST) helped to determine the role of carotid endarterectomy in the treatment of asymptomatic patients. The principal outcomes are summarised in table 1. Note that each trial reported on different endpoints and that ACAS never published 5-year risks of ipsilateral stroke (including the perioperative risk). The general tendency has been to assume that both trials reported an approximate 5-year stroke risk of 12% for medically treated patients versus approximately 6% for those randomised to surgery. Table 1 shows this not to be strictly true (ie, one is comparing ipsilateral stroke in ACAS with any stroke in ACST), but it has become conventional to do so.

The results from ACAS and ACST led to an unprecedented increase in the volume of carotid endarterectomies performed worldwide, but they also unmasked a number of issues that many would probably prefer not to have been highlighted. First, ACAS showed no evidence that carotid endarterectomy significantly reduced the number of disabling or fatal strokes. Second, although men benefited considerably from surgery in ACAS, women derived no significant benefit (absolute risk reduction=1·4% at 5 years versus 8·0% for men). Even when all perioperative events were

<table>
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<tr>
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<th>ACAS (n=1662)</th>
<th>ACST (n=3120)</th>
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<tr>
<td></td>
<td>Medical therapy</td>
<td>Surgery</td>
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<tr>
<td>5-year risk of ipsilateral stroke + any perioperative stroke or death</td>
<td>11.0%</td>
<td>5.1%</td>
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<tr>
<td>5-year risk of any stroke + any perioperative stroke or death</td>
<td>17.5%</td>
<td>12.4%</td>
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<tr>
<td>Number needed to treat to prevent one stroke of any type at 5 years</td>
<td>20</td>
<td>19</td>
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<tr>
<td>Number of strokes of any type prevented at 5 years per 1000 procedures</td>
<td>50</td>
<td>53</td>
</tr>
<tr>
<td>Number needed to treat to prevent one ipsilateral stroke at 5 years</td>
<td>17</td>
<td>..</td>
</tr>
<tr>
<td>Number of ipsilateral strokes prevented at 5 years per 1000 procedures</td>
<td>59</td>
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Table 1: Outcomes from ACAS and ACST, comparing best medical therapy with carotid endarterectomy.
excluded, no benefit was seen in women. Third, the 5-year data in ACAS were projected—the median follow-up period was only 2.7 years due to the trial being stopped prematurely. Fourth, there were concerns over the surgeon selection process in that 40% of surgeon applicants were rejected from trial participation following review of their records. Accordingly, the 2.3% operative risk was considered unlikely to be generalisable into routine clinical practice. Fifth, no association was noted between stenosis severity and long-term risk of stroke, in fact the relationship was inverse. Finally, surgery in patients with contralateral occlusion had no apparent benefit.

Publication of ACST results in 2004 appeared to provide definitive answers to many of the concerns raised by ACAS. The principal conclusions from ACST (which randomised twice as many patients as ACAS) were that: (1) immediate carotid endarterectomy significantly reduced the risk of fatal or disabling strokes by 50%; (2) males and females appeared to gain significant benefit from prophylactic carotid endarterectomy and; (3) immediate carotid endarterectomy benefited asymptomatic patients only if they were older than 75 years.

Accordingly, ACST was seen as having provided gold-standard evidence to support using carotid endarterectomy in asymptomatic females. However, a few commentators observed that ACST did not include the operative risk when publishing their long-term data regarding gender. However, when the perioperative risk was included, all significant benefit in women disappeared. ACST are due to publish their 10-year outcomes in 2009. Preliminary data from national presentations suggest that women still gain significantly less benefit than do men (ie, we still do not know which female subgroups will gain maximum benefit from intervention). Additional evidence suggests that improvements in best medical therapy have significantly reduced the annual risk of stroke in medically treated patients. At present, I consider doing carotid endarterectomy in otherwise fit males aged younger than 75 years and to similarly fit females under 70 years.

Angioplasty or endarterectomy?

Unlike the symptomatic and asymptomatic trials comparing carotid endarterectomy with best medical therapy, randomised controlled trials have not helped to achieve consensus regarding which patients might benefit from carotid endarterectomy or carotid artery stenting. Angioplasty does offer important potential advantages over endarterectomy (no incision, less invasive, no cranial nerve injury), but the 2007 Cochrane review still recommended that carotid stenting should be done only within ongoing randomised controlled trials.

Figure 2 shows a summary of the principal findings from the Cochrane review of 11 randomised controlled trials, many of which were either methodologically flawed or stopped early. The outcome of any stroke or death within 30 days of treatment significantly favoured endarterectomy. There was also a very highly significant reduction in the risk of cranial nerve injury favouring carotid stenting. Death within 30 days, death or disabling stroke within 30 days, and late stroke showed no significant difference between stenting and endarterectomy.

Two very large randomised controlled trials in symptomatic patients are about to close recruitment (ICSS and CREST) and their combined total of 4000 patients will greatly inform the debate. Accordingly, the next Cochrane Review will be of considerable importance. The role of carotid artery stenting in asymptomatic patients is now under review and I urge doctors reading this article to participate in one of the three randomised trials about to start recruiting asymptomatic patients (the Asymptomatic Carotid Trial 1 [ACT-1], Asymptomatic Carotid
Surgery Trial II [ACST-II], and Transatlantic Asymptomatic Carotid Intervention Trial [TACIT]). Otherwise, continuing to recommend surgery in standard-risk symptomatic and asymptomatic patients is probably safest.

Conclusion

Notwithstanding potential differences of opinion regarding the respective roles of carotid endarterectomy and carotid artery stenting, a few simple pieces of advice are indisputable. Above all else, the treatment of symptomatic patients must remain the first priority. Expedited referral and surgery will prevent many more strokes in the long term than would treating myriads of asymptomatic individuals. Some asymptomatic individuals would undoubtedly gain from intervention, although just how much recent improvements in what now constitutes best medical therapy will affect the risk–benefit equation remains to be seen, but asymptomatic patients must remain secondary in importance to the treatment of symptomatic patients. Finally, it is beholden upon all of us to change the perception of stroke and transient ischaemic attacks so that they are considered with the same importance as heart disease and cancer. Only then will the Government’s 48-hour treatment aspirations be met.

I have no conflict of interest.

References