Two large trials (NASCET and ECST) have shown carotid endarterectomy (CEA) reduces the risk of cerebral infarction in patients with a recently symptomatic (<6 months), severe (50–99%) stenosis of the ipsilateral internal carotid artery.1,2 The original analyses suggested that the degree of benefit gained was related, in part at least, to the severity of the stenosis. Subsequent analysis of the pooled data on 5893 patients has shown that the benefit from surgery was greatest in men (p = 0.003), those over the age of 75 years (p = 0.03) and those randomised within 2 weeks after their last ischaemic event (p = 0.009).3 The only large trial of endovascular intervention versus (angioplasty or stenting) has shown no difference in early or late outcomes in the 504 randomised patients4 and a larger international trial (ICSS) is now underway.5

There remains a question as to whether carotid intervention (CEA or stenting) should be performed as an emergency, within hours or days after onset of ischaemic stroke, as the risk of a further stroke has been shown to fall exponentially with time. Early studies showed that emergency CEA carried a high risk of cerebral haemorrhage and that the risk of stroke or death in patients with unstable neurological symptoms was about 20%.6 Whilst there is no evidence that early surgery (within a week) after stroke in patients who are neurologically stable is associated with increased operative risk7 there is little evidence to suggest that there is any benefit in reducing early stroke recurrence and current available evidence would support a policy of immediate medical therapy, i.e. antiplatelet agents followed by carotid intervention as soon as patients have achieved independence.

The use of antiplatelet drugs (aspirin) in the acute setting has been well validated by both the International Stroke Trial (IST), and the Chinese Acute Stroke Trial (CAST) using slightly differing treatment regimes.8,9 The IST collaborators used 300 mg of aspirin for 2 weeks, or until discharge, and the Chinese study used 160 mg in the acute phase for 4 weeks.

Hypertension, particularly accelerated or malignant hypertension after acute cerebral infarction is likely to increase the risks associated with early carotid intervention as in the post operative period it is associated with hyperperfusion syndrome. Tight blood pressure control pre operatively conflicts with current American and European post stroke recommendations for blood pressure control which suggest avoidance of artificial blood pressure lowering in the acute stroke period.10 This issue of artificial blood pressure reduction is currently the subject of several randomised controlled trials and until the results of these trials is available extreme caution with blood pressure alteration in the acute stroke period must be advised.

The place of statin therapy in the acute stroke remains unclear at this time. The Heart Protection Study (HPS) has demonstrated clear benefits in secondary prevention, and a statin at the highest tolerated daily dose should probably be prescribed for all patients with vascular disease, irrespective of their total cholesterol.11

Angiographic studies within 6 h of stroke demonstrate that 75–89% of patients with an acute ischaemic stroke have a visible occlusion of an extracranial and/or intracranial artery related to the ischaemic area. In the majority of cases this occlusion will be of
either the M1 or M2 segment of the middle cerebral artery due to distal embolisation of thrombus from the internal carotid. The aim of early surgical revascularisation in patients with carotid stenosis is to prevent early stroke recurrence due to further embolisation from a stenosed ulcerated plaque, however there are no randomised trials in patients with stroke secondary to carotid occlusion in whom the aim would be to reduce the area of irreversible cerebral ischaemia by enhancing reperfusion. These patients are ideally treated with systemic agents either intravenous or intra arterial.

Meta-analysis of the randomised trials of intravenous thrombolysis (2775 patients) with recombinant tissue plasminogen activator (rt-PA) has shown that treatment started within 3 h leads to fewer dependent patients at 3 months. These findings have now also been confirmed outside of the trial setting. The benefits of thrombolysis after 3 h may be outweighed by the risk of cerebral haemorrhage (5%) but remain unclear and are currently the subject of two randomised controlled trials looking at up to 4.5 h (ECASS III) and 6 h (IST3). Intra-arterial thrombolysis probably results in quicker and better recanalisation rates but this benefit likely to be offset by the delays incurred in performing selective carotid catheterisation and a higher risk of cerebral haemorrhage (10%). It has been suggested that mechanical clot disruption or aspiration might shorten the time to flow restoration, and improve overall recanalisation rates, but the data on this is confined to single reports or small case series. In the small number of patients with poor collateral flow acute carotid occlusion may result in stroke without any distal embolisation. A small case series using angiographic thrombolysis and immediate surgery has shown some success in these patients. Emergency carotid thromboembolectomy may also produce high recanalisation rates of over 80%, but again, any benefits are likely to be offset by the delays incurred in performing emergency surgery.

In summary, the pragmatic management of patients with stroke is to start intravenous thrombolysis in those who can be treated up to 3 h after onset of symptoms only after performing a CT head scan to exclude cerebral haemorrhage. Patients who cannot be treated under 3 h under the present licence for tPA and those presenting between 3 and 6 h of onset of symptoms should be included in current randomised trials e.g. IST3 (www.IST3.com)

Patients who improve and achieve independence (i.e. a Modified Oxford Handicap Score of three or less) require early investigation as to the cause of their stroke and if carotid imaging suggests a significant ipsilateral carotid stenosis then intervention (CEA or stenting) can and should be performed sooner rather than later in addition to the medical therapy already outlined. Carotid stenting should only be performed as part of a randomised trial in comparison with CEA. There is no evidence to support emergency carotid intervention at this time.

References


Accepted 9 September 2005