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Long term effect of carotid surgery in asymptomatic stenosis

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A 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomized trial is reviewed.

Why is this study of clinical importance?

Asymptomatic patients with substantial (eg, 60-90%) carotid artery narrowing but no recent neurological symptoms are at increased long-term risk of ischaemic stroke, especially in parts of the brain supplied by that artery (the ipsilateral carotid territory). Carotid endarterectomy (CEA) can remove the arterial narrowing, but the procedure itself causes some immediate risk of:

Stroke or death.

ACAS investigators designed a study to find out whether the addition of CE to aspirin plus risk factor modifications will affect the incidence of TIA or infarctions in patients with asymptomatic but haemodynamically

significant carotid stenosis in at least one artery in 1987. This study randomly assigned patients during 1993-2003 to immediate CEA or deferral of any carotid artery procedure until a more definite indication was thought to have arisen, and followed them up until 2006-08. In 2004, ACST-1 reported the medium-term benefits of CEA during the first few years after randomization. This article describes the immediate hazards and 10-year benefits of CEA, subdividing the benefits by participants' characteristics and medical treatment.

Who were the participants?

In asymptomatic patients with substantial carotid artery narrowing, ACST-1 compared immediate CEA versus deferral. All other aspects of treatment were left to the clinician, but usually included long-term antithrombotic therapy, antihypertensive therapy, and, particularly in recent years, lipid-lowering therapy. In all 126 centers in 30

countries participated. Patients were eligible if: (1) they had severe unilateral or bilateral carotid artery stenosis (generally carotid artery diameter reduction at least 60%, although there was no fixed minimum percentage); (2) this stenosis had not caused stroke, transient cerebral ischaemia, or any other relevant neurological symptoms in the past 6 months; (3) no circumstance or condition precluded long-term follow-up; and (4) doctor and patient were both substantially uncertain whether to choose immediate CEA or deferral of any CEA. A total of 3120 patients entered the study between April, 1993, and July, 2003, with no significant differences in baseline characteristics between those randomly allocated immediate CEA and deferral.

What was the intervention?

In asymptomatic patients with substantial carotid artery narrowing, ACST-1 compared immediate CEA versus deferral. All other aspects of treatment were left to the clinician, but usually included long-term antithrombotic therapy, antihypertensive therapy, and, particularly in recent years, lipid-lowering therapy. They allocated patients equally to immediate CEA or deferral of any carotid surgery by minimized randomization.

Follow-up was scheduled at 4 months and 12 months and then yearly until 2006-08, irrespective of any nonfatal strokes.

What was the outcome?

In all 1560 patients were allocated immediate CEA versus 1560 allocated deferral of any carotid procedure. The proportions operated on while still asymptomatic were 89.7% versus 4.8% at 1 year (and 92.1% vs 16.5% at 5 years).

Perioperative risk of stroke or death within 30 days was 3.0% (95% CI 2.4-3.9; 26 non-disabling strokes plus 34 disabling or fatal perioperative events in 1979 CEAs). Excluding perioperative events and non-stroke mortality, stroke risks (immediate vs deferred CEA) were 4.1% versus 10.0% at 5 years (gain 5.9%, 95% CI 4.0-7.8) and 10.8% versus 16.9% at 10 years (gain 6.1%, 2.7-9.4); ratio of stroke incidence rates 0.54, 95% CI 0.43-0.68, $p < 0.0001$. The results showed that 62 versus 104 had a disabling or fatal stroke, and 37 versus 84 others had a non-disabling

stroke. Combining perioperative events and strokes, net risks were 6.9% versus 10.9% at 5 years (gain 4.1%, 2.0-6.2) and 13.4% versus 17.9% at 10 years (gain 4.6%, 1.2-7.9). Medication was similar in both groups; throughout the study, most were on antithrombotic and antihypertensive therapy. Net benefits were significant, both for those on lipid-lowering therapy and for those not, and both for men and for women up to 75 years of age at entry (although not for older patients).

What were the conclusions?

Successful CEA for asymptomatic patients younger than 75 years of age reduces 10 year stroke risks. Half this reduction is in disabling or fatal strokes. Net benefit in future patients will depend on their risks from unoperated carotid lesions (which will be reduced by medication), on future surgical risks (which might differ from those in trials), and on whether life expectancy exceeds 10 years.

How does this impact us?

For men and women younger than 75 years with asymptomatic stenosis, successful carotid surgery could usefully add to the beneficial effects of good medical therapy (antihypertensive and statin regimen) in reducing long term stroke risks as long as perioperative risks remain low. This is especially in patients who would otherwise have more than 10 years of reasonable life expectancy. We need to be aware of the local risks and benefits before we can routinely recommend this procedure due to the perioperative risks.

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Recommended Reading

1. Alison Halliday, Michael Harrison et al. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. *Lancet* 2010; 376: 1074-84.