

## References

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## IN THE LITERATURE

## Should people with asymptomatic carotid artery stenosis undergo endarterectomy for primary stroke prevention?

Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, et al; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004;363:1491-502.

**Background:** Carotid endarterectomy (CE) is well established as a beneficial procedure for reducing the risk of stroke among patients with symptomatic high-grade carotid artery disease.<sup>1</sup> However, its role in reducing the risk among patients with asymptomatic carotid artery stenosis (i.e., no prior cerebral or retinal transient ischemic attack [TIA] or stroke) has been less certain and the subject of much controversy.<sup>2</sup>

**Design:** This multicentre randomized trial is the world's largest vascular surgery trial. From 1993 to 2003, it enrolled 3120 asymptomatic patients with carotid artery stenosis  $\geq 60\%$  (on ultrasound). Patients were randomly allocated to either immediate CE or medical therapy and deferral of CE. Patients with poor surgical risk or a cardiac source of emboli were excluded. Surgeons were required to have a perioperative risk of stroke or death of 6% or less. Medical treatment was left to the discretion of the treating physician. The main outcomes were perioperative morbidity and mortality, and the incidence of nonperioperative stroke.

**Results:** The risk of stroke or death within 30 days of CE was 3.1%. The overall 5-year risk of stroke (including perioperative stroke) was lower in the immediate surgery group than in the medical therapy group (6.4% v. 11.8%,  $p < 0.0001$ ), for a relative risk reduction of about 50%. Subgroup analyses showed a statistical benefit in favour of immediate CE for both men and women, but not for patients aged 75 years and older. CE was particularly beneficial in those with elevated cholesterol.

**Commentary:** Asymptomatic carotid artery stenosis (unlike symptomatic carotid artery stenosis) is a relatively low-risk condition, and this study confirms its natural history. The annual risk of stroke without surgery was about 2%, which is consistent with findings from previous studies; the annual risk of disabling or fatal stroke was only about 1%.

This trial provides evidence that CE is efficacious for primary stroke prevention, but the absolute benefit is small (annual absolute risk reduction about 1%). The study's main end point included *all* stroke types. If one

focuses only on prevention of a disabling or fatal carotid territory ischemic stroke (the main indication for CE), the absolute benefit derived from surgery is even smaller. For every 100 patients operated on, about 7 carotid territory strokes (but only 3 disabling or fatal carotid territory ischemic strokes) would be prevented at 5 years and 3 additional strokes or deaths would be caused as a perioperative complication. With advances in medical management, including aggressive reduction of risk factors and more widespread use of preventive treatments, the benefit of surgery may be further narrowed.

The patients in this trial faced an extremely low surgical morbidity and mortality that is difficult to achieve outside of a clinical trial. Because complication rates of CE are inversely proportional to both hospital and surgeon case volumes, the procedure should not be performed in asymptomatic patients in centres with low case volumes or where the perioperative stroke and death rate exceeds 3%. Independent audits of perioperative complication rates should be made readily available to referring physicians and patients contemplating this procedure. Furthermore, caution is urged when surgical decisions are based solely on carotid ultrasonography, which may misclas-

sify the degree of stenosis. Newer techniques to identify "high-risk" carotid plaques (e.g., transcranial Doppler emboli detection, magnetic resonance direct thrombus imaging, 3-dimensional ultrasonography) are under investigation.

**Practice implications:** When faced with an individual patient, the decision to opt for surgical management of asymptomatic carotid artery disease is not straightforward (see reference 3 for a comprehensive review). CE should be considered only for carefully selected patients with carotid artery stenosis of at least 60% who are less than 75 years old, have a good life expectancy and are at low surgical risk. Evidence of subclinical infarcts on brain imaging should be sought, as this may identify patients who actually have symptomatic carotid artery disease even though the symptoms are unrecognized clinically. Improved risk stratification methods are still needed to identify patients who will benefit most

from CE and those who may be most harmed. On the basis of previous reports, patients with a higher degree of carotid artery stenosis, plaque ulceration or subclinical infarcts on brain imaging may be at increased risk of stroke and therefore may benefit more from CE; those with contralateral carotid artery occlusion, atrial fibrillation, congestive heart failure and diabetes may have a higher risk of perioperative stroke or death.

Conservative patients and their physicians will opt for medical management with aggressive reduction of risk factors and antiplatelet, antihypertensive and statin therapies (for plaque stabilization or perhaps plaque regression), although CE for asymptomatic carotid artery stenosis is now a more valid alternative. Asymptomatic carotid artery disease is a marker for coronary artery disease and peripheral vascular disease, which may also require attention. All patients should be educated about symptom recognition and monitored for the development

of cerebral or retinal TIA or stroke, which would then indicate urgent referral for CE. Ultimately, patients who will benefit most from CE are those with recent stroke symptoms, and improved efforts directed at recognizing and referring these patients must remain top priority.

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