The investigators of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) are reporting the results of an interim analysis of the findings of a randomized controlled clinical trial of carotid endarterectomy for patients with a recent hemispheric, transient ischemic attack (TIA) or a mild (nondisabling) stroke and ipsilateral narrowing of the internal carotid artery. Two groups in the trial received best medical care, including antiplatelet therapy; one of the two groups also had endarterectomy. For patients with high-grade stenosis (70-99% narrowing in the luminal diameter), surgery was highly beneficial. Consequently, patients with high-grade stenosis are no longer being entered into the trial. Because the question of surgical benefit for patients with moderate stenosis (30-69%) has not yet been answered, that part of the trial dealing with symptomatic patients with moderate stenosis will continue. Because it also is not yet known whether asymptomatic patients will benefit from carotid endarterectomy, other trials for those patients will also continue.

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The primary question of efficacy addressed by the trial was the following: Among symptomatic patients with high-grade carotid stenosis (70-99%), does carotid endarterectomy, despite perioperative risk of any stroke or death from any cause, reduce the overall risk of fatal and nonfatal ipsilateral carotid stroke? The interim analysis that follows answers the primary question as well as this question: Among symptomatic patients with high-grade stenosis, is the risk of any severe stroke or death from any cause reduced by carotid endarterectomy?

The trial was conducted at 50 US and Canadian centers, all of which had documented surgical and neurological expertise. To be eligible for the trial, patients <80 years of age must have had a hemispheric TIA or a nondisabling stroke within 120 days and angiographic evidence of 30-99% stenosis in a carotid artery (appropriate for the symptoms) that was accessible to endarterectomy. To measure stenosis, the investigators used the linear diameter at the site of greatest narrowing as the numerator (N) and the diameter of the normal artery distal to the bulb as the denominator (D). The degree as a percentage of stenosis then becomes \((1 - N/D) \times 100\).

Patients were classified into two predetermined stenotic strata: 30-69% and 70-99%. The 595 patients with 70-99% narrowing were identified as the high-grade stenosis patients. Patients were excluded if they refused informed consent or had had a possible cardiac source of embolic stroke, uncontrolled hypertension, uncontrolled diabetes, mental incapacity, clinically important impairment of major organs, recent myocardial infarction, or other serious illnesses that would reduce their chances of survival to <50% during the next 5 years.

All patients were given optimal medical care, including antiplatelet treatment (usually aspirin) and, as indicated, antihypertensive, antilipid, and antidiabetic therapy. More than 99% of both medical and surgical patients were on some antithrombotic drug during the trial. Patients randomly allocated to surgery underwent carotid endarterectomy by neurosurgeons or vascular surgeons who met strict performance standards and had previously demonstrated expertise in the procedure. Surgery was performed an average of 2 days after randomization. Surgical technique, including anesthetic method, use of intraoperative monitoring, shunting, and patch-grafting, were at the discretion of the surgeon.

Medical, neurological, and functional status were assessed by participating neurologists for all patients 1 month after entry, every 3 months for the next year, then every 4 months for the remainder of the trial. All perioperative complications were reported, and all deaths in the first month after randomization were included for both groups, along with the main study outcome measure of stroke.

Main Results: The results reported here apply only to symptomatic patients who were entered in the high-grade stenosis group; there are no conclusive
results at this time for the patients with moderate stenosis. Randomization created balanced treatment groups of medical (295) and surgical (300) patients with respect to important prognostic characteristics and underlying vascular lesions. The median age of patients was 66 (range 35–80) years, and one third were women. The qualifying event was a nondisabling stroke in 32% and one or more TIA’s for the remainder of the group.

No patients were lost to follow-up, none were withdrawn, and the average duration of follow-up among surviving patients was 18 months. Among the medical patients, 16 (5.4%) crossed over and underwent carotid endarterectomy on the same side as the lesion for which they were randomized (five after a stroke, six after a TIA, two as preliminary to other required surgery, and three for miscellaneous reasons). Of the 300 patients randomized to surgery, all but one underwent carotid endarterectomy.

The perioperative period was defined as the period from randomization to 30 days after surgery. There was a total perioperative stroke morbidity and mortality rate of 5%, which included a major stroke and mortality rate of just over 2% and a mortality rate alone of less than 1%. During a period of similar duration (32 days), just over 3% of the medical group had stroke morbidity or mortality.

Interim analysis shows that among symptomatic patients with high-grade carotid stenosis (70–99%), carotid endarterectomy does indeed reduce the overall risk of fatal and nonfatal ipsilateral carotid stroke, despite any perioperative risk of any stroke or death from any cause. Including perioperative morbidity and mortality, or its equivalent time in the medical group, over 24% of medical patients, but only 7% of surgical patients, had experienced fatal or nonfatal ipsilateral stroke at 18 months. This result yields an absolute risk reduction of 17% ($p<0.001$). Furthermore, carotid endarterectomy remained beneficial overall in the prevention of stroke, even when strokes in other vascular territories were included in the analysis.

The investigators also found that among symptomatic patients with high-grade stenosis, the risk of any severe stroke or death from any cause was indeed reduced by carotid endarterectomy. By 18 months, more than 12% of medical patients, but only 5% of surgical patients, had experienced major or fatal stroke in any territory or death from any cause. This result yielded an absolute risk reduction of over 7% ($p<0.01$).

The early risk of perioperative stroke and death is rapidly overcome by endarterectomy, with benefit to the patient appearing within 3 months after surgery. Moreover, benefit of surgery increases for as long as 30 months, which suggests that the beneficial effects of surgery persist at least that long.

A secondary analysis determined that a finer division of the degree of high-grade carotid stenosis (70–79%, 80–89%, 90–99%) correlated with the degree of relative risk reduction after surgery in symptomatic patients. This analysis reinforces the imperative need to continue to study the efficacy of carotid endarterectomy for carotid stenosis in the 30–69% range.

Carotid endarterectomy is highly beneficial for patients with recent hemispheric, transient ischemic attacks or nondisabling strokes and ipsilateral high-grade (70–99%) stenosis. At this time, conclusions cannot be drawn about possible benefits for symptomatic patients with moderate stenosis (30–69%) or for asymptomatic patients; these patients will continue to be studied in this and other trials.

KEY WORDS • carotid artery diseases • endarterectomy

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