Editorial

Carotid Endarterectomy:
Three Critical Evaluations

North American Symptomatic Carotid Endarterectomy Study Group

Carotid endarterectomy is an operation which emerged when three important but separate scientific developments converged: Moniz introduced cerebral angiography, the techniques of surgical arterial repair were refined to deal with trauma on the battlefields and in the bombed cities of World War II, and, finally, the phenomenon of transient cerebral ischemia as a marker for extracranial carotid disease was identified. More than 30 years ago, the first carotid endarterectories were reported, and by now the number that have been performed world-wide can be no less than one million. The growth in popularity of the procedure has been exponential, with good data indicating an increase from 15,000 carried out in the United States in 1971 to 150,000 estimated as the number performed in 1987.

A variety of reasons explain this burgeoning in the operative repair of the atherosclerotic carotid bifurcation: the medical profession has been educated to recognize transient ischemic attacks and their significance as indicators of stroke risk, physicians have been trained to examine the neck for bruits as part of a thorough physical examination, surgical training programs have schooled an increasing number of young surgeons in the technique of endarterectomy, and the hazards of directly invasive arteriography have been replaced by safe noninvasive studies capable of giving images of the cervical portion of the carotid arteries that vary from reasonable to excellent.

Three facts preclude a universal and hearty endorsement of the surge of activity in the performance of carotid endarterectomy. First, there is no published study that can claim without equivocation that the procedure, even in the most skilled hands, leads to a better stroke-free survival more often than may be anticipated in those treated without surgery. Second, it is a procedure that may cause immediate stroke, stroke-death, and complicating myocardial infarction in a small but possibly irreducible number of patients. Figures from the National Hospital Discharge Survey have alerted us to a national average of 2.8% mortality from the procedure. A survey conducted by senior surgeons, based on an anonymous questioning of their colleagues at major centers active in performing the procedure, indicates an average combined mortality and permanent neurologic morbidity of approximately 6%; 8.5% was the morbidity-mortality figure when transient neurologic disability was included. Third, all this is coming into focus at the same time that ischemic stroke continues to decline at a rate approaching 5% per year. Moreover, this decline in most developed countries began before and would seem to be independent of the recent major increase in the performance of endarterectomy.

It would be naive to claim that there is a universal consensus in North America that the time has come to expend the requisite time, energy, and money to submit this procedure to the rigors of a randomized clinical trial, embracing the null hypothesis, asking patients and practitioners to enter into a disciplined study of the procedure. Criticisms have been published that question the wisdom of subjecting any surgical procedure to a comparison with medical therapy, and there are a multitude of papers expressing satisfaction with the "results" of carotid endarterectomy obtained in uncontrolled surgical series. Nevertheless, it would be equally naive to claim that the profession has universally agreed that carotid endarterectomy is efficacious. Serious reservations have been registered, and these have increased in number and persuasiveness as the performance of the procedure has gained momentum.

These reservations about the benefit of this surgical treatment led the Committee on Health Care Issues of the American Neurological Association to pose the question of efficacy to a group of medical and surgical experts: does carotid endarterectomy decrease stroke and death in patients with transient ischemic attacks (TIAs)? Whisnant et al., reporting for this committee, concluded that "carotid endarterectomy may be of value, provided the procedures are performed with a very low surgical complication rate. No clinical trial has adequately addressed the benefit or lack of benefit of the procedure. It is possible that the net effect of carot-
id endarterectomy in patients with carotid TIAs in the United States is unfavorable."

This committee based its conclusions on a review of the available data from symptomatic patients, which documented a stroke rate in untreated or medically-treated patients of 5% per year for the first 3 years and 3% per year thereafter. When these figures were contrasted with a theoretical surgical group with a perioperative morbidity and mortality of 4% and a subsequent stroke rate of 2% per year, this committee concluded that the detrimental effect of surgery would be negated in 1 year, and that by 5 years there would be a net 33% reduction of stroke. This beneficial reduction drops to 25% if the surgical morbidity-mortality figure is 6% and to 0% if the complication rate is 10%. Finally, this expert committee showed that to achieve a 50% reduction of stroke in 5 years would require the attainment of a surgical morbidity-mortality rate of 1% or less. No independently compiled or audited series of operated symptomatic patients with such a low perioperative complication rate has been reported.

Thus, there is uncertainty within the experienced and objective medical and surgical communities about the efficacy and indications for carotid endarterectomy. Even though this uncertainty is not unanimous, it is both genuine and sufficiently widespread to provide the ethical prerequisite to a clinical trial described by Freedman in his recent essay. Moreover, if carotid endarterectomy were not a surgical procedure but a pharmaceutical product, it is reasonable to argue that its documented risks of associated morbidity and mortality would lead the United States Food and Drug Administration to demand its validation in a rigorous randomized trial prior to its approval and licensure. Indeed, the call for a rigorous evaluation of the procedure is already bearing fruit on two continents. The Europeans have already entered nearly 1,500 patients into a randomized study of patients with symptomatic carotid artery disease, and another randomized trial has been approved by the Veterans Administration and is about to commence patient entry; as this editorial goes to press, its authors are joining forces with colleagues in 50 institutions in the United States and Canada to perform a randomized trial of carotid endarterectomy among symptomatic patients.

Readers are assured that these studies have not been designed to "prove that endarterectomy is useless" nor to show that "medical therapy is better." Rather, these studies have been designed to establish objectively, with a credible and simultaneously studied nonsurgical control group, the relative incidence of stroke and death in thousands of patients on two continents, all subjected to the best available medical care under the supervision of expert neurologists; half of the patients have been randomized to receive carotid endarterectomy performed by surgeons expert in carrying out this procedure. Both groups will be followed for an average of 5 years.

This American-Canadian study, the North American Symptomatic Carotid Endarterectomy Study (NASCES), will complement a parallel study of asymptomatic carotid stenosis; both are supported by the National Institute of Neurological and Communicative Disorders and Stroke. The NASCES is expected to delineate clearly which patients are appropriate for endarterectomy, to identify the upper limits of acceptable operative morbidity and mortality compatible with anticipated benefit from the procedure, and to identify which clinical-radiological subgroups and which patients with combinations of risk factors may expect benefit.

The organizers of these studies recognize that the completed trial may not meet universal acceptance by the medical and surgical communities. For example, the EC/IC Bypass Study sufficiently disappointed some readers that they have criticized its generalizability (but not its internal validity). Occasional critics have suggested that some of the participating surgeons knew in advance which patients would benefit most from the procedure and arranged to omit them from the trial. In fact, however, the evidence that this occurred in more than a handful of the 62 active centers is lacking, and the nonrandomized patients have been neither identified nor published as a group dissimilar to those in the trial.

Nonetheless, to obviate this criticism, great care will be taken in the NASCES to record both the baseline characteristics and the subsequent course of those patients of participating physicians who are clinically eligible but not submitted to randomization. As in all clinical trials, it will be more meaningful to analyze the results in those who were in the trial than to expect important answers to emerge from the analysis of those who were not. This will apply even though the nonrandomized patients will be prospectively studied. The goal of the organizers of the NASCES trial is to have a team of collaborators who will be committed to entering all clinically eligible patients who consent.

Experienced surgeons can be expected to have a lower postoperative morbidity and mortality than those who perform few endarterectomies. It may be that there are exceptional surgical maestros leading unusually capable teams of anesthesiologists and technicians whose results can be shown to indicate that they perform these operations more safely than their peers. No surgical trial can or should be composed of only maestros. Even in the most renowned orchestra there is only one first violinist, but the skill of the support violinists must be as close to flawless as careful selection and dedicated effort can achieve. In the same way, the surgical team in a multicenter trial must be constituted of individuals whose records denote nothing short of excellence in surgical skills and experience. To this end, NASCES has a Surgical Committee that has selected only competent surgeons and whose ongoing duty is to monitor the surgical results. At the beginning of the EC/IC Bypass Study, concerns were expressed that several of the most experienced surgeons (the world's microvascular maestros) had decided not to commit themselves to participate in the randomized study. It was speculated that their absence would deny a valid evaluation of the procedure and that true results
would apply only to centers where surgeons with less experience would be performing the surgery. As it turned out, there were no parameters by which surgical success of the participating surgeons could be measured to suggest that the surgical activity of the participants did not equal or exceed any of the results reported by the recognized experts. Obviously there was modest variation between the centers, but the average was exceedingly satisfactory. The selection of surgical participants in the evaluation of symptomatic carotid endarterectomy is expected to follow this pattern and to lead to a credible result.

An editorial in this journal in 1984 expressed concern about the status of endarterectomy in symptomatic carotid disease. The European, the Veterans Administration, and the NASCES randomized trials are expected to address this concern. Neurologists, neurosurgeons, vascular surgeons, and the readers of Stroke who share the disquiet about this common procedure will wish to cooperate with one of these three studies. We believe that carotid endarterectomy is a procedure that will be shown to be of benefit in the prevention of stroke. It is an exciting prospect to think that in 6 or 7 years the uncertainty that today lingers over carotid endarterectomy will be replaced by a set of credible guidelines for its use.

**References**


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