We announce the completion of acquisition of patients for a prospective randomized clinical trial designed to determine the role of carotid endarterectomy in the treatment of patients with asymptomatic carotid stenosis. We also respond to a previous editorial concerning this trial.

This on-going multicenter trial (Cooperative Studies Protocol #167, Asymptomatic Carotid Stenosis: Etiological Importance in Development of Stroke) has been conducted in 10 Veterans Administration Medical Centers during the last 5 years. Randomization of 451 adult male patients with a mean age of 64 years to treatment with carotid endarterectomy plus aspirin versus treatment with aspirin alone was completed in November 1987. Mean clinical follow-up is currently 36 months, and a 60-month follow-up is planned before the outcome results are reported. Compared with other studies on carotid bruit, this trial included only patients with hemodynamically significant stenoses defined as luminal reductions on lateral arteriography of ≥50%, a luminal area reduction of ≥75% in the presence of positive noninvasive testing. Contrary to Dyken's editorial opinion, these lesions are associated with an increased rate of transient ischemic attack (TIA) and stroke. Chambers and Norris reported an 18% annual rate of TIA and stroke in an asymptomatic population with area reductions of ≤75% compared with a rate of <3% in patients with lesser stenoses. Furthermore, significantly higher annual neurologic event rates were observed in patients with progressing carotid artery stenoses and heart disease and in male patients. Consequently, the concept of identifying asymptomatic patients with high-grade stenoses or noninvasive evidence of increasingly severe stenoses as a stroke-prone group is valid and forms the basis for this trial.

The magnitude of operative stroke and death is of paramount importance in the decision for carotid endarterectomy in patients with asymptomatic carotid stenosis. The principal investigators in this trial, one vascular surgeon and one neurologist at each center, submitted narrative summaries and operation reports for all carotid endarterectomies performed during a prior 2-year period. While Dyken calculated the potential operative risk at 5.9% in the 10 participating centers, his figure included a transient neurologic event rate of 2.2%. Since he suggested an innocuous course for transient neurologic events in his editorial, a more realistic operative stroke and death rate would be 3.7%. This reduced estimate of operative complications coupled with an annual neurologic event rate as reported in the Toronto experience may then allow a statistically significant conclusion in this trial.

The goal of concluding that the risk of stroke alone can be reduced significantly by operative intervention may not be achievable in this trial due to sample size considerations. However, clinicians are reminded that the efficacy of aspirin in symptomatic patients was not substantiated for stroke alone but required the reporting of a combined stroke and death rate to achieve a significant result. Furthermore, the presumption that TIA is an innocuous event constitutes a clinical generalization that awaits further analysis. As many as 30–40% of patients thought to have only transient neurologic events were reported as having results diagnostic of stroke on computed tomography or magnetic resonance imaging. The conclusion that “the more important endpoints of stroke and death could never be determined” is speculative and awaits analysis of 5-year follow-up data.

While we agree with Dyken that the diagnosis of TIA may be ill-defined, this problem was not ignored by the Planning Committee of this trial. Each clinical diagnosis of TIA required confirmation by the principal investigators at each center. Furthermore, each neurologic event (TIA or stroke) and each death is reviewed by an End Points Committee, whose members are otherwise uninvolved with the trial and review summary statements and are blinded to the treatment of each patient. These provisions are consistent with achieving the highest possible diagnostic accuracy.
Until outcome results are reported from this prospective multicenter trial as well as the more recently initiated clinical trial supported by the National Institutes of Health, clinical groups must conduct periodic audits of their complication rates associated with the performance of carotid endarterectomy. Clinicians are advised to refer patients for surgery only in institutions that document acceptably low operative stroke and death rates. Since performance of these clinical trials has been recommended by surgeons and neurologists for the last decade or more, we are delighted on behalf of the Cooperative Studies Program, Veterans Administration, to be one of the currently active groups in this effort. We agree with the opinion that "At last from the darkness there is a glimmering of science."

References
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Stroke endarterectomy for asymptomatic carotid stenosis.
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