

### SYMPOSIUM: CONTROVERSIES IN CEREBROVASCULAR DISEASE

## 3. CURRENT INDICATIONS FOR CAROTID ENDARTERECTOMY

Paul M. Walker, MD, PhD\*

Randomized, prospective trials examining the effectiveness of carotid endarterectomy have given distinct information into the mechanisms and prevention of embolic strokes. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the Asymptomatic Carotid Atherosclerosis Study (ACAS) have demonstrated the benefits of carotid endarterectomy for patients who meet the precise selection criteria and are treated according to established study protocols. The existing challenge to clinicians lies in the application of trial results to the individual patient.

Les études prospectives randomisées sur l'efficacité de l'endartérectomie carotidienne ont produit des renseignements distincts sur les mécanismes des embolies et la prévention. L'étude nord-américaine sur l'endartérectomie de la carotide symptomatique (NASCET) et l'étude sur l'athérosclérose de la carotide asymptomatique (ACAS) ont démontré les avantages de l'endartérectomie carotidienne pour les patients qui satisfont aux critères de sélection précis et sont traités conformément à des protocoles d'étude établis. Pour les cliniciens, le défi réside dans l'application des résultats d'étude à chaque patient.

In 1986, when I presented my own results of carotid artery surgery, I stated that there was still no adequate proof that endarterectomy reduced strokes. I tried to engender some support for the idea of a randomized, prospective, controlled study that was being conceptualized by Dr. Henry Barnett. However, this idea was perceived as unnecessary at the time.

Eventually, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) did proceed and proved that under certain circumstances carotid endarterectomy is the

most effective intervention in reducing not only the mortality, but particularly the horrific morbidity associated with stroke.<sup>1</sup> As part of the executive committee of NASCET, I recall when the decision was made to stop the trial for patients with greater than 70% carotid stenosis because surgical treatment proved far more effective than medical therapy in reducing the stroke rate. It was a high point in my surgical career.

In 1993, a symposium on carotid endarterectomy was organized whereby we reviewed these results. We also discussed specific technical considerations

for performing carotid artery surgery, stressing the importance of reducing the complication rate to maintain the benefit of surgery.<sup>2</sup> Since then, however, the waters have become somewhat muddied with respect to the indications for carotid endarterectomy. Nevertheless, it is clear that there has to be some ability to generalize the positive results of the original NASCET. Thus, although the degree of stenosis was measured in a specific and perhaps controversial way, the trial identified a clear relationship between the degree of stenosis and the incidence of stroke. Unfortunately, this fact is often forgot-

*From The Toronto Hospital, University of Toronto, Toronto, Ont.*

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*\*James Wallace McCutcheon Chair, Surgeon-in-Chief, Vice President, Surgical Directorate, The Toronto Hospital, University of Toronto*

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**Correspondence to:** Dr. Paul Walker, Bell Wing 1-635, General Division, The Toronto Hospital, 585 University Ave., Toronto, ON M5G 2C4; tel 416 340-5051, fax 416 340-5054

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ten when we talk about indications for asymptomatic patients. In the NASCET, the transient ischemic attack (TIA) had to have occurred within 120 days for the patient to be eligible for endarterectomy.<sup>1</sup> Although it is difficult to believe that a patient who has had a TIA at 122 days is any different from a patient who has had a TIA at 120 days, the question of when that benefit of en-

arterectomy fades due to the remoteness of the TIA is clearly unknown.

A 1992 consensus conference, examining the current status of carotid surgery, reviewed and graded the literature up to that point.<sup>3</sup> Some of the results of this consensus are presented in Table I. It is important to understand both the results and the definitions under which the results are clas-

sified. Although it is highly improbable that there will ever be a clear set of guidelines for the management of all carotid surgery, it is important to know where firm evidence exists and where true questions remain. The NASCET<sup>1</sup> did show that the perioperative risk of major stroke and death must not exceed 2.1% or the benefit diminishes and that if the rate of com-

**Table I**

**Indications for Carotid Endarterectomy in Symptomatic Patients**

Proven benefit (based on the NASCET<sup>1</sup>)\*

Patients' cumulative risk of any ipsilateral stroke after 2 yr of treatment: 26% after medical treatment, 9% after carotid endarterectomy (absolute risk reduction 17% [3.5%])

Patients' cumulative risk of major or fatal ipsilateral stroke after 2 yr of treatment: 13.1% after medical treatment, 2.5% after surgical treatment (absolute risk reduction 10.6% [2.6%])

Carotid endarterectomy still beneficial when all strokes and deaths are included in the analysis

Carotid endarterectomy highly beneficial in patients with

recent hemispheric and retinal TIAs

nondisabling strokes

ipsilateral high-grade stenosis (70%–99%) of internal carotid artery

Acceptable indication but not proven benefit†

TIAs (single, multiple or crescendo) in the past 6 mo with stenosis > 70%

Progressive stroke with stenosis > 70%

Mild or moderate stroke, and stenosis of 50% to 69%

Ipsilateral carotid endarterectomy combined with required CABG in a patient with TIAs with unilateral or bilateral stenosis of ≥ 70%

Uncertain benefit‡

TIAs or mild stroke with stenosis < 50%

TIAs with stenosis < 70% combined with CABG

Moderate or evolving stroke with stenosis < 69%

Global ischemic symptoms

Ipsilateral stenosis > 75% but contralateral stenosis < 75%

Acute dissection of ICA with persistent symptoms while taking heparin

Acute carotid occlusion within 6 h of diagnosis, producing TIA or mild stroke

Proven inappropriate§

Single TIA, moderate or evolving stroke with stenosis < 50%, not taking acetylsalicylic acid

Global ischemic symptoms with stenosis < 50%

Asymptomatic, acute ICA dissection while taking heparin

Medical centres with a combined perioperative stroke-related morbidity and mortality > 5%

\*This is the strongest indication for carotid endarterectomy. Data are supported by results of prospective, contemporary, randomized trials (e.g., NASCET).

†This is a good indication for endarterectomy that is supported by promising but not scientifically certain data.

‡Data are insufficient to define risk:benefit ratio.

§Current data show that the operative risk outweighs any benefit.

TIA = transient ischemic attack, CABG = coronary artery bypass grafting, ICA = internal carotid artery

plications approaches 10%, all benefit is lost.

With regard to the dilemma of asymptomatic carotid artery stenosis, perhaps the most confusing piece of the puzzle with respect to carotid artery surgery is the results of the Asymptomatic Carotid Atherosclerosis Study (ACAS).<sup>4</sup> The National Institutes of Health certainly increased the credibility of these results by issuing clinical directives to stop the trial and surgery for asymptomatic patients with stenosis greater than 60%. However, my major concern is that a statistical difference has been extrapolated into a tangible clinical difference, and I question the results of this study. The indications for surgery according to the ACAS are listed in Table II.

Barnett, Meldrum and Eliasziw<sup>5</sup> stated that the ACAS produced some interesting, statistically significant findings that do not translate into clinical importance or practice: the incidence of disabling strokes was not reduced by surgery, and benefit to women was not shown.

Another question remains that does not have a well-defined answer: How often do people present with a TIA before a major cerebral vascular event? The data in NASCET would

suggest that it is common for a TIA to precede a major ipsilateral stroke, thus presenting a window of opportunity to intervene appropriately. However, the most frequently cited paper on asymptomatic patients states that this scenario is a rarity and that most people actually present with a severe ipsilateral stroke without any previous TIA. Of note, however, is that this paper was published in 1974.

There appears to be a paradox to the problem of patients with asymptomatic stenosis. If the data firmly support surgery for patients with an asymptomatic 60% carotid stenosis, why should surgery be limited to those patients who happen to appear in one's office? If this intervention is indeed appropriate for these individuals, we should be offering this endarterectomy to all who have an asymptomatic 60% carotid stenosis.

Let us explore further this line of thinking. What are the direct benefits and risks for mass screening for carotid stenosis? The direct hospital costs of stroke per admission in Ontario are Can\$27 000. Annually, 50 000 Canadians are afflicted with stroke. Screening identifies patients who are at 1% to 2% risk per year. Arteriography, the standard screening procedure, carries

a risk of stroke of 0.5% to 1.0%. The ACAS trial stated that, to prevent 1 stroke, 17 selected patients must receive carotid endarterectomy in centres of excellence that have a perioperative morbidity and mortality of less than 3%. However, major stroke was not prevented by endarterectomy, and the generalizability of these study results is a major concern.

If we consider the cost-effectiveness of carotid endarterectomy in stroke prevention, the direct lifetime medical cost of stroke is between US\$30 000 and \$60 000. Trials of symptomatic patients suggest that performing endarterectomy on 100 patients results in 17 fewer strokes over 2 years. Therefore, the savings due to reduction in stroke risk ranges from US\$5100 to \$10 200 per surgical patient.<sup>3</sup>

The prevalence of carotid stenosis greater than 50% is estimated as follows:

- 5% of the general population over the age of 60 years
- 10% of the population over the age of 60 years with atherosclerotic risk factors
- 20% of the population with coronary artery disease (CAD) and peripheral vascular disease (PVD).<sup>6-8</sup>

Therefore, to prevent 1 stroke, the numbers of individuals who need to be screened in each group are:

- 370 by Doppler ultrasonography (followed by 19 angiographic examinations and 17 endarterectomies) in the 5% prevalence group (individuals older than 60 years with no atherosclerotic risk factors)
- 91 by Doppler ultrasonography (followed by 18 angiographic examinations and 17 endarterectomies) in the 20% prevalence group (population with CAD and PVD).

However, the possible risks of screening patients for asymptomatic carotid stenosis are of concern. False-positive tests can result in angiogra-

**Table II**

**Indications for Carotid Endarterectomy in Asymptomatic Patients**

Proven benefit (based on ACAS trial <sup>4</sup> )
Asymptomatic carotid stenosis > 60% confirmed by arteriography
Medical centres with perioperative morbidity and mortality < 3%
Carefully selected patients in whom risk factors have been managed aggressively
After endarterectomy, patients' absolute risk of stroke reduction is 5.8% within 5 yr and relative risk reduction is 55%.
Uncertain benefit
Stenosis > 75% in a high-risk patient/surgeon combination (surgical morbidity and mortality rates > 3%)
Combined carotid and coronary operations
Ulcerative lesions without hemodynamically significant stenosis

phy, which carries a 1% risk of stroke. Also, unnecessary anxiety may be inflicted on healthy people.

The position of the American Heart Association is clear: "It appears that the cost of large-scale screening programs would likely negate any potential cost benefit of surgery of asymptomatic stenosis. Unless we can further identify subsets of patients who are at particularly high risk for stroke, the benefit of performing CE indiscriminately on asymptomatic patients with carotid stenosis will likely be largely outweighed by the cost of screening."<sup>3</sup>

In many other areas of health care, the concept of evidence-based medicine is becoming an important topic for discussion and will clearly be a guiding force in the future of surgical practice, particularly with respect to funding. Even though we may believe, think or want to think that certain interventions are appropriate, unless we can prove it and be accountable for the intervention, the funds for it will not be available.

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## ADDENDUM

Since the presentation of this material at the 18th meeting of the Canadian Society for Vascular Surgery in September 1996, there have been new developments in the indications for carotid endarterectomy for preventing stroke.

The North American Symptomatic Carotid Endarterectomy Trial (NASCET), a 12-year study sponsored by the National Institute of Neurological Disorders and Stroke, examined the benefit of carotid endarterectomy for patients with symptoms of stroke associated with 30% to 39% carotid artery stenosis. In 1991, early data were released regarding the benefit of surgery for patients with 70% to 99% carotid artery stenosis in the prevention of stroke. Since then the study has focussed on carotid endarterectomy for symptomatic patients with moderate (30% to 69% carotid artery stenosis). The results of the final phase of the NASCET were announced at the American Heart Association's 23rd International Joint Conference on Stroke and Cerebral Circulation in February 1998. The results demonstrated that patients with carotid artery stenosis greater than 50% clearly benefit from surgery.