EXPERT REVIEW

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Surgical Versus Percutaneous Therapy of Carotid Artery Disease: An Evidence-Based Outcomes Analysis

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STROKE IS A MAJOR cause of morbidity and mortality worldwide and is a leading cause of long-term, acquired adult disability in most developed countries.[1,2] In the United States, stroke affects approximately 800,000 people each year and currently is the fifth leading cause of death.[2] Carotid artery stenosis from atherosclerotic changes of the vessel wall contributes to 10% to 20% of all strokes.[2–4] As such, carotid artery stenosis is considered to be a modifiable and treatable factor for the risk reduction of subsequent stroke.[5]

Current guidelines and recommendations for surgical intervention in patients with symptomatic disease are based on the results of the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[6,7] and the European Carotid Surgery Trial (ECST).[8] In the NASCET trial, the annual stroke rate without controlled medical treatment (within 2 years of follow-up) was reported at 26% for high-grade stenosis (>70% stenosis) and 22.2% for moderate stenosis (50%-69%). Similar results were obtained in the ECST trial[5]; however, these early studies were marked by several key limitations. Diagnosis of carotid stenosis was based on a patient's history of transient ischemic attack (TIA) or stroke without considering other potential sources such as atrial fibrillation. In addition, medical treatment at the time of these studies mainly consisted of aspirin (ASA), whereas current treatment standards use a combination of statins, ASA, and anticoagulants.

Improvements in diagnostic modalities have led to the earlier detection of carotid stenosis and have increased the knowledge base regarding the risks and spontaneous course of the disease.[9] Whereas auscultation of carotid bruits was the initial diagnostic gold standard, the advent of vascular ultrasound permitted screening of a larger number of patients. Presently, sophisticated ultrasound systems, computed tomography, and magnetic resonance imaging angiographies allow for visualization of the vessel wall very early in disease progression while patients still are asymptomatic.[9]

Today, the definitive treatment for carotid disease remains carotid revascularization. However, the decision to perform carotid endarterectomy (CEA) versus carotid artery stenting (CAS) remains controversial given the conflicting results of clinical trials. This article reviews the evolution of these 2 procedures and discusses the current evidence with respect to their perioperative and long-term outcomes.

CAROTID ENDARTERECTOMY: HISTORY, EVOLUTION, OUTCOMES, AND LARGE-SCALE TRIAL DATA

History

The first successful CEA was performed by DeBakey on August 7, 1953. A 53-year-old bus driver presented with intermittent episodes of right arm weakness associated with expressive aphasia. The diagnosis of carotid stenosis was made based on history and physical examination findings of an extremely weakened left carotid and left superficial temporal pulse. The patient underwent thromboendarterectomy of the left ICA with primary repair of the vessel. The patient experienced an uncomplicated postoperative course with resolution of his neurologic symptoms.[10]

Evolution

Since that first endarterectomy, several advances have been made in the surgical treatment of extracranial carotid disease. The use of a carotid shunt was first described by Al-Naaman and Cooley in 1956 to maintain cerebral perfusion during carotid cross-clamping.[11] Patch closure of the carotid arteriotomy to preserve luminal diameter was first described in 1965, with the first

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Table 1. Incidence of Cerebrovascular Accident in Major CEA RCTs

Trial	Symptoms	Degree of Stenosis (%)	Perioperative (≤30 days) Stroke/Death Rate (%)	Overall CVA: CEA	Overall CVA: Medical (%)	p Value
NASCET[7,15]	Symptomatic	70-99	5.8	9% at 2 y	26	<0.001
	Symptomatic	50-69	6.7	15.7% at 2 y	22.20	0.045
ECST[8]	Symptomatic	80-99	7.0	14.9% at 3 y	26.50	0.001
ACAS[16]	Asymptomatic	60-99	2.3	5.1% at 5 y	11	0.004
ACST[17]	Asymptomatic	60-99	3.1	6.4% at 5 y	11.78	<0.0001

Abbreviations: ACAS, the Asymptomatic Carotid Atherosclerosis Study; ACST, Asymptomatic Carotid Surgery Trial; CAS, carotid artery stenting; CEA, carotid endarterectomy; CVA, cerebrovascular accident; ECST, European Carotid Surgery Trial; NASCET, North American Symptomatic Carotid Endarterectomy Trial; RCT, randomized controlled trial.

randomized trial in 1987 showing its benefit over primary closure.[12] Eversion carotid endarterectomy has evolved as an alternative to conventional longitudinal arteriotomy. Etheredge[13] was the first to describe complete transection of the internal carotid to facilitate removal of carotid plaque with end-to-end closure. Since then, randomized trials have demonstrated comparable results with either conventional or eversion techniques.[14]

Outcomes

Several large, randomized trials have been conducted over the last 30 years demonstrating the benefit of CEA in both symptomatic and asymptomatic patients. The primary outcome data of 4 major randomized controlled trials (RCTs) regarding CEA are shown in Table 1.

Results of Randomized Trials

Symptomatic Disease

North American Symptomatic Carotid Endarterectomy Trial. NASCET was the major trial demonstrating the benefit of CEA in symptomatic patients.[7,15] NASCET was a randomized, prospective, multicenter trial designed to compare the efficacy of CEA versus medical therapy in patients with symptomatic extracranial carotid disease. The study included 659 patients with hemispheric symptoms and severe ICA stenosis (70%-99%) who were assigned randomly to either CEA or antiplatelet therapy. Another 865 patients with moderate ICA stenosis (50%-69%) were assigned randomly in a similar fashion. At 2-year follow-up, there was a significant reduction in ipsilateral stroke in the group with severe stenosis undergoing CEA versus medical therapy (9% *v* 26%, respectively). At 5 years, patients with moderate stenosis demonstrated a reduced ipsilateral stroke rate of 15.7% versus 22.2% in the medical arm ($p = 0.45$). The benefit seen in both groups persisted throughout the trial's 8-year follow-up.

Trial investigators concluded that CEA was highly beneficial for reducing the stroke rate in patients with severe ICA stenosis. Moderate benefit was demonstrated in patients with moderate stenosis. No benefit was seen in patients with <50% stenosis. A subset analysis of NASCET found that patients older than 75 years with ICA disease (50%-99%) benefited more from CEA than did younger patients.[18]

European Carotid Surgery Trial. ECST was the largest European trial comparing CEA and medical therapy. ESCT was a prospective, multicenter trial that randomly assigned 3,024 patients with symptomatic ICA stenosis to either CEA or ASA therapy. At 3 years, patients undergoing CEA demonstrated a significantly reduced ipsilateral major stroke rate compared with patients randomly assigned to ASA alone (2.8% *v* 16%, respectively). The frequency of all major stroke or death at 3 years was 14.9% in the CEA group and 26.5% in the medical therapy group, with an absolute benefit of CEA of 11.6%. When stratified by severity of carotid stenosis, the 3-year risk of any major stroke (including surgical events) in patients with 80% to 99% stenosis was 6.8% in the CEA group versus 20.6% in those treated medically ($p < 0.0001$). At 5 years, the absolute risk reduction (ARR) of stroke within the CEA group was 21.2% ($p < 0.0001$). The authors concluded that symptomatic patients with high-grade (80%-99%) ICA stenosis benefit more from CEA than from medical therapy alone. The risk of succumbing to major stroke was found to increase based on severity of the stenosis.[8]

There is a discrepancy in the definition of severe stenosis for which CEA is most beneficial between NASCET and ECST (70% *v* 80%, respectively). Subsequent analysis was performed by the ECST investigators, who attributed the difference to several factors. First, varying methods were used to quantify the degree of carotid stenosis used in both trials. In the NASCET trial, the luminal diameter at the area of maximum stenosis was compared with the diameter at the distal healthy ICA segment. ECST measured the diameter at the greatest area of stenosis and compared it with the original ICA diameter at the carotid bulb (typically larger diameter). The authors of ECST suggested that the method used in NASCET could underestimate the actual degree of stenosis. Figure 1 depicts the differences in carotid anatomy measurements between the 2 trials. Second, the 2 trials differed on their definition of stroke. NASCET defined stroke as any event with symptoms lasting longer

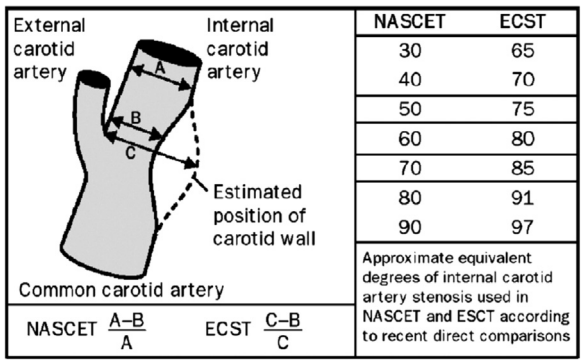

Fig 1. Differing methods for determining the percent of carotid artery stenosis. From Yang EH, Holmes DR Jr: Surgical and Percutaneous Management of Carotid Artery Stenosis. Curr Probl Cardiol 33:291-316, 2008.