

# Endarterectomy Is Superior to Stenting in Patients with Symptomatic Severe Carotid Stenosis

Mas JL, Chatellier G, Beyssen B, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. *N Engl J Med* 2006;355:1660–71.

## Study Overview

**Objective.** To compare carotid artery stenting (CAS) with carotid endarterectomy (CEA) in patients with severe symptomatic carotid stenosis.

**Design.** Multicenter, randomized noninferiority trial (the Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis [EVA-3S] trial).

**Setting and participants.** 527 patients aged  $\geq 18$  years with severe symptomatic carotid stenosis, defined as a transient ischemic attack (TIA) or nondisabling stroke within 120 days before enrollment and stenosis of 60% to 99% in the symptomatic carotid artery, were randomized to CEA or CAS. Stenosis was confirmed by catheter angiography or duplex scanning and magnetic resonance angiography.

**Main outcome measures.** The primary endpoint was a composite of any stroke or death occurring within 30 days posttreatment. Secondary outcomes were myocardial infarction; TIA; cranial nerve injury; major local complications within 30 days posttreatment; and composites of any stroke or death within 30 days posttreatment plus ipsilateral stroke, any stroke, or any stroke or death within 31 days through the end of follow-up.

**Main results.** Baseline characteristics between the CEA and CAS groups were similar; however, more patients in the CEA group were aged  $> 75$  years or had a history of stroke, and more patients in the CAS group had contralateral carotid occlusion. The study was stopped early by the safety committee based on the observed 30-day risk of stenting. Incidence of any stroke or death at 30 days was 3.9% in the CEA group compared with 9.6% in the CAS group ( $P = 0.01$ ), with a relative risk of 2.5 (95% confidence interval, 1.2–5.1). At 6 months, the incidence of any stroke or death was 6.1% after CEA compared with 11.7% after CAS ( $P = 0.02$ ). Cranial nerve injury was significantly more common after CEA as compared with CAS (7.7% versus 1.1%;  $P < 0.001$ ). The median length of hospital stay was shorter after CAS than after CEA (3 days versus 4 days;  $P = 0.01$ ).

**Conclusion.** In patients with symptomatic severe carotid artery stenosis, CAS is inferior to CEA.

## Commentary

Recently, there has been extensive debate regarding the safety and efficacy of CAS compared with CEA. In centers with complication rates below the accepted threshold of 6% [1], CEA has proven benefit over medical therapy for patients with symptomatic and asymptomatic stenosis. CAS has only shown benefit in patients with symptomatic stenosis who are at high perioperative cardiovascular risk, which is currently the only U.S. Food and Drug Administration–approved indication for CAS [2].

A number of noninferiority trials have recently been published and others are undergoing recruitment in an attempt to broaden the indications for CAS. In contrast to clinical trials comparing a treatment with placebo, noninferiority trials are designed to show that a new treatment is not inferior to standard treatment by a predefined clinically acceptable amount. If noninferiority is established, the utility of the new treatment can be based on ancillary advantages in safety, convenience, or cost [3]. CAS offers potential advantages over CEA in these areas, but strong evidence supporting CAS in a broad population is lacking.

The EVA-3S trial showed a significantly increased risk of stroke or death with CAS. A number of criticisms have been raised about the study, including inadequate training of the operators and lack of standardized techniques. In this trial, an operator was considered “experienced” after placement of 12 carotid stents of any kind. Verzini et al [4] recently demonstrated a learning curve for CAS and concluded that 195 procedures needed to be performed by an operator before the complication rate consistently matched that of CEA. To become competent in CAS, U.S. guidelines recommend a minimum of 25 stenting procedures. In a subgroup analysis in the EVA-3S, however, there was no difference in complication rates based on operator experience.

The SPACE trial [5] was a multicenter, prospective, randomized trial designed to test the noninferiority of CAS and CEA in patients with symptomatic carotid artery stenosis. The rate of ipsilateral stroke or death at 30 days was 6.8% in

the stenting arm and 6.3% in the surgical arm; however, this difference was not statistically significant for noninferiority. Results at 6 to 24 months are forthcoming. The SPACE and EVA-3S trials both failed to prove the noninferiority of CAS versus CEA in patients at average surgical risk. The CREST [6] and ACT I [7] trials are ongoing large randomized studies evaluating CAS versus CEA in symptomatic and asymptomatic carotid artery stenosis, respectively, which may help end the current debate.

### Applications for Clinical Practice

Until more data become available, CAS should generally be reserved for patients with symptomatic carotid artery stenosis who are at high surgical cardiovascular risk at centers with an acceptably low (< 6%) complication rate.

—Review by Michael P. Janjigian, MD (New York University School of Medicine, New York, NY), and Nirav R. Shah, MD, MPH

### References

1. Furlan AJ. Carotid-artery stenting—case open or closed [published erratum appears in *N Engl J Med* 2006;355:2712]? *N Engl J Med* 2006;355:1726–9.
2. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493–501.
3. Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. *Ann Intern Med* 2006;145:62–9.
4. Verzini F, Cao P, De Rango P, et al. Appropriateness of learning curve for carotid artery stenting: an analysis of periprocedural complications. *J Vasc Surg* 2006;44:1205–12.
5. The SPACE Collaborative Group; Ringleb PA, Allenberg J, Bruckmann H, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomized non-inferiority trial [published erratum appears in *Lancet* 2006;368:1238]. *Lancet* 2006;368:1239–47.
6. Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). Available at [www.clinicaltrials.gov/ct/show/NCT00004732?order=1](http://www.clinicaltrials.gov/ct/show/NCT00004732?order=1). Accessed 10 Jan 2007.
7. Carotid stenting vs. surgery of severe carotid artery disease and stroke prevention in asymptomatic patients (ACT I). Available at [www.clinicaltrials.gov/ct/show/NCT00106938?order=1](http://www.clinicaltrials.gov/ct/show/NCT00106938?order=1). Accessed 10 Jan 2007.

Copyright 2007 by Turner White Communications Inc., Wayne, PA. All rights reserved.