



# ARTICLE OF THE MONTH

## Long-term Outcomes after Stenting Versus Endarterectomy for Treatment of Symptomatic Carotid Stenosis: The International Carotid Stenting Study (ICSS) Randomised Trial

Bonati LH, Dobson J, Featherstone RL, Ederle J, van der Worp HB, de Borst GJ, Mali WP, Beard JD, Cleveland T, Engelter ST, Lyrer PA, Ford GA, Dorman PJ, Brown MM; for the International Carotid Stenting Study investigators. *Lancet*. 2014 Oct 14. pii: S0140-6736(14)61184-3. doi: 10.1016/S0140-6736(14)61184-3. [Epub ahead of print] PMID: 25453443

In this inaugural 2015 installment of the SNACC Article of the Month, we start things off right with an important article of the highest possible methodology. The article by Bonati *et al.* is a very large (N = 1713), prospective, multi-center (50 centers), multi-national, long-term (4.2 year median follow-up), randomized trial comparing carotid stenting *versus* endarterectomy in symptomatic patients. The primary outcome of this *Lancet* article was “fatal or disabling strokes”, which did not differ between groups, although total strokes were more common in the stenting group. To shed more light on this subject and this article, we have enlisted the expertise of Guy Edelman, MD, who is the Chief of Neuroanesthesia at the University of Illinois at Chicago. Guy is a long-time SNACC member with a passion for education and was actually the first Neuroanesthesiologist I ever worked with (as a CA-1). We hope you will find this article, and Dr. Edelman’s commentary, enlightening and ask you to share your thoughts by signing on to the [SNACC LinkedIn Feed](#). Hope your holidays were excellent!

~John F. Bebawy, MD

### Commentary

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In the setting of carotid occlusive disease, the evolving evidence base has posed questions regarding the relative safety and efficacy of endovascular therapy. Several well conducted randomized trials and meta-analyses have now been published comparing the results of carotid artery stenting (CAS) to carotid endarterectomy (CEA). Questions remain regarding the internal and external validity for many of these studies. In this month’s AOTM, Bonati *et al* present the long-term results of the ICSS trial. This study represents the largest prospective, randomized trial to date comparing CAS and CEA in symptomatic patients.

In the ICSS, 1713 patients with symptomatic atherosclerotic carotid stenosis were randomized to receive either CAS or CEA procedures. Patients were followed for a median of 4.2 years (IQR 3.0-5.2 years, maximum follow-up 10.0 years). An available online supplement reveals substantial variation in procedural technique for both the CAS and CEA groups. The primary study endpoint was the incidence of fatal or disabling stroke, with secondary endpoints including all-cause mortality, overall stroke incidence and procedural stroke or death. Serial modified Rankin scores measured neurological outcome. Data was analyzed by both intention-to-treat (ITT) and per-protocol basis. By ITT analysis, the incidences of fatal or disabling strokes (CAS 6.4% vs. CEA 6.5%; NS) and all cause mortality were similar. Functional neurological outcome did not differ between treatment groups at one and five year time points. The overall stroke rate was higher in the CAS group (15.2% vs. 9.4%; HR 1.71, 95% CI 1.28-2.30), with the difference ascribed to a higher incidence of non-disabling stroke. In addition, the rate of peri-procedural stroke or death and any ipsilateral stroke was higher in the CAS patients. It was concluded that while CAS and CEA were equivalent in efficacy for preventing severe strokes, the higher risk of non-disabling stroke following CAS must be balanced by the increased risk of myocardial infarction and procedural complications following CEA.

It is unclear whether the CAS methodology used in ICSS reflects current practice in endovascular therapy. In their discussion, the authors addressed the limitations inherent in the ICSS, including the role of operator experience in performing CAS and the fact that carotid artery stenting was a relatively new procedure when the ICSS project began in 2001. In the same issue of *Lancet*, an editorial by Roffi points out that relative endovascular inexperience in the ICSS may have influenced the observed high rate of peri-procedural strokes, as only ten prior CAS procedures were required for surgeon participation. When taking into consideration the limited endovascular experience early in the conduct of the ICSS, plus the subsequent introduction of newer cerebral protection devices for CAS, it could be speculated that current stroke rates may be more favorable for endovascular treatment.

Importantly, the ICSS was inadequately powered to perform patient subgroup analysis. Endovascular treatment is a potential option for patients deemed to be at high medical or surgical risk. As a counterpoint to this study, one is directed to a retrospective review by Spangler (*J Vasc Surg* 2014;60:1227-31). In this series of over 11,000 patients, symptomatic patients undergoing CAS had consistently higher peri-procedural rates of stroke or death than CEA patients, with the highest rates occurring in the medical high-risk subgroup (CAS 9.3% vs CEA 1.5%;  $P < 0.01$ ). While the ICSS offers new long-term neurological outcome data in which CAS is comparable to CEA, the most attractive patients for this modality are frequently those at elevated risk. Going forward, risk-stratified outcome analysis will further define which patients, if any, will be best served by endovascular cerebral reconstruction.