



# Treating symptomatic carotid artery disease: deciding between carotid artery stenting and carotid endarterectomy – balancing the risks

*“While the debate regarding which technique is superior has been ongoing for more than a decade, it is prudent to conclude that each technique has its strengths and limitations and the need of the hour is to individualize patient care based on the risk for myocardial infarction versus the risk for stroke.”*

**KEYWORDS:** carotid artery stenosis ■ endarterectomy ■ stenting

Ischemic stroke is the third leading cause of death in the USA [1,2] and is an important cause of major morbidity and mortality both in the USA and worldwide. Carotid artery disease amenable to revascularization accounts for 5–12% of new strokes [3,4]. Carotid artery angioplasty and stenting (CAS) has evolved as an alternative therapeutic option for the treatment of extracranial carotid artery occlusive disease and the concept was first introduced in 1980 by Kerber *et al.* [5]. The initial problems associated with carotid angioplasty included vessel recoil and dissection and have been successfully addressed with the use of stents. The problems of luminal narrowing due to external compression forces and torsion, have been greatly reduced by the use of self-expanding stents, and distal embolization has been reduced by the use of embolic protection devices. However, CAS has raised much controversy regarding its safety, efficacy and criteria for patient selection.

## Guidelines

The 2010 American Heart Association (AHA) and American Stroke Association guidelines for the prevention of stroke in patients with stroke or transient ischemic attack recommend CAS as an alternative to carotid endarterectomy (CEA) for symptomatic patients at an average or low risk of complications associated with endovascular intervention, when the diameter of the lumen of the internal carotid artery is reduced by greater than 70% by noninvasive imaging, or greater than 50% by catheter angiography (Class I; Level of Evidence B) [6]. In addition, among patients with symptomatic severe stenosis (>70%) in whom the stenosis is difficult to access surgically, medical conditions are

present that greatly increase the risk for surgery, and when other specific circumstances exist, such as radiation-induced stenosis or restenosis after CEA, CAS may be considered (Class IIb; Level of Evidence B). Of note, the former indication has been upgraded from a Class IIa recommendation [7] to a Class I recommendation, largely based on the results of the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST), and this is controversial. The later indication is less controversial and includes patients at high risk for open endarterectomy, defined as patients with severe co-morbidities (Class III/IV congestive heart failure, Class III/IV angina, left main coronary artery disease, greater than or equal to two-vessel coronary artery disease, left ventricular ejection fraction less than or equal to 30%, recent myocardial infarction [MI], severe lung disease or severe renal disease), or challenging technical or anatomic factors, such as prior neck operation (e.g., radical neck dissection) or neck irradiation, post-endarterectomy restenosis, surgically inaccessible lesions (e.g., above C2 or below the clavicle), contralateral carotid occlusion, contralateral vocal cord palsy or the presence of a tracheostomy.

## Evidence

Two recently published large-scale randomized trials comparing CAS versus CEA have reached opposite conclusions. In the International Carotid Stenting Study (ICSS), comparing CEA with CAS in 1713 patients with recently symptomatic carotid stenosis eligible for either procedure, CEA was demonstrated to be superior to CAS at 120 days postprocedure, with increased risk of death/stroke/MI, any stroke



**Sripal Bangalore**

New York University School of Medicine, New York, NY 10016, USA  
sripal.bangalore@nyumc.org

and all-cause death in the CAS group, and a significantly higher risk of cranial nerve palsy was observed with CEA [8]. Of note, the risk of periprocedural MI was similar between the groups (CAS vs CEA: 0.35 vs 0.47%). In the CREST, comparing CEA with CAS in 2502 patients with symptomatic or asymptomatic carotid stenosis, the risk of a 4-year rate of composite primary outcome (periprocedural stroke/MI or death and post-procedural ipsilateral stroke) did not differ significantly between the two groups. However, CAS was associated with a significantly higher risk of 4-year death or stroke, 4-year stroke and periprocedural stroke, and CEA was found to be associated with significantly higher periprocedural MI (2.3 vs 1.1%) and cranial nerve palsy. The rate of MI was substantially higher in the CREST (routine evaluation of cardiac biomarkers and electrocardiogram) than in the ICSS (clinical MI). In addition, the rate of death or any stroke at 30 days was substantially higher in the ICSS than in the CREST, even in the CEA group (3.4 vs 2.3%), which is likely due to enrollment of asymptomatic patients in CREST.

.....  
 “...there will be increasing recognition of the complementary role for a less invasive, percutaneous option in the armamentarium for the treatment of patients with symptomatic carotid artery disease.”  
 .....

We have shown, in an analysis of 13 randomized controlled trials enrolling over 7000 participants, that CAS was associated with an increased risk of both periprocedural (death/MI/stroke; death/stroke and any stroke) and intermediate-to long-term outcomes, but with a lower risk of periprocedural MI and cranial nerve injury [9] when compared with CEA.

### Debate

Proponents of CEA and those of CAS have debated on a number of contentious issues in these trials.

#### ■ Relative importance of stroke versus MI

Carotid artery angioplasty and stenting has been associated with an increased risk of stroke while CEA has been associated with an increased risk of MI. While the value of routinely evaluated periprocedural MI has been questioned, even in contemporary trials of percutaneous coronary intervention, the CREST showed that both major and minor stroke affected mental health at 1 year, while periprocedural MI did not. In

the ICSS, the risk of post-procedural MI (clinical) was similar between the groups. Moreover, all MIs in the CAS group were fatal while those in the CEA groups were not.

#### ■ Relative importance of cranial nerve palsy

Carotid endarterectomy has been consistently associated with an increased risk of cranial nerve palsy. One can argue that from a patient perspective, a cranial nerve palsy is equivalent to a minor stroke, at least in the short term. While even a minor stroke affected health status in CREST, the impact of cranial nerve palsy was not evaluated. Of note, in most of the studies, there was no difference between CAS and CEA for disabling stroke.

#### ■ Operator experience

The question of the impact of relatively inexperienced operators performing stenting versus a well-experienced surgeon performing CEA has not been resolved [10]. This has been hypothesized to be a major player in the difference in outcomes seen in US compared with non-US trials. However, in our meta-analysis, we did not notice any substantial interaction for US versus non-US trials for any of the outcomes tested [9].

#### ■ Optimal embolic protection device

In a meta-analysis of 32 studies, CAS was associated with significantly higher (37 vs 10%;  $p < 0.01$ ) new diffusion-weighted imaging lesions (consistent with distal emboli) compared with CEA [11]. The use of embolic protection devices (EPD) has significantly reduced this incidence [11,12]. In a meta-analysis involving more than 3000 patients, the 30-day rate of death or stroke was 1.8% in patients treated with EPD compared with 5.5% in those who underwent CAS without EPD [13]. However, in the MRI substudy of the ICSS, new ischemic lesions were three times more common in the stenting group than in the endarterectomy group post-treatment [14], and embolic protection devices were not effective in preventing cerebral ischemia during stenting. It is not clear if this was due to embolization during deployment of EPDs.

### Conclusion

Carotid artery stenting and CEA offer complementary options for patients with symptomatic carotid artery disease. While the debate regarding which technique is superior has been ongoing for more than a decade, it is prudent to conclude that each technique has its strengths and

limitations and the need of the hour is to individualize patient care based on the risk for MI versus the risk for stroke. While subgroup analyses from randomized controlled trials have identified certain characteristics (younger patients) [15] as being associated with better outcomes for CAS, these can be best described as hypothesis-generating only. The questions of operator experience, patient selection and optimal EPD can only be resolved by randomized trials designed to address these issues. As the technology for carotid stenting improves with better EPDs used in conjunction with better patient selection, the big debate as to which technique is superior will likely become a thing of the past and there will

be increasing recognition of the complementary role for a less invasive, percutaneous option in the armamentarium for the treatment of patients with symptomatic carotid artery disease.

#### Financial & competing interests disclosure

*The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

*No writing assistance was utilized in the production of this manuscript.*

#### Bibliography

- Mohr JP, Caplan LR, Melski JW *et al.*: The Harvard Cooperative Stroke Registry: a prospective registry. *Neurology* 28, 754–762 (1978).
- Thom T, Haase N, Rosamond W *et al.*: Heart disease and stroke statistics – 2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 113, E85–E151 (2006).
- Inzitari D, Eliasziw M, Gates P *et al.*: The causes and risk of stroke in patients with asymptomatic internal-carotid-artery stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N. Engl. J. Med.* 342, 1693–1700 (2000).
- Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB: The Stroke Data Bank: design, methods, and baseline characteristics. *Stroke* 19, 547–554 (1988).
- Kerber CW, Cromwell LD, Loehden OL: Catheter dilatation of proximal carotid stenosis during distal bifurcation endarterectomy. *AJNR Am. J. Neuroradiol.* 1, 348–349 (1980).
- Furie KL, Kasner SE, Adams RJ *et al.*: Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack. A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 42(1), 227–2276 (2011).
- Sacco RL, Adams R, Albers G *et al.*: Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 37, 577–617 (2006).
- Brown M, Ederle J, Bonati L *et al.*: Safety results of the International Carotid Stenting Study (ICSS): early outcome of patients randomised between carotid stenting and endarterectomy for symptomatic carotid stenosis. Presented at: *European Stroke Conference*. Stockholm, Sweden, 26–29 May 2009.
- Bangalore S, Kumar S, Wetterslev J *et al.*: Carotid artery stenting vs carotid endarterectomy: meta-analysis and diversity-adjusted trial sequential analysis of randomized trials. *Arch. Neurol.* DOI: 10.1001/archneurol.2010.262 (2010) (Epub ahead of print).
- Roffi M, Sievert H, Gray WA *et al.*: Carotid artery stenting versus surgery: adequate comparisons? *Lancet Neurol.* 9, 339–341 (2010).
- Schnaudigel S, Groschel K, Pilgram SM, Kastrup A: New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke* 39, 1911–1919 (2008).
- Wholey MH, Al-Mubarek N: Updated review of the global carotid artery stent registry. *Catheter Cardiovasc. Interv.* 60, 259–266 (2003).
- Kastrup A, Groschel K, Krapf H, Brehm BR, Dichgans J, Schulz JB: Early outcome of carotid angioplasty and stenting with and without cerebral protection devices: a systematic review of the literature. *Stroke* 34, 813–819 (2003).
- Bonati LH, Jongen LM, Haller S *et al.*: New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). *Lancet Neurol.* 9, 353–362 (2010).
- Bonati LH, Dobson J, Algra A *et al.*: Short-term outcome after stenting versus endarterectomy for symptomatic carotid stenosis: a preplanned meta-analysis of individual patient data. *Lancet* 376, 1062–1073 (2010).