Carotid Artery Disease: Current Treatment Strategies

Written by Mary Mosley

Medical treatment, lifestyle management, and revascularization are complementary strategies to treat carotid artery disease to reduce stroke and cardiovascular events. The degree of carotid stenosis increases the risk of stroke, with an annual incidence of about 3% for an 80% to 89% stenosis and nearly 5% with a 90% to 99% stenosis in asymptomatic patients. Clinical trial data showed the annual stroke risk was 2% to 2.5% in asymptomatic and 4.4% to 13% in symptomatic patients who had a standard surgical risk. However, advances in medical therapy such as inhibitors of the renin angiotensin system and statins since these trials were conducted and the variability in lesion severity and morphology, among other factors, may impact these stroke rates, noted Rajeev L. Narayan, MD, Hackensack University Medical Center, Hackensack, New Jersey, USA.

Medical therapy is required for all patients with carotid artery disease and includes antiplatelet agents, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and statins. As a class, antiplatelet therapy reduced stroke or transient ischemic attack by 22% in a meta-analysis by the Antiplatelet Trialists' Collaboration. Notably, aspirin is not recommended for primary prevention of stroke because of the lack of a consistent benefit [Goldstein LB et al. *Circulation*. 2006].

For secondary prevention of stroke, ticlopidine or dipyridamole added to aspirin reduced stroke, with a 21% relative risk reduction in nonfatal or fatal stroke in the Ticlopidine Aspirin Stroke Study and about a 10% reduction in the European Stroke Prevention Study. However, the PROFESS study [Sacco RL et al. *N Engl J Med*. 2008] showed a similar reduction in the first recurrent stroke with aspirin plus dipyridamole compared with clopidogrel (HR, 1.01; 95% CI, 0.92 to 1.11) and for the combination of stroke, myocardial infarction (MI), and death (HR, 0.99; 95% CI, 0.92 to 1.07). A similar reduction in ischemic stroke was also found with aspirin plus clopidogrel vs clopidogrel alone in patients who had a transient ischemic attack in the MATCH study. An anticoagulant provided similar outcomes to an antiplatelet for primary and secondary stroke prevention, according to data from the TAIST trial.

Treatment to control blood pressure to reduce the risk of stroke should include a diuretic and an ACE inhibitor or ARB, stated Dr Narayan. Statins have been shown to reduce the risk of stroke, and high-dose statins produced even greater reductions for primary and secondary prevention in the JUPITER [Ridker PM et al. *N Engl J Med*. 2008] and SPARCL studies.

Revascularization with carotid endarterectomy (CEA) and carotid artery stenting (CAS) are associated with excellent long-term patency and prevention of ipsilateral stroke, but the keys are judicious patient selection and experienced, high-volume operators with good technique, according to D. Christopher Metzger, MD, Wellmont CVA Heart Institute, Kingsport, Tennessee, USA. The choice of CEA or CAS should be personalized to a patient's level of risk.

CEA was established as the gold standard for revascularization; however, Dr Metzger noted the results are not the same as in the clinical trials when it is performed by inexperienced operators or in high-risk patients. The relative risk reduction in ipsilateral stroke was 53% in asymptomatic patients in the ACAS study and 65% in symptomatic patients in the NASCET study with CEA vs medical therapy ($P < .001$ for both). But, even with experienced operators and low-risk patients with contralateral lesions, 14.3% of patients had a stroke or died, he stated.

CAS is reserved for high-risk patients who have a higher 30-day risk of stroke and death. CAS was better than CEA in reducing major adverse events, which included stroke, death, and MI, at 30 days (12.0% vs 20.1%; $P = .05$) and had lower rates of cranial nerve injury (0% vs 5.3%; $P = .003$) and target vessel revascularization (0.7% vs 4.6%; $P = .04$) in the SAPPHIRE trial.

The CREST trial [Brott TG et al. *N Engl J Med*. 2010] showed that outcomes were similar with CAS and CEA. The event rate for the primary outcome of stroke, MI, or death during the

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Table 1. CREST Trial Outcomes

	CAS	CEA	HR (95% CI)	*P* Value
Primary outcome[a]	7.2	6.8	1.11 (0.81 to 1.51)	.51
Periprocedural stroke	4.1	2.3	1.79 (1.14 to 2.82)	.012
Periprocedural major stroke	0.9	0.6	1.35 (0.54 to 3.36)	.52
Periprocedural MI	1.1	2.3	0.50 (0.26 to 0.94)	.032
Postprocedural ipsilateral stroke	2.0	2.4	0.94 (0.50 to 1.76)	.85
Cranial nerve injury	0.3	4.7	0.07 (0.02 to 0.18)	NR

Data presented in percentages.

CAS, carotid artery stenting; CEA, carotid endarterectomy; MI, myocardial infarction; NR, not reported.

[a]Primary outcome comprised stroke, MI, or death during the periprocedural period plus ipsilateral stroke thereafter.

Source: Brott TG et al. *N Engl J Med*. 2010.

periprocedural period plus ipsilateral stroke thereafter was similar for both, and no significant difference was seen for major strokes during the periprocedural period (Table 1). After the periprocedural period, there was a low rate of ipsilateral stroke out to 4 years. Cranial nerve injury was significantly lower with CAS ($P < .001$).

Outcomes with CAS continue to improve as shown by large, prospective registries. The final results are expected soon from the phase 3 ACT I trial [NCT00106938] with standard-risk patients, which aims to show the noninferiority of CAS with embolic protection against CEA.

Carotid ultrasound (CUS) is not recommended for all patients, but it may be a useful tool, stated Ido Weinberg, MD, Massachusetts General Hospital, Boston, Massachusetts, USA, to evaluate patients with hemispheric neurologic symptoms, cervical bruit, pulsatile neck mass, subclavian steal, or nonatherosclerotic carotid artery pathology. CUS is also used to follow patients with proven carotid artery disease and for evaluation after CEA or CAS.

The routine use of CUS to identify and quantify carotid intimal media thickness is not recommended because of a low level of evidence, and it has only incremental value for reclassifying risk. The ankle brachial index, coronary calcium score, and inter-arm blood pressure measurement provide the same information, without the technical skill required to use CUS, including the ability to differentiate plaque from the intima and media layers of the artery. Finally, there appears to be little value to assess the presence of coexisting carotid disease in patients undergoing a coronary artery bypass surgery, because the outcomes and adverse events are similar whether the surgeries are simultaneous or consecutive [Tomai F et al. *JACC Cardiovasc Interv*. 2011].