Trials to Evaluate CEA Versus CAS in Carotid Artery Stenosis

Written by Emma Hitt Nichols, PhD

Several large trials evaluating the efficacy of carotid endarterectomy (CEA) versus carotid artery stenting (CAS) are currently underway, with a large meta-analysis to include data from over 5000 patients planned for 2019. Alison Halliday, MD, University of Oxford, Oxford, United Kingdom, reflected on the results of the ACST-2 [Halliday A et al. *Eur J Vasc Endovasc Surg* 2013], SPACE-2 [Reiff T et al. *J Stroke* 2009], and CREST-2 trials.

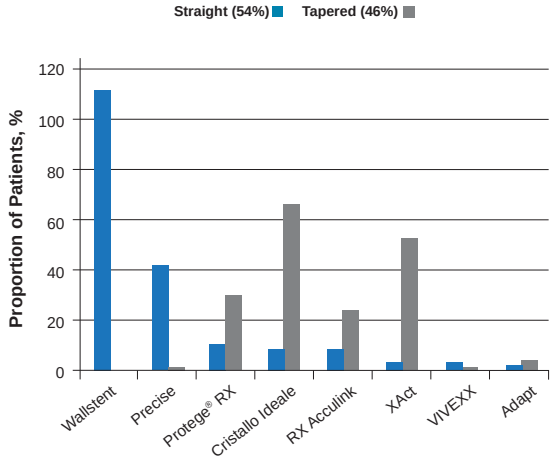
Carotid stenosis can be attributed to ~20% of ischemic strokes. Over the past 40 years, multiple clinical trials have evaluated the efficacy of CEA versus no intervention and CEA versus CAS. In the 1990s, the ACST-1 trial evaluated immediate versus deferred CEA, in which both physician and patients were substantially uncertain about the need for immediate CEA [Halliday A et al. *Lancet* 2004]. In the ACST-1 trial, the hazard of surgery was ~3%, but the absolute risk of stroke was decreased by 6% over 10 years in both men and women. In 2010, the CREST trial randomized 1183 asymptomatic patients with carotid artery stenosis to undergo CAS or CEA [Brott TG et al. *N Engl J Med* 2010]. The primary endpoint of the trial was the composite of stroke, myocardial infarction, or death from any cause during the periprocedural period or any ipsilateral stroke within 4 years after randomization. There was no difference in the primary endpoint of the trial between CAS and CEA (7.2% vs 6.8%; HR, 1.11; 95% CI, 0.81 to 1.51; p=0.51).

It would be ideal to design a randomized controlled trial that evaluates the efficacy of CEA, CAS, and best medical treatment (BMT) simultaneously; however, the number of patients required is too large. Therefore, several trials are currently ongoing that will evaluate the best intervention for carotid artery stenosis separately.

The SPACE-2 study will have two sub-trials: SPACE-2A will evaluate CEA plus BMT versus BMT alone and SPACE-2B will evaluate CAS plus BMT versus BMT alone [Reiff T et al. *J Stroke* 2009]. Approximately 1636 patients will be enrolled and randomized in each sub-trial.

In 2010, the multicenter ACST-2 trial began enrollment to directly evaluate CEA versus CAS in asymptomatic patients with tight stenosis requiring intervention [Halliday A et al. *Eur J Vasc Endovasc Surg* 2013]. Enrollment reached 1287 in 2013, and the first 1000 patients had a median age of 71, with 96% of patients having 70% to 99% stenosis and 20% of patients having 70% to 100% contralateral stenosis. In addition, 30% of patients had diabetes, 11% renal failure, 6% atrial fibrillation, and 37% ischemic heart disease. In ACST-2, 93% of patients were receiving antiplatelet therapy, 89% antihypertensive therapy, and 85% lipid-lowering therapy at study entry. In the first 800 patients, 54% received a straight stent and 46% received a tapered stent (Figure 1). Preliminary results demonstrate that the rate of disabling and fatal stroke or myocardial infarction at ≤30 days is 1%, which is reduced from 1.7% in the previous ACST trial. By 2019, it is expected that enrollment for ACST-2 will reach ~3000 patients, and a metaanalysis including CREST-2, SPACE-2, and ACST-2 is planned that will include >5000 patients.

Figure 1. Stents Used in the First 800 Patients of ACST-2



Data from large trials that evaluate CEA versus CAS head-to-head is greatly anticipated and has the potential to provide a foundation for evidence-based medicine in the treatment of carotid artery stenosis.

System Changes to Ensure Patient Safety and Access to Innovative Devices

Written by Mary Mosley

The Center for Devices and Radiological Health (CDRH) of the United States Food and Drug Administration (US FDA) has undertaken work to refine its direction towards smart regulation, to protect public health by ensuring safe devices, and to promote public health by facilitating device innovation, according to Christy Foreman, Director of the Office of Device Evaluation at CDRH. She reviewed the updated mission, vision, and strategic plan for the CDRH, and its impact on regulatory science, clinical trials, feasibility trials, and pre- and postmarketing data.

In particular, the CDRH strives to ensure that patients in the US have access to high-quality, safe, and effective medical devices that will be available in a timely fashion. In accordance with this mission and vision, six strategic priorities have been developed to achieve the CDRH goal: