Treatment for routine, symptomatic, carotid bulb atherosclerosis

Carotid endarterectomy and stenting are comparable

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The results of recent carotid artery stenting (CAS) vs carotid endarterectomy (CEA) randomized studies (CREST,¹ SPACE,² EVA3S,³ and ICSS⁴) have created conflict among surgical and endovascular communities over which procedure is preferred for secondary stroke prevention for symptomatic carotid stenosis. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) established CEA as the gold standard for surgical treatment in the early 1990s. Carotid stenting has been held to the high standard of CEA, and in order to present

a viable alternative surgical therapy, it must be effective at preventing strokes, durable, and safe, with complication rates comparable to CEA.

Carotid stenting is a clinically effective procedure. CREST, SPACE, and EVA3S showed equivalent annual stroke rates for the 2 treatments in symptomatic patients after the initial 30

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days (CEA vs CAS: 0.8 vs 0.6, 1.3 vs 1.4, and 0.7 vs 0.4, percent per year, respectively). The stroke-free survival curves in CREST for CEA and CAS are parallel after the perioperative period out to 4 years, indicating clinical durability.

Perioperative safety remains the controversial point; the 30-day stroke and death rate for the stented patients was over 2 times that of the surgical group in the EVA3S trial. In the ICSS trial, the CAS group suffered stroke or death twice as often as the CEA group. Complications rates were, at best, equivalent in the 2 groups in the SPACE trial (6.3% for CEA and 6.8% for CAS), with CAS not achieving noninferiority. Why the difference between the 2 treatment cohorts in these trials? When discussing complications, one has to consider the technical experience of the treating physicians, and in these trials, the required training of the carotid stenting physicians was minimal to nonexistent. In the EVA3S and ICSS trials, operators could enroll patients without ever having performed a carotid stenting procedure, or a cerebral angiogram. Operators in the SPACE trial had to have placed 25 carotid or vertebral stents before enrolling patients, but there was no specific required carotid stenting experience, and no scrutiny of technique or results before physicians were allowed to enroll patients.

Conversely, in the CREST trial, a rigorous process was implemented to credential physicians to perform CAS. Operators had to submit records of CAS cases, including admission notes, indications for CAS, procedure reports, and discharge summaries. Criteria used for consideration were low complication rate, experience with at least 15 procedures, and use of proper technique. Once approved, candidates were trained on the trial devices and then proceeded with enrollment in the “lead-in” phase, requiring performance of 5 to 20 procedures, depending upon their previous experience, which was closely monitored for major complications. In this “lead-in” period of the study, the 30-day stroke and death rate for symptomatic patients was 5.8%, which fell to 4.5% if subjects older than 75 years were excluded.⁵

The primary combined endpoint of stroke, death, and myocardial infarction (MI) was statistically equivalent between CEA and CAS in CREST. Predictably, the attention to credentialing of CAS physicians in CREST resulted in the lowest reported 30-day stroke and death rate in symptomatic patients in a randomized trial—6%—which is equivalent to the complication rate in the CEA arm of NASCET. Hence both CEA and CAS enjoy a wide margin of superiority over medical treatment for this disease. However, the perioperative stroke rate in the CEA arm was also the lowest yet reported, and so there were statistically more perioperative strokes in CREST in the CAS group than in the CEA group (6% vs 3%). The difference was entirely due to minor stroke, as major stroke and death were equivalent. Conversely, there was a statistically higher incidence of MI in the CEA group than in the CAS group. The increase in minor stroke in the CAS group and the increase in perioperative MI in the CEA group offset one another, leading to the equivalent primary endpoint.

Minor stroke is important. Patients who experienced a minor stroke were more likely to have a diminished health-related quality of life (HRQOL) at 1 year, even though their modified Rankin Scale and NIH Stroke Scale scores were equivalent to other patients at 6 months. However, perioperative MI is also important. Affected patients did not have a diminished HRQOL, but were statistically more likely to die in the follow-up period than patients who did not have a perioperative MI. Therefore, the cumulative endpoint of stroke, death, and perioperative MI is clinically relevant and all components are important. As CREST demon-

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strates statistical equivalence of CEA and CAS for this endpoint, both carotid stenting and CEA should be considered for all symptomatic patients with significant carotid stenosis.

There are other considerations. First, cranial nerve palsy was not a component of the primary endpoint in CREST, but 5% of CEA patients experienced cranial nerve palsy. This is surely one component leading to the initial superiority of CAS over CEA in the HRQOL scores—a superiority that is not maintained long term, but does seem to be important to patients, as does the idea of a “minimally invasive” procedure with a faster recovery time. Second, as seen with CEA, the perioperative risk of CAS will likely decline, primarily due to increasing experience with the procedure. A recent study⁶ confirms the importance of operator experience and procedural volume in clinical outcomes. In an observational study using Medicare data, an increased 30-day mortality rate was seen in patients treated by operators with lower annual volumes (<6 = very low volume to >24 = high volume) and patients treated by operators early in their experience (first–11th procedure). The mortality rate was double (1.9%) in the elderly patients treated by novices, when compared to mortality rates in other clinical trials with more seasoned operators, such as SAPHIRE and CREST. In fact, the risk of the procedure trended downward during the CREST trial, despite no significant change in the technology. Better patient selection will also play a role. Patients considered “high risk” for CEA were excluded from CREST. For example, patients with anatomic risk factors which make CEA more difficult, such as prior CEA, neck dissection, and neck radiation, were excluded. However, there was no uniform attempt to exclude patients at high risk for CAS within CREST. Factors such as tortuosity and disease of the aortic arch, heavy calcification of the carotid stenosis, and long length of the lesion increase the risk of carotid stenting. These features do not adversely affect CEA, but they were unknown in most patients prior to randomization in CREST because most patients were randomized based on ultrasound, where evaluation for high-risk CAS features is often not performed. The increased rates of stroke and death in the over-70 years of age population may be due to the increased incidence of these anatomic features in the elderly. Avoiding patients with high-risk CAS features should lower the perioperative risk of the procedure. Next, the technology of carotid stenting continues to advance, with improved “cerebral protection” devices and techniques, such as flow reversal, which may be more effective at preventing small cerebral emboli. In addition, advanced imaging of carotid plaques may help stratify patients to CAS or CEA based upon plaque morphology. Finally, there may be additional gain from standardization of adequate antiplatelet therapy during and after the procedure.

The CREST trial has proven the equivalence of CEA and CAS for symptomatic carotid stenosis. We now have 2 effective surgical treatments for this disease, and both enjoy a large margin of superiority over medical treatment alone. Both should be considered for all patients, and patients should be educated about both treatment options.

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DISCLOSURES

Dr. Jensen serves on a speakers bureau for and has given lectures on behalf of eV3; is listed as an author on patents re: Trocars designed for vertebroplasty, Percutaneous spinal fusion device, and Breast localization needle; serves as a consultant for Kuros Inc.; performs acute stroke therapy and carotid stenting (5% of clinical effort); and receives royalties from Stryker for a patent re: Percutaneous spinal fusion device. Dr. Heck serves as a consultant for Gore and receives research support from Cordis, Abbott, and Penumbra.