Carotid Artery Stenting in 2007

An overview of some of the issues, controversies, and recent data.

BY GERALD ZEMEL, MD

Stroke is the third leading cause of death in the US today. Because many ischemic strokes are linked to carotid artery disease, it is not surprising that treatment of the disease is the focus of one of the most intense debates in vascular medicine. At the center of the debate is, what is the best approach? Is it medical management, carotid endarterectomy, or carotid angioplasty and stenting? While we await results of hopefully definitive trials, such as TACIT (Transatlantic Asymptomatic Carotid Intervention Trial) and CREST (Carotid Revascularization Endarterectomy versus Stenting Trials), it is becoming clear that the answer is not so simple. In fact, the best treatment is likely dependent on a number of patient-specific issues, ranging from the nature of the plaque to risk factors.

Currently, surgery is considered the standard of care, except for patients at high surgical risk. The US Food and Drug Administration (FDA) has approved carotid angioplasty and stenting only for use in symptomatic patients with ≥70% stenosis who are at high surgical risk.

Even staunch supporters of surgery likely realize that stenting will not remain so limited in use (officially and unofficially) for long. Until fairly recently, many skeptics, including interventionists, doubted that stent placement would negate the risk of stroke, but with the advent and subsequent improvement of distal protection devices, improved stents, and new techniques such as flow reversal, it is clear that carotid stenting is here to stay. This is undoubtedly true, despite recently published prosurgery studies (including EVA-3S)[1] that cast aspersions on the procedure but were flawed in design.

Compared to endarterectomy, stenting is less invasive, has a faster recovery time, and eliminates the risk of nerve injury. Also, anecdotally, stenting appears to be very durable, with 1-year restenosis rates reported as low as 1%, although longitudinal studies are required for validation. Existing longitudinal registries may shed some light; unfortunately, they do not provide a comparison to surgery. Restenosis rates after surgery—reported from trials as a byproduct, not a specific complication—range from 3% to 10% at 1 year. Interestingly, with the exception of patients who have had neck radiation, carotid stenting appears to be one of the most, if not the most, durable of all stenting procedures, presumably due to low resistance blood flow.

"Even staunch supporters of surgery likely realize that stenting will not remain so limited in use (officially and unofficially) for long."

Many interventionists strongly believe that stenting is likely to overtake endarterectomy as the standard of care, much as endovascular repair of abdominal aortic aneurysms is surpassing open surgical repair. In the not too distant future, in fact, surgery may be reserved for patients who are at high risk for stenting, rather than the converse.

That said, there are a number of ongoing controversies and issues regarding carotid stenting that must be resolved, ranging from defining the high-risk stent patient and agreeing on the best selection criteria to determining appropriate use of embolic protection devices.

WHEN TO INTERVENE?

Through the years, specialists in carotid artery disease have continued to struggle with the question of when to intervene. Stroke and death are risks of both stenting and surgery, and while the definitive acceptable stroke and death risk of each treatment has not been determined, obviously the risk of treatment should not outweigh the risk of stroke or death due to disease. Generally, accepted risk of perioperative stroke or death from intervention is less than 6% and 3%, for symptomatic and asymptomatic patients, respectively.

Currently, asymptomatic patients with stenosis of less than 60% typically are managed medically. Symptomatic patients with greater than 50% stenosis may be candidates for more invasive treatment, whether stenting or surgery. In

contradistinction to the 70% high-risk symptomatic FDA requirement, two-thirds of strokes occur in previously asymptomatic patients. In the real world, 75% of people undergoing stenting or endarterectomy today are asymptomatic.

Newer evidence suggests that, in assessing risk for carotid stenting, we should be less concerned about restriction of blood flow (due to stenosis) and more concerned about the type of plaque involved. Although there is some correlation between the percentage of stenosis and the likelihood of embolization, newer findings suggest that the type of plaque involved is as much of a concern as stenosis, if not more. Plaque that is lipid-laden, nonfibrous, and noncalcified—so-called "vulnerable" plaque—likely poses greater embolic risk during a stenting procedure. Many patients with this vulnerable plaque may not have a high degree of stenosis, or symptoms, and yet, due to the nature of the plaque, are in fact at high risk for stroke and death. We need to identify the best diagnostic approaches to determine the morphology of the plaque prior to treatment, as well as which patients are more likely to be at risk from vulnerable plaque.

Furthermore, a relatively new finding being reported at ISET by Rodney Raabe, MD, challenges the conventional definition of symptomatic carotid artery disease. Using a series of sophisticated psychological and cognitive tests, Dr. Raabe found that cognitive function is more likely to decline in asymptomatic patients with carotid artery disease who are treated medically than in those who undergo angioplasty and stenting, suggesting that the disease leads to neurological deficits. Although it is not clear what percentage of stenosis results in reduced cognitive function, it is intuitive that we are likely defining symptomatic carotid artery disease too narrowly.

CHOOSING THE PROCEDURE

The two major controversies facing interventionists today are choosing the appropriate stent and protection device based on the variables, such as the type of plaque, age, and anatomy that will define the high-risk stent patient.

> "Newer evidence suggests that . . . we should be less concerned about restriction of blood flow (due to stenosis) and more concerned about the type of plaque involved."

Despite early skepticism regarding the benefit of distal embolic protection devices, placing these devices has become commonplace to the extent that it is the rare carotid stenting procedure today that does not include one. Although there likely never will be a definitive study comparing use of embolic protection to stenting without such a device, findings from CAPTURE (the Carotid RX Acculink/RX Accunet Post-Approval Trial to Uncover Unanticipated or Rare Events) suggest protection devices are necessary because predilatation without protection, prior to stent placement, resulted in a fourfold increase in major ischemic events. Updated results of 2,500 patients tracked through the CAPTURE registry are being presented at ISET.

Although it is early, evidence is emerging that different stents and distal protection devices may be more or less effective depending on the anatomy of the patient, the characteristics of the plaque, as well as other risk factors. We continue to study these variables, and it is likely that

ISET PRESENTATIONS

The following presentations, and more, will be explored at the upcoming International Symposium on Endovascular Therapy (ISET), January 28 – February 1, 2007, in Hollywood, Florida. Included among the nearly three dozen CAS-related presentations and talks at ISET are:

- "A Perspective on Carotid Stenting in 2007," a keynote lecture given by William A. Gray, MD, an interventional cardiologist at Columbia University College of Physicians and Surgeons and a principal investigator for several CAS trials (including CREST).
- "Carotid Stenting Should Be More Widely Utilized," a debate featuring Mark Wholey, MD, taking the pro side, and Anthony Comerota, MD, taking the con.
- Three entire sessions focusing on carotid stenting, including assessment of the postmarket trials, the relationship of outcome to device characteristics, a discussion of the true meaning of "asymptomatic," and various talks on embolic protection.

Additionally, a session is being devoted to imaging and diagnosis of carotid disease, and ISET 2007 will continue its signature dedication to presenting live cases.

For complete conference information, please contact Complete Conference Management at questions@ccmcme.com.

a protocol will be developed to guide interventionists in the use of the appropriate devices, depending on particulars of the patient. Current evidence suggests that stenting is riskiest in patients who have extremely tortuous vasculature that is heavily calcified, who are of advanced age, and whose plaque is friable and embologenic.

Tortuous vessels make placement of the stent and deployment of embolic protection devices risky. In some cases, stent placement is less of a concern than the ability to advance the embolic protection device distally. In cases in which it is determined during the procedure that the protection device cannot be placed safely, the question remains whether to continue to stent or to abort the procedure entirely. This is an area that requires more thorough study.

We know that cerebral reserve decreases with age, and, therefore, older patients may not be able to tolerate the emboli that are inevitable as a result of nearly every stenting procedure. Atherosclerotic debris may be minimized with the use of embolic protection devices, but it is not negated and may continue to be cause for concern. Younger patients with greater cerebral reserve are more likely to tolerate tiny emboli than older patients with less reserve. Investigators are exploring alternative protection devices, including a new approach that utilizes carotid flow reversal to eliminate the risk of emboli to the brain.

THE FUTURE

We have clearly established that the carotid stent procedure is a viable, effective, and durable alternative to carotid endarterectomy. Its appropriate place in the treatment of carotid disease has yet to be firmly defined. Consider that it is possible we may find that asymptomatic disease is best treated medically, and that the symptomatic patient should undergo endarterectomy, thus relegating the stent procedure to the very small group of symptomatic, high-surgical-risk patients (sound familiar?). ■

Gerald Zemel, MD, is from the Baptist Cardiac and Vascular Institute, Miami, Florida, and is ISET Course Director. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Zemel may be reached at (786) 596-5990; geraldz@baptisthealth.net.

1. Mas JL, Chatellier G, Beyssen B, et al. Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med. 2006;355:1660-1671.