INVITED COMMENTS

Scientific evidence demonstrating the safety of carotid angioplasty and stenting: Do we have enough to draw conclusions yet?

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At two national conferences in November 1997, the American Heart Association conference and the Montefiore Medical Center Current Issues and Techniques in Interventional Radiology conference, the treatment of carotid atherosclerosis by carotid angioplasty and stenting was represented by prominent speakers as a proven form of treatment. The speakers recommended that this new treatment for the prevention of stroke be used by cardiologists and interventional radiologists because the results are known to be safe and cost-effective. This view appears to be held increasingly by specialists who use catheter-based therapy as the only form of interventional or procedural therapy in vascular disease.

Specialty partisanship is a poor basis for recommendation of treatment to patients, especially if the partisanship is motivated by turf-control issues or economic anxiety. The best foundation for perspective on a new therapy is scrutiny of the best available scientific evidence. This familiar process has served well for a long time. What evidence is available now to form a conclusion about carotid stenting? A peer-reviewed, externally adjudicated, randomized trial has never compared carotid stenting and carotid endarterectomy. The experience that has been reported can be classified into the following three categories: abstracts, anecdotal reports, and clinical series.

Many reports are available only in abstract form. These reports usually have been accompanied by verbal presentations at scientific meetings where personality and audiovisual aids also influence the message. For example, a large carotid stent series from Europe with more than 600 cases was presented verbally and summarized only in abstract form. Such a large amount of clinical information cannot be adequately described so briefly. Yet, this particular series is cited frequently during public discussions of carotid stenting.

Two abstracts on carotid stenting from the American Heart Association meeting illustrate how brief reports provide incomplete evidence. One study compared two groups of patients who received bilateral carotid stenting either simultaneously at a single procedure or sequentially by staged procedures.[1] Two strokes and one death occurred in the first group, and four strokes occurred in the second group. The authors concluded that "bilateral carotid stenting can be successfully performed during the same procedure" and that the "risk of neurologic complications is not higher when compared with staged procedures." An alternative analysis might conclude that because bilateral carotid stenting yielded six strokes and one death in the total of 42 patients, bilateral carotid stenting is unacceptably dangerous whether staged or simultaneous. No details are available to help understand how the authors could conclude that this experience was "successful."

In another presentation, comparison was made between carotid stenting and carotid endarterectomy in patients who were more than 80 years old.[2] In the group of 30 patients who underwent stenting there were one major stroke, three minor strokes, and one death. In the group that underwent endarterectomy there were no strokes or deaths, but there were three temporary cranial nerve palsies. The following conclusions were made: "1. Minor neurologic complica-

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tions (minor stroke and cranial nerve palsies) are comparable," and "2. Even though the stented patients had higher co-morbidity, the non-neurological complications were lower and the hospital stay was shorter compared to patients undergoing endarterectomy." An alternative analysis would be that cranial nerve palsy and minor stroke have not been counted as equal endpoints in previous studies. By the usual stroke and death endpoints, carotid endarterectomy was significantly more successful than stenting ($p = 0.024$, Fisher's exact test). Again, we should await a detailed report before we draw conclusions. Although abstracts and verbal presentations play an important role in the process of information distribution, they nevertheless do not provide the best level of scientific evidence to draw conclusions regarding the safest remedy for serious conditions, such as those that threaten stroke.

From 1983 to the present, many manuscripts that appeared in all types of journals have reported groups of patients treated by a variety of catheter-based procedures. The following problems exist with these reports: in general, the number of patients treated is small; the data that describe their condition are incomplete; the process used to select for this type of intervention is not described; and outcome beyond the immediate time of the procedure is not provided. Perhaps the greatest difficulty with these anecdotal reports is their tendency to group together patients with different types of lesions and dissimilar natural histories or stroke risks. Thus anecdotes in a collection remain anecdotes even with larger numbers. Still, such reports do have value: they at least show technical feasibility, and they help lead to more systematic examinations at higher levels of evidence. However, the reports do not provide the best level of evidence themselves.

Few reports of carotid stenting published in complete manuscript form describe patient characteristics, indications for treatment, and objectively assessed results.[3-7] These clinical series have come from single institutions, and the participants have described their own results. Sometimes these same investigators have been involved with the development of medical devices that pertain to carotid stenting. They cannot be expected to be free of bias under such circumstances.

Now, in 1997, we have entered an era of industry-sponsored trials of carotid stenting devices. At least four such trials are open in the United States, and others exist in Europe. Some of these trials are designed to directly compare carotid stenting with carotid endarterectomy, and other trials function, at least initially, as registries to document safety and efficacy issues. An industry-sponsored trial may yield well-documented data and certainly involves outside review of results. Nevertheless, the focus of this type of trial is different from that of a trial funded by an independent agency with an external peer review. Although an industry-sponsored trial may be scrupulously organized and may include an endpoints adjudication committee and a data safety and monitoring board, the trial nevertheless is aimed at getting a product to market. Such a study, no matter how carefully executed, cannot be expected to provide the best level of evidence because of the overlying intention to support the development of commercial enterprise.

In 1997, two proposals were submitted to the National Institutes of Health (NIH) for randomized trials to compare carotid endarterectomy and carotid stenting, Carotid Revascularization Endarterectomy versus Stent Trial (CREST) and Carotid Artery Stenting versus Endarterectomy Trial (CASET). Each proposal was offered by an interspecialty group of physicians with expertise in cerebrovascular disease and clinical investigations. The process of review is ongoing. The process is complex partly because the two proposals are from separate groups. Major issues include establishment of a level of procedural expertise required to most safely apply catheter-based therapy, anticipated changes in the relevant medical devices, and consensus on whether clinical equipoise exists to the extent required to ethically randomize patients between the two treatments.

Consideration of these difficult and critically important issues takes time. Meanwhile, the promotion of carotid stenting at many continuing-education programs and the expanding experience of institutions that participate in industry-sponsored trials continues. These forces conceivably may generate so much enthusiasm and momentum for carotid stenting that the procedure may become accepted practice without the best level of evidence available.

In this event, comparison to the history of carotid endarterectomy may be drawn. The fundamental premise for two prominent NIH-sponsored trials on carotid endarterectomy, the North American Symptomatic Carotid Endarterectomy Trial[8] and Asymptomatic Carotid Atherosclerosis Study[9] was that the procedure had come into general use without the support of the best level of evidence. The lack of such evidence lead to contentious differences of opinion among specialties about the proper place of carotid endarterectomy during the 1970s and 1980s.

Patients were not served well by conflicting advice about the safest course of action. Will carotid stenting repeat this history?

Major patient morbidity rates and enormous financial costs are at stake in the management of carotid disease. An effort to acquire the best level of evidence as soon as possible would be the most beneficial for patient care and conservation of health care resources. The proponents of randomized clinical trials between carotid endarterectomy and carotid stenting should meet the requirements of the NIH so that a properly funded trial can be approved quickly. We need to have the best level of evidence before we draw conclusions.

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