Carotid Artery Balloon Angioplasty and Stenting (CABAS): A Neuroradiologic Perspective

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Stroke is the third leading cause of death in the United States, with at least half a million strokes newly diagnosed per year. Most are noncardiogenic, and the majority of those are related to carotid artery atherosclerosis. The cost of treating stroke totals more than $30 billion a year, which does not include the emotional and social costs involved (1). There are effective treatments for carotid artery disease. Randomized prospective surgical trials (North American Symptomatic Carotid Endarterectomy Trial [NASCET] and European Carotid Surgery Trial [ECST]) have shown a significant reduction in the risk of stroke in symptomatic patients with severe carotid stenosis (>70%) who undergo carotid endarterectomy versus optimal medical therapy. In the NASCET study, symptomatic patients with greater than 70% stenosis had a 2-year cumulative risk of stroke of 26% with optimal medical therapy, versus 9% risk with carotid endarterectomy ($P < .001$). For major stroke and death, a risk reduction of 10.6% was identified with surgery. A recent reassessment by the American Heart Association (AHA) Stroke Council indicates that carotid endarterectomy is three times as effective as medical therapy alone in reducing the frequency of stroke (2). The benefits are dependent on maintaining a low complication rate. The perioperative stroke/death rate for symptomatic patients in the NASCET study was 5.8%, and the rate of major stroke and death was 2.1%. For the ECST study, the rate of stroke and death was 7.5%. These rates include any event after randomization, even when preoperative.

While the demonstrated utility of surgery for improving outcome in patients with severe carotid stenosis is an important advance, the complication rates, while acceptable, leave room for improvement. In fact, some authors suggest that since surgical expertise varies in the community, overall complication rates are higher than reported by NASCET. One report suggests that endarterectomy in high-risk patients may have a stroke risk of up to 18% (3).

Progressive advances in catheter-based techniques and equipment have led to active pursuit of alternative endovascular approaches to carotid stenosis that might offer the same efficacy as carotid endarterectomy with less morbidity. Carotid artery balloon angioplasty and stenting (CABAS) may be such an approach. Theoretical advantages of CABAS include the ability to monitor neurologic status during the entire procedure (local anesthesia is not uniformly employed for endarterectomy), to reach very high cervical and petrous level stenosis, and to avoid the 7.6% risk of cranial nerve injury reported in NASCET. In addition, primary stenting during angioplasty may trap potential emboli from plaque between the stent mesh and the arterial wall, and help prevent cerebral embolization. It is also likely that a reduced hospital stay will lead to lower costs. The major disadvantage is destabilization of a friable plaque under conditions of no cerebral protection when surgeons typically clamp the carotid for protection during endarterectomy. Indications for considering an endovascular approach include such conditions as radiation-induced carotid fibrosis, fibromuscular dysplasia, and severe medical comorbidity. The question remains about whether the initial approach to atherosclerotic disease of the carotid bifurcation should be endovascular.

Initially, under the guise of clinical trials, the practice of CABAS has now rapidly spread to community practice sites with varying degrees of institutional or national regulatory oversight. In many locations, there is little or no involvement of radiologists. This may seem surprising, since many have preached caution. An editorial by Beebe et al (4) suggested that the out-of-study performance of CABAS is poorly supported by small series of cases with limited outcome and follow-up data, and that despite its investigational status, the procedure is widely promoted by some physicians and manufacturers. The authors went on to outline the need for controlled trials, which at a minimum must include independent neurologic assessment, pre- and postprocedural neuroimaging, life-table reporting of follow-up information for at least a year, and interdisciplinary review by impartial experts. Although two groups of investigators have currently organized trials along these lines (Carotid Artery Stenting vs. Endarterectomy Trial [CASET] and Carotid Revascularization Endarterectomy vs. Stent Trial [CREST]), both are unfunded. A study comparing surgery and angioplasty, with few cases of stenting, is ongoing in Europe (Carotid and Vertebral Artery Transluminal Angioplasty Trial [CAVATAS]), although no results have yet been reported, and the number of patients recruited is likely...
to be insufficient, for carotid disease alone, to be statistically valid. Company-sponsored studies are in progress.

There are a few reports, and some large but non-randomized series of CABAS, suggesting that short-term results may compete with surgery. Yadav et al reported a prospective evaluation of 107 patients in a relatively high-risk population that included patients with prior endarterectomy and serious medical comorbidity (3). Mean stenosis was reduced from 78% to 2% (18% at 6 months). A combined endpoint of stroke and death was recorded in 7.9%, and for ipsilateral major stroke and death, in 1.6%. Another large review of over 2200 cases performed at 27 centers presented recently at the AHA reported a major stroke rate of 1.3%, a minor stroke rate of 3.2%, and mortality of 1.4% (<6% total) (5). No long-term outcome information is available, however. The definition of stroke in these reports was clinical: no MR or CT scans were obtained as part of the protocols.

As Becker discussed in a review of this subject, “...stents have proved to be the most important advance since balloon angioplasty. When properly sized and deployed, they resist elastic recoil of the vessel wall and become incorporated into the wall, covered by thin neointima with a functioning endothelial coat” (5). He points out, however, that stents may thrombose acutely, especially those with poor outflow. More significantly, late restenosis caused by intimal hyperplasia may occur in as many as 50% of femoral and coronary artery stents, a complication that would be particularly problematic in the carotid circulation. In fact, fishmouthing (deformation of the ends of the stent) may require repeat angioplasty, and over time could render the carotid unsalvageable. One recent report of a 6-month follow-up of carotid arteries stented with the Palmaz device revealed that stent collapse occurred in 11 (16%) of 70 cases, with repeat angioplasty required in five, and additional stenting with an alternative device in three (4%) (6). Further complicating the issue, angioplasty in the carotid/cerebral circulation is quite different from that performed in other locations. Coronary disease, for example, is a stenotic problem: decreased flow to the myocardium is the symptomatic problem. In the cerebral circulation, most symptomatic events are related to embolism from friable atherosclerotic lesions and manipulation produces a higher end-organ risk. No surgical rescue is available for procedural failure, unlike bypass grafting, should coronary angioplasty fail. Also, complete occlusion of the carotid artery is not necessarily synonymous with end-organ damage, given the potential of collateral circulation. Furthermore, as recently outlined by Hurst et al in an editorial on this topic, stratification has not been accomplished in any of the groups of patients currently under study (7). Little has been reported to date about the independent effects of calcified or ulcerated lesions and lesions with free thrombus adherent to plaque. Little information is available concerning the special difficulties encountered in crossing very high-grade stenosis (7). Cerebral protection during stent placement, either proximal or distal to the treated lesion, has been all but ignored. Finally, aside from the current risks to patients, the possible future for this technique may be retarded, since if currently available devices prove inadequate, the development of more compatible devices may be delayed by a lack of public acceptance or funding of future trials.

Now let us consider the AHA statement that prompted this commentary (8). It is hard to disagree with most of its substance and intent. Generated by a multidisciplinary committee of the AHA, and recently published in the journals Stroke, JVIR, and Circulation, the document expresses the concerns of physicians in several of the AHA councils regarding the uncontrolled proliferation of CABAS. The AHA is a national organization that provides a forum for clinical and research activities in cerebrovascular disease and stroke, and publishes two journals, Circulation and Stroke. AHA working groups have rigorously explored and issued position papers on many topics that impact neuroradiologic practice, including intravenous and intraarterial thrombolysis.

Through its involvement in stroke, this organization can profoundly affect neuroradiologic practice. Why then was only one neuroradiologist involved in the formulation of this document? Most likely this is a reflection of the relative lack of involvement of neuroradiologists in the Councils on Cardiovascular Radiology and Stroke of the AHA. The Cardiovascular Radiology Council is a forum for the participation of radiologists in AHA deliberations; it is led by vascular/interventional radiologists who have realized the importance of multidisciplinary efforts. The Stroke Council is attended regularly by neuroradiologists, although other specialists dominate it. Recently, the leadership of the American Society of Neuroradiology has begun to promote membership in these councils, and has begun to have input into AHA affairs.

The current AHA document, supported by a multidisciplinary group of leaders in their respective fields, preaches caution; a position easy to support in view of the lack of any real safety and efficacy data about CABAS. It clearly outlines the need for randomized, well-controlled prospective trials. To the average neuroradiologist, however, portions of the document may seem a bit too generic. In an effort not to offend any one group, it avoids a critical assessment of a key topic—the qualifications necessary to perform such procedures. The writing group’s recommendation is that a team of experts participate in this procedure. The team as named, however, consists of neurologists, interventional radiologists, vascular surgeons, interventional cardiologists, and neurosurgeons, and therefore lacks the only subspecialist formally and extensively trained to perform cerebral angiography and more delicate endovascular procedures in the carotid territory; i.e., the neuroradiologist. Why?

We live in a time when physicians of different specialties compete more than ever for patients and for the shrinking health care dollar. Some see the
current heightened activity in promoting and performing CABAS as an outgrowth of this competition, while others see it as an honest effort to explore the application of advances in endovascular materials and techniques to this territory. Some criticize interventional cardiologists for performing these procedures and for the recent proliferation of short educational courses and live procedural demonstrations at cardiology and other meetings that are being held before controlled studies have been performed to prove safety and efficacy.

On the other hand, some criticize neuroradiologists for being slow to grasp the importance of competing for this facet of stroke therapy. Many neuroradiologists are hesitant to become involved in an unproved procedure for which there is a good surgical alternative. Perhaps this is partly related to our intimate knowledge of the dangers of carotid artery embolization, and the gross appearance of ulcerated plaque, because we have long performed cerebral angiography. Conventional diagnostic neuroangiography is done with great care to guard against thromboembolic complications. The dogma that crossing a severely diseased internal carotid origin should be avoided has merit, and for some, this remains a barrier. Also, the controversy surrounding the justification of surgical treatment of carotid stenosis has only recently been clarified, but still controversy remains concerning treatment of asymptomatic lesions. Many highly competent neuroradiologists are not eager to tackle invasive procedures, and the number of interventional neuroradiologists, highly skilled physicians expert at navigating diseased arteries and managing possible intracranial vascular complications, including dissection and thromboembolism, is growing but remains relatively small. Members of the Society of Cardiovascular and Interventional Radiology (SCVIR) are beginning to pursue carotid disease, and in fact many are already involved in carotid angiography and CABAS, in some cases because neuroradiologists at their institutions shy away from performing invasive procedures altogether.

So, who should do these procedures? Technical skill is a requisite, and is available in the hands of qualified neuroradiologists, interventional radiologists and cardiologists, as well as some neurosurgeons. Technical skill is not, however, the only issue when considering carotid angioplasty and stent placement. Of paramount importance is the understanding of cerebrovascular anatomy and pathophysiology, as well as the ability to recognize and treat potential complications of therapy. The acute management of intracranial vascular complications requires a physician skilled in intracranial microcatheter navigation and local intraarteral thrombolysis. Interventional neuroradiologists and some others who have training and experience in endovascular cerebral vascular therapy (vascular/interventional radiologists, neurosurgeons) have the skills needed for this, whereas the majority of cardiologists do not. For this reason, if cardiologists are to be involved in these procedures, it is essential that others who do have special skills and training in interventional neuroradiology be involved also.

Where do we stand in 1998? As suggested by Beebe et al, promotion far outstrips proved safety and efficacy (4). There is still no controlled long-term outcomes information, and yet more than a dozen companies are actively marketing stents in the U.S. The lay press has picked up on this. In a recent New York Times article concerning the conduct of an interventional cardiology meeting known as Transcatheter Cardiovascular Therapeutics (TCT), it was written that, “there is so much promotion, that some say that heart patients may find themselves being treated with expensive devices, not because they have been shown to be the most effective, but because they were intensely promoted” (9). Much money is at stake for the businesses that supply materials. Larry Best, the Chief Financial Officer at Boston Scientific, was quoted as saying that his company spent $5 million at the last TCT meeting, but the effort was worth the cost, considering the $10 billion market for the devices promoted. Should current devices prove inadequate, we risk a public backlash against other proven devices, particularly those approved but used in “off label” sites successfully.

We all must be aware that the Food and Drug Administration (FDA) and the Health Care Financing Administration (HCFA) have taken a special interest in carotid stents, which are considered significant risk (Class B) devices. FDA guidelines require an investigational device exemption (IDE) and local institutional review board (IRB) approval for its use in the carotid artery. The policy of the HCFA indicates that Medicare will deny payment for an entire hospital admission if the purpose of the admission is to perform carotid angioplasty and stenting, and will downgrade payment should the procedure be performed on a patient admitted for another reason. Furthermore, it was not long ago (1994) that the FDA and HCFA launched an initiative through the Office of the Inspector General, which resulted in subpoenas to several hospitals for billing for devices either unapproved or approved but used off label, in hopes of recovering penalties for Medicare fraud. In 1996, a letter from the FDA to the journal Stroke indicated that to that date, all published reports of carotid stenting were improperly conducted, and future publications would be carefully surveyed (10). The authors went on to write that, “considerable responsibility for surveillance of innovative interventions is delegated to individual institutional review boards to ensure that patients are adequately protected from undue risk caused by the use of unproven interventions. When such procedures involve experimental devices of significant risk to patients, the IRB is directed to refer investigations to the FDA for study approval via an investigational device exemption. The IRBs have failed to execute this obligation in the case of percutaneous angioplasty and stenting for carotid arterial disease. While anecdotal reports of extensive use of carotid percutaneous angioplasty and stents abound, these unapproved and uncontrolled studies...
do not provide the data necessary for accurate assessment of the appropriateness of the procedure. Procedures such as these, performed without an IDE, are in contravention of FDA regulations. Most importantly, they do not address the highest, scientific manner the benefits and risks to the patients” (10). Nothing has changed since that time.

How have manufacturer-based trials handled this issue? One trial supported by Schneider, the manufacturer of the Wallstent, is underway. As is written by the organizers, this is the first randomized prospective study aimed at determining the safety and efficacy of CABAS vs. endarterectomy in patients with symptomatic high-grade (60% to 99%) stenosis (11). The end point is cumulative occurrence of any ipsilateral stroke, periprocedural death (30 days), or vascular death within 1 year. Stroke is divided into major and minor according to a 90-day postevent examination. Follow-up with carotid sonography is required. Twenty-one hospitals/medical centers are involved, and up to 700 patients will be recruited (44 patients enrolled up to December 1997). Schneider has IDE and FDA approval to conduct the trial. Of interest, however, are the guidelines for the performance of these procedures. All centers have formed a multidisciplinary team to perform assessments and follow-up. The team must include, at a minimum, an interventionist, a surgeon, a neurologist, an experienced sonographer, and a study coordinator. The specialties of the interventionist and the surgeon may vary. Cardiology, radiology, neuroradiology, neurology, and other appropriate specialty training fall within the guidelines. Each center must document 10 cases of symptomatic or asymptomatic patients who are treated with the Wallstent in the carotid who present with a 30-day complication rate of 10% or less. Otherwise, the “interventionalist” could document experience with the Wallstent in other arteries, and then take a “preceptorship” with another “interventionalist” with carotid experience with the Wallstent. If the latter is done, the investigator must treat five patients before randomization, two of whom must be supervised. The neurologist must complete an NIH stroke scale training video, and a Barthel scale certification examination. All patients must undergo head CT or MR imaging within 30 days of the procedure. If duplex sonography indicates the need, an angiogram is to be done. To the credit of the study design, the angiogram must include views of the arch as well as both carotid and vertebral artery territories, including intracranial vessels. Selective carotid artery injections must be done. Problems, however, persist. What are the necessary qualifications for the specified “interventionalist”? What is the “experience” of the preceptor? Why are there no requirements for real training and certification in carotid and cerebral angiography? Do the patients undergoing these procedures really understand this lack of standards?

It is clear to me that CABAS is an investigational procedure that requires a group of specialists who use strict guidelines for patient selection. Operator expertise must be substantiated through recognized training programs, and documentation of a sufficient number of cases performed. Expertise by an individual or a team is essential. All physicians involved need to adhere to strict guidelines.

Now I would like to consider separately the role that neuroradiologists should play in view of these developments. First, publication of ASITN/ASNR/SCVIR quality improvement guidelines for cerebral angiography will address the need to set a high standard for the knowledge-based qualifications of the operator. These will contain literature-based thresholds for indications and complications that are realistic and patient-oriented. They will also stress the need for a high-quality angiographic study recorded with digital subtraction or cut film (not cine), and formal interpretation for the record. ASITN/ASNR quality improvement guidelines already exist for the performance of many specific neurointerventional procedures, and the angiography guidelines should eventually serve as the basis of guidelines for CABAS, when appropriate. Operator expertise must be substantiated through recognized training programs, and documentation of a sufficient number of cases performed, with success rates and outcomes that meet or exceed those outlined in fair quality improvement guidelines, before clinic or hospital credentialing is awarded.

Neuroradiology should further develop a clinically directed, patient-oriented goal as part of its overall mission. A clinically oriented home page, stressing the training and experience available through consultation with fully trained, and in many cases, subspecialty certified, diagnostic and interventional neuroradiologists, should be considered. Links to neuroradiologic sites from all pages referring to diagnostic neuroangiography and neurointervention, and from any clinical sites dealing with the diagnosis and treatment of stroke and cerebrovascular diseases, could be accomplished. The patient is an informed consumer. The ease of Internet research is leading to an increased patient knowledge base, and this is to the advantage of the qualified physician. The development of a nationwide database containing vital information including patient outcome data related to these procedures is desirable. A potential model exists currently, as the SCVIR HI-IQ database is linked nationally.

We need to promote the involvement of neuroradiologists in the Stroke and Cardiovascular Radiology Councils of the AHA. The mission of the AHA is one we can support: to reduce disability and death from cardiovascular diseases and stroke. There are 29,000 members who sit on 13 scientific councils. Council representatives serve on research committees that determine how to allocate roughly $100 million in research funds each year. The Stroke Council conducts the Joint International Conference on Stroke and Cerebral Circulation, which is co-sponsored by the Cerebrovascular Surgery Section of the American Association of Neurological Surgeons, the Canadian Stroke Society of the Canadian Heart Foundation, the American Neurological Association, and the So-
ciety for Vascular Surgery. The American Society of Neuroradiology should also participate. The Cardiovascular Radiology Council focuses on radiology as it relates to cardiac and circulatory diseases including MR, sonography, and nuclear medicine, and it provides a multidisciplinary meeting ground. It is involved in setting standards for imaging equipment and the practice of cardiovascular and interventional radiology. Membership in the AHA is $25 per year, and includes reduced registration fees for AHA scientific sessions, and a 25% discount on AHA scientific journals such as *Stroke, Circulation, Arteriosclerosis, Thrombosis, and Vascular Biology*.

We must strive to improve communication and cooperation with our colleagues in cardiology, surgery, and vascular/interventional radiology in order to arrive at the best solution for the patient. Interventionalists pioneered intracranial vascular navigation. Skills have been developed while performing local intraarterial thrombolysis and treating cerebral aneurysms and fistulas that are essential for immediate salvage of intracranial complications of CABAS, such as dissection and thromboembolism. Time is essential in managing such events in order to salvage viable brain tissue, and neuroradiologists should participate in all such cases for this reason alone. An interventional neuroradiologist should preferably be present to lead CABAS procedures, and cardiologists, surgeons, and others who perform the procedure should be required by IRB design to have a neuroradiologist present to conduct the radiologic portion of the procedure and to handle intracranial complications. Of course, a team approach is necessary. We must take advantage of the considerable skills that our colleagues in interventional radiology, cardiology, neurology, vascular surgery, and neurosurgery bring to the table, and devise the best possible cooperative efforts to conduct clinical trials and, then, clinical practice should CABAS ultimately prove safe and effective. Peripheral vascular and coronary interventionalists have highly developed skills in balloon inflation and stent deployment. The clinical neuroradiologist is most knowledgeable about clinical stroke diagnosis and medical therapy, and the vascular/neurovascular surgeons are experienced in open rescue measures should embolectomy or vascular repair become necessary. A multidisciplinary team is required, since all these skills are usually not present in a single individual.

The neuroradiology community should take primary responsibility to ensure that these procedures prove safe and effective, that appropriate performance guidelines and training standards are in place for best patient care and outcome possible, and that any practitioner who can meet these requirements and outcomes should be able to practice with institutional controls in place to review performance continuously. Such qualifications should include in-depth knowledge of cerebrovascular angiographic anatomy and physiology and proven skills in managing intracranial complications. The required skills do not appear magically overnight, or after a brief day- or week-long course, but require concentrated, supervised training and experience, as is offered and certified by our ACGME-approved residency and fellowship programs and the Neuroradiology CAQ certification process. So called “minimally invasive” techniques are not best performed by “minimally trained” physicians of any subspecialty. We need to continue to assure that neuroradiologists are well trained in angiography and endovascular techniques in order to support our involvement should the widespread use of CABAS and proximal local intracranial fibrinolysis be supported by good clinical trials.

We must support the Academy of Radiology Research, the formation of an NIH Biomedical Imaging Institute, and the promotion of research in stroke and endovascular treatment of cerebrovascular disease through the Foundation of the ASNR. We have already begun to work on these issues, but we must move forward purposefully, and without delay.

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**References**