Angioplasty and stenting for carotid artery stenosis: indications, techniques, results, and complications

Giuseppe Lanzino, M.D., Richard D. Fessler, M.D., Robert A. Mericle, M.D., Ajay K. Wakhloo, M.D., Ph.D., Lee R. Guterman, Ph.D., M.D., and L. Nelson Hopkins, M.D.

Department of Neurosurgery and Toshiba Stroke Research Center, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, New York

Following the favorable results obtained in the treatment of coronary artery disease, combined angioplasty and stenting has been advocated for the treatment of carotid artery stenosis as well. Although widespread application of angioplasty and stenting for carotid artery disease is neither indicated nor recommended, it may be a viable alternative therapy for select patients who are high-risk patients for surgery. The results of early series have suggested that endoluminal revascularization in these high-risk patients can be performed with an acceptable degree of safety. Although the incidence of death and major stroke rates following angioplasty and stenting procedures compares favorably with surgery, results of more recent clinical series have suggested that the incidence of perioperative transient neurological events and minor strokes may be higher than suggested by earlier reports, especially in patients with recent neurological symptoms and "unstable" plaques. In this article, the authors review the current potential indications for and preliminary results of angioplasty and stenting and describe their procedural technique. In addition, potential applications of stenting to intracranial thromboocclusive carotid artery disease are reviewed.

Key Words * angioplasty * stenting * carotid artery stenosis * endarterectomy * complications

Following the encouraging and long-lasting results obtained in the treatment of coronary and peripheral circulations with angioplasty and stenting, a natural extension was the application of these new technologies to the last frontier: the cerebral vasculature. Results of preliminary clinical series have suggested that carotid artery angioplasty and stenting could be performed safely with excellent angiographically demonstrated results immediately and at 6 months postprocedure.[6,13,14,34,62,64] Although long-term follow-up data is not yet available, the reported low rates of procedure-related morbidity and mortality appear to make it a viable alternative therapy to carotid endarterectomy (CEA) in a select group of patients.

In this article, we review the current potential indications for combined angioplasty and stenting, discuss our preliminary results, and describe our procedural technique. In addition, potential applications of
stenting to intracranial thromboocclusive carotid artery disease are reviewed. Based on excellent coronary circulation results attained using stenting with or without angioplasty over angioplasty alone, as well as the improved immediate angiographically demonstrated results obtained following stent placement, numerous interventionists have progressed to using routine stenting for endoluminal carotid artery revascularization. The present review concentrates on this current technique.

WHICH PATIENTS SHOULD BE CONSIDERED FOR CAROTID ANGIOPLASTY AND STENTING?

Several large cooperative randomized trials have proven the efficacy of CEA for extracranial carotid artery stenosis.[17,18,48] However, the benefits of CEA are critically dependent on the rate of perioperative complications. If the combined perioperative morbidity and mortality rate exceeds 3% in asymptomatic patients and 6% in symptomatic patients, the benefits of this procedure are quickly lost.[24]

To evaluate the possible role of carotid stenting, it is important to recognize that patients in whom CEA has been proven beneficial were carefully selected.[17,18,24,48] In the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[48] European Carotid Surgery Trial,[17] and Asymptomatic Carotid Atherosclerosis Study,[18] patients with risk factors that might have created confounding variables in the data analysis were excluded. These factors included 1) age greater than 79 years; 2) heart, kidney, liver, or lung failure; 3) cancer likely to cause death within 5 years; 4) cardiac valvular lesion or rhythm disorder likely to be associated with cardioembolic stroke; 5) previous ipsilateral CEA; 6) angina or myocardial infarction in the previous 6 months; 7) progressing neurological signs; 8) contralateral CEA within 4 months; or 8) a major surgical procedure within 30 days. Thus, a substantial number of patients with high-risk carotid artery lesions do not meet the criteria established for enrollment in these studies. Arguably, NASCET,[48] Asymptomatic Carotid Atherosclerosis Study,[18] and European Carotid Surgery Trial[17] may have selected a low-risk subgroup to undergo CEA, leaving the indications for CEA in a large number of elderly patients with carotid stenosis to be determined. Indicative of the high degree of selection in NASCET is the observation that, although the published mortality rate in the NASCET series was 0.6%,[48] the mortality rate among Medicare beneficiaries undergoing CEA was 3% during the same period.[33]

Widespread use of angioplasty and stenting for the entire spectrum of carotid artery occlusive disease is neither indicated nor recommended. However, certain patient subgroups may benefit from this procedure if the low morbidity and mortality rates indicated by early clinical series are sustained.[5,11,35] Included in these subgroups are patients with one or more of the following conditions: significant medical coexisting disease, recurrent high-grade stenosis, contralateral occlusion, radiation-induced stenosis, surgically difficult-to-access high-cervical stenosis, "tandem" lesions, and intraluminal clot.

Patients With Significant Medical Comorbidities

There is a direct relationship between significant (clinically important) coexisting medical deficits and perioperative complications associated with CEA. This is true for nonneurological complications, such as myocardial infarction,[52] as well as for neurological deficits and death. In a subgroup analysis of the NASCET, diabetic patients undergoing CEA had significantly higher perioperative morbidity and mortality rates (above 10%) (HJM Barnett, unpublished data). Because patients with other significant coexisting disease were excluded from the major CEA trials, the indications for and results of surgery in this subgroup of patients are not established.
The coexistence of severe carotid artery stenosis and symptomatic coronary artery disease presents the physician with a management dilemma.\cite{23,27} The operative repair of one condition is accomplished only at the cost of a substantial risk of complication from the other. Coronary artery disease is one of the most important factors when evaluating the perioperative risk of CEA.\cite{52} In addition, when long-term results of CEA were reviewed, cardiac disease was the leading cause of death.\cite{65} Conversely, significant carotid artery disease places patients who are undergoing coronary artery bypass grafting (CABG) at increased risk for stroke and/or air or atheromatous embolization during cardiopulmonary bypass.\cite{19} Faggioli, et al.,\cite{19} reported on a series of 539 patients undergoing CABG who underwent preoperative noninvasive evaluation (with carotid Doppler ultrasound and oculor pneumoplethysmography) for the detection of carotid artery occlusive disease. They found that a carotid artery stenosis above 75% was an independent predictor of stroke risk (odds ratio 9.9).

In patients with significant coexistent carotid and coronary artery diseases, there is little debate that revascularization is appropriate for both; however, the timing is difficult. The surgical approach is either a simultaneous procedure or a staged approach in which one procedure is performed several days before the other. Published reports on combined CEA and CABG suggest that the risk of stroke or death ranges from 7.4 to 9.4%, roughly 1.5 to 2.0 times the risk of each operation alone.\cite{23} On the other hand, patients who undergo CEA as a prelude to CABG are at highest risk for complications.\cite{45} In this subgroup of high-risk patients, avoiding a major operation or general anesthesia by performing angioplasty and stenting may represent a valid alternative to CEA.\cite{3,41,51} We recently reviewed our experience in the treatment of 20 patients with coexistent coronary and carotid artery disease who underwent prophylactic angioplasty and stenting prior to CABG.\cite{41} Thirteen patients (65%) experienced unstable angina. The mean interval between stenting and CABG was 8 days. After angioplasty and stenting, one patient died of a cardiac event, and one patient suffered a transient neurological deficit. The mean length of stay was 14 days, and no patient suffered a permanent cerebrovascular event after undergoing angioplasty and stenting. These results support the use of angioplasty and stenting as a valid alternative to CEA for the management of carotid artery disease in patients with coexistent symptomatic coronary artery disease that requires urgent cardiac revascularization.

**Carotid Restenosis**

Postendarterectomy recurrent carotid artery stenosis has been increasingly recognized because long-term follow-up evaluation using noninvasive methods is routinely performed following CEA (Fig. 1).\cite{45} Patterns of early and late restenosis are observed after successful CEA. Early recurrent stenosis (within 24 months after surgery) is usually caused by a myointimal fibroblastic reaction, whereas late restenosis occurs as a consequence of recurrent atherosclerotic formation.\cite{7}
Fig. 1. A 69-year-old man with a history of hypertension, peripheral vascular disease, coronary artery disease, and hypercholesterolemia was evaluated for recurrent left carotid artery stenosis (A) 10 years after undergoing left CEA. Although the patient had been asymptomatic, serial Doppler studies had documented progression of the degree of stenosis. Endoluminal revascularization was performed. B: Left CCA digital subtraction angiogram, lateral projection, showing improvement in the degree of stenosis after balloon angioplasty. C: Left CCA angiogram, lateral projection, non-subtracted view, showing a self-expanding stent across the stenosis. D: Lateral cervical fluoroscopy revealing a partially deployed intravascular stent. Note the proximal and distal markers at the proximal and distal ends of the stent, respectively. The middle black marker shows the distal end of the protective sheath that is withdrawn as the stent is deployed. E: Lateral cervical fluoroscopy. The intravascular self-expandable stent is deployed. Note the microguidewire across the stent. F: Left CCA angiogram, nonsubtracted view, poststent deployment, showing the restored carotid artery lumen. No perioperative neurological complications were encountered. The patient was discharged the next day.

Surgery for recurrent carotid artery stenosis is technically challenging. Dense scar tissue surrounds the carotid bifurcation and its branches, and the planes of dissection are difficult to delineate from the surrounding tissue, making dissection more traumatic.[45] In early-stage restenosis with myointimal hyperplasia, diffuse thickening of the intima and media results in fibrous hypertrophic scarring throughout the CEA site. A distinct cleavage plane between the recurrent plaque and the underlying media is usually impossible to identify. In late-stage recurrent atherosclerosis, the recurrent plaque is
often friable and associated with intraluminal clot, which increases the risk of clot embolization during carotid artery dissection. In addition, the presence of scarring and the absence of a clear cleavage plane make performing a standard CEA impossible in some cases. Excision of the diseased segment and reconstruction by using an interposition graft is preferred in these cases. Because of all of these challenges, the major complication rate of repeated CEA approximates 10%, even when performed by the most experienced surgeons.[45]

Recently, angioplasty and stenting of the extracranial carotid artery has been suggested as a valid alternative to carotid artery reexploration in patients with recurrent disease. Angioplasty and stenting obviates the need for dissection, and the presence of periarterial scarring poses no problem because dissection is not required. Thus, cranial nerve injury, a significant problem in cases of reexploration, is eliminated.

In the past 4.5 years, we have performed a total of 25 endoluminal revascularization procedures in 21 patients (mean age 69 years) with recurrent carotid artery stenosis.[39] The mean interval from the primary CEA was 57 months (range 8-220 months). Early in our experience, angioplasty alone was performed to treat seven vessels. Recent experience suggests that in this subgroup of patients the addition of stents (in the next 18 vessels) prevents the recoil phenomenon that is observed when treating more fibrous lesions.[6,12,63] The mean degree of stenosis, measured using the strict criteria developed by NASCET for calculation of de novo stenosis,[49] was 75% before and 9% after angioplasty with or without stenting in 24 of 25 treated vessels for which angiograms were available for review (angiograms were not available for one patient). No major neurological or cardiac complications occurred, and there were no deaths. There was one periprocedural transient neurological event, and one patient developed a femoral pseudoaneurysm at the access site. No neurological events ipsilateral to the treated artery occurred after a mean of 27 months in the 16 patients each of whom underwent at least 6 months of follow up. These early results indicate that angioplasty and stenting of carotid artery restenosis can be safely performed and that it represents a valid alternative to carotid artery reexploration procedures in this high-risk group.

**Carotid Stenosis With Contralateral Occlusion**

Patients with recent symptoms referable to severe carotid stenosis and coexistent contralateral carotid artery occlusion face a serious prognosis (HJM Barnett, unpublished data).[21] In the NASCET,[21] the risk of ipsilateral stroke in medically treated patients with severe stenosis of the symptomatic carotid artery and occlusion of the contralateral carotid artery was 69.4% at 2 years. Although CEA significantly reduces the risk of stroke in this cohort of patients, the perioperative risk is high. In the same trial, the perioperative risk of stroke or death in the presence of a contralateral carotid artery occlusion was 14.3%. Carotid artery shunting is used in 67 to 83% of patients with contralateral occlusions.[9,21] However, shunt insertion may increase the risk of stroke from emboli.[26] As expected, patients with contralateral occlusions have an increased prevalence of significant risk factors, commensurate with systemic vascular disease. Combined angioplasty and stenting in this subgroup represents a valid alternative to CEA, obviating the need for temporary occlusion in the presence of reduced cerebrovascular reserve. In a consecutive series of 26 procedures that treated carotid artery stenosis and contralateral occlusion in 23 patients who underwent angioplasty and stenting at our institution during a 5-year period, no perioperative neurological events occurred (Mericle, et al., unpublished data). In addition, there were no strokes or cardiac events in the 1st month. The average ipsilateral stenosis was 78% preprocedure and 5% postprocedure. The clinical follow-up period (mean, 18 months) was available for all patients but
one. Nineteen patients were independent and well; two patients died (one of metastatic prostate carcinoma 12 months after carotid artery revascularization and the other of respiratory arrest after a prolonged hospital course and multiple complications); and one patient suffered a contralateral (to the treated vessel) hemispheric stroke 41 months postprocedure.

**Radiation-Induced Carotid Artery Stenosis**

Results of human and animal studies have shown that concentrated cervical-region radiotherapy damages large arteries and leads to atherosclerosis-like occlusive disease. The spectrum of the disease varies and is not dose related. As patients with head and neck malignancies survive for longer periods, radiation-induced carotid artery stenosis is sometimes observed.

Patients in whom symptomatic carotid artery occlusive disease occurs as a result of cervical radiation often require treatment because the disease progresses rapidly. Although successfully treated with direct endarterectomy or bypass of the involved arterial segments, these lesions undoubtedly present surgical challenges. Angiographic findings in this disorder include disproportionate involvement of the distal common carotid artery (CCA). Lesions are typically confined to the irradiated field and are unusually long and difficult to resect. Direct exposure of the involved carotid artery by performing standard endarterectomy is most often reported. However, nearly all authors emphasize that a marked amount of periarterial scarring is encountered, and the planes of dissection are obscured by fibrous changes. This periarterial scarring is probably related to radiation effects on the microvasculature. The wall of the artery is weakened as the vasa vasorum, which provide nutrients to the outer vessel wall, are extremely vulnerable to radiation-induced damage. Infections and wound problems are increased by previous radiation treatment. Furthermore, the risk of airway obstruction (as a result of endotracheal tube trauma to the fixed irradiated vocal cords and laryngeal edema caused by surgical dissection in an irradiated field) can be increased in these cases. The potential advantages offered by the endovascular approach for these patients are obvious.

**High Cervical Stenosis and "Tandem" Lesions**

A high bifurcation near the skull base, especially in a patient with a short or thick neck, or a long carotid artery stenosis that extends to the skull base can be difficult to expose surgically. Dissection of the carotid artery in these cases can be troublesome and at times quite traumatic. These patients should be considered for stenting.

"Tandem" lesions have long been considered an angiographic risk factor for perioperative neurological events. The NASCET excluded patients in whom an intracranial lesion was more severe than the surgically accessible lesion. For example, the presence of carotid siphon disease has been proposed as a contraindication to CEA because of concern of postoperative occlusion secondary to decreased flow during endarterectomy. Patients harboring such lesions may benefit from angioplasty and stenting because only a few seconds of occlusion time are needed to perform the procedure. If the distal stenosis is severe, angioplasty can be performed in both lesions at the same sitting (Fig. 2). At our institution, 11 patients with tandem stenosis (two upper cervical, two petrous, six cavernous, and one supraclinoid) underwent angioplasty to treat carotid segments with and without stenting. The proximal lesion was considered the flow-limiting lesion in 10 of the 11 patients and treated accordingly. In the remaining patient, both lesions were treated (Fig. 2). No permanent neurological events and no perioperative cardiac deficits and death were encountered. This experience suggests that this procedure may be a viable alternative to CEA in patients with inaccessible tandem carotid artery lesions.
Fig. 2. A 64-year-old man was evaluated for an irregular stenosis of the right internal carotid artery origin. Because of the presence of tandem intracranial lesions, the patient was considered a high-risk surgical candidate. A: Right CCA angiogram, lateral view. Careful measurements of the lesion are obtained before selecting the appropriate angioplasty balloon and stent. Measurements are taken of the lesion length, including any tapering segments, as well as the diameter of the artery proximal and distal to the lesion. B: Right CCA angiogram, lateral intracranial view, revealing a proximal tandem lesion at the skull base (black arrow) in addition to sluggish intracranial flow, as suggested by coexistent distal filling of the distal external carotid artery branches. C: Right CCA angiogram following angioplasty and stenting showing excellent revascularization of the carotid artery stenosis. D: Right CCA angiogram, lateral intracranial view, after placement of two stents at the level of the petrous portion of the internal carotid artery in addition to angioplasty and stenting of the internal carotid artery origin. Two stents were used to cover both the focal tandem stenosis and a long segment of the vessel that appeared irregular. There is resolution of the tandem lesion with dramatic improvement in middle and anterior cerebral artery filling. (E) Plain x-ray film showing the two intracranial stents (white arrows). F: Right CCA digital subtraction angiogram, anteroposterior view revealing an iatrogenic dissection proximal to the stented intracranial carotid artery segment. Because of the excellent distal flow, it was decided to treat this dissection conservatively. G: Right CCA angiogram, lateral view, at 3-month follow up revealing excellent patency of the bifurcation stent without significant myointimal hyperplasia. H: Right CCA angiogram, lateral intracranial view, at 3-month follow-up examination showing excellent intracranial flow with no evidence of in-stent stenosis at the petrous segment of the internal carotid artery. I: Right CCA angiogram, oblique intracranial view, at 3-month follow up revealing remodelling of the internal carotid artery at the level of the iatrogenic dissection with persistent stenosis but no significant
limitation of distal flow.

**Carotid Stenosis With Intraluminal Clot**

Patients with intraluminal thrombus superimposed on an atherosclerotic plaque are at risk for imminent stroke. However, CEA is associated with a significant perioperative neurological morbidity rate. In a subgroup analysis of 53 patients enrolled in the NASCET study with an intraluminal clot identified by angiography, the 30-day risk of stroke was 10.7% in those randomized to medical treatment and 12% in those who underwent surgery.[60] The high morbidity rate in this subgroup is related to the presence of fresh clot and the substantial risk of emboli dislodgment during surgical dissection of the carotid artery. The use of endoluminal revascularization may be advantageous for these patients (Fig. 3), although the safety of this approach in such cases has not been demonstrated.

![Fig. 3. Right CCA angiogram. A 61-year-old man underwent cerebral angiography for evaluation of recurrent right hemispheric TIAs. A: Digital subtraction angiogram revealing a mild to moderate stenosis of the right internal carotid artery origin. Intraplaque irregularities are evident. The patient was considered for possible CEA. However, 72 hours after diagnostic angiography, while receiving continuous intravenous heparin infusion, he sustained a new neurological event (left hand paresthesias and weakness) without full recovery within 24 hours. Magnetic resonance imaging showed a small (2-mm) infarction in the right parietal area. Because of the progressive nature of his symptoms, he was considered for endovascular treatment. B: Lateral projection, 96 hours after diagnostic angiography, showing intraluminal clot. C: Lateral view, after local infusion of 250,000](image-url)
units of urokinase, showing improvement of the intraluminal filling defects. D: Lateral projection, following angioplasty and stenting, revealing restoration of the carotid lumen. Postprocedure, he experienced a hypotensive episode (systolic blood pressure, 75 mm Hg) which lasted approximately 5 to 10 minutes. He was also noted to have worsening of his preexisting left hand weakness. Right carotid artery angiograms, intracranial lateral views, before (E) and after (F) angioplasty and stenting revealing improved intracranial perfusion without evidence of vessel dropout after endoluminal revascularization. The patient's neurological status returned to his preprocedure baseline in 24 hours. No neurological deficits were noted at the 6-week follow-up visit, although he reported decreased fine motor skills with the left hand, especially while typing or playing guitar.

To reduce the possibility of emboli formation from fresh thrombotic material while crossing the lesion with either the microguidewire, the angioplasty balloon, or the stent itself, we inject 100,000 to 200,000 units of urokinase (Abbokinase; Abbott Laboratories, Chicago, IL) across the lesion before any endoluminal manipulation. In several cases, we have documented widening of the vessel lumen following local thrombolysis, which suggests clot lysis and improvement of the amount of intraluminal clot (Fig. 3 C).[25] In patients with intraluminal clot, the local injection of urokinase before angioplasty and stenting may increase the safety of the procedure by digesting the friable portion of the thrombus, which has a higher potential for distal embolism than well-organized thrombus.

**PREPARATION OF PATIENTS FOR CAROTID ARTERY ANGIOPLASTY AND STENTING**

In all patients scheduled for angioplasty and stenting, a baseline neuroimaging study must be performed, preferably brain magnetic resonance imaging, to ensure that postprocedural infarction is not attributed to preexisting disease and to rule out the presence of an intracranial process (that is, tumor) manifesting with symptoms that are indistinguishable from transient ischemic attacks (TIAs).

A complete angiographic study in all patients provides critical information regarding the presence of collateral circulation and coexistent intracranial disease that may be responsible for the clinical symptomatology. In addition, intracranial views are particularly useful for baseline comparison if embolic complications were to occur during the procedure (Fig. 4).
Fig. 4. A 66-year-old man with multiple medical coexisting disease underwent successful angioplasty and stenting of a high-grade left carotid artery stenosis (not shown). Neurological examination after stent deployment demonstrated a mild word-finding problem, clearly a change from the patient’s baseline status. Poststent deployment, digital subtraction angiogram, left internal carotid artery injection, anteroposterior (upper left) and lateral (upper center) views, showing faint opacification of the angular artery origin (arrows). Upper Right: Capillary parenchymal blush seen on digital subtraction angiogram (parenchymogram) revealing absence of flow in the territory of the left angular artery. Lower Left and Center: Digital subtraction angiogram. Left internal carotid artery injection after local thrombolysis, showing good filling of the large angular artery (arrows). Lower Right: Parenchymogram after thrombolytic therapy revealing reestablished flow in the territory of the left angular artery. (Hopkins, et al. Reprinted with permission.)

Before the procedure, patients undergo aspirin (325 mg daily) and ticlopidine therapy (250 mg twice daily) or clopidogrel therapy (75 mg daily) beginning 2 days before admission. Baseline laboratory values are obtained, including electrolytes, serum creatinine, blood urea nitrogen levels, and prothrombin and thromboplastin times. Proper informed consent is obtained. Patients are allowed to consume clear fluids and medications only starting at midnight the day of the procedure. Insulin-dependent diabetic patients receive half of their usual morning dose of insulin and are scheduled as the first case of the day. Solutions containing dextrose are used for hydration. Patients maintained on oral anticoagulation therapy discontinue its use 72 hours prior to the procedure and are admitted 24 hours preprocedure for heparinization. For patients with renal disease and elevated serum creatine levels, hydration is ideally begun 24 hours before the procedure. In general, we ensure that patients are well hydrated (except those with congestive heart failure) and receive limited contrast volume or isoosmolar contrast media.

The access site is shaved and cleansed with disinfectant solution. Distal pedal and medial tibial pulses (or
ulnar and radial pulses if a transbrachial approach is planned) are felt and marked for later reference (this becomes particularly important in elderly patients with peripheral vascular disease). Because of the very low risk of infection following diagnostic or therapeutic endovascular procedures, prophylactic antibiotics are not routinely administered. A Foley catheter is inserted to decrease patient discomfort and restlessness as well as to allow for detailed monitoring of urinary output.

**PROCEDURE AND PERIOPERATIVE CARE**

All patients receive a local anesthetic at the puncture site as well as intravenous sedative hypnotic and analgesic medications. Initially, we routinely placed a transvenous cardiac pacemaker preoperatively if the lesion was located near the carotid sinus. More recently, we place a venous sheath only in patients with a calcified plaque that involved the carotid sinus and we have a pacemaker immediately available should malignant bradycardia or asystole develop during balloon inflation. Intravenous atropine (0.5-1.0 mg) is administered before angioplasty is performed in the stenotic lesion (except in patients with unstable coronary disease). Prior to manipulation of the lesion, heparin (50 units/kg) is administered intravenously to maintain an intraoperative activated clotting time at approximately 300 seconds throughout the procedure.

Arterial access is usually obtained through the femoral artery. We usually use the Cook introducer system (Bloomington, IN) and a standard 0.035-inch hydrophilically coated guidewire to avoid inadvertent endothelial damage during abrupt manipulation of the catheter tip. Optimum placement of the guide catheter proximal to the lesion can be arduous. This is particularly true in elderly patients in whom a tortuous atherosclerotic arch is often present. To overcome resistance to proper placement of the large guide catheter by the very tortuous origin of the great vessels from the aortic arch, navigation of the guide catheter over a very stiff wire is sometimes necessary. Catheterization of the right CCA is often easier than catheterization of the left CCA. During placement of the guide catheter, care must be taken to avoid plaque disruption. The introducer is removed when the guide catheter is placed in the appropriate location in the CCA (proximal to the lesion). Meticulous attention must be given to catheter hygiene to avoid air bubbles or thrombus formation. Heparanized saline is gently flushed through each catheter used during the procedure via a rotating hemostatic adaptor.

Following guide catheter positioning, the stenosis is carefully crossed with a 0.14 to 0.18-inch microguidewire. We use a wire with a soft tip and a stiff proximal end, such as the All Star (ACS, Temecula, CA). The wire is navigated across the lesion with the assistance of biplanar road-map fluoroscopy. Once the wire extends through the lumen of the lesion, it is advanced past the stenosis. High-resolution biplanar digital subtraction angiography runs are performed to document stability of the lesion. Measurements of the lesion are obtained to guide further decisions regarding angioplasty balloon and stent selection. Measurements performed include lesion length as well as the diameters of the artery proximal and distal to the lesion (Fig. 2A).

A microcatheter (Rapid Transit; Cordis Endovascular, Miami Lakes, FL) is placed proximal to the lesion, and 150,000 units of urokinase are infused across the lesion at a rate of 50,000 units per minute. The urokinase is infused through the microcatheter, around the guidewire that has already been placed across the lesion. If postinfusion angiography demonstrates a morphological change in the lesion, an additional 100,000 units of urokinase are infused. After infusion of urokinase and posturokinase angiography, the microcatheter is removed and the angioplasty balloon is pushed along the guidewire into the lesion and inflated to a pressure appropriate for the balloon type, typically between 8 and 15 atmospheres (Fig. 5).
We prefer using an oscillating balloon inflation technique in which the balloon is inflated submaximally and then pressure is oscillated over 1 or 2 atmospheres for 10 to 15 seconds. Usually, we find that the degree of the stenosis is improved after angioplasty (Fig. 1B), even when the angioplasty balloon is deliberately undersized. The most important parameters for angioplasty balloon selection are the balloon length, maximum inflation diameter, and burst strength compliance. In general, it is desirable to cover the entire length of the lesion with the angioplasty balloon. Placement of the balloon in arterial segments that are not diseased is avoided because this may induce intimal damage with secondary hyperplasia and arterial dissection. Ideally, the diameter of the diseased artery is reconstructed to its prediseased caliber. Overinflation of the balloon may result in intimal dissection or rupture of the balloon or the artery.

Although primary stenting for carotid artery stenosis can be performed in select cases, angioplasty-assisted stenting has merit. The main purpose of balloon angioplasty is to facilitate stent placement. Tight stenotic lesions may be too small to primarily accept a stent. Angioplasty allows safe navigation of the relatively voluminous stent-delivery-system complex through the lesion. The angioplasty balloon is deliberately undersized to avoid overinflation and to open the artery only enough to permit passage of the stent.

Two types of stents are currently used in the carotid artery: self-expanding and balloon-expandable stents. The most common balloon-expandable stent is the Palmaz (Johnson & Johnson Interventional Systems, Warren, NJ), which is available in several sizes that can be inflated to predetermined lengths and diameters. The most commonly used self-expanding stent is the Wallstent (Schneider/Boston
This endovascular stent has been used and approved for treatment of tracheobronchial strictures and is also available in several sizes that have a predetermined length for each diameter reached after deployment. One stent specifically designed for the carotid arteries and currently undergoing clinical feasibility trials is the INTEGRA self-expanding stent (SCIMED/Boston Scientific, Maple Grove, MN). This device is a multisegmented nitinol (nickel-titanium alloy) stent that expands to a predetermined size based on its surrounding temperature. Other manufacturers have developed stents for specific use in the carotid artery that we are evaluating in preliminary clinical trials. Stent selection is determined by the normal arterial caliber and lesion length. Stents are typically oversized by 1- to 2-mm diameter and should completely cover the lesion proximally and distally. Each stent has advantages and disadvantages that must be considered when choosing the most appropriate stent for each particular case. Balloon-expandable Palmaz stents are generally used only for short lesions because they are long and cannot be easily navigated around intravascular curves. The self-expanding Wallstent is sold premounted on its deployment device (Fig. 6). The Wallstent is currently preferred for use in most carotid artery lesions. Frequently, there is a "waist" at the center of the stent at which the atherosclerotic lesion is generally most dense. The waist is remodelled by using postdeployment balloon angioplasty. Serial neurological examinations are performed after each step of the procedure involving manipulation across the stenosis for prompt recognition of any changes from the patient's baseline status.

![Fig. 6. Photographs showing the Wallstent self-expanding stent. A: Distal (left) and proximal (right) delivery system. The stent is deployed by progressively withdrawing the sheath (B-D).](image)

After satisfactory revascularization is achieved, final digital subtraction angiograms are obtained, including views of the ipsilateral intracranial circulation. Usually, the intraoperative heparin is allowed to reverse on its own, and the femoral sheath is removed once the activated clotting time has returned to baseline. Alternatively, in select cases, we use a percutaneous closure system (Perclose, Menlo Park, CA) that allows percutaneous suturing of the femoral arteriotomy and early mobilization of the patient. Special attention is given to the femoral artery site both before and after sheath removal to detect thrombosis or emboli in the distal leg, hematoma, or pseudoaneurysm formation.

Postprocedure, patients are admitted to the intensive care unit for overnight observation, and they are monitored closely for at least 18 hours postoperatively. At discharge, we prescribe aspirin for patients who underwent angioplasty alone. After stenting, we prescribe ticlopidine or clopidogrel and aspirin.
When ticlopidine is prescribed, a blood cell count with differential is obtained 2 and 4 weeks posttreatment to detect possible ticlopidine-induced neutropenia, a potentially fatal complication.

RESULTS AND COMPLICATIONS

Initial reports have shown the feasibility of carotid artery angioplasty and stenting with acceptable low morbidity rates. A multicenter experience at seven United States centers was recently reviewed.[34] A total of 484 patients underwent balloon angioplasty followed by stent deployment for the treatment of stenosis in 543 extracranial carotid arteries. The stenosis was symptomatic in 56% and asymptomatic in 44%. Of the treated patients, 69% had coronary artery disease and 5.3% had contralateral carotid artery occlusion. There was a very high technical success rate (97%) and a low incidence of major strokes (3.3%).

Yadav and coworkers[65] have detailed their experience in 107 patients who underwent endoluminal revascularization procedures to treat 126 extracranial carotid arteries. In their experience, 68% of the patients had sustained a previous myocardial infarction, and undergone CABG, and/or coronary angioplasty; 77% met the NASCET exclusion criteria;[48,59] 9% had a contralateral carotid artery occlusion; and 11% had undergone a previous ipsilateral CEA. Approximately 45% of these patients were referred for endovascular treatment by a neurosurgeon or a vascular surgeon. This series confirmed the technical feasibility of angioplasty and stenting and an acceptable complication rate for this procedure considering the coexisting diseases of the treated patients. There was one case of acute stent thrombosis (0.8%). The mean stenosis was 78 ± 14% before and 2 ± 5% after stenting. The minimum lumen diameter was 1.3 mm before and 5.0 mm after stenting, for an acute gain of 3.7 mm. There was a single periprocedural myocardial infarction (0.9%) and a major stroke and death rate of 3%. In an update of this series, the late outcome in 150 patients who underwent stenting of 180 arteries was reported:[64] 86 percent of the patients had undergone either ultrasonography (24%) or follow-up angiography (62%) at 6 months. The mean stenosis was 17 ± 13%, with only 4% of the patients experiencing restenosis, which was defined as greater than 50% stenosis. Five patients required repeated angioplasty and one had to undergo CEA at follow up. Some degree of deformation was noted in eight stents and was considered significant only in two patients who then underwent repeated angioplasty.

These early series demonstrate that angioplasty and stenting can be a valid alternative to CEA in a select group of patients. However, at this time angioplasty and stenting is neither an indicated nor recommended treatment for patients who are good surgical candidates because the effectiveness of CEA has already been proven. Unfortunately, angioplasty and stenting has been prematurely compared to CEA. As a result, a recent randomized trial undertaken in the United Kingdom at a single institution that compared angioplasty and stenting with CEA has been prematurely discontinued because a significant incidence of perioperative strokes was observed in the endoluminal revascularization group.[47]

When considering the effectiveness and safety of angioplasty and stenting, it is important to realize that, despite the relatively low rates of mortality and major stroke, minor strokes and perioperative TIAs following endovascular treatment of carotid artery stenosis are not infrequent.[2,36,42] Jordan and coworkers[36] have retrospectively reviewed the complications encountered in 268 patients who underwent revascularization of 312 hemispheres (some patients underwent bilateral procedures either simultaneously or in separate settings). Minor strokes, which the authors defined as a new neurological deficit that resolved with minimal or no deficit within 1 month of the procedure, occurred in 7.1% of patients. Perioperative TIAs occurred in 4.1%. These numbers are significant because 63% of the
patients were being treated for asymptomatic carotid artery stenoses. In a preliminary report from a single center at the University of Oregon on 17 patients who underwent angioplasty and stenting, minor strokes (two ischemic and one hemorrhagic) occurred in three patients (18%).[42] All of these patients eventually recovered from their neurological deficits. Similarly, we have identified a significant number of transient events in patients with recent symptoms and "unstable" plaques (that is, those irregular lesions, often causing severe stenosis, with or without intraluminal clot, causing recurrent symptoms despite antiplatelet or anticoagulant therapy) (Figs. 3 and 7). It should be emphasized that these events may not be detected in the absence of diligent neurological evaluation.

Fig. 7. A 72-year-old man was evaluated for recurrent left hemispheric TIAs. A: Left CCA digital subtraction angiogram, lateral view, showing a high-grade carotid artery stenosis. B: Left CCA angiogram, after angioplasty and stenting, revealing a reestablished carotid artery lumen. The patient suffered an intraoperative TIA (expressive aphasia) that lasted 45 seconds and occurred immediately after the tight stenosis was crossed with the guidewire. No evidence of vessel dropout was found on the intracranial angiography (not shown) performed a few seconds after symptom development. No grossly detectable neurological deficits were present at discharge 2 days after revascularization.

This relatively high incidence of minor strokes and TIAs may be due to microemboli. In a study in which patients undergoing angioplasty and stenting were compared with those undergoing CEA, the median number of cerebral emboli detected by transcranial Doppler study during the procedure was significantly higher in the angioplasty and stenting group (average 284 signals) (unpublished data). The surgical group averaged 12 signals (p = 0.0007). Similar observations have been reported by others.[1,16,30,47] The endovascular procedures primarily associated with microemboli were those related to catheter manipulation across the plaque, prestent angioplasty, and stent deployment. Patients with very severe disease and a small residual lumen may be at particular risk as the balloon-catheter and stent combination is invariably wider than the residual lumen. Most microemboli are likely lysed by endogenous fibrinolysis in the presence of adequate cerebral blood flow. A prospective study conducted in The Netherlands[16] in which patients undergoing endoluminal revascularization were evaluated using
cerebral magnetic resonance imaging pre- and postprocedure failed to demonstrate any signal intensity change referable to emboli in 14 patients even though two of these patients sustained perioperative neurological events. To obviate the risk of microemboli, distal protection with a balloon system has been proposed. This approach has been pioneered by Théron, et al.[55] in France. Several manufacturers are currently working on cerebral protection by using temporary occlusion balloons or microfilters.

Factors associated with a higher incidence of neurological complications include advanced age, plaque characteristics, severity of the stenosis (Fig. 7), and the presence of tandem lesions.[43] In our experience, neurologically unstable patients, such as those with crescendo TIAs or stroke in evolution, and patients with symptomatic plaques are at increased risk for neurological complications during the angioplasty and stenting procedure (Figs. 3 and 7). If an embolic complication occurs during endovascular intervention, combined superselective pharmacological thrombolysis and mechanical thrombolysis are warranted because a spectacular result can be obtained and otherwise debilitating deficits can be reversed (Fig. 4).[32]

**Restenosis After Angioplasty-Assisted Stenting**

Following early experience in the coronary circulation, concerns existed regarding the long-term durability of carotid artery stents and the possible incidence of restenosis. In an early series reported by Yadav, et al.[62] in 81 patients, either follow-up angiograms (71 patients) or Doppler studies (10 patients) were obtained. A minor degree of myointimal hyperplasia (mean angiographic stenosis 18 ± 12%) occurred in most patients. Hemodynamically significant restenosis (> 50%) was less common, occurring in four patients (4.9%), and was not associated with clinical symptoms. Our experience supports these findings. Repeated balloon angioplasty can be performed for significant restenosis. Carotid endarterectomy and stent removal can also be performed, although this is more technically demanding than CEA for de novo stenosis.[58]

The long-term durability of angioplasty and stenting is unknown. Long-term clinical follow-up review is imperative. We do not perform routine follow-up cerebral angiography in these patients because of the small but definite associated risk of complication. On the day after endoluminal revascularization, our patients undergo Doppler studies to assess baseline Doppler velocities proximal to, within, and distal to the stented segment. These studies are repeated at 3, 6, and 12 months and yearly thereafter. Follow-up angiography is reserved for patients with increased Doppler velocities (peak systolic velocity, > 200 seconds). In our experience, increased Doppler velocities do not always correlate with angiographically significant (> 50%) restenosis. Differences in compliance between stented and adjacent nonstented vessel segments may produce artificially elevated Doppler velocities.

**Nonneurological Complications**

A review of device-related technical complications is beyond the scope of the present report. The reader is referred to other reviews that have specifically addressed this issue.[31] Nonneurological complications include those occurring at the access site, and cardiac, renal, and hemodynamic instability.

Complications at the access site are more likely in patients with peripheral vascular disease. If any resistance is encountered during advancement of the guide catheter in the femoral or iliac arteries, immediate angiography should be performed to study the anatomy. In some cases, the coexistence of atherosclerotic disease and tortuous vessels makes navigation difficult and increases the risk of femoral artery dissections.
In patients with calcified rigid vessels, compression alone is not enough to induce hemostasis at the access site after removal of the introducer sheath. Persistent hemorrhage at the access site after removal of the introducer sheath can be a harbinger of pseudoaneurysm or hematoma. Retroperitoneal hemorrhage can be fatal and is often overlooked as a cause of hemodynamic instability.[62] In our experience, the incidence of these complications has progressively decreased with experience and meticulous attention to the postprocedural access site. In addition, the availability of new percutaneous closure devices may have a significant impact on reducing these complications.

Endoluminal carotid artery revascularization is often performed in high-risk patients with significant coronary artery disease. However, the incidence of cardiac complications is relatively low because the procedure is performed while the patient receives intravenous sedation, and this avoids the need for general anesthetic. In addition, in patients with unstable angina awaiting urgent coronary revascularization, the procedure can be performed while the patient receives a continuous heparin infusion. In our recent experience, the availability of new percutaneous closure devices has eliminated the need to stop the heparin infusion for removal of the femoral sheath.

Bradycardia, hypotension, and temporary asystole related to manipulation in the region of the carotid baroreceptors during angioplasty and stenting are not unusual and are clinically significant in at least 25% of patients.[36] These transient hemodynamic changes are less common when self-expanding stents are used. Postprocedure intensive care unit admission is mandatory because refractory hypotension may require treatment with continuous vasopressor infusion for titration of systolic blood pressure. Patients with critical unstable coronary artery disease are less likely to tolerate such hemodynamic changes. Whether the temporary significant hypotension observed intraoperatively in some of these patients has any role in the development of perioperative neurological symptoms is unknown at this point.

Renal complications, although unusual, can occur in patients with renal insufficiency due to contrast load. However, in such patients, the risk of these complications is reduced with proper perioperative hydration and, more recently, with the use of novel, less nephrotoxic contrast agents. Particular care must be taken to reduce the contrast load and use diluted media.

**POTENTIAL APPLICATIONS OF STENTS TO INTRACRANIAL THROMBOOCCLUSIVE CAROTID ARTERY DISEASE**

Further improvements in stent technology and the availability of stents designed exclusively for neurovascular use may enable successful stent treatment of select intracranial diseases. These include intracranial occlusive disease and prevention of acute and subacute vessel occlusion after successful intracranial intraarterial thrombolysis.

**Angioplasty and Stenting of Intracranial Occlusive Disease**

Stenotic lesions located in surgically difficult-to-access areas such as the intracranial carotid artery, the intracranial vertebrobasilar system, and the proximal middle cerebral artery (MCA) are responsible for 5 to 10% of ischemic strokes.[51] Although different extracranial-intracranial bypass procedures (superficial temporal artery-MCA, occipital artery-posterior inferior cerebellar artery, and superficial temporal artery-superior cerebellar or posterior cerebral artery) have been advocated for the treatment of stenotic lesions in these areas, they are technically demanding and difficult to perform. Additionally, no clear-cut evidence supports their efficacy.
The potential advantages of endoluminal revascularization of these inaccessible intracranial vessels by performing angioplasty and stenting are immediately intuitive. Previous experience with intracranial angioplasty alone for the treatment of atherosclerotic lesions has shown some promising results.[8,28,53,54,56,57] However, significant complications (such as intimal dissections and subacute thrombosis) have been reported:[28,53,54] this is reminiscent of the initial experience with coronary angioplasty prior to the introduction of stents and antiplatelet agents. Current studies are underway to evaluate the efficacy of new stents with improved flexibility specifically designed for intracranial use (Fig. 2). We believe that these devices will improve the efficacy of cranial vessel repair and enhance the safety of angioplasty alone by reducing subacute thrombosis and reestablishing lumen patency if a dissection occurs.[15]

**Angioplasty and Stenting for Acute Stroke**

The indications for angioplasty and stenting in patients with crescendo TIAs and stroke evolution have been previously mentioned. One more potential application of angioplasty and stenting is for the treatment of acute stroke related to occlusion of intracranial vessels after intraarterial thrombolytic therapy.

The authors of several reports have suggested the potential advantages of superselective intraarterial thrombolysis over other modes of delivery. The Prolyse in Acute Cerebral Thromboembolism Trial [10] was a randomized, controlled, double-blind trial that tested the rate of recanalization, safety, and clinical efficacy of local intraarterial recombinant pro-urokinase administered within 6 hours of stroke secondary to occlusion of the MCA. Recanalization of the MCA was found in 58% of patients who received the study drug as opposed to only 14% of those who received placebo, and this was statistically significant. The frequency of brain hemorrhage, the most feared complication of acute thrombolysis, was not significantly different in the two groups.

Unfortunately, thrombolytic agents, although effective for thrombus lysis, have a paradoxical effect on platelet activation. There is far more experience with the coronary vessels, and the cardiac literature suggests that rethrombosis occurs more commonly in vessels with significant underlying stenoses.[22,59] Thus, in stenotic vessels, immediate or delayed reocclusion after successful revascularization procedures is a major concern. This phenomenon has been observed in the anterior and posterior circulations: the incidence of reocclusion after successful vertebrobasilar recanalization is as high as 30% and is uniformly fatal.[4] Therefore, a select subgroup of patients with acute ischemic stroke, namely those in whom an atherosclerotic lesion is with superimposed acute thrombosis, is likely to benefit from the addition of stenting to emergency thrombolysis.

Occlusion of the ostia of small perforating vessels by angioplasty and stenting, with the obvious risk of ischemia or infarction in branches of the basilar artery, anterior artery, or MCA, is a poorly understood risk and is probably the most dreaded one. In this respect, the safety of intracranial angioplasty has been reported by several investigators.[8,28,50,53,54,56,57] Additional experimental and clinical experience suggests that the risk with intracranial stents is only a theoretical one. Lateral carotid artery branches in dogs, which approximate the size and angle of origin of human perforating branches, tend to stay patent after stenting of the carotid artery.[61] In addition, in one patient whose fusiform aneurysm of the basilar trunk (a segment notoriously rich in critical small perforating branches) was treated by stenting, no problems with perforating branches occlusions were reported.[29] Similarly, we have not encountered problems with side vessel occlusion in four patients who have undergone intracranial stent placement for
the treatment of aneurysms (three patients) or stenosis (1 patient).[39] The ophthalmic artery (two patients) and the anterior inferior cerebellar artery (two patients) were covered by intracranial stents. In all four patients, vessel patency was angiographically documented 24 hours after stent placement. None of these four patients has experienced any symptoms or signs referable to occlusion of these branches at follow up.

CONCLUSIONS

As new technologies and operative experience evolve, it may be reasonable to consider carotid artery angioplasty and stenting as an alternative procedure to CEA for high-risk patients in whom the complications of CEA may exceed the potential benefits.[35] This subgroup includes patients at risk for carotid artery clamping (such as those with contralateral carotid artery occlusion, previous cerebral infarction, or tandem lesions); those with concomitant unstable angina that requires surgery or other significant medical comorbidities; and those with lesions difficult to treat surgically (such as very high cervical stenosis, radiation-induced stenosis, restenosis). The endovascular technique is well tolerated because it can be performed with minimal sedation without a general anesthetic, providing easy communication with the patient and serial assessments of neurological status while avoiding anesthesia-related complications. Because no postoperative anticoagulation therapy is required, patients are usually discharged after 24 hours.

Although early clinical series have convincingly shown the feasibility and safety of carotid artery angioplasty and stenting, a word of caution is necessary before widespread application of this approach is undertaken. The long-term durability of the angiographic result in the carotid artery is unknown, despite the existence of extensive cardiology experience that has demonstrated a relatively low long-term restenosis rate in the coronary circulation. Also, despite the low incidence of major strokes, the incidence of minor strokes and perioperative transient neurological deficits is relatively high and does not compare favorably with that associated with CEA in low-risk patients. Significant potential for improvement of the devices used exists. The catheter, balloon, and stent technologies used in the preliminary studies reported here were all adapted from coronary, neurovascular, or peripheral vascular applications; none was specifically developed for carotid artery applications.

References


17. European Carotid Surgery Trialists' Collaborative Group: MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. Lancet 337:1235-1243, 1991


Manuscript received October 20, 1998.
Accepted in final form November 17, 1998.
The authors received research support from Arterial Vascular Engineering (Santa Rosa, CA), Boston Scientific Corporation (Natick, MA), and Cordis Endovascular Systems (Miami Lakes, FL).
Address reprint requests to: Giuseppe Lanzino, M.D., Department of Neurosurgery, State University of New York at Buffalo, 3 Gates Circle, Buffalo New York 14209-1194.