Carotid Stents to Prevent Stroke: A Nonsurgical Option

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Angioplasty and stent placement have become accepted alternatives to surgery in many vascular territories. The most recent application of percutaneous intervention has been to explore its clinical utility and safety for stroke prevention in carotid arteries. Over the past 8 years, from January 1994 until Nov 2002, we performed 449 elective carotid stent procedures in 426 patients and in 481 vessels. Informed consent was obtained from each patient. Success was achieved in 97.3% of the patients treated. After one month of follow-up, 12 (2.8%) patients experienced stroke or death. After an average of 2.8 ± 1.7 years (range 1 month to 8.8 years) of follow-up, restenosis was found in 11 (2.6%) patients and was treated with balloon angioplasty. Our results, in a predominantly high-risk surgery group of patients, suggest that carotid stent placement is a viable treatment alternative to conventional surgery. It is likely that as the technology continues to evolve, the procedural risks of stroke and death will be minimized by embolic protection devices, making carotid stenting an option for low-risk surgical patients.

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In general, percutaneous revascularization with stent placement offers a less invasive alternative to surgery, without the risk of general anesthesia, a lower procedural morbidity and mortality, a shorter hospital stay, and a lower cost. Nonsurgical options become particularly attractive in patients with medical comorbidities or other conditions that increase their risk of surgical complications.

Over the past 20 years, angioplasty and stent placement have become accepted alternatives to surgical revascularization of aorta, renal, lower extremity, and brachiocephalic vessels. The most recent application of percutaneous intervention has been to explore its clinical utility and safety for stroke prevention in carotid arteries.

At the Ochsner Clinic Foundation, we became interested in the feasibility of carotid stent placement to prevent stroke in January of 1994. Our program began as a multidisciplinary effort among the Departments of Cardiology, Vascular Surgery, Vascular Medicine, and Neurology. Very early in our experience we realized the benefit of having an independent review of our clinical outcomes. This was accomplished by having a physician who was not a member of procedure team, a neurologist or a vascular internist, examine the patients before and after the procedure.

METHODS

Over the past 8 years, from January 1994 until November 2002, we performed 449 elective carotid stent procedures in 426 patients and in 481 vessels. Informed consent was obtained from each patient. Initially, our primary interest was to investigate the feasibility of carotid stent placement in patients at increased risk for adverse events with surgery (Table 1) (1-3). Subsequently, we have extended our investigations to low surgical risk populations in both randomized and nonrandomized trials. Patients were generally enrolled in investigational trials or registries with systematic clinical follow-up prospectively planned. Contraindications to carotid stenting are listed in Table 2.

Premedication

Effective antiplatelet therapy has been a major advance in the prevention of coronary stent thrombosis and has been adopted as the standard therapy for carotid stent patients. Pretreatment of patients with both aspirin (325 mg/qd) and ticlopidine (250 mg/bid) or clopidogrel (75 mg/qd) has become standard practice. Clopidogrel has generally become the preferred agent due its better safety profile, ability to achieve a more rapid onset of activity with a loading dose, no requirement for surveillance blood counts during follow-up, and its lower daily cost.

Table 1. High risk criteria for carotid stent selection.

- Carotid stenosis above the angle of the jaw.
- Intrathoracic (below the clavicle) carotid stenosis.
- Excessive neck scarring from radiation or infection.
- Prior carotid endarterectomy with recurrent stenosis.
- Contralateral severe carotid stenosis or occlusion.
- Severe coronary artery disease (> 2 vessel CAD).
- Severe pulmonary disease.
- Severe congestive heart failure (NYHA III/IV).
- Left ventricular ejection fraction < 30%.
- Open heart surgery needed within 6 weeks.
- Patient age > 80 years.
- Contralateral laryngeal nerve palsy.
- Severe tandem carotid stenoses.

Table 2. Contraindications to carotid stent placement.

- Active septicemia.
- Visible thrombus within the lesion.
- Unable to gain vascular access.
- Neurovascular rescue not available.
- Inability to obtain informed consent.

Procedure

The femoral artery is the preferred approach, although direct carotid puncture and in extreme circumstances even the brachial approach may be used. We prefer to use either no sedation or very little conscious sedation in order to be able to observe the patient for intraprocedural neurologic deficits. Patients are frequently interrogated for symptoms and asked to perform motor functions relative to the distribution of the target carotid artery to ensure no neurologic event has occurred during the procedure.

Internal Carotid and Extrathoracic Common Carotid Artery Lesions

From the femoral approach, arterial access is obtained and either a long 7 Fr introducer sheath (Shuttle Sheath, Cook, IN) or, if a multipurpose shape coronary guide catheter is to be used, a short 9 Fr/10Fr sheath is inserted. The patient is anticoagulated with 5000 to 10,000 U of heparin. A 125 cm long, 6 Fr diagnostic catheter (JR-4, IMA, Simmons, Headhunter [H5N] or Vitek) is placed through the 7 Fr sheath or 9 Fr/10 Fr coronary guide catheter and functions as an introducer. Either the innominate or the left common carotid artery is engaged using the 6 Fr diagnostic catheter. An exchange length 0.035-in Wholey wire or 0.038-in steerable guidewire is advanced into the external carotid artery, and the diagnostic catheter is advanced (over the wire) several centimeters into the common carotid artery. For gentle curves, the softer wires are often sufficient to support the 7 Fr sheath or 9Fr/10Fr multipurpose coronary guide catheter to enter the common carotid artery over the 6 Fr diagnostic catheter. However, for more acute angles or tortuous arteries, the soft steerable wires are exchanged for an extra-stiff 0.035-in Amplatz wire to provide more support. The diagnostic catheter is then used as an introducer to assist the atraumatic advancement of the sheath or guiding catheter into the common carotid artery. The 0.035-in guidewire and 6 Fr diagnostic catheter are removed leaving the 7 Fr sheath or 9Fr/10Fr coronary guide catheter in the common carotid artery. It is useful at this time to confirm that the activated clotting time (ACT) is approximately 250 seconds and to give additional heparin if necessary prior to crossing the lesion with a guidewire.

Baseline carotid angiography is performed and intracranial views (PA and LAT) are obtained. Quantitative angiographic measurements of the internal carotid artery distal to the lesion and the common carotid artery are obtained to assist in balloon and stent sizing. The lesion is crossed either with an exchange length, extra-support coronary guidewire (0.014-in or 0.018-in) or with a soft-tipped steerable wire and then exchanged for an extra-support wire. Care is taken to control the distal portion of the guidewire to avoid intimal damage or spasm in the intracranial portion of the carotid artery.

Predilation of the carotid lesion is often performed with undersized balloons to avoid the "Dotter" effect of advancing the bulky stent delivery catheter across the lesion. For lesions involving the carotid bifurcation, some investigators prophylactically place a temporary right ventricular pacemaker to treat bradycardia that may occur with balloon inflation. Others premedicate the patient with 0.5 mg of atropine prior to balloon inflation, and some operators only use atropine if bradycardia occurs.

Most operators prefer self-expanding stents for lesions not protected by the axial skeleton or skull from external compression. Self-expanding stents are generously sized at least 1 mm larger than the reference diameter. For lesions at the carotid bifurcation, the stent is sized to be larger than the common carotid artery. There does not appear to be any disadvantage in placing self-expanding stents across the origin of the external carotid artery. Many operators routinely use self-expanding stents that are 8 mm or 10 mm in diameter and either 2 cm or 4 cm in length for all internal carotid lesions.

After stent deployment, final balloon inflation is performed to further dilate the lesion and appose the stent struts to the arterial wall. The balloon size is determined by quantitative measurement of the internal carotid artery distal reference segment. Experienced operators emphasize the importance of conservative balloon sizing (< 1:1) for post-deployment balloon dilations and accept a residual diameter stenosis of < 20% as a good final result. This conservative approach avoids the risk of vessel rupture, minimizes distal dissections, minimizes barotrauma to the carotid body, and potentially decreases the risk of distal embolization that may occur with high pressure inflations.

Following post-deployment balloon dilation, final angiograms of the carotid lesion with intracerebral views are performed. It is important to confirm that there are no missing intracerebral branches and there are no distal internal carotid artery dissections secondary to guidewire manipulation. Before the catheters are withdrawn, a neurologic examination is performed to insure that the patient is intact. If a deficit is discovered, the angiograms are reviewed to look for a culprit lesion, and if discovered, attempts to relieve the ischemia are made (neurologic rescue). The ability to perform a neurologic rescue procedure is an essential element to ensure the safety of the carotid stent procedure.

Aorto-ostial and Intrathoracic Common Carotid Lesions

These lesions present special circumstances because they are protected by the upper thorax from stent compression and require precision placement of the stent at the ostial portion of the vessel. In these "ostial" lesions, most operators favor the use of balloon-expandable stents.

Femoral access is obtained with either an 8 Fr or 9 Fr sheath depending on the diameter of balloon and stent to be deployed. Anticoagulation with 5000 IU to 10,000 IU (1000 IU/kg) of heparin is administered. A 6 Fr diagnostic catheter (JR-4, IMA, Headhunter, or Vitek) is advanced to the aortic arch and the ostium of the common carotid artery is gently engaged. The lesion is crossed with a 0.035-in exchange length Wholey guidewire (Malinckrodt, St. Louis, MO). The diagnostic catheter is exchanged for the coronary guiding catheter (Multipurpose, or Hockey stick) and baseline angiography of the lesion and intracranial angiography are performed. The ostial lesion is then predilated with a balloon sized 1:1 with the common carotid artery reference diameter. Upon deflation of the balloon, the guiding catheter is advanced over the balloon into the target vessel. This allows the guide catheter to act as a sheath and protect the stent during delivery to the lesion. The balloon catheter is removed and a balloon expandable stent (Palmaz 154 or Palmaz 204; Cordis, Miami, FL) is hand-crimped onto the same balloon used for predilation. The balloon mounted stent is then advanced to the ostial carotid lesion within the guiding catheter. The guiding catheter is withdrawn and final positioning of the stent is performed with contrast injections from the guiding catheter. It is preferable to have the stent slightly protrude into the aorta to ensure that the ostium of the target vessel is covered by the stent struts. The stent is deployed with balloon inflation, usually 10 to 12 atm. After the final inflation, the guiding catheter is once again advanced over the deflating balloon to selectively intubate the stent segment. This allows easy access to the stent if a second stent is required. Final angiography is performed including intracranial views and a neurological assessment is performed.

Post-Procedure Care

Patients who have had an uneventful procedure are observed in a post-angioplasty recovery area with frequent neurologic examinations over the next several hours. Arterial sheaths are removed when the ACT falls to less than 170 seconds. Alternatively, femoral closure devices may be used to assist hemostasis.

Patients who are moderately hypertensive (systolic = 180 mmHg), should be observed, as their blood pressure will generally fall to an acceptable range over several hours. Hypotension may lead to relative hypoperfusion of the brain and neurologic symptoms due to a delay in the cerebrovascular autoregulatory vasomotor response.

If a patient becomes hypotensive during carotid body stimulation, it is important to pharmacologically support blood pressure to maintain brain perfusion and to vigorously administer fluids to counteract the reflex vasodilation that may occur. Vasoconstrictor medications (neosynephrine) may be titrated intravenously to achieve a target systolic blood pressure of > 140 mm Hg. Most patients' blood pressure will normalize over several hours, but in severe cases hypotension may persist for 24 to 36 hours. It is also important to investigate potential bleeding sources in any patient who becomes hypotensive during or following an invasive vascular procedure.

Carotid stent patients should have a complete neurological examination within 24 hours of the procedure. It is preferable to have this examination done by an unbiased observer (neurologist or vascular internist) who is not a member of the interventional team. Patients are usually discharged from the hospital the morning after the procedure. Aspirin (325 mg/qd) is prescribed indefinitely if there are no contraindications to its use. Clopidogrel (75 mg/qd) is given for a minimum of 30 days following the procedure. A follow-up clinical examination and carotid duplex ultrasound are scheduled for 1 month.

RESULTS

Acute Procedural Outcome

Patient demographic data are shown in Table 3. Procedural success, defined as a successful angiographic result without a major complication, was achieved in 97.3% of the patients treated (Figure 1). The mean baseline diameter stenosis was reduced from 88.3% to 3.9% after stent placement.

Thirty-Day Outcome

The mean follow-up of patients has been 2.8 ± 1.7 years (range 1 month to 8.8 years). Only 12 (2.8%) of 426 patients experienced stroke or death within 30 days of the procedure. Restenosis after 6 months (defined as > 50% diameter stenosis) was found in 11 (2.6%) patients and was treated with balloon angioplasty. One patient who had a recurrent lesion after endarterectomy had recurrent restenosis after repeat angioplasty or in-stent restenosis and received local vascular irradiation (brachytherapy). He has subseqently done well, without further recurrence.

Table 3. Patient demographics.

Variable	Number (%)
Age	70 ±8.7 (range 43 to 95 yrs)
Sex (M)	282 (63%)
Symptomatic	237 (55% [TIA = 38%; Stroke = 17%])
High surgical risk	365 (86%)
Distal emboli protection	38 (9%)

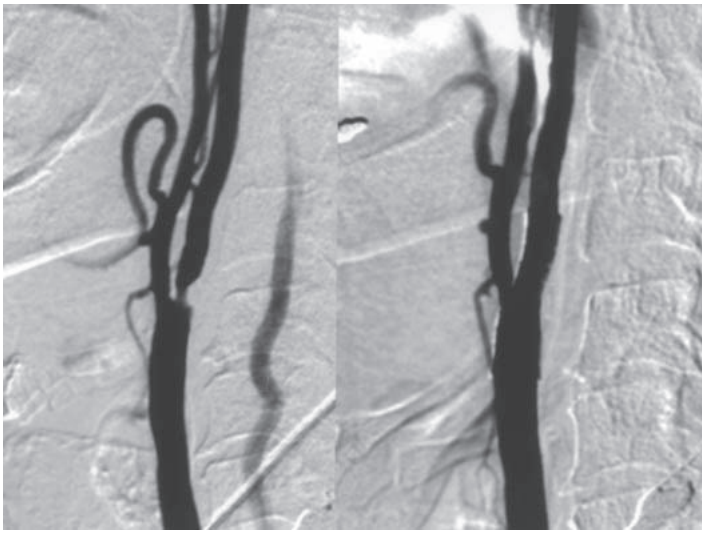

Figure 1. Angiography of carotid stent placement.

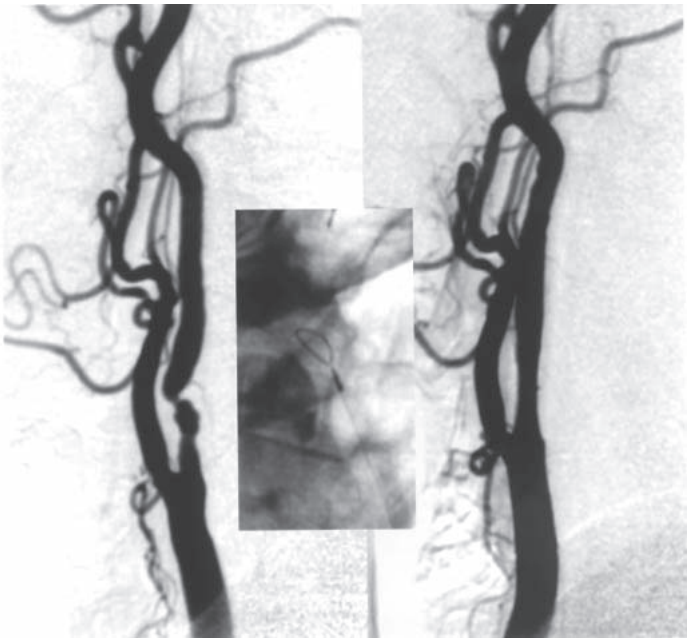

Figure 2. Angiography of the Filterwire (insert) distal protection device.

Table 4. Embolic protection devices.

Distal balloon occlusion with aspiration
Percusurge (MAVERICK/SHELTER) n = 9

Distal filter
Filterwire (BEACH) n = 11
Accunet (CREST/ARCHER) n = 15
Angioguard (SAPPHIRE) n = 3

Embolic Protection Devices

Embolic protection devices have been used with carotid stenting in 38 patients enrolled in FDA approved protocols (Figures 2-4) (Table 4). One (2.6%) of those patients suffered a post-procedural minor stroke. There were no technical failures of the devices and no local complications related to their use. In virtually every case, visible debris was retrieved in the aspirate (Percusurge) or filter (Filterwire, Angioguard, and Accunet).

DISCUSSION

The benefit of surgical revascularization for stroke prevention in selected patients with extracranial carotid artery stenotic lesions has been well established in randomized controlled trials (4-7). Controversy exists over the risks of carotid surgery in everyday practice which may not be reflected in the highly selected population of patients and surgeons participating in the randomized trials. Wennberg and colleagues analyzed mortality results for all Medicare patients (n = 113,300) undergoing carotid endarterectomy during the same period that randomized surgical trials were being conducted (8). They found that the 30-day mortality rate in the Medicare population was three times higher than reported in the randomized trials. They also reported a strong relationship between increasing age and perioperative mortality, with patients more than 85 years old three times more likely to die than those less than 70 years of age. Given the higher mortality results in the Medicare population, which represents the majority of patients receiving carotid surgery, the authors argued that the results of carotid surgery in highly selected patients and performed by highly selected surgeons were not representative of everyday practice.

Carotid Stent Results

Several groups have published their early results for carotid stent placement in various populations of patients with extracranial carotid disease (Table 5). Our data from the past 8 years, in a predominantly high-risk cohort of patients, compare favorably with the published literature.

Early randomized trial data suggest that carotid stenting will emerge as a viable alternative to surgical therapy for stroke the

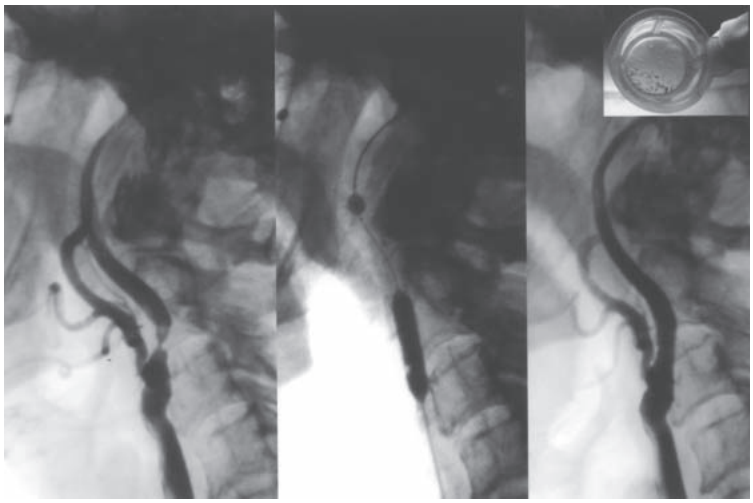

Figure 3. Angiography of the Accunet (center frame) protection device.

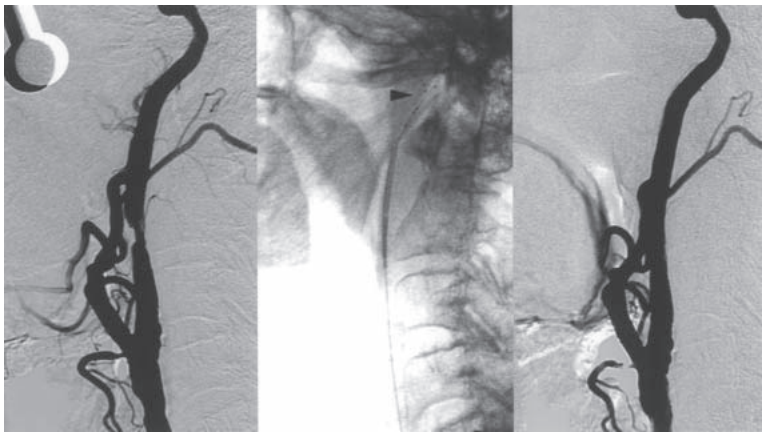

Figure 4. Angiography of the Percusurge distal occlusion balloon (middle), with aspirated debris (insert upper right).

Table 5. Thirty-day complications of carotid stent placement.

Study (Ref)	Arteries (n)	All Stroke & Death (%)	Major Stroke & Death (%)	Death (%)
Yadav et al (9)	126	7.9	2.4	0.8
Wholey et al (10)	2,048	5.8	2.7	1.4
Bergeron et al (11)	99	1	0	0
Henry et al (12)	174	2.8	1.7	0
Al-Mubarak et al (13)	44	6.8	4.5	4.5
Yadav et al (14)	25	4.0	0	0
Waigand et al (15)	53	1.9	1.9	1.9
	2,569	**4.3**	**1.9**	**1.2**

prevention in patients with extracranial carotid artery occlusive disease. The results of the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS), a randomized trial of carotid intervention versus surgery, have been favorable (16). A total of 504 patients (> 90% symptomatic) were randomized to either carotid endarterectomy (n = 253) or carotid angioplasty (n = 251). Only 26% of the angioplasty patients received a carotid stent for a failed angioplasty result; the remainder were treated with balloon angioplasty alone.

The 30-day endpoint of disabling stroke or death showed no difference between the angioplasty arm (10%) and the surgical arm (9.9%). The 95% confidence intervals for the surgical event rate (9.9%, 95% CI 6.2% - 13.6%) overlapped with the complication rates of both the European Carotid Surgery Trial (7.0%, 95% CI 5.8% - 8.1%) and the North American Symptomatic Carotid Endarterectomy Trial (6.5% 95% CI 5.2% - 7.8%). Complications of cranial nerve injury and myocardial ischemia were only seen in the surgical arm. Long-term follow-up has shown no difference in neurological events between the groups. The authors concluded that angioplasty and surgery were equivalent for safety and efficacy but the angioplasty group experienced less procedural morbidity.

Recently, a landmark trial (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy [SAPPHIRE]) was reported at the American Heart Association annual meeting that compared carotid stenting with distal protection to endarterectomy in high-risk surgery patients (17). A total of 723 patients were entered into the trial, with 156 randomized to carotid stenting with distal protection, 151 randomized to endarterectomy, and 416 patients treated in a nonrandomized registry (409 stent, 7 surgery).

For the randomized patients, the 30-day stroke/death/myocardial infarction rate was significantly lower

Table 6. SAPPHIRE: Carotid stent with distal protection versus endarterectomy in high-risk surgery patients (30-day stroke, death, an myocardial infarction) (17).

	Stent	Surgery	P value
Symptomatic	4.2	15.4	ns
Asymptomatic	6.7	11.2	ns
All	5.8	12.6	0.047

in carotid stent group (5.8%) compared with the surgical group (12.6%, $p < 0.05$) (Table 6). In the nonrandomized registry patients, the 30-day stroke/death/myocardial infarction rate was 7.8% for stents and 14.7% for surgery. The surgical group also had an excess of cranial nerve injury (5.3%), which was not seen in the stent group. Long-term follow-up in this trial is on-going, but if the results continue to show a benefit for carotid stent patients, this study will provide strong evidence that stent placement with distal protection is the procedure of choice in patients at increased risk for surgery.

CONCLUSION

It is desirable for carotid stent placement to be performed by a multidisciplinary team composed of members with the skills needed to deliver optimal care. The team should include an experienced vascular interventionist to perform the procedure and a neurologist or vascular internist to screen patients for appropriate indications and to independently assess outcomes. Finally, in centers performing carotid stenting, it is essential that the capability exist to perform an emergency neurovascular rescue procedure.

Given the encouraging results of the two largest randomized trials, CAVATAS in low-risk surgery patients and SAPPHIRE in high-risk surgery patients, carotid stenting is a viable treatment alternative in patients at risk for stroke from carotid artery atherosclerotic lesions. As the technology continues to evolve, it is very likely that embolic protection devices will become routinely available and easier to use, further reducing the risk of a periprocedural stroke and improving the results of carotid stent placement.

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