Early results of carotid stent placement for treatment of extracranial carotid bifurcation occlusive disease

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Objective: The purpose of this study was to review the initial results of carotid artery angioplasty with stenting (CAS) performed by vascular surgeons to treat bifurcation occlusive disease. Most patients were selected for CAS if they had indications for endarterectomy (CEA) but were considered at high risk for surgery.

Methods: Since December 2000, 74 carotid arteries in 69 patients underwent CAS, with distal balloon embolization protection in 96%. Mean patient age was 72 years; 82% of patients were men. Indications for CAS included asymptomatic disease (62%), transient ischemic attack (TIA; 23%), and cerebrovascular accident (18%). Mean internal carotid artery diameter stenosis was 82%. CAS was chosen over CEA because of cardiac (49%) or pulmonary (4%) comorbid conditions, hostile neck (25%), distal extent of disease (6%), and contralateral cranial nerve injury (1%). CAS was performed in 15% of patients who were good surgical candidates, because of patient preference. Pathologic conditions were primary atherosclerosis (81%), recurrent carotid stenosis (18%), and dissection (1%). Procedures were transfemoral in 95% of cases and transcarotid in 5%. In 30% of cases the contralateral carotid artery had 80% or greater stenosis or was completely occluded.

Results: Technical success was achieved in 96% of cases. There were no deaths, no major strokes, one minor stroke (National Institutes of Health Stroke Scale, 3), and one TIA (neurologic event rate, 2.6%). The single minor stroke resolved completely by 1 month. One patient (1.3%) had a perioperative myocardial infarction. Transient neurologic changes occurred in 8% of patients during the protection balloon inflation, and all resolved with deflation. Bradycardia requiring pharmacologic treatment occurred in 14% of patients. At mean follow-up of 6 months there have been two instances of recurrent stenosis greater than 50% as noted at duplex scanning. During the same period, 266 carotid CEAs were performed, with a neurologic event rate of 0.8% (major stroke, 0.4%; no minor strokes; TIA, 0.4%) and a myocardial infarction rate of 3%. Combined stroke and death rate was 1.3% in patients who underwent CAS and 0.5% in patients who underwent CEA.

Conclusion: CAS with cerebral protection can be performed safely in patients at high surgical risk, with low perioperative morbidity and mortality. The durability of the procedure must be determined with longer follow-up. (J Vasc Surg 2004; 39:1193-9.)

Carotid endarterectomy (CEA) has been used to successfully treat extracranial carotid bifurcation occlusive disease for more than four decades. Randomized multicenter clinical trials have demonstrated the effectiveness of CEA in selected patients with both symptomatic and asymptomatic carotid stenosis.1-6 Carotid artery angioplasty with stenting (CAS) to treat extracranial carotid occlusive disease has slowly evolved as a possible alternative therapy that may be beneficial in patients who are at increased risk for complications after CEA.

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial (SAPPHIRE), a multicenter randomized trial comparing CAS with CEA in patients at high surgical risk with symptomatic and asymptomatic disease with severe extracranial carotid stenosis demonstrated a 5.8% combined stroke, myocardial infarction, and death rate, compared with a 12.5% rate in the CEA group.7,8 This is the first study to suggest that CAS may have a better outcome than CEA in selected patients. The role of CAS in the treatment of extracranial carotid occlusive disease remains unclear. At least initially, this procedure seems best suited in patients who are at high risk for CEA. Two groups of patients have been considered at increased risk for CEA: patients with anatomic challenges, such as previous carotid surgery, neck dissection, and lesions that extend above the level of the C2 vertebral body; and patients with significant associated medical comorbid conditions, such as unreconstructed coronary artery disease, congestive heart failure, and recent myocardial infarction.
We describe our initial experience with CAS in patients deemed at increased risk for complications after CEA. This includes all patients to date who have undergone CAS performed by vascular surgeons, including patients who would be included in the “learning curve.” We also focus on the use of embolization protection during CAS.

METHODS

Data for all patients who underwent CAS to treat extracranial carotid bifurcation occlusive disease from December 2000 through September 2003 were reviewed. Patients who had stent-graft placement because of trauma (n = 3), stents placed at the time of CEA because of distal flap (n = 4), or combined coronary bypass and CAS (n = 1) were excluded. Data were prospectively entered into a database. The study was not carried out under a research protocol, but the risks and benefits of CAS compared with CEA were reviewed in detail with each patient before proceeding with CAS, and this review was approved by the institutional review board.

For purposes of this review, patients at high risk were classified as having either anatomic high risk or medical high risk. Anatomic high risk included previous carotid surgery, neck dissection, radiation therapy to the neck, lesions extending above the C2 vertebral body, presence of a stoma, and contralateral cranial nerve injury. Medical high risk included cardiac comorbidity, such as myocardial infarction or congestive heart failure within 3 months or unreconstructed coronary artery disease; and pulmonary comorbidity, such as need for home use of oxygen. Initially only patients at high risk were offered CAS; later in this experience, some patients at normal risk were offered CAS if this was their distinct preference.

Patients received either clopidogrel, 75 mg/d for 1 week, or a single 300-mg loading dose of clopidogrel orally on the morning of the procedure. In addition, patients were given oral aspirin throughout the perioperative period. Procedures were performed either in the operating room, with an OEC 9800 portable C-arm with 12-inch image intensifier (OEC Medical Systems, Salt Lake City, UT) and four-way floating carbon fiber table, or in a radiology suite, with a fixed GE system (GE Medical Systems, Milwaukee, Wis) with a 16-inch image intensifier. An anesthesiologist was present throughout the procedure. Procedures were performed with the patient under local anesthesia, with minimal or no conscious sedation, and an arterial catheter for monitoring blood pressure.

Thoracic arch aortography was performed via a femoral approach. Patients received 3000 to 5000 units of heparin intravenously during the diagnostic portion of the procedure. In most cases only the ipsilateral carotid artery was moved with the aspiration catheter into the external carotid artery. This is similar in theory to the practice many surgeons use when performing CEA of initially dilated with either a 5-mm or 6-mm balloon (Gazelle; Boston Scientific). The aspiration catheter was then placed over the wire, and the ICA proximal to the GuardWire balloon was aspirated twice, then gently flushed with 20 mL of heparinized saline solution. Flushing was performed to promote removal of larger debris that may not be removed with the aspiration catheter into the external carotid artery. This is similar in theory to the practice many surgeons use when performing CEA of initially flushing the common carotid artery flow into the external carotid artery before restoring flow to the ICA. After this, the GuardWire balloon was deflated, flow was restored through the ICA, and completion ipsilateral carotid bifurcation and intracranial arteriograms were obtained.

Patients underwent a neurologic examination performed by the general surgery chief resident or vascular fellow plus the surgical attending physician on postoperative day 1 and at each clinic visit. Patients were not examined by an independent protocol neurologist. Any new neurologic deficits were scored with the National Institutes of Health (NIH) Stroke Scale. A major stroke was defined as a new neurologic event that lasted longer than 24 hours, with an increase in the NIH Stroke Scale greater than 3. A minor stroke was defined as a new neurologic event that lasted longer than 24 hours and was associated with an increase in the NIH Stroke Scale of less than 3. A transient map arteriographic image of the carotid bifurcation was then obtained. With use of the road map image, the stiff guide wire was advanced into the external carotid artery and advanced into the third-order branches. The diagnostic catheter and 6F shuttle sheath were then advanced coaxially into the mid–common carotid artery below the carotid bifurcation. Adequate heparin was given to elevate activated clotting time to 300 seconds. Ipsilateral intracranial arteriograms in lateral and AP views were obtained. The lesion was then crossed with a 200-cm long PercuSurge GuardWire antiembolization device (Medtronic/AVE, Sunnyvale, Calif), which was positioned 3 cm beyond the stenosis in a straight portion of the internal carotid artery (ICA). In all cases the PercuSurge device crossed the lesion without the need for predilation. The GuardWire balloon was serially inflated as described by the manufacturer, from 4 mm to 6 mm in diameter, until flow was occluded through the ICA, as determined at arteriography. Once flow was occluded through the ICA and no neurologic deficit developed, the lesion was predilated with a 3-mm rapid-exchange balloon (Gazelle; Boston Scientific). Based on the GuardWire balloon diameter required to occlude the ICA, either an 8-mm or 10-mm rapid-exchange WallStent (Boston Scientific) was placed across the lesion and dilated with either a 5-mm or 6-mm balloon (Gazelle; Boston Scientific). The aspiration catheter was then placed over the wire, and the ICA proximal to the GuardWire balloon was aspirated twice, then gently flushed with 20 mL of heparinized saline solution. Flushing was performed to promote removal of larger debris that may not be removed with the aspiration catheter into the external carotid artery. This is similar in theory to the practice many surgeons use when performing CEA of initially flushing the common carotid artery flow into the external carotid artery before restoring flow to the ICA. After this, the GuardWire balloon was deflated, flow was restored through the ICA, and completion ipsilateral carotid bifurcation and intracranial arteriograms were obtained.

Patients remained in the recovery room for 4 to 6 hours. If no hemodynamic instability occurred, they were transferred to a standard hospital room. The next morning a carotid duplex scan was obtained, and patients were subsequently discharged to home with aspirin and clopidogrel, 75 mg/d orally for 1 month. Carotid duplex scanning was performed at 1 and 6 months, and yearly thereafter.
ischemic attack (TIA) was defined as a new neurologic deficit that lasted less than 24 hours. A neurologic deficit that developed during inflation of the GuardWire embolization protection balloon that completely resolved with deflation of the balloon was not considered a TIA, but as failure of embolization protection.

Myocardial infarction was defined as a troponin T level greater than 0.03 ng/mL or an abnormal postoperative electrocardiogram compared with preoperative findings suggestive of myocardial infarction.

Recurrent stenosis was defined as stenosis greater than 50% with duplex ultrasound scanning criteria.

Data are presented as mean ± SEM. Statistical analysis was performed with analysis of variance (ANOVA) with post hoc t test, with StatView Software (SAS Institute, Cary, NC).

RESULTS

Patient demographic data. Seventy-four carotid arteries were treated in 69 patients. Mean patient age was 72 ± 1 years, and 82% of patients were men. Comorbid conditions included diabetes in 39% of patients, coronary artery disease in 77% of patients, hypertension in 80% of patients, creatinine concentration greater than 1.8 mg/dL in 17% of patients, and active or recent tobacco use in 86% of patients. A previous reconstruction for peripheral vascular or coronary artery disease had been performed in 51% of patients. Medical management of this cohort of patients included an angiotensin converting enzyme inhibitor in 69% and statins in 76%. Antiplatelet medications were used in the perioperative period in all patients, including clopidogrel in 95% and aspirin in 81%. Eleven percent of patients received warfarin sodium (Coumadin) for reasons unrelated to carotid artery disease. Cardiac comorbidity was the most common reason for selecting CAS over CEA, followed by previous neck operations (Table I). Anatomic high risk was present in 32% of patients, and medical high risk in 53% of patients. Fifteen percent of patients who underwent CAS had no associated increased risk factor for CEA, and received treatment later in the series, on the basis of clear patient preference.

Lesions. Primary atherosclerotic lesions were treated in 81% of patients, recurrent stenosis after previous CEA in 18% of patients, and ICA dissection in 1% of patients. A history of stroke was present in 15% of patients, and previous TIA in 23% of patients; 62% of patients had asymptomatic disease. Mean radiographic ICA stenosis in patients with asymptomatic disease was 85% ± 2%, and in patients with symptomatic disease was 78% ± 3%. In patients without symptoms, 30% had a contralateral ICA occlusion or stenosis greater than 80%, compared with 18% in patients with symptoms (Fig).

Perioperative data. A femoral approach was used in 95% of patients, and a common carotid approach through a limited neck incision with the patient under local anesthesia in 5% of patients. Predilation with a 3-mm balloon before stent placement but after balloon protection was performed in 99% of patients. Self-expanding WallStents were placed in 99% of patients, and Precise stents (Cordis) in 1% of patients. The diameters of the stents used were 8 mm in 48% of procedures and 10 mm in 52% of procedures. A 5-mm angioplasty balloon was used for final angioplasty in 65% of patients, a 6-mm balloon in 34% of patients, and a 4-mm balloon in 1% of patients. Embolization protection was established in 96% of patients. The PercuSurge GuardWire system was used in 95% of patients, reversed internal carotid artery flow in 1%, and no protection in 4%. The procedures in which no cerebral protection was used were to treat recurrent stenosis, early in our experience. Neurologic changes occurred in 8% of patients when the PercuSurge GuardWire was inflated. Neurologic function recovered promptly in all patients but one, once the balloon protection device was deflated. In the one instance, complete neurologic recovery required 30 minutes. This procedure was also complicated by persistent bradycardia and hypotension during this period. In the 8% of patients who did not tolerate balloon inflation initially, all patients but one tolerated subsequent inflation after systolic blood pressure was increased by 30 to 40 mm Hg. Mean operative time was 75 ± 3 minutes; fluoroscopy time was 25 ± 1 minutes; and mean volume of contrast agent (Visipaque) used was 124 ± 7 mL.

Early outcome. Technical success was achieved in 96% of procedures. The two causes of failure were intolerance of GuardWire balloon protection device deployment in one patient, and one episode of congestive heart failure after thoracic flush aortography. The early complication rate is shown in Table II. There were no deaths or major strokes within 30 days. Minor stroke and TIA each occurred in 1.3% of patients. The single patient with a minor stroke had symptoms preoperatively, and normal results of neurologic examination at 1-month follow-up. The single TIA was manifested as a transient episode of expressive aphasia in a patient with asymptomatic disease preoperatively. Patients with primary atherosclerosis had a combined stroke and death rate of 2%; no stroke or death occurred in patients with recurrent stenosis or dissection. Additional complications occurred in 14% of patients (Table III). Mean hospital stay was 1.4 ± 0.2 days. Eighty percent of patients were discharged to home in less than 24 hours. Ten percent of patients required a monitored bed for monitoring of blood pressure or bradycardia.

| Table I. High-risk categories |
|-----------------------------|---|
| Category                     | % |
| Anatomic                    |   |
| Hostile neck                | 25 |
| Distal extent               | 6  |
| Contralateral cranial nerve | 1  |
| Medical                     |   |
| Cardiac                     | 49 |
| Pulmonary                   | 4  |
| None                        | 15 |

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A, Pre-intervention arteriogram demonstrates a critical internal carotid stenosis (arrow). B, Arteriogram after intervention with $8 \times 24$-mm Wallstent and 5-mm balloon angioplasty.
Late outcome. Mean follow-up was 6 ± 1 months. There have been two cases of recurrent stenosis greater than 50% at duplex scanning. No patient had stenosis greater than 80% or required repeat intervention. The number of deaths and of major and minor strokes has remained unchanged since the 30-day follow-up.

Comparison with concurrent CEA. Although the patients were not comparable, a comparison of our concurrent experience with CEA is provided for reference. During the same period as this study of CAS, 266 carotid CEAs were performed at our institution, with a neurologic event rate of 0.8% (major stroke, 0.4%; no minor strokes; TIA, 0.4%) and a myocardial infarction rate of 3%.

DISCUSSION

CEA has achieved outstanding results in the treatment of extracranial carotid occlusive disease. Multicenter randomized trials comparing CEA with medical management in patients with symptomatic disease include the North American Symptomatic Carotid Endarterectomy Trial,1,4 the European Carotid Surgery Trial,4 and the Aspirin and Carotid Endarterectomy trial,10 which have a combined stroke and death rate of 2.3% in patients at good surgical risk. The Asymptomatic Carotid Atherosclerosis Study similarly showed a stroke and death rate of only 2.3% in patients with asymptomatic disease with severe extracranial carotid bifurcation occlusive disease.6

The use of CAS in patients with extracranial carotid occlusive disease has been controversial. Early single-center reports were encouraging.11 However, two subsequent trials that directly compared CEA and CAS were stopped early because of a significantly higher incidence of stroke in the CAS group.12,13 The Carotid and Vertebral Artery Transluminal Angioplasty Study was the first to demonstrate a better outcome in the CAS group compared with the CEA group.14 This trial was not thought representative of contemporary surgical results, however, because there was a stroke rate of 9.9% in patients who underwent CEA. The SAPPHIRE Trial was a randomized multicenter trial that compared the results of CEA with those of CAS in patients at high risk with symptomatic and asymptomatic disease.7 This study was the first to demonstrate a better outcome in the CAS group compared with the CEA group.8 The major difference between the two treatment groups was in the incidence of myocardial infarction; there was no significant difference in major or minor stroke, or death. These results have been maintained at 1-year follow-up, at which time the multiple adverse events rate was 12% in the CAS group and 20% in the CEA group.15 Whether these results can be extrapolated to a patient population at low risk is unknown. At present, Hobson16 is conducting an NIH-sponsored trial (Carotid Revascularization and Endarterectomy vs Stent Trial) that seeks to answer this question.

The present study demonstrated a stroke and death rate similar to that reported in previous CAS trials and lower than that reported in the SAPPHIRE trial. There are several explanations for the low stroke rate reported in our study. First, our single-center experience is similar to that of previous single-center reports, which tend to have lower complication rates than those reported in multicenter trials. Second, our patients were not examined by an independent protocol neurologist, as in the SAPPHIRE trial, which may have detected more subtle neurologic deficits. Third, the cerebral protection device and stent system used in the present study were different from those used in the SAPPHIRE trial. Fourth, we did not prospectively determine cardiac enzyme levels in all patients, which could have disclosed more subtle cardiac events. Last, a focused angiographic approach was used in the performance of CAS in this report. Only the target carotid artery was cannulated, rather than performing four-vessel arteriography. This focused approach may have limited the wire and catheter manipulation within the aortic arch, resulting in a lower incidence of neurologic events.

There did not appear to be a significant learning curve effect on the outcome of carotid stent placement by vascular surgeons in the present study. Previous investigators have found a significant learning curve effect in the outcome of CAS,17 and suggest that a minimum of 50 such procedures must be performed to overcome the learning curve effect. One possible explanation for the lack of a learning curve effect in this report may be the endovascular experience previously accumulated by the two vascular surgeons (R.J.P., M.S.) who performed CAS procedures in this study. Both surgeons had extensive experience with the use of the embolization protection device and low-profile systems in mesenteric and renal vascular beds before using these devices in the carotid artery. In addition, both surgeons had observed more than 15 CAS procedures at outside institutions before beginning the carotid stent program.

### Table II. Thirty-day operative outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>%</th>
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<tbody>
<tr>
<td>Death</td>
<td>0</td>
</tr>
<tr>
<td>Major stroke</td>
<td>0</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>1.3</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>1.3</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.3</td>
</tr>
</tbody>
</table>

### Table III. Additional post-procedure complications*

<table>
<thead>
<tr>
<th>Complication</th>
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<tbody>
<tr>
<td>Bradyarrhythmia</td>
<td>3</td>
</tr>
<tr>
<td>Reperfusion syndrome (unilateral headache)</td>
<td>1</td>
</tr>
<tr>
<td>Groin hematoma</td>
<td>3</td>
</tr>
<tr>
<td>Blood pressure control for management of hypotension</td>
<td>1</td>
</tr>
<tr>
<td>Seizure</td>
<td>1</td>
</tr>
<tr>
<td>Groin infection</td>
<td>1</td>
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*Post-procedure (30 days) complications occurred in 14% of all patients.
Some form of embolization protection was used in all but two patients in this study. Patients who did not receive embolization protection received treatment only for recurrent stenosis early in our experience. Ohki et al. demonstrated in an ex vivo model that atheroembolic particles are generated during CAS from human carotid plaque specimens. Although previous reports have demonstrated that the use of embolization protection is safe, to date no randomized report has demonstrated the superiority of embolization protection in prevention of perioperative neurologic events during CAS. A meta-analysis performed by Kastrup et al. does support the use of cerebral protection devices. These investigators have shown a reduction in neurologic events, from 5.5% to 1.8%, after use of cerebral protection devices. Similarly, Wholey et al., using a multicenter registry, demonstrated a stroke and death rate of 4.2% without cerebral protection and 1.7% with protection. Despite the lack of conclusive evidence suggesting the superiority of embolization protection, the use of such devices has become widespread as CAS has evolved.

In a randomized multicenter trial, use of the PercuSurge GuardWire balloon embolization protection device resulted in a 42% decrease in cardiac events after angioplasty of saphenous vein graft lesions. Henry et al. demonstrated a neurologic event rate of 1.8% when this device was used in CAS. The GuardWire has a low crossing profile, and was effective at crossing all lesions in this report. The major drawback to this device is that in 8% of patients in the present study neurologic compromise developed with balloon inflation. All patients but one recovered promptly after immediate balloon deflation. An explanation for the delay in neurologic recovery in the one patient was potentially the persistent bradycardia and hypotension, which when resolved resulted in complete neurologic recovery. This patient underwent successful repeat CAS the next day, during which blood pressure was maintained at 30 to 40 mm Hg higher than at the initial procedure. In general, if a patient did not tolerate initial balloon occlusion of the ICA with the GuardWire, the balloon was deflated, blood pressure was elevated 30 to 40 mm Hg above baseline, and the balloon was subsequently re-inflated. All patients but one tolerated a second attempt at balloon inflation.

The unknown incidence of stent-related recurrent stenosis is an additional area of concern with CAS. The incidence of recurrent stenosis in the present study at mean follow-up of 6 months was 2%. This compares favorably with previous CAS studies, which have shown an average recurrent stenosis rate of 4.8%. As a result of the limited follow-up in this group of patients, the durability of this procedure will need further evaluation.

In conclusion, our initial experience with CAS, mainly in patients at high surgical risk, was comparable with our concurrent CEA experience, although follow-up was too short to determine the ultimate durability of CAS. We found that some patients have a very strong preference for CAS over CEA, and may refuse an operative approach despite its potential benefit. For this reason, vascular surgeons must develop skills to perform and evaluate CAS, so that all appropriate treatment options are available to patients.

REFERENCES


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