Long-Term Outcome After Angioplasty for Symptomatic Extracranial Carotid Stenosis in Poor Surgical Candidates

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Background and Purpose—The optimal treatment of patients with symptomatic carotid stenosis who are poor surgical candidates is uncertain. The purposes of this study were to report the long-term outcome after angioplasty in a series of these patients and to compare these data with historical control data from the North American Symptomatic Carotid Endarterectomy Trial (NASCET).

Methods—We identified 42 consecutive patients with >70% carotid stenosis and ipsilateral ischemic symptoms within 120 days of treatment with angioplasty. All were considered poor surgical candidates by experienced surgeons. Baseline epidemiological stroke risk factors were obtained from review of medical records. Follow-up was from clinic records and by telephone.

Results—Baseline epidemiological stroke risk factors were similar to those of medically treated NASCET patients. Angioplasty patients tended to have higher degrees of stenosis (45% with >90% stenosis versus 24% in NASCET) and more frequent contralateral stenosis or occlusion (30% versus 9%) than NASCET patients. Three patients suffered procedural strokes; 2 of the 3 made nearly complete recoveries. One additional patient suffered a central retinal occlusion 48 hours after angioplasty. No ipsilateral strokes occurred during the mean follow-up period of 1.7 years. Three patients were lost to follow-up. The cumulative risk of stroke was 9.5% (4 of 42) compared with 26% at 2 years for medically treated patients in NASCET.

Conclusions—These pilot data suggest a beneficial effect of angioplasty for patients with high-grade symptomatic carotid stenosis who are not good surgical candidates. (Stroke. 2002;33:2877-2880.)

Key Words: angioplasty ▪ carotid endarterectomy ▪ carotid stenosis ▪ stents

Carotid endarterectomy has been shown to be a durable and effective procedure for the prevention of stroke in patients with recent ischemic symptoms and associated high-grade stenosis of the cervical carotid artery.1,2 However, some patients with symptomatic carotid stenosis may not be good candidates for surgery because of age, anatomic factors, prior neck irradiation, previous surgery, or poor medical condition. Both the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) excluded many such patients to the extent that these factors could be explicitly defined.1–3 Thus, the optimal treatment of these excluded patients remains unresolved.

Angioplasty and stenting may be a good option for this subset of patients; however, the current data supporting endovascular therapy are limited.4–7 There have been no randomized studies of angioplasty versus medical therapy for patients considered to be poor surgical candidates, and the natural history for these patients remains to be defined. Most of the literature for carotid angioplasty and stenting consists of case series that include both symptomatic and asymptomatic patients, as well as patients with different degrees of surgical risk.4–9 These factors have a strong impact on the procedural complication rate for both angioplasty and surgical endarterectomy.10–13 One prospective, randomized study of angioplasty versus surgical endarterectomy has shown similar stroke risk at 3 years in symptomatic patients who are good surgical candidates.14

The purpose of the present study was to compare the outcome of a consecutive series of symptomatic patients with high-grade carotid stenosis treated with endovascular techniques with the outcome observed in historical control subjects. All patients were considered to be poor surgical candidates by referring surgeons; the current practice at our institution is for patients with surgically amenable carotid stenosis to undergo endarterectomy. The outcome data from this consecutive series of poor surgical candidates were compared with those of historical control subjects: medically treated patients in NASCET.

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Materials and Methods

Patients
Between October 1996 and November 2001, 102 patients were referred to our institution for angioplasty and stenting of 110 extracranial carotid artery stenoses. The medical histories of these patients, their procedural reports, and immediate clinical outcomes were recorded in a prospective database maintained for quality assurance purposes by a nurse-coordinator. We reviewed this database for patients who met 2 criteria: ipsilateral ischemic symptoms within 120 days and stenosis of the symptomatic carotid of \( >70\% \). Ipsilateral ischemic events were defined as stroke, transient ischemic attack (TIA), and transient or permanent monocular blindness. Carotid artery stenosis was measured by NASCET criteria. Patients with carotid stenosis resulting from dissection were excluded. Forty-two patients who met these criteria were identified. This retrospective review was approved by the Human Studies Committee of our institution.

Angioplasty Procedure
All patients received antiplatelet prophylaxis with ticlopidine, clopidogrel, and/or aspirin. Angioplasty and stenting procedures were performed with intravenous conscious sedation in 39 patients (93%); the remaining 3 patients had the procedure while under general anesthesia. Transthoracic pacing pads were placed in case of symptomatic bradycardia or asystole but were never used. Vascular access was obtained via standard sterile Seldinger technique at the common femoral artery in all patients. In all patients, a 5F diagnostic catheter was placed in the target common or external carotid artery. This was exchanged over a wire for a 7F long sheath (Shuttle, Cook Inc). The tip of this sheath was placed in the common carotid artery close enough to the stenosis to allow stability of angioplasty and stent devices but not so close as to interfere with deployment. Heparinization was administered as an intravenous bolus, generally calculated at 100 U/kg, either just before or after placement of the 7F sheath. Serial activated clotting times were measured at 30-minute intervals with a target activated clotting time of \( >300\) seconds. Diagnostic images of the stenosis and distal circulation were obtained. The degree of stenosis was measured by NASCET criteria. Robinol (9 of 42) or atropine (8 of 44) was administered for prophylaxis or treatment of bradycardia with balloon expansion at the discretion of the operator. The lesion was then crossed under road-map control with a 300-cm 0.018-inch wire (Roadrunner, Cook Inc). An angioplasty balloon was guided across the lesion and inflated 1 or 2 times to the nominal pressure. Generally, this was a 4-mm balloon (n=37). A self-expanding stent was placed in 41 of the 42 patients after initial angioplasty. Poststen intromioplasty with a high pressure was required for stent apposition or residual stenosis in 30 patients. Control angiography was performed, followed by a brief neurological examination in patients not under general anesthesia. Control of the common femoral arteriography site was by manual compression (n=17) or by use of a closure device (Perclose, Abbott Inc [n=20] or AngioSeal, St Jude’s Medical, Daig Division [n=6]). Heparinization was continued after the procedure in 18 patients for up to 24 hours. Patients were maintained on combined antiplatelet therapy after the procedure for 30 days, followed by aspirin alone indefinitely.

Clinical Data
Hospital records and office charts were reviewed for the following information: age, sex, race, presenting symptoms and date of onset, percentage of stenosis, presence and degree of contralateral carotid stenosis, contralateral carotid occlusion, hypertension, diabetes, peripheral vascular disease, coronary artery disease, smoking, prior ischemic stroke, and prior myocardial infarction. Presenting symptoms were categorized as stroke, TIA, and ocular stroke and TIA (amaurosis fugax). Reasons for surgical referral were recorded, as were details of the angioplasty procedure and any procedural complications.

Clinical Follow-Up and End Points
Follow-up was obtained through review of medical records and clinic notes or by direct contact by a nurse-coordinator. Patients were asked if they had experienced any sudden episodes of weakness, blindness, numbness, or speech difficulty, including events similar to their index event. The specific end points assessed were the occurrence of ipsilateral stroke, any stroke, and death, as in NASCET. A minor stroke was defined as a neurological deficit lasting \(<7\) days or a stroke with no disabling residual symptoms. Possible TIs were also recorded. Cause of death was ascertained from medical records.

Data Analysis
Baseline epidemiological stroke risk factors and demographic data were tabulated. The occurrence of an end point was calculated at 30 days (perioperative) and through the time to the most recent follow-up.

Results
Patient demographics and baseline epidemiologic stroke risk factors are shown relative to NASCET medically treated patients in Table 1. Patients in the present series had more severe stenosis and more frequent contralateral disease than patients in the NASCET study. Five patients (11.6%) were found to have contralateral occlusion, with 13 patients (30.2%) having contralateral stenosis of \( >50\% \).

The reasons for referral for angioplasty are listed in Table 2. Seventeen patients (40.5%) had recurrent stenosis after prior carotid endarterectomy, and 4 patients (9.5%) had stenosis after cervical irradiation. High and low anatomic location of the stenotic lesion and long segment lesions were angiographic risk factors that led to referrals for endovascular therapy in 26 patients. Significant medical conditions such as severe cardiac conditions accounted for the remainder of referrals. Of the 42 patients, 14 had \( >1\) reason for referral.

Procedural Results and Complications
Angioplasty was completed in all patients, and a stent was placed in all but 1 patient. Thirty-nine patients had no residual stenosis after the angioplasty procedure. The patient who was unable to have a stent placed had residual stenosis of 40%. Three patients suffered strokes during the procedure; 2 of the 3 patients had minor, nondisabling strokes with nearly complete clinical recovery. In 1 patient, ischemic symptoms developed after angioplasty and before stent placement. Angiography showed a distal thrombus in the middle cerebral artery that was successfully treated with direct intra-arterial thrombolysis. No obstructive lesion was found in the second patient. The third patient suffered a major stroke immediately after stent deployment. Angiography showed no arterial occlusions. CT scanning several days later showed multiple infarctions consistent with a shower of emboli. The patient died of a myocardial infarction 6 months later while in long-term rehabilitation. A fourth patient developed monocular blindness 48 hours after the procedure. Retinal examination showed cholesterol emboli. None of these 4 patients suffered any further ischemic events. The 30-day risk of stroke in this series was 4 of 42 or 9.5%. There were no perioperative deaths.

Two patients had periprocedural ipsilateral TIs, with 1 occurring during the procedure and the other on the first postoperative day. The latter patient had a second TIA 20 days
later. An angiogram obtained at that point was normal. The patient had no further neurological symptoms.

Three patients suffered arterial access site complications within 30 days of the angioplasty procedure. The complications consisted of a groin infection requiring surgical exploration in 1 patient, a common femoral artery occlusion requiring emergent bypass in 1 patient, and a retroperitoneal hemorrhage requiring prolonged hospital stay in 1 patient.

Long-Term Outcome
Mean follow-up was 1.7 years (range, 1 to 62 months). Three patients were lost to follow-up after 5.5, 6, and 12 months. No ipsilateral strokes occurred during the follow-up period. Therefore, the overall incidence of any ipsilateral stroke for all 42 patients was 9.5% (4 of 42) over a mean follow-up period of 1.7 years. Outcome data are detailed in Table 3 with comparison to the medical and surgical arms of the NASCET trial.

Two patients suffered nonipsilateral strokes during the follow-up period. One had a fatal contralateral stroke; the other patient had a minor posterior circulation stroke. Four deaths occurred: 2 from myocardial infarctions at 6 and 18.5 months, 1 from a contralateral stroke at 17 months, and 1 from cancer at 12 months.

Discussion
In this series of 42 poor surgical candidates with recently symptomatic, high-grade carotid stenosis, angioplasty and stenting yielded a long-term outcome that compared favorably to that of medically treated patients in NASCET. In the absence of data from a randomized, controlled trial of angioplasty and stenting against best medical therapy, these results support the use of angioplasty and stenting over medical treatment in this highly selected patient population.

Is the NASCET cohort a reasonable historical control for comparison? It must be acknowledged that most, if not all, of the patients in the present series would have been excluded from NASCET for the reasons listed in Table 2. In addition, 3 patients were 80 years of age. Despite this clear limitation, it is reasonable to assume that the patients in the present study would have had a similar natural history risk of stroke if left untreated as the NASCET medically treated patients. First, all patients in the present series had documented ischemic symptoms within 120 days of treatment in the territory supplied by a carotid artery with at least 70% luminal diameter narrowing in its extracranial portion. These were 2 key inclusion criteria for NASCET.1,3 Second, the data from Table 1 demonstrate very similar baseline stroke risk factors for patients in NASCET and from the present series. The only difference between the 2 groups was that patients in the present study tended to have greater degrees of stenosis and more frequent severe contralateral disease, factors that might be expected to indicate a higher risk for stroke.12,13 Third, the underlying pathology in most patients in the present series was likely to be atherosclerotic disease. Six patients had a
history of neck irradiation. The nature of the stenosis in these patients is likely to be atherosclerotic. Radiation-induced endothelial injury may result in atherosclerotic disease in the carotid vessel, often occurring at an increased pace in patients with elevated serum cholesterol and triglycerides. Recurrent stenosis after endarterectomy has been shown to have varying pathology, with restenosis occurring within 2 to 3 years more likely to result from myointimal hyperplasia and stenosis occurring after 3 years more likely to be from the reformation of atherosclerotic plaques.

The limitations of the present study, regarding comparison with NASCET data, are as follows. First, 3 patients were lost to follow-up. If all 3 had suffered late ipsilateral strokes, the ipsilateral stroke rate would have been 16.7% (7 of 42). This still compares favorably with the 26% reported for the medically treated cohort of NASCET, however. Second, NASCET data were reported as 2-year cumulative follow-up in contrast to our series with a mean follow-up of 1.7 years. Third, although follow-up data were collected prospectively, data regarding procedural complications were collected retrospectively. Fourth, follow-up was obtained by telephone interview for many patients. The validity of a similar telephone interview for verifying stroke-free status in a patient population with a high prevalence of previous stroke has been well-established.

The periprocedural stroke rate of 9.5% in the present study is higher than in many prior case series of carotid artery angioplasty and stenting but are nearly identical to those reported in the Carotid and Vertebral Artery Transluminal Angioplasty Study. In this prospective, randomized study of angioplasty and stenting versus surgical endarterectomy, the 30-day stroke and death rate was 10.0% for endovascularly treated symptomatic patients. Many prior case series have included asymptomatic patients and combined their procedural and outcome analyses. Periprocedural stroke rates are higher for symptomatic patients than asymptomatic patients. These findings extend to surgical endarterectomy as well: the periprocedural stroke and death rate in the Asymptomatic Carotid Atherosclerosis Study was 2.3% in asymptomatic patients compared with the 5.8% seen in symptomatic patients in NASCET. Complications of stroke may be reduced in the future by the use of recently developed protection devices that prevent distal embolization of plaque fragments or thrombus.

In conclusion, the pilot data from the present study support the use of angioplasty and stenting in patients with symptomatic, severe extracranial carotid stenosis who are poor surgical candidates. Although there are substantial differences between the NASCET group and the patients in our cohort, namely that they would have been excluded from NASCET, it is reasonable to assume that they would have had a similar outcome with medical treatment given the presence of high-grade carotid artery stenosis and recent ischemic symptoms. It is likely that angioplasty and stenting in these patients provide a better long-term outcome than would be achieved with medical treatment.

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