Safety of Latest-Generation Self-expanding Stents in Patients With NASCET-Ineligible Severe Symptomatic Extracranial Internal Carotid Artery Stenosis

Italo Linfante, MD; Joshua A. Hirsch, MD; Magdy Selim, MD, PhD; Gottfried Schlaug, MD, PhD; Louis R. Caplan, MD; Arra S. Reddy, MD

Background: Patients with symptomatic extracranial internal carotid artery stenosis (≥70%) benefit from carotid endarterectomy when compared with medical management. However, independent risk factors can significantly increase the combined stroke and death risk after carotid endarterectomy. Carotid angioplasty and stenting (CAS) is a therapeutic option in patients who are otherwise at high risk or ineligible for carotid endarterectomy. Previous-generation self-expanding stents were hampered by length foreshortening, which limited their application in multifactorial occlusive extracranial internal carotid artery stenosis.

Methods: This is a single-center, prospective, open-label, safety study of CAS with the latest-generation self-expanding stents in patients with extracranial internal carotid artery symptomatic stenosis (≥70%). All patients included were adjudicated to be ineligible for carotid endarterectomy by a vascular surgeon and/or a neurologist according to the exclusion criteria. Primary adverse events included death and all strokes (ipsilateral and contralateral). Secondary adverse events included transient ischemic attack, myocardial infarction, stent thrombosis, need for reintervention, and presence of hematomas. All adverse events were recorded at 24 hours, 30 days, and 6 months after CAS.

Results: Between June 1, 2001, and January 30, 2003, 23 consecutive patients (14 women and 9 men; mean age, 65 years; age range, 48-85 years) underwent 24 extracranial CAS procedures with the latest-generation self-expanding stents. All patients had one or multiple criteria for ineligibility according to the North American Symptomatic Carotid Endarterectomy Trial. Extracranial CAS was successful in all patients, with average residual stenosis of less than 20%. One patient (4%) experienced a stroke by the 30-day periprocedure examination. The total number of primary adverse events at 6 months after CAS was 2 strokes (9%), 1 of which was contralateral to the stent placement; there were no deaths. Twenty-two patients were asymptomatic at 6 months, with a modified Rankin scale score of 1 or less. Of the 2 patients who had a stroke, 1 had a follow-up modified Rankin scale score of 3.

Conclusion: Extracranial CAS with the latest-generation self-expanding stents is a valid alternative treatment in high-risk or North American Symptomatic Carotid Endarterectomy Trial–ineligible patients.

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asymptomatic patients who were good surgical candidates. Similar to CEA, medical and radiological risk factors can negatively impact outcome after CAS.7,8 To our knowledge, there are no published randomized trials of CAS on symptomatic severe ICA stenosis in high surgical risk or NASCET-ineligible patients. Nonrandomized, single-institution, retrospective database analyses of CAS in this group of patients reported periprocedural risks for strokes and death comparable to those of CEA.9-11

Recently, technology has improved the type of stents used in extracranial occlusive ICA disease.12 In particular, self-expanding nitinol stents use the high continuous outward force that results in expansion of the ICA contour over time, decreasing short-term endothelial injury and thrombogenicity.13 However, previous-generation self-expanding stents were hampered by a decrease in length on the vertical axis as the stent expanded (length foreshortening).14 The latest-generation self-expanding stents are not significantly affected by length foreshortening and may be more suitable for complex, multifactorial, extracranial ICA stenosis.

**METHODS**

This is a single-center study evaluating the safety of CAS with the latest-generation self-expanding stents in multifactorial 70% or more symptomatic extracranial ICA stenosis. The study was a retrospective analysis from June 1, 2001, to July 30, 2002, and a prospective analysis from August 1, 2002, to January 30, 2003. We included consecutive patients who (1) experienced strokes, transient ischemic attacks, or retinal symptoms in the territory of the ipsilateral carotid stenosis within 30 days of the procedure; (2) had extracranial ICA stenosis of 70% or more, measured by digital subtraction angiography by NASCET criteria; and (3) were adjudicated to be NASCET ineligible for CEA by the referring vascular surgeons and/or neurologist. The adjudication was based on the patient's medical history and neurological examination and imaging results. Risk factors for CEA were subdivided into 2 groups: medical (unstable neurological status, recent history of myocardial infarction, unstable congestive heart failure with an ejection fraction <28%, difficult-to-treat hypertension, cancer with a life expectancy of <5 years, and aged >80 years) and radiological (restenosis after CEA, high or complex plaques, carotid dissections, contralateral ICA occlusion, and severe intracranial stenosis). Patients with ICA stenosis resulting from dissection were included.

**PROCEDURE**

All patients or a patient's relative signed the informed consent stating the risks and possible complications of the procedure. All patients received antiplatelet prophylaxis with clopidogrel bisulfate and aspirin. Extracranial CAS was performed with monitored anesthesia care in most patients. Preprocedure trans-thoracic pacing pads were placed as a precautionary measure, but never used. Access was via the common femoral artery in all patients. A 4-vascular angiogram by digitally subtracted images (Integris-Allura Biplane N 5000; Philips Medical Systems, Best, the Netherlands) was obtained in all patients before and after the stenting procedure to evaluate the extent of intracranial occlusive disease, collateral flow, and hemodynamics. The degree of stenosis was measured by NASCET criteria on the carotid angiograms. The ICA lesion was crossed with a 250-cm wire with a 0.036-cm diameter (Agility 14; Cordis Corp, Miami, Fla). The artery was accessed by either a 7F guiding catheter or a 6F long arterial sheath. When necessary, an exchange-length wire was placed and anchored in the ipsilateral external carotid artery. Heparin was administered with an intravenous bolus, 100 U/kg, before starting the actual stenting procedure, and monitored by serial activated clotting times, with a target of longer than 300 seconds. An angioplasty balloon was used only in patients with severe stenosis. Glycopyrrolate, 0.1 to 0.2 mg as a single dose intravenously, was administered for prophylaxis of bradycardia before balloon expansion. Twenty-four latest-generation self-expanding stents (PRECISE; Cordis Corp) were placed in 23 patients after initial angioplasty. Gentle positioning angioplasty was required for stent dilatation in 20 patients. After CAS, patients received combined antiplatelet therapy (aspirin, 325 mg/d; and clopidogrel, 75 mg/d) for at least 6 weeks, followed by aspirin, 325 mg/d, given alone indefinitely.

**SAFETY EVALUATION**

A neurological examination was performed on all patients by a stroke neurologist (I.L. or M.S.) at baseline, during the procedure, and at 30 days and 6 months after CAS. The modified Rankin scale score was included in the 30-day and 6-month follow-up examinations. Primary adverse events recorded for the safety evaluation included death and any stroke (ipsilateral or contralateral). Secondary adverse events recorded were transient ischemic attack, myocardial infarction (Q wave or non-Q wave), stent thrombosis, need for reintervention, and the presence of hematomas. Successful stent deployment and patency were determined immediately by angiography and carotid ultrasonography at 30 days and 6 months after CAS. All examination results and events were recorded immediately postprocedure and at 24 hours, 30 days, and 6 months after the procedure. Medical histories, procedural reports, and clinical outcomes were recorded in a prospective database maintained for quality assurance purposes by the interventional neuroradiology service.

The guideline for stopping the study was an incidence of primary adverse events that exceeded twice the rate of such events reported in patients with 70% or more stenosis in the NASCET surgical group.

**RESULTS**

Patient data are shown in Table 1. Between June 1, 2001, and January 30, 2003, we performed CAS in 23 consecutive NASCET-ineligible patients and placed 24 stents. Criteria that would exclude the patients from CEA, according to NASCET, are listed in Table 2.

The stent deployed successfully, without significant length foreshortening, in all 23 patients, with residual stenosis of less than 20%. During the procedure, there was a progressive increase in the ICA diameter secondary to stent expansion (Figure 1 and Figure 2). At the 30-day postprocedure follow-up examination, there was 1 stroke and 1 transient ischemic attack. One patient developed a right inferior division middle cerebral artery stroke secondary to stent occlusion 2 weeks after CAS. The stent occlusion was likely secondary to a severely tortuous ICA with an irregular, long, and severe stenosis. Another patient who was not adequately anticoagulated with heparin experienced a transient ischemic attack immediately postprocedure.

The number of primary adverse events at 6 months included the sum of the events recorded at 30 days plus the events recorded at 6 months. Overall, there were 2 strokes (9%) and no deaths. The second stroke oc-
curred in a patient who had a less than 2-cm-diameter anterior cerebral artery infarction contralateral to the stent placement. This patient recovered completely in 1 week. Secondary adverse events included 1 non-Q-wave myocardial infarction and 4 hematomas postprocedure, 1 retroperitoneal hematoma, and 3 groin hematomas. All hematomas resolved without surgical intervention. Twenty-two stents were patent at the 6-month follow-up Doppler examination. Twenty-two patients had a modified Rankin scale score of 1 or less at 6 months after CAS. The patient who experienced the stroke secondary to stent occlusion had a modified Rankin scale score of 3.

Extracranial ICA angioplasty and stenting with the latest-generation self-expanding stents yielded a satisfactory safety profile in our series of 23 NASCET-ineligible patients with symptomatic 70% or more stenosis. In the present series, there was a higher frequency of severe stenosis (>90%) compared with that in NASCET, and there were multiple NASCET exclusion criteria (Table 2). The NASCET exclusion criteria have been associated with a significant increase in the risk of stroke or death after CEA. To our knowledge, the natural history of patients with 70% or more, symptomatic, NASCET-ineligible ICA stenosis has not been evaluated in a large control study. Therefore, the evaluation of a treatment in NASCET-ineligible patients is not optimal because of the lack of a historical control group. It may be reasonable to assume that the risk of stroke or death in medically treated patients with 70% or more, symptomatic, NASCET-ineligible ICA stenosis should be either similar or higher compared with the medically treated NASCET-eligible patients.

In the 70% or more stenosis asymptomatic group of NASCET, the 30-day periprocedural stroke and death rate was 5.8%. Therefore, a new treatment for this patient population should have a 30-day stroke and death rate that is at least similar to 5.8%. In our series, there was 1 stroke (4%) at the 30-day follow-up examination. In larger series of high-risk surgical patients with 70% or more symptomatic stenosis, Fox et al and Malek et al reported a periprocedural stroke and death rate of 3.8% and 9.5%, respectively. Perioperative stroke rates for CEA are lower in asymptomatic patients with balanced surgical risk stenosis compared with symptomatic patients with high surgical risk, severe stenosis. In particular, the risk of stroke and death in the Asymptomatic Carotid Atherosclerosis Study was 2.3%, compared with 5.8% for the 70% or more stenosis symptomatic group of NASCET. Similar to CEA, CAS also resulted in higher periprocedural complication rates in high-risk and/or NASCET-ineligible patients compared with patients with a balanced risk for surgery. Nevertheless, if we combine all the data on CAS in 70% or more stenosis, symptomatic, high-risk, NASCET-ineligible patients (including ours), the average 30-day perioperative stroke rate is 6.2%, which is similar to the 5.8% of the NASCET surgical group.

In the present series, the total number of primary adverse events at 6 months after CAS was 2 strokes (9%), 1 of which was contralateral to the stent placement; there were no deaths. In longer-term follow-up studies, Fox et al reported an incidence of all strokes or death of 17.8% during a median follow-up of 14 months.

The most significant limitations of our study are the small cohort of patients and the short follow-up. Even with these limitations, CAS with the latest-generation self-expanding stents had a satisfactory safety profile despite factors that significantly increase the risk for any procedure. Altogether, the safety data on CAS in high-risk symptomatic patients with 70% or more ICA stenosis are in range with the stroke and death rates of CEA.
in patients with a balanced risk for surgery. In our se-
ries, the original study design did not include the use of
a distal protection device. Recent advancements in stent
technology, such as stents that are more suitable for ex-
tracranial ICA occlusive disease and emboli protection
devices, seem promising for improving the safety of CAS.
In particular, the improvements in safety of distal pro-
tection devices may result in further reduction of em-
bolic complications.16,17

In conclusion, although larger series are needed, our
preliminary data indicate that CAS with the latest-
generation self-expanding stents represents a valuable
treatment option in patients with severe extracranial ICA
stenosis and multiple risk factors for surgery.

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material support (Drs Linfante, Hirsch, Caplan, and Reddy);
study supervision (Drs Hirsch, Caplan, and Reddy).

Corresponding author and reprints: Italo Linfante, MD,
Division of NeuroEndovascular Surgery and Interven-
tional Neuroradiology, Department of Radiology, Univer-
sity of Miami, Jackson Memorial Hospital, 1611 NW 12th
Ave, West Wing 279, Miami, FL 33136 (e-mail:
ilinfant@med.miami.edu).

Figure 1. A, A 73-year-old woman with severe right internal carotid artery stenosis, lung cancer, congestive heart failure, severe intracranial stenosis, and an
anterior communicating artery aneurysm. B, There was satisfactory recanalization after balloon angioplasty and stenting. C, An angiogram 6 months after carotid
angioplasty and stenting showed expansion in the diameter of the stent.

Figure 2. A 63-year-old man with a left internal carotid artery (ICA) restenosis after carotid endarterectomy, a recent myocardial infarction, crescendo transient
ischemic attacks, and contralateral ICA occlusion. A-C, During the procedure, there was a progressive increase in ICA diameter secondary to stent expansion.
REFERENCES


