Drug-Eluting Stents for the Treatment of Intracranial Atherosclerosis
Initial Experience and Midterm Angiographic Follow-up

Alex Abou-Chebl, MD; Qasim Bashir, MD; Jay S. Yadav, MD

Background and Purpose—Intracranial stenting is associated with a 32% rate of restenosis. Drug-eluting stents (DES) have revolutionized the treatment of coronary artery disease and have greatly reduced the risk of in-stent stenosis. We present our experience with the feasibility and safety of using DES for patients with symptomatic intracranial atherosclerosis.

Methods—All of the patients had >70% stenoses and had failed maximal medical therapy. They were pretreated with aspirin, clopidogrel, and intraprocedural heparin. All of the lesions were predilated, and balloons and stents were slightly undersized. Clopidogrel and aspirin were continued for 1 year, and patients had clinical follow-up and vascular imaging at 30 days, 6 months, and 1 year.

Results—Eight patients with intracranial internal carotid artery (3), middle cerebral (2), basilar (2), and vertebral artery (1) stenoses were successfully treated with 4 Cypher (Cordis Corp) and 4 Taxus (Boston Scientific Inc) stents. The mean stenosis severity was reduced from 84.4% to 2.5% ± 4.6%. One patient had an intraprocedural retinal embolism, but there were no other complications. Over a mean follow-up of 11.1 ± 4.9 months (range, 2 to 17.3 months), patients have had repeat angiography (5) or transcranial Doppler with or without CT angiography (3). None of the patients have had clinical or significant angiographic restenosis or required target vessel revascularization.

Conclusions—Elective intracranial stenting with DES appears to be feasible and safe, but additional clinical experience is required to assess its efficacy. (Stroke. 2005;36:e165-e168.)

Key Words: angiography ■ intracranial arterial diseases ■ ischemia ■ stents
Interventional Technique
All of the patients underwent thorough cerebral angiography with an emphasis on defining the following lesional and anatomical characteristics: vessel reference diameter, lesion length, eccentricity, and the presence of perforating vessels or branches within the lesion or adjacent vessel segments. Via a transfemoral approach, a 70- to 80-cm–long 7 to 8F sheath was placed in the distal common carotid artery or proximal subclavian artery. A 6F guide catheter (Envoy, Cordis Corp) was then placed into the distal cervical internal carotid artery (ICA) or vertebral artery (VA) at the C2 level. Interventions were performed with 0.014-inch coronary balloon and stent delivery systems over soft-tipped, hydrophilic guide wires. Wire manipulation and placement were guided by patient discomfort; if any, angioplasty was performed with an undersized coronary balloon (Maverick, Boston Scientific Inc), which was slowly inflated to its nominal pressure. Balloon inflations were guided by patient discomfort; if pain developed, then additional balloon inflation was stopped, and a neurological assessment was performed.

Provisional stenting was performed when dissection, residual stenosis, or lesion recoil occurred. Stents were sized to match the diameter of the smallest normal arterial segment into which they were to be implanted. As with angioplasty, pain or discomfort were used to guide stent delivery and deployment. Postdilation with a balloon sized 1:1 with the treated segment was performed when needed to ensure complete stent expansion.

Postprocedural Management
Postprocedure patients were sent to the neurological intensive care unit for observation and continuous arterial blood pressure monitoring to keep systolic blood pressures < 140 mm Hg. Patients were discharged to home the following day on a regimen of 325 mg of aspirin lifelong and 75 mg of clopidogrel daily for 1 year. All were followed clinically and with transcranial Doppler ultrasound (TCD) at 30 days, 6 months, 1 year, and yearly thereafter. All of the patients were also asked to return for a follow-up angiogram between 6 months and 1 year after treatment.

Outcome Measures
All of the adverse events were noted prospectively. Technical success was defined angiographically as a reduction in stenosis severity to ≥50% luminal narrowing without angiographic evidence of distal embolization, flow-limiting dissection, or contrast extravasation. Angiographic restenosis was defined as ≥50% stenosis within the stent or just outside the stent margins.

Results
Eight patients were successfully treated, 4 with Cypher (Cordis Corp) and 4 with Taxus (Boston Scientific Inc) DES. Three ICA, 2 middle cerebral, 2 basilar (BA), and 1 vertebral artery were treated. All 8 of the patients had recurrent cerebral ischemia despite medical therapy with aspirin and clopidogrel (6) or warfarin (2). Patient clinical details are listed in Tables 1 and 2.

The mean stenosis severity was reduced from 84.4%±10.2% to 2.5%±4.6% (Table 2). There was 1 clinical complication not related to the stent itself (retinal embolism during guide catheter removal) and 1 poststenting complication (nonflow-limiting, asymptomatic BA dissection). During the mean follow-up period of 11.1±4.9 months, there have been no recurrent cerebral ischemic events, and all of the patients remain neurologically independent.
Follow-up cerebral angiography has been obtained in 5 of 8 patients at a mean of 9.6 ± 4.3 months (range, 2 to 15.2) after stenting (Table 3). There was no evidence of aneurysm formation or other arterial abnormality by angiography (Figure). Two patients have refused additional angiography but have returned for follow-up with TCD, combined with CT angiography in 1 patient. In both cases, there was a normal flow pattern proximal to and distal to the stent, and in the patient with the middle cerebral stent, the instent mean flow velocities were normal, suggesting that there was no hemodynamically significant stenosis. One patient has not reached the 6-month angiographic follow-up point, but on TCD at 2 months, the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Duration of Clinical Follow-up, Months</th>
<th>Clinical Outcomes</th>
<th>Time to Follow-up Imaging, Months</th>
<th>Follow-up Angiography Findings, % Stenosis</th>
<th>TCD MFV, Initial/Latest Follow-up, cm/s*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17.3</td>
<td>No Recurrent Events</td>
<td>15.2</td>
<td>0</td>
<td>†/108</td>
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<tr>
<td>2</td>
<td>14.7</td>
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<td>12.6</td>
<td>29%</td>
<td>258/130</td>
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<tr>
<td>3</td>
<td>14.7</td>
<td>No Recurrent Events</td>
<td>12.6</td>
<td>0</td>
<td>†/60</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
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<td>2</td>
<td>†</td>
<td>170/50</td>
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<td>5</td>
<td>12.9</td>
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<td>10.8</td>
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<tr>
<td>6</td>
<td>10.6</td>
<td>No Recurrent Events</td>
<td>10.4</td>
<td>†</td>
<td>†/40§</td>
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<tr>
<td>7</td>
<td>9.6</td>
<td>No Recurrent Events</td>
<td>7.5</td>
<td>†</td>
<td>†/68¶</td>
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<td>8</td>
<td>7.6</td>
<td>No Recurrent Events</td>
<td>5.5</td>
<td>0</td>
<td>†/88</td>
</tr>
<tr>
<td>Mean</td>
<td>11.1</td>
<td></td>
<td>9.6</td>
<td></td>
<td></td>
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<tr>
<td>Std. Dev.</td>
<td>4.9</td>
<td></td>
<td>4.3</td>
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</tbody>
</table>

TCD indicates transcranial Doppler ultrasound; MFV, mean-flow velocities; Std. Dev, standard deviation. *All follow-up TCD’s performed same day as angiogram or within 1 week of angiogram; †Preprocedure TCD not done; ‡Patient refused angiography or too early for angiographic follow-up; †Internal carotid pulsatility index of 1.2 (contralateral 1.1) and normal MFV proximal and distal to stent suggest no hemodynamically significant instent stenosis; ¶Middle cerebral artery MFV are in normal range and good opacification distal to stent by computed tomography angiography suggest no significant instent stenosis.

Angiographic images of the 5 patients for whom a follow-up angiograms were obtained. Each series (A–E) contains (left to right) the initial pretreatment angiogram, the immediate poststenting angiogram, and the most recent angiographic follow-up image. In each image, the arrow points to the stented segment. Note in B the 1 year follow-up image shows a mild degree of neointimal growth indicated by the white arrow.
BA stent was widely patent. None of the patients had significant angiographic or clinical restenosis or required target vessel revascularization. The asymptomatic BA dissection complicating a Taxus (Boston Scientific Inc) DES was completely healed on the 6-month angiogram (Figure 1).

**Discussion**

To our knowledge, this is the first report of the use of DES in the intracranial vasculature with angiographic and clinical follow-up. In this series, the use of DES was feasible and safe, because there were no untoward effects associated with the stents. The midterm safety of these devices appears to be favorable with no evidence of arterial toxicity. Importantly, there have been no delayed recurrent ischemic events or cases of stent thrombosis over a mean of 11.1 months of follow-up.

The use of DES in the intracranial vasculature is desirable because of the high restenosis risk (∼32%) associated with bare metal stents (BMS). In the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries trial of a BMS developed for intracranial stenoses, restenosis was associated with a 39% rate of recurrent symptoms. Drug-eluting stents have revolutionized the treatment of CAD by reducing the risk of in-stent restenosis from 30% to ∼1%, and they should have a similar effect on intracranial atherosclerotic lesions. The ultimate goal of stenting is to maintain adequate cerebral perfusion over the lifetime of the patient; by preventing restenosis with DES, patients may be spared the risk of recurrent ischemia, as well as the risks associated with intracranial interventions, which may be between 10% and 30%.

The histological structure of the intracranial arteries differs from that of the coronary arteries, and, as a consequence, there are theoretical risks (eg, vessel toxicity and delayed endothelialization) associated with DES that are not associated with BMS. Vessel toxicity occurs by a direct effect of the drugs. The safety of DES in the intracranial vasculature was assessed in the current series by angiography, and no evidence of arterial toxicity was noted. Therefore, DES was feasible and safe for the treatment of intracranial atherosclerotic lesions.

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In summary, in this series, we found that the use of DES was feasible and safe for the treatment of intracranial atherosclerosis. Larger, longer-term studies are needed, but DES are a promising new therapy for this potentially devastating disease.

**References**

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