Angioplasty for Symptomatic Intracranial Stenosis

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Background and Purpose—Medical treatment of symptomatic intracranial stenosis carries a high risk of stroke. This study was done to evaluate the clinical and angiographic outcomes after intracranial angioplasty for this disease.

Methods—A total of 120 patients with 124 intracranial stenoses were treated by primary angioplasty. All patients had neurologic symptoms (stroke or transient ischemic attack) attributable to intracranial stenoses ≥50%. Angiograms were evaluated before and after angioplasty for the degree of stenosis.

Results—Pretreatment stenoses varied from 50% to 95% (mean 82.2±10.2). Post-treatment stenoses varied from 0% to 90% (mean 36.0±20.1). There were 3 strokes and 4 deaths (all neurological) within 30 days of the procedure, giving a combined periprocedural stroke and death rate of 5.8%. A total of 116 patients (96.7%) were available for a mean follow-up time of 42.3 months. There were 6 patients who had a stroke in the territory of treatment and 5 additional patients with stroke in other territories. Ten deaths occurred during the follow-up period, none of which were neurological. Including the periprocedural stroke and deaths, this yielded an annual stroke rate of 3.2% in the territory of treatment and a 4.4% annual rate for all strokes.

Conclusion—Intracranial angioplasty can be performed with a high degree of technical success and a low risk of complications. Long-term clinical follow-up of intracranial angioplasty patients demonstrates a risk of future strokes that compares favorably to patients receiving medical therapy. (Stroke. 2006;37:1016-1020.)

Key Words: angioplasty ■ arteriosclerosis ■ basilar artery ■ carotid arteries ■ middle cerebral artery

Intracranial atherosclerotic stenosis accounts for 8% to 10% of ischemic strokes and is particularly prevalent in the black and Asian population.1,2 Medical therapy with antiplatelet and antithrombotic agents has been widely used, but there is a high rate of failure, resulting in recurrent transient ischemic attack (TIA), stroke, and death in symptomatic patients.3–6 Endovascular therapy using primary angioplasty or stenting has been used to treat this condition, although reports have generally documented smaller, single center experiences, and consequently, recommendations for the use of endovascular techniques have been controversial.7 We report the immediate results and long-term clinical follow-up using intracranial angioplasty in the treatment of 120 patients with symptomatic intracranial stenosis treated at 3 centers.

Methods

All patients who underwent primary balloon angioplasty for symptomatic atherosclerotic intracranial stenoses between July 1993 and December 2004 at 3 institutions (Borgess Medical Center, Kalamazoo, Mich; Our Lady of Lourdes Regional Medical Center, Lafayette, La; Stanford University Medical Center, Stanford, Calif) were included in this study. There were a total of 120 patients with 124 lesions. During this period, there were 6 additional patients for whom treatment was attempted, but they were not treated because the lesion could not be safely accessed by the angioplasty balloon. All patients had intracranial stenoses with symptoms referable to the target lesion. A total of 118 (98%) were on antiplatelet or anticoagulant medication at the time of symptoms; 76 patients (63%) were on antiplatelet medication (aspirin, ticlopidine, clopidogrel, dipyridamole), 27 (22%) were on anticoagulant therapy (warfarin or heparin), and 15 (13%) were receiving both types of agents.

Intracranial lesions were defined as being located in the internal carotid artery at or above the precavernous or upper petrous portion and in the posterior circulation as being above the C-1 portion of the distal vertebral artery. Patients were excluded if the lesion was attributable to etiology other than atherosclerosis such as vasospasm, if there was a tandem extracranial lesion undergoing treatment, or if the treatment was occurring during an acute stroke. If patients had a preprocedure stroke, they were generally not treated until 4 to 6 weeks after the acute event because of concerns about reperfusion hemorrhage. Some patients had tandem intracranial lesions treated (eg, internal carotid artery and middle cerebral artery or vertebral and basilar). In these cases, when multiple lesions were present in the same circulation, the most profound stenosis was reported before and after angioplasty. Patients were only considered to have a separate lesion if there was an angioplasty performed on a lesion in a completely separate vascular distribution. Patients were treated with semicompliant coronary angioplasty balloons varying in size from 1.5×9 mm to 4×20 mm that were...
introduced through 5F to 7F guide catheters. Balloons were deliberately undersized by 0.5 mm diameter to reduce the risk of arterial damage or rupture by using angiographically obtained measurements. The shortest available length to fully cross the lesion was chosen to improve balloon tracking. Slow inflation times were used to minimize rupture and dissection. Balloons were inflated at ~1 atmosphere every 30 to 60 seconds until nominal pressures were achieved. These pressures were generally in the range of 6 to 8 atmospheres for the balloons that were used. Stents were placed at the discretion of the treating physician in some the cases. This was done if the stenosis was felt to be worse or not improved after angioplasty or if a postangioplasty dissection was felt to require treatment. The outcome data were analyzed on an “intention-to-treat” basis, and these patients were therefore included in the study.

In advance of the procedure, patients were placed on antiplatelet medication if they were not already using it. There was no standard for timing the start of therapy or medication type. During the procedure, patients were systemically anticoagulated, generally by bolus injection, but there was no standard. After the procedure, patients were generally continued on antiplatelet medication on a chronic basis, although earlier in the experience, anticoagulation was also used.

Stenosis was measured at the individual centers using available software provided by the digital subtraction angiography equipment manufacturer. The measurement was based on the ratio of the narrowest diameter on any projection to the nearest portion of the artery that is judged to be normal. When severe preocclusive stenosis made it too difficult to perform an accurate measurement the stenosis was reported as 95%. The annual stroke rate was calculated using the ratio of stroke rate to follow-up time.

**Results**

There were 84 men and 36 women ranging in age from 31 to 82 years (mean 62.3±12.2 years). Sixty-six patients (55%) had a stroke before angioplasty, and 54 (45%) had TIAs. Table 1 shows the vascular risk factors of the patient population, and Table 2 shows the lesion locations. There was an even distribution of lesions in the anterior and posterior circulations.

The pretreatment stenosis varied from 50% to 95% (mean 82.2±10.2). A total of 118 (95.2%) of the lesions had >70% stenosis, with only 6 (4.8%) having stenosis in the 50% to 69% range. All the lesions were crossed and dilated. Post-treatment stenosis varied between 0% and 90% (mean 36.0±20.1).

Stents were placed after the angioplasty in 16 (12.9%) of the angioplasty procedures. Eleven of these were placed because the stenosis was judged to be the same or worse after angioplasty. Five were placed after the angioplasty when a dissection was noted. Post-treatment stenosis for the group treated with angioplasty alone was 5% to 90% (mean 39.4±18.7). Sixty-four patients (59.3%) had <50% residual stenosis, 35 (32.4%) had 50% to 69% stenosis, and 9 (8.3%) had >70% residual stenosis. In addition to the 5 dissections treated with stent placement, there were 20 other patients with dissection (visible luminal flaps) not treated by stent placement (20.2% of all angioplasties). There were no occlusions at the time of the postangioplasty angiogram.

There were 3 periprocedural strokes occurring within 30 days of the procedure and 4 periprocedural deaths, yielding a 5.8% periprocedural stroke and death rate. None of the periprocedural strokes were disabling or resulted in a change in modified Rankin score. Six of these events occurred in the first day postprocedure, and 1 occurred in a delayed fashion in the 30-day period. Two deaths were attributable to vessel rupture, 1 to reperfusion hemorrhage, and 1 to complications associated with an ischemic infarct.

A total of 116 patients were available for follow-up, and the follow-up time varied from 1 to 128 months (mean 42.3 months). Ninety-three had follow-up >12 months. During this period, there were 10 deaths attributable to various etiologies, including myocardial infarct, multiorgan system failure, cancer, sepsis, and spinal cord injury. There were no deaths attributable to ischemic or hemorrhagic stroke. During the follow-up period, there were 6 strokes that occurred in the vascular distribution of the treated vessel and 5 strokes that occurred outside of the area of treatment. Six TIs were also reported in the follow-up period, although it is not known to what territory they are attributable.

The annual stroke rate in the territory of treatment including the periprocedural strokes and deaths was 3.2%. The annual stroke rate for all strokes including periprocedural events was 4.4%. The annual stroke rate for those patients who had angioplasty without stent placement was 3.0% for the territory of treatment and 4.3% for stroke in any territory. The annual rate of strokes in the treated territory for those patients showing dissection (not treated with stent placement) was 1.5%. Kaplan–Meier analysis demonstrated a 5-year stroke-free survival of 88.6% for strokes in the territory of angioplasty including the periprocedural events (Figure 1). The 5-year stroke-free survival for all strokes including the periprocedural complications was 83.1% (Figure 2).

During the follow-up period, 14 patients (12.1%) had a repeat angioplasty, and 8 patients (6.9%) had a stent placed. All were accomplished without complication. These procedures were done based on the individual decision of the treating physician because the angiographic stenosis had worsened, the patient had additional symptoms (stroke or TIA), or the treating physician felt that a better result could be achieved in a repeat procedure.

**TABLE 1. Vascular Risk Factors**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Hypertension</td>
<td>90 (75)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>69 (58)</td>
<td></td>
</tr>
<tr>
<td>Smoking history</td>
<td>56 (47)</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>83 (69)</td>
<td></td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>61 (31)</td>
<td></td>
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</table>

**TABLE 2. Lesion Locations**

<table>
<thead>
<tr>
<th>Location</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior circulation</td>
<td></td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>43 (35)</td>
</tr>
<tr>
<td>Middle cerebral artery</td>
<td>20 (16)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td></td>
</tr>
<tr>
<td>Vertebral</td>
<td>37 (30)</td>
</tr>
<tr>
<td>Basilar</td>
<td>22 (17)</td>
</tr>
<tr>
<td>Posterior cerebral artery</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>
Table 3 shows the aggregate modified Rankin scores before and after treatment at the time of last follow-up. Fifty-seven patients (49%) had improved scores, 53 (45%) were unchanged, and 7 (6%) had poorer scores.

Routine angiographic follow-up was not performed on all patients. Sixty-seven patients (57.8%) had follow-up angiogram, with the last angiographic follow-up done between 1.0 and 84.0 months postprocedure (mean 20.5 ± 22.7 months). Eighteen (26.9%) showed improvement in the stenosis compared with postangioplasty angiogram, 33 (49.3%) were unchanged, and 16 (23.9%) displayed worsening stenosis at the time of last follow-up.

**Discussion**

The clinical outcome after primary angioplasty for the treatment of symptomatic intracranial atherosclerosis reported here compares favorably with the recent reported results for the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial. WASID found a high rate of stroke for patients with symptomatic intracranial stenosis treated with medical therapy. WASID was prematurely stopped because of safety concerns in the warfarin-treated group and concluded that aspirin should be used in preference to warfarin. However, the study found there was a 12% 1-year and a 15% 2-year probability for recurrent stroke in the territory of the stenotic artery in patients treated with aspirin. The annual rate of same territory strokes calculated from the reported aggregate follow-up was 8.5%. Our results show a 3.2% annual stroke rate, including periprocedural strokes, a 1-year stroke rate of 8.8% (including periprocedural strokes), and a 2-year cumulative stroke rate of 11.8%. We did not include the 6 patients who did not undergo angioplasty because the balloon could not safely access the lesion. Two of these 6 patients had strokes in the first year, 1 of them fatal.

The patients in the current study may have been at a higher risk of stroke than discussed previously in natural history studies and higher than the aggregate reported in WASID. It is true that >50% of the WASID patients had middle cerebral artery or basilar lesions, whereas 33% of our patients had lesions in the locations. These locations may contribute to a higher stroke rate in the WASID group. However, in agreement with known pathophysiology for vascular lesions in all
other territories, post hoc analysis of the WASID data suggests that patients presenting with stroke and those with >70% stenosis have higher rates of subsequent stroke when compared with patients presenting with TIA and 50% to 69% stenosis. Fifty-five percent of our patients had a stroke in the territory of treatment before angioplasty, and 61% of the WASID patients had strokes in the territory of stenosis. A total of 118 (95.2%) of the lesions treated in the current study had >70% stenosis, whereas only 37.4% had >70% stenosis in the WASID study. It has also been suggested that patients who fail previous treatment with antiplatelet or anticoagulant medication are at a high risk for developing recurrent symptoms. A total of 118 (98%) of the patients in this series had failed some combination of these agents.

Previously reported single center experiences with angioplasty have suggested that the procedure can be done with a high degree of technical success,9–14 although some centers have reported higher rates of complication.15 Long-term

### TABLE 3. Modified Rankin Scores

<table>
<thead>
<tr>
<th>Score</th>
<th>Pretreatment (%)</th>
<th>Post-Treatment (%)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>18 (15%)</td>
<td>42 (37%)</td>
</tr>
<tr>
<td>1</td>
<td>32 (27%)</td>
<td>28 (24%)</td>
</tr>
<tr>
<td>2</td>
<td>28 (23%)</td>
<td>32 (28%)</td>
</tr>
<tr>
<td>3</td>
<td>24 (20%)</td>
<td>9 (8%)</td>
</tr>
<tr>
<td>4</td>
<td>11 (9%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>5</td>
<td>4 (3%)</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>

Figure 2. Kaplan–Meier plots showing the stroke-free survival for all strokes. The plots show the percentage of patients still alive without having had a stroke in any territory after their angioplasty. Solid line represents the outcome for all treated patients. Dashed line represents the stroke-free survival after excluding strokes occurring as procedural complications.
outcome data after angioplasty, although less frequently reported, has shown similar low rates of stroke to the rates reported here. Clark et al reported on 17 patients treated with intracranial angioplasty followed for a mean of 22 months and found no neurological events in the territories of the angioplasty vessels. Marks et al recently reported a mean follow-up time of 52.9 months in 36 patients showing a 3.36% annual stroke rate in the territory appropriate to the site of angioplasty. Intention to treat using primary stenting has also been used for symptomatic intracranial atherosclerosis. Stenting may improve the degree of post-treatment residual stenosis and treat dissections; however, the procedure involves additional instrumentation with more complex devices in the intracranial circulation. It has not been shown that stenting can be performed with an improved safety profile over angioplasty or that the procedure will improve clinical outcomes compared with angioplasty alone. There has been 1 prospectively reported series of stenting for intracranial atherosclerosis. Forty-three patients with intracranial atherosclerotic stenosis were treated with a stent designed for use in the intracranial circulation. There were 6 strokes in the first 12 months of the follow-up (13.9%), 4 of these in the periprocedural period. Recent single center experience with stenting has also reported similar rates of periprocedural complications and follow-up strokes. Nevertheless, in the study reported here, stents were used in 16 (12.9%) of the initial procedures when the angioplasty did not appear to achieve an adequate result. As stents specifically designed for use in the intracranial circulation become available, they might play a greater role in the endovascular management of this disease.

Limitations of these data should be mentioned. Because this is a retrospective evaluation, bias may have been introduced to select patients that would have a high success rate and low complication rate with the procedure and that would have a lower risk of stroke. However the incidence of vascular risk factors reported here and the mean age of our patient population are very similar to the population reported in the WASID trial. In addition, as has already been pointed out, the degree of stenosis seen in our patients and the failure of medical therapy may suggest these patients were at very high risk of stroke. In addition, these data are derived from 3 centers, and the absence of a uniform management protocol or procedural technique is an inherent limitation of the data.

Fourteen patients (12.1%) had a repeat angioplasty, and 8 patients (6.9%) had a stent placed in the period of follow-up. These additional procedures were performed in this series without complication; however, they do expose the patients to additional intraprocedural risk and do involve an extra health care cost, which would have to be factored into any treatment paradigm for this disease. However, repeat treatment of many diseases is necessary, and clinical success is the goal of any therapy.

In conclusion, this study reports treatment results and long-term clinical follow-up in 120 patients with symptomatic intracranial stenosis undergoing primary angioplasty for their disease. This study documents a high rate of technical success and a low rate of subsequent stroke that compares quite favorably with recently published data in patients with these lesions treated with medical therapy.

Acknowledgments

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References

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