Results using a self-expanding stent alone in the treatment of severe symptomatic carotid bifurcation stenosis

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Object. Conventional endovascular therapy for carotid stenosis involves placement of an embolic protection device followed by stent insertion and angioplasty. A simpler approach may be placement of a stent alone. The authors determined how often this approach could be used to treat patients with carotid stenosis, and assessed which factors would preclude this approach.

Methods. Over a period of 6 years, 97 patients with symptomatic carotid stenosis were treated with the intention of using a “stent-only” approach. Arteries in 77 patients (79%) were treated with stents alone, 13 required preinsertion balloon dilation, 6 postinsertion dilation, and 1 both pre- and postinsertion dilation.

Results. The mean stenosis according to North American Symptomatic Carotid Endarterectomy Trial criteria was reduced from 82 to 40% in the stent-only group and from 89 to 37% in the stent and balloon angioplasty group. The 30-day stroke and death rate was 7.2%. Patients were followed for a mean of 15 months. In the stent-alone group, the mean preoperative Doppler peak systolic velocity (PSV) was 409 cm/second, with an internal carotid artery/common carotid artery (ICA/CCA) ratio of 7.2. At follow-up review, the PSV decreased to 153 cm/second and the ICA/CCA ratio to 2.1. In the angioplasty group the mean preoperative PSV was 496 cm/second and the ICA/CCA ratio was 9.2, decreasing to 163 cm/second and 2, respectively, at follow-up evaluation. Restenosis occurred in 12.8% of patients at 6 months and in 15.9% at 1 year. One stroke occurred during the follow-up period in each group. Using multivariable analysis, factors precluding the “stent-only” approach were as follows: severity of stenosis, circumferential calcification, and no history of hyperlipidemia.

Conclusions. Balloons may not be required to treat all patients with carotid stenosis. A stent alone was feasible in 79% of patients, and 79% of patients were alive and free from ipsilateral stroke or restenosis at 1 year. Restenosis rates with this approach are higher than with conventional angioplasty and stent insertion. Carotid arteries with very severe stenoses (> 90%) and circumferential calcification may be more successfully treated with angioplasty combined with stent placement. (DOI: 10.3171/JNS/2008/109/9/0454)

Key Words • carotid angioplasty and stent placement • carotid endarterectomy • carotid stenosis • stroke

CAROTID angioplasty and stent placement is an increasingly used alternative therapy for the treatment of carotid stenosis. The results of recent clinical trials, however, have called into question the widespread use of this therapy followed by stent insertion and angioplasty. A simpler approach may be placement of a stent alone. The authors determined how often this approach could be used to treat patients with carotid stenosis, and assessed which factors would preclude this approach.

Methods. Over a period of 6 years, 97 patients with symptomatic carotid stenosis were treated with the intention of using a “stent-only” approach. Arteries in 77 patients (79%) were treated with stents alone, 13 required preinsertion balloon dilation, 6 postinsertion dilation, and 1 both pre- and postinsertion dilation.

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of an SES alone can dilate severely stenosed CAs.\textsuperscript{16,20} We wanted to determine how often this “stent only” approach could be used to treat patients with severe carotid stenosis successfully, and which factors would preclude such an approach and require concurrent angioplasty.

\textbf{Methods}

\textbf{Patient Population}

Between March 2000 and August 2006, 97 patients with 102 symptomatic, severely stenosed CAs were prospectively identified and treated. All patients presented with a transient ischemic attack or stroke referable to the appropriate CA territory. All patients were deemed by a neurosurgeon to have relative contraindications to carotid endarterectomy, including prior neck irradiation, prior ipsilateral carotid endarterectomy, age > 80 years, or concurrent serious illness such as recent myocardial infarction, congestive heart failure, or chronic pulmonary disease.

\textbf{Patient Baseline Characteristics}

As shown in Table 1, patients were on average 72 years old (range 50–91 years), and most of them were men (71%). Significant vascular risk factors were present in all patients, including a history of diabetes mellitus (28%), hypertension (90%), hyperlipidemia (81%), current or history of smoking (79%), and coronary artery disease (65%). Ten patients (10%) had undergone a previous ipsilateral carotid endarterectomy and 4 (4%) had received prior neck irradiation.

\textbf{Stent Placement Technique}

Informed consent was obtained in all patients. Acetylsalicylic acid and clopidogrel were coadministered for 5 days prior to stent insertion. The aim at the outset of the procedure was to deploy an SES alone without use of angioplasty balloons. After induction of intravenous sedation, an 8 Fr femoral artery sheath was placed into the common femoral artery. Systemic heparinization was instituted and an activated clotting time of 2–3 times the baseline level was maintained during the procedure.

The CCA was cannulated with a 5 Fr catheter, and an exchange-length 0.035-in guidewire was used to exchange for a 6 Fr (inner diameter) guiding catheter (Cook Shuttle catheter). Under roadmap guidance, the stenosis was crossed with a 0.014-in exchange-length guidewire. The guidewire was advanced to the petrous segment of the ICA. Embolic protection devices were not used. The stenosis was then crossed with an 8-mm-diameter and 40-mm-long SES. Preinsertion balloon dilation was only performed if required to enable the stent physically to cross the stenosis. A balloon with a diameter of 2–3 mm was generally sufficient for this purpose. The most commonly used stents were as follows: Precise (Cordis, 67 arteries), Smart (Cordis, 12 arteries), and Wallstent (Boston Scientific, 13 arteries). Following stent delivery, angiographic views of the head and neck were obtained. Postinsertion balloon dilation was not routinely performed and there was no minimum lumen diameter required at the end of the procedure. The heparinization was allowed to wear off gradually. Acetylsalicylic acid and clopidogrel were coadministered for 1 month, after which time one of these agents was discontinued.

\textbf{Carotid Artery Imaging}

Angiographic views of the head and neck were obtained at the outset of the procedure and then after successful placement of the SES. Radiographs of the stent were assessed in both anteroposterior and lateral neck projections, and the most severe degree of stent narrowing on either projection was recorded. The degree of stenosis before and after the procedure was quantitated using the NASCET criteria.\textsuperscript{21}

Serial CA Duplex ultrasonography was performed in all patients to assess the treated artery over time. The mean peak systolic velocities in the ICA and the ICA/CCA ratio were determined before the procedure (baseline), immediately following the procedure and within 1 week, once or twice in the next 4 months, once again during the next 12 months, and annually thereafter.

The degree of lesion calcification was assessed by examination of at least 2 orthogonal views of the neck at the time of angiography or on CT angiography, if available. It was quantified on a scale of 0 to 4 based on the extent of circumferential calcification: Grade 0 indicated no calcification; Grade 1 indicated flecks of calcification involving < 25% of the circumference of the artery; Grade 2 involved 25–50% of the circumference of the artery; Grade 3 involved 50–75% of the circumference of the artery; and Grade 4 indicated circumferentially calcified plaque.

Restenosis was defined as a mean PSV of > 230 cm/second, in addition to consecutive measurements demonstrating a trend toward increasing velocities. This definition was chosen because a PSV of 230 cm/second approximately correlates with a > 70% stenosis.\textsuperscript{10} In addition, SESs can demonstrate gradual expansion over time\textsuperscript{16,20} and therefore, although initial velocities may be elevated in some patients, subsequent velocity values fall as the stent expands. Severe restenoses were confirmed on CT angiography.

\textbf{Statistical Analysis}

For patient demographics and baseline imaging characteristics, descriptive statistics were calculated for all patients and for the 2 groups separately. To avoid clustering effects, only the first artery treated was included for further analysis in patients in whom both CAs were treated with stents (5 patients). Logistic regression techniques were used to calculate ORs, 95% CIs, and to compare the combined stent- and angioplasty-treated patients statistically with those treated with stents alone. The Kaplan–Meier technique was used to calculate the time required to achieve a residual stenosis of < 30% by NASCET criteria after treatment.

\textbf{Results}

\textbf{Degree of Stenosis}

The majority of patients were found to have high-
grade (> 70%) carotid stenoses (90%) at the time of angiography (Table 1). Only 8 patients (8%) had moderate (50–69%) carotid stenosis. The average degree of stenosis was 83% (range 58–99%) by NASCET criteria. The contralateral ICA was severely stenosed in 29 patients (30%) and occluded in 14 patients (14%).

### Immediate Anatomical Outcome

An SES was successfully deposited without use of angioplasty in 77 patients (79%). In the remaining 20 patients (21%), angioplasty was required. Thirteen patients required preinsertion balloon dilation to enable the stent physically to cross the stenosis. Postinsertion balloon dilation was not performed in any patient due to persistent residual stenosis after stent insertion, but was required in 7 patients due to the following considerations: 1) placement of overlapping stents required to cover the stenosis (2 patients); 2) acute thrombus formation and/or plaque extrusion at the time of stent deployment, causing severe stenosis or occlusion (3 patients); or 3) severe restenosis on early follow-up (2 patients, at 1 and 3 months follow-up). Angioplasty both before and after stent placement was required in 1 patient.

Figure 1 demonstrates the degree of carotid stenosis before and immediately after treatment. The average stenosis in the stent-only group according to NASCET criteria was reduced from 82% (range 58–95%) to 40% (range 0–73%). In patients requiring angioplasty, the mean stenosis was reduced from 89% (range 73–99%) to 37% (range 7–64%) after angioplasty and stent placement.

### Long-Term Anatomical Outcome

The mean follow-up period was 15 months (range 2 days–69 months), with plain radiographs of the neck obtained to assess the stent, and carotid ultrasonography used to assess the vessel lumen. A follow-up duration of 6 months was available for 70 patients, and follow-up reached the 1-year point for 44 patients. Figure 2 demonstrates long-term follow-up of the stent expansion by using neck radiography. Maximal stent expansion occurred dur-
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ing the procedure, although gradual, continued expansion was observed over the following year. Similar results were obtained whether patients received stent insertion alone or combined stent placement and angioplasty. Figure 3 demonstrates the time after treatment required for the stent to achieve a residual stenosis of < 30%. Fifty percent of patients treated with angioplasty and stent insertion achieved this residual stenosis within 2 weeks of the stent placement procedure and 75% within 5 months. In the group treated with stents alone, half of the patients achieved a residual stenosis of < 30% within 2 months and 75% within 16 months of the stent placement procedure.

Figure 4 demonstrates the long-term follow-up of the lumen of treated CAs by using ultrasonography. The mean PSV fell most dramatically at the time of stent placement and continued to decrease gradually over the following year. Similar outcomes were obtained whether patients received stent treatment alone or stent insertion and angioplasty. As shown in Table 1, in patients treated with stents alone, the mean preprocedural PSV in the ICA was 405 cm/second (range 152–1038 cm/second), with a mean ICA/CCA ratio of 6.9 (range 1.7–18.7). At 1 year of follow-up, the PSV decreased to a mean of 154 cm/second (range 58–623 cm/second) in the stent-only group, with an ICA/CCA ratio of 2.1 (range 1–7.8). In the stent and angioplasty group, the mean PSV fell from 496 cm/second (range 272–618 cm/second) to 162 cm/second (range 129–222 cm/second) and the ICA/CCA velocity ratio fell from 9.2 (range 4.9–12.6) to 1.9 (range 1.6–2.3) at 1 year of follow-up.

Clinical Outcome

In this cohort, the combined 30-day rate of stroke or death was 7.2%, with 5 ipsilateral strokes and 2 deaths (Table 2). Other perioperative complications included vessel injury (2 patients), retroperitoneal hematoma (1 patient), and sublingual hematoma (1 patient). There were no perioperative myocardial infarctions.

Restenosis occurred in 9 arteries (9%); 6 (7.8%) in the group treated with stents alone and 3 (15%) in those treated with stents and angioplasty (Table 2). In patients with at least 6 months of follow-up, the restenosis rate was 9 (12.8%) of 70, and in patients with 1 year of follow-up the rate was 7 (15.9%) of 44. Four arteries progressed to occlusion between 12 and 18 months after treatment.

Excluding the periprocedural period, at the longest follow-up point ipsilateral strokes had occurred in 2 patients (2.5% overall); 1 was major (at 8 months) and 1 was minor (at 18 months). At 6 months of follow-up the ipsilateral stroke rate was 0 of 70 and at 1 year it was 1 (2%) of 44. Thirteen patients died during the course of follow-up of causes unrelated to the carotid stenosis or its treatment. Thus, the short- and long-term success rates with placement of an SES alone (excluding patients with perioperative stroke or death, restenosis, and ipsilateral stroke during follow-up) were 48 (80%) of 60 at 6 months and 31 (79%) of 39 at 1 year.

Factors Predicting Increased Risk of Unsuccessful Treatment With Stent Alone

As shown in Table 1, by using univariable logistic regression analysis, 3 factors were identified that predicted an increased risk of unsuccessful treatment with stent alone: the absence of hyperlipidemia (OR 3.23, 95% CI 1.05–9.89), severity of stenosis (OR 1.10, 95% CI 1.03–1.18), and degree of circumferential calcification (OR 1.67, 95% CI 1.05–2.66). All 3 factors were found to be independent predictors on multivariable regression analysis. Although a greater proportion of patients requiring angioplasty had high-grade stenoses and 50% had near occlusions, 13 (56%) of the 23 patients with near occlusions were successfully treated with stent placement alone. Similarly, of the 40 patients with > 75% circumferential calcification (Grade 3 or 4), 29 (73%) were successfully treated with stent alone. The combination of a near occlusion and high degree of circumferential calcification (Grade 3 or 4) was strongly predictive of unsuccessful
treatment with stent alone (OR 8.11, 95% CI 1.75–37.66; p = 0.008).

Discussion

Protected carotid angioplasty and stent placement has become the standard of practice in many centers for the endovascular treatment of patients for whom surgery for symptomatic or asymptomatic severe carotid stenoses carries high risks.9,24,25 Based on our experience, balloon angioplasty may not be required to treat all these patients. Deployment of an SES alone was possible in 77 (79%) of 97 patients in our symptomatic cohort. Eighty percent of patients (48 of 60) at 6 months and 79% (31 of 39) at 1 year were alive and free of ipsilateral stroke or restenosis. The rate of recurrent ipsilateral stroke alone (excluding the periprocedural period of 30 days) was 0% at 6 months and 2% at 1 year, which compares favorably with rates found in patients enrolled in registries of large trials of carotid stent placement for symptomatic stenosis.9,11,19,25 The 30-day composite rate of any stroke or death in our series, which included only symptomatic patients at high surgical risk, was 7.2%. Embolic protection devices were not used in this cohort, and therefore it is possible that this rate would have been lower had they been used. This periprocedural adverse event rate, however, is in line with those of published trials of carotid stent placement and case series involving symptomatic patients. The 30-day rate of stroke or death was 10% in the CAVATAS,3 12.1% in the WALLSTENT,1 4.8% in the SAPHIRE,30 6.8% in the SPACE,23 and 9.6% in the EVA-3S study.19 Seventy-one percent of patients randomized into SAPHIRE were asymptomatic, which at least partially explains the lower periprocedural rates observed in this trial. The 30-day combined vascular event rates in published case series and registries with mixed symptomatic and asymptomatic patients range from 1.2 to 10.9%.9,11,12,26,29 The importance of reporting periprocedural event rates in terms of symptomatic status is highlighted by the results of 2 recent registries, the ARChER11 and the CAPTURE.12 The overall 30-day combined rate of death, stroke, or myocardial infarction in the CAPTURE registry was 6.3%, and it was 8.3% in the ARChER. For symptomatic patients, these rates were 12 and 13%, respectively, compared with 5.4 and 6.8% for asymptomatic patients.

With conventional carotid angioplasty and stent placement, reported restenosis rates range from as low as 0.6% to as high as 11% at 1 year.4,9,11,22,25,27,30 This wide range may reflect variability in the imaging modalities used to assess the vessel lumen (ultrasonography, CT, or MR angiography), how closely patients are monitored during
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Follow-up, the definition of restenosis, and the criteria for reintervention. One of the major limiting factors in treating patients with severe carotid stenoses with SESs alone appears to be the higher rate of in-stent restenosis, which was 12.8% at 6 months and 15.9% at 1 year in our cohort. Poor stent expansion immediately postprocedure and prior or neck cancer have been found to be associated with a higher risk of restenosis. Angioplasty can be an effective treatment for in-stent restenosis. Retreatment carries additional risk, however, and the criteria for reintervention are not well defined. Fortunately, the great majority of in-stent restenoses are asymptomatic, as evidenced by the low rates of ipsilateral stroke during follow-up.

Using multivariable logistic regression analysis, 2 imaging features were independently associated with an increased risk of failure of SES treatment alone: the severity of stenosis and the degree of circumferential calcification. A very severe stenosis or near occlusion was more likely to impede passage of a stent across the stenosis. Also, severe concentric calcification was more likely to prevent stent expansion. It is important to note, however, that 14 (58%) of the 24 patients with near occlusions and 30 (73%) of 41 patients with > 75% circumferential calcification (Grade 3 or 4) were still successfully treated with stents alone.

Unexpectedly, a history of hyperlipidemia was also independently associated with success using the stent-only approach. The interpretation of this finding is difficult, given that serum lipid levels were not known at the time of stent insertion, all patients were receiving lipid-lowering medications, and carotid plaque composition was not examined. Softer carotid plaques have a higher content of lipid. It is possible that patients with a history of hyperlipidemia had softer, more compressible atherosclerotic plaque, leading to easier stent passage through the stenosis and greater stent expansion. Intensive statin therapy, however, has been found to decrease plaque’s lipid content.

In other studies, several other clinical and angio-

Table 2

Clinical Outcome in 97 Patients with Carotid Bifurcation Stenosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall</th>
<th>Stent Alone</th>
<th>Stent &amp; Angio</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>97</td>
<td>77</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Periop complications (w/in 30 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>5 (5)</td>
<td>3 (4)</td>
<td>2 (10)</td>
<td>0.273</td>
</tr>
<tr>
<td>Death</td>
<td>2 (2)</td>
<td>2 (3)</td>
<td>0</td>
<td>1.000</td>
</tr>
<tr>
<td>Other</td>
<td>4 (4)</td>
<td>2 (3)</td>
<td>2 (10)</td>
<td>0.187</td>
</tr>
<tr>
<td>Periop period (incl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restenosis§</td>
<td>9 (9)</td>
<td>6 (8)</td>
<td>3 (15)</td>
<td>0.386</td>
</tr>
<tr>
<td>Occlusion</td>
<td>4 (4)</td>
<td>3 (4)</td>
<td>1 (5)</td>
<td>1.000</td>
</tr>
<tr>
<td>Ipsilateral stroke</td>
<td>7 (7)</td>
<td>4 (5)</td>
<td>3 (15)</td>
<td>0.152</td>
</tr>
<tr>
<td>Death</td>
<td>13 (13)</td>
<td>11 (14)</td>
<td>2 (10)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

* FU = follow-up; incl = including.
† Based on the Fisher exact two-tailed test.
‡ Included arterial injury, retroperitoneal hematoma, and sublingual hematoma.
§ Defined as a mean PSV of > 230 cm/second, in addition to consecutive measurements demonstrating a trend toward increasing velocities.

Strokes arising from carotid stenosis are most often due to atheroembolism. Treatments, therefore, should be aimed at eliminating the potential for plaque embolization. Restoration of a normal lumen diameter should be considered a secondary goal. In the CREST, the largest ongoing randomized controlled trial comparing stent placement and endarterectomy, a final stenosis of < 30% is required at the end of the procedure. In our series of patients who were successfully treated with SESs alone, only 25% of them achieved this degree of stenosis at the end of the procedure (Fig. 3). Within 16 months of follow-up, however, the majority of these patients had a residual stenosis of < 30% and therefore would have been subjected to potentially unnecessary angioplasty, exposing them to increased peri procedural risk.

Several limitations of the present study are acknowledged. First, the data arise from a nonrandomized registry. Second, there was no direct comparison made to conventional angioplasty and stent placement. Third, there are significant differences in the characteristics of available SESs for the treatment of carotid stenosis, such as the stent’s free cell area, flexibility, conformability, and continuous outward force. In particular, the variability in the continuous outward force exerted by different devices may affect the ability of a particular stent to expand gradually and dilate a stenosed artery over time. In this regard, we did not note any advantage of a particular device used in this study, although more than two-thirds of patients were treated with the same type of stent. Last, follow-up duration was short (mean 15 months). A longer follow-up will be required to determine the durability of this technique.

Conclusions

Based on our experience, balloon angioplasty may not be required to treat all high surgical risk patients who have symptomatic severe carotid stenosis. An SES alone may suffice in up to 80% of such patients. In-stent restenosis rates with this approach are higher than with conventional angioplasty and stent placement. Therefore, CAs with very severe stenoses (> 90%) and heavy circumferential calcification may be more successfully treated with balloon angioplasty combined with stent placement.

Disclosure

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