Carotid Artery Stenting in Acute Stroke

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Objectives
The purpose of this study is to demonstrate the technical success of carotid artery stenting in acute extracranial internal carotid artery (ICA) occlusion as well as the benefit in clinical outcome.

Background
Stroke caused by acute occlusion of the ICA is associated with a significant level of morbidity and mortality. For this type of lesion, treatment with standard intravenous thrombolysis alone leads to a good clinical outcome in only 17% of the cases, with a death rate as high as 55%. Recanalization of the occluded ICA can lead to an improvement in acute symptoms of stroke, prevent possible deterioration, and reduce long-term stroke risk. At present, there is no consensus treatment for patients with acute ischemic stroke presenting with severe clinical symptoms due to atherosclerotic occlusion of the extracranial ICA.

Methods
Carotid artery stenting was performed in 22 patients with acute atherosclerotic extracranial ICA occlusion within 6 h of stroke symptom onset. In 18 patients, there was an additional intracranial occlusion at the level of the terminal segment of the ICA (n = 4) and at the level of the middle cerebral artery (n = 14). Intracranial occlusions were either treated with the Penumbra system or the Solitaire stent–based recanalization system, or a combination of mechanical recanalization and intra-arterial thrombolysis. Recanalization results were assessed by angiography immediately after the procedure. The neurologic status was evaluated before and after the treatment with a follow-up as long as 90 days using the National Institutes of Health Stroke Scale and the modified Rankin Scale.

Results
Successful recanalization of extracranial ICA with acute stent implantation was achieved in 21 patients (95%). There was no acute stent thrombosis. After successful recanalization of the origin of the ICA, the intracranial recanalization with Thrombolysis In Myocardial Infarction flow grade 2/3 was achieved in 11 of the 18 patients (61%). The overall recanalization rate (extracranial and intracranial) was 14 of 22 patients (63%). Nine patients (41%) had a modified Rankin Scale score of ≤2 at 90 days. The mortality rate was 13.6% at 90 days.

Conclusions
Carotid artery stenting in acute atherosclerotic extracranial ICA occlusion with severe stroke symptoms is feasible, safe, and useful within the first 6 h after symptom onset. (J Am Coll Cardiol 2011;58:2363–9) © 2011 by the American College of Cardiology Foundation

Stroke is the most common cause of permanent disability, the second most common cause of dementia, and the third most common cause of death in the Western world (1). Intravenous (IV) thrombolysis with tissue plasminogen activator (tPA) has become established as the standard therapy in acute ischemic stroke (2). The treatment of extracranial internal carotid artery (ICA) occlusions is a dramatic challenge because IV thrombolysis has low recanalization rates, ranging from 4% to 32% depending on the vessel (4% for ICA occlusions and 32% for middle cerebral artery [MCA] occlusions) (3,4). For these types of lesions, treatment with standard IV thrombolysis alone leads to a good clinical outcome in only 17% of the cases with a death rate of as high as 55% (5). Also, recanalization of the occluded ICA can lead to an improvement in acute symptoms of stroke, prevent possible deterioration, and reduce long-term stroke risk (6).

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At present, there is no consensus treatment for patients with acute ischemic stroke presenting with severe clinical symptoms due to atherosclerotic occlusion of the extracranial ICA. The literature consists of only isolated studies and case reports on recanalization of acute occlusion of the ICA (6–12).
In the past decade, carotid artery stenting (CAS) has emerged as a less invasive alternative to surgical treatment of carotid artery stenosis (13). We reviewed 22 patients who were interventionally treated with CAS for an atherosclerotic extracranial ICA occlusion within 6 h of acute stroke symptom onset.

**Methods**

From 2006 to 2010, a total of 367 patients were treated endovascularly for acute stroke in our department. We retrospectively collected and analyzed the data for 22 of the 367 patients with acute ischemic stroke due to an atherosclerotic extracranial carotid artery occlusion. Neurologic evaluation with the National Institutes of Health Stroke Scale (NIHSS) was performed on admission and discharge, and the modified Rankin Scale (mRS) score was evaluated at 90 days after therapy by 2 experienced stroke neurologists (S.W., S.B.). The patient’s outcome was defined as a good outcome if the patients had an mRS score of 0 to 2, whereas a poor outcome was an mRS score of 3 to 6. Computed tomography (CT) and CT angiography of the supra-aortic vasculature were performed on admission to rule out intracranial hemorrhage (ICH), to assess the carotid artery occlusion, and to evaluate intracranial circulation for additional occlusions. Control CT was performed 24 h after treatment and before discharge or if the patient’s symptoms worsened.

**Patient selection.** Patients matching the following criteria were included in our analysis: acute stroke symptom onset and arrival at the hospital within 6 h with a major neurologic deficit (NIHSS score of ≥10), atherosclerotic occlusion of the ICA at the origin of the vessel, no “marked ischemia” on the CT scan defined as hypodensity that is already visible because hypodensity defines nonreversible brain damage.

Patients presenting with subacute, fluctuating neurologic symptoms were excluded from the analysis. We also excluded patients in which a dissection of the ICA was diagnosed due to the different nature of the disease. The diagnosis of ICA dissection was based on imaging criteria (e.g., detection of vessel wall hematoma in magnetic resonance imaging). Patients with radiologic signs of chronic ICA occlusions were also excluded.

After the diagnosis of an extracranial atherosclerotic ICA occlusion and blood sample analysis, treatment was started with IV tPA for patients within 3 h of symptom onset, and after publication of the ECASS (European Co-operative Acute Stroke Study) III, the time window was altered to 4.5 h after symptom onset. Patients were then transferred to the angiography suite located on the same floor for interventional treatment. Depending on the patients’ neurologic status, they were either treated while they were under sedation or under intubation and ventilation. Table 1 summarizes the patients’ clinical characteristics.

**Interventional treatment.** The interventional treatment consists of 2 steps: first, extracranial revascularization, and second, intracranial recanalization.

**EXTRACRANIAL REvascularization.** Once an acute occlusion of the ICA had been identified, a long 6-F guide sheath was placed in the distal common carotid artery. A long 0.014- or 0.018-inch microwire was used to pass the occlusion. If this was unsuccessful, a 0.035-inch guidewire (e.g., a Terumo [Terumo Medical Corporation, Somerset, New Jersey] standard wire) was used together with a 4-F multipurpose catheter. Once the wire had successfully passed the occlusion, the catheter was advanced into the occluded vessel segment and contrast medium was injected to verify the intraluminal position of the catheter and rule out the possibility of manipulation having caused a dissection. To remove the 4-F catheter, a long 0.014-inch wire was introduced if necessary. A self-expanding carotid stent was placed in the area of the occlusion, to appose the stent to the vessel wall and to eliminate a residual stenosis, balloon angioplasty was performed. In most of the cases, a Wallstent (Boston Scientific, Natick, Massachusetts) was used because the closed-cell design of the stent makes it easier to place a catheter in the distal ICA for intracranial recanalization if necessary. After successful stent placement, 500 mg of IV aspirin (Aspisol, Bayer, Leverkusen, Germany) were given. Clopidogrel was started 24 h after treatment. No IV heparin was given. In cases of no additional intracranial occlusion, a proximal protection device (Gore, NeuroProtection System, W. L. Gore & Associates, Inc., Newark, Delaware) was used, if possible.

**INTRACRANIAL REcANALIZATION.** The entire length of the ICA and the intracranial area was then imaged to determine whether there was any further stenosis or occlusion of the ICA or MCA. If an additional occlusion in the terminal

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Overview of Patient Population and Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>64.8 ± 19.5 (49–85)</td>
</tr>
<tr>
<td>Female</td>
<td>5/22</td>
</tr>
<tr>
<td>NIHSS score at baseline</td>
<td>17.2 ± 5.3 (12–25)</td>
</tr>
<tr>
<td>Time from stroke symptom onset to recanalization, min</td>
<td>246 ± 95 (123–395)</td>
</tr>
<tr>
<td>Door to ICA lesion crossing time, min</td>
<td>86 ± 32 (48–128)</td>
</tr>
<tr>
<td>Extracranial recanalization</td>
<td>21/22 (95)</td>
</tr>
<tr>
<td>Additional intracranial occlusion</td>
<td>18/21 (85.7)</td>
</tr>
<tr>
<td>Intracranial recanalization</td>
<td>11/18 (61)</td>
</tr>
<tr>
<td>Overall recanalization (extracranial and intracranial)</td>
<td>14/22 (63)</td>
</tr>
<tr>
<td>Mortality at 90 days</td>
<td>3/22 (13.6)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>4/22 (18)</td>
</tr>
</tbody>
</table>

Values are mean ± SD (range), n/N, or n/N (%).

ICA = internal carotid artery; NIHSS = National Institutes of Health Stroke Scale.
segment of the ICA or MCA was present, the long 6-F sheath was advanced as far as possible into the recanalized ICA. The devices used for mechanical thrombectomy were the Penumbra system (Penumbra Inc., Alameda, California) or the Solitaire AB/FR (ev3 Europe SAS, Paris, France) with or without additional intra-arterial (IA) thrombolysis with tPA. In the cases in which the Penumbra system was used, we introduced the 0.42-inch catheter in combination with a soft 0.010- or 0.014-inch microwire to access the occluded vessel segment. After placement of the catheter within the thrombus, aspiration was started. If the 0.42-inch catheter was unable to pass the carotid siphon due to vessel tortuosity, the smaller catheter (0.32 inch) was used. When we used a Solitaire-based approach, we placed a Rebar microcatheter (ev3, Plymouth, Minnesota), depending on the size of the stent system used, and with the help of a soft 0.010-inch or 0.014-inch microwire, we passed the occlusion. Contrast medium was injected to confirm placement of the microcatheter distal to the thrombus. We then advanced the stent through the microcatheter and placed it with at least two-thirds of the stent system within the thrombus, through removal of the microcatheter. We then waited approximately 3 min to give the stent time to migrate into the thrombus and then pulled the system out under continuous aspiration into the long 6-F sheath. If necessary, these steps were repeated until we could reach a Thrombolysis In Myocardial Infarction (TIMI) score of 2 or 3. Intracranial TIMI scores before and after recanalization were assessed (14). Successful intracranial recanalization was defined as a TIMI score of 2 or 3.

In every case, an immediate post-treatment CT scan was performed to rule out ICH caused by the treatment.

Results

Patient population and angiographic outcome. The 22 patients treated for acute ICA occlusion were selected from the group of patients presenting at our institution with acute ischemic stroke and with proven occlusion of the extracranial part of the ICA. The mean time from stroke onset to recanalization was 246 ± 95 min. The patients’ mean NIHSS score on admission was 17.2 ± 5.3. All patients had an NIHSS score of at least 10 on admission (Table 1). Eight patients had contraindications to IV tPA, but the others received a standard 10% bolus of the maximum dose (0.9 mg/kg body weight). IV administration of tPA was halted in all cases when the occlusion site was accessed to save the remaining tPA for IA administration if necessary. Fifteen patients (68%) were treated while they were under general anesthesia with intubation because of agitation; in the remaining 7 patients (32%), treatment with mild sedation was possible.

In 21 of 22 patients (95%), the proximal ICA was recanalized successfully (Fig. 1). In 3 patients, no further vessel occlusion could be detected after successful recanalization of the extracranial ICA (Fig. 2). In 2 of these patients, a proximal protection device was used. Of 21 patients, 18 (85.7%) showed an additional intracranial occlusion after flow restoration in the proximal ICA: at the level of the terminal segment of the ICA (n = 4) and at the level of the MCA in 14 patients. These patients were either treated with the Penumbra system or the Solitaire stent–based recanalization system or a combination of mechanical recanalization and IA tPA (Fig. 3, Online Video 1). The IA tPA was given to support the mechanical devices in 10 patients with a dose of 5 to 20 mg. The intracranial recanalization to a TIMI score of ≥2 was achieved in 11 of 18 patients (61%). With the aid of the Penumbra system, we were able to recanalize the occluded vessel to a TIMI score of ≥2 in 3 of 9 patients (33.3%). The Solitaire system was successful in 9 of 9 patients (Table 2). The overall recanalization rate (extracranial and intracranial) was 14 of 22 patients (63%) (Tables 1 and 2).

Clinical outcome. Forty-one percent of the patients showed a good clinical outcome with an mRS score of 0 at 90 days. Four patients (18%) had an ICH. These hemorrhages occurred within 72 h after treatment. The immediate post-treatment CT scans were negative for ICH. There was no difference regarding the occurrence of ICH in patients treated with sedation or with mechanical ventilation. Three patients (13.6%) in this population died of a large infarction and swelling of the brain, all of them in combination with ICH. In 2 patients, the ICH was symptomatic with neurologic deterioration of more than 4 points on the NIHSS (Table 1). Figure 1 shows an overview of the NIHSS, TIMI flow, and mRS before and after treatment.

Discussion

Acute extracranial ICA occlusion resulting in ischemic stroke is different from other forms of acute occlusion of the
cerebral vessels. The occluded segments in other cerebral vessels, such as the MCA and the terminal segment of the ICA, usually consist of an occlusive embolus in a normal vessel (15). Successful recanalization of the occluded vessels is associated with improved outcome after acute ischemic stroke (16). The ECASS III showed that IV tPA is effective in treating acute ischemic stroke if given to patients within 4.5 h of stroke symptom onset (2). More patients had a favorable outcome with IV tPA than with a placebo (52.4% vs. 45.2%; \( p = 0.04 \)). However, the patients included in this study only rarely correspond to patients whom we currently consider to be candidates for IA approaches. The patients treated in the ECASS III had a relatively low NIHSS score compared with a patient population with a proven large vessel occlusion (10.7 to 11.6 compared with 17). However, the recanalization rates achieved with IV tPA for large-vessel arterial occlusion are low, ranging from 4% to 32% depending on the vessel (4% for ICA occlusions and 32% for MCA occlusions) (3,4).

The pathophysiologic processes involved in occlusion of the extracranial ICA are similar to processes observed in acute occlusion of the coronary arteries. The occluded segment of the ICA consists of predominantly atherosclerotic plaque and a superimposed thrombus. Therefore, large
contributions of atherosclerotic plaque and platelet activation do not provide an ideal substrate for thrombolytics alone (15,17). In acute myocardial infarction, primary stent placement has provided the best treatment outcomes (18,19). The results of our study combined with the results of the 2 largest series indicate that this approach is also feasible for acute atherosclerotic extracranial ICA occlusions (8–10). Table 3 shows an overview of the studies in which more than 10 patients were treated with this approach.

Interventional treatment consists of 2 steps. The first step is extracranial revascularization of the ICA with stent implantation, as in the treatment of atherosclerotic stenosis. The second step is intracranial, mechanical recanalization of the occluded vessel, if necessary.

In our study, the technical success rate of CAS for this acute extracranial ICA occlusion was 95%. This high technical success rate was similar to that of the other 2 studies (84% and 100%). A recent study of 22 patients with
acute ICA occlusion found a technical success rate of 77.3%; however, the patient collective consisted of cardioembolic and atherosclerotic ICA occlusions as well as dissections (8). In our study, proximal protection was used in 2 of the patients with no additional intracranial occlusion. However, because an intracranial occlusion is present in the majority of cases (85.7% in our study), it seems that the use of protection devices is required only in patients with no evidence of additional occlusion of the intracranial arteries to prevent secondary embolization into the intracranial vessels (20). Distal protection is difficult to perform in such cases because the distal parts of the ICA are not visible. Therefore, proximal protection should be used in these cases. In most of the cases, a closed-cell stent was used because a closed-cell design makes it easier to place a catheter in the distal ICA for intracranial recanalization, if necessary.

For elective treatment of atherosclerotic stenosis of the ICA with stent implantation, it is common practice to administer dual antiplatelet therapy with clopidogrel and aspirin at least 1 day before the intervention (21,22). After emergency stent implantation, antiplatelet medication is necessary to prevent acute stent thrombosis. In the acute phase administration of IV aspirin, if available, or IV glycoprotein IIb/IIIa receptor antagonist, such as abciximab, would be possible (23,24). However, the ideal medical regimen in CAS for acute stroke is not known, and it must be borne in mind that aggressive anticoagulation, especially in combination with thrombolysis, may increase the risk of ICH. To minimize this risk, it is probably an option to disclaim thrombolysis in this special group of patients. In our series, no cases of acute stent thrombosis occurred with this medical regimen. Secondary prophylaxis with a combination of 75 mg clopidogrel and 100 mg aspirin daily is administered for at least 6 weeks, followed by lifelong treatment with a platelet inhibitor (25).

After successful CAS of an ICA occlusion, an additional occlusion may be present in the terminal segment of the ICA or the MCA. The rate of additional intracranial occlusion was 85.7% in our study compared with 66% and 100% in the other 2 series (9,10). In the event of additional intracranial occlusion, further recanalization measures should be taken. A mechanical approach should be the first option to treat these lesions. For these cases, we used the Penumbra system or the Solitaire stent (26–28). The highest recanalization rate (100%) was achieved by the use of the Solitaire device, which provides a new approach to the treatment of acute intracranial occlusions. This new technique, in which the Solitaire stent was placed and deployed in the occluded vessel during thrombus formation and was then withdrawn in its unfolded state, was described recently (27). The device combines the advantages of prompt flow restoration and mechanical thrombectomy, and the first results of the use of this technique show high recanalization rates and a high rate of favorable clinical outcome (28).

Patients’ neurologic recovery and functional outcome resulted in a favorable clinical outcome with a 90-day mRS score of 0 to 2 in 41% of patients. The highest rate of functional outcome for an mRS score of ≤2 after 90 days (56%) was achieved in the series of Nedeltchev et al. (10). For these types of lesions, treatment with IV thrombolysis alone leads to a good clinical outcome in only 17% of cases (3). In our study, mortality rate was 13.6% at 90 days. The ICH rate of 18% (n = 4) in the present study is higher than the previously reported rates for CAS in acute stroke (6% and 8%) (8–10). This may reflect the fact that in our series, IV and IA tPA was used more often than in the other studies. The ICH risk is expected to be higher in acute CAS compared with mechanical recanalization studies because of the aggressive anticoagulation that is required (29). More-

### Table 2

**Overview of the Intracranial Recanalization Devices**

<table>
<thead>
<tr>
<th>Intracranial Recanalization Device</th>
<th>Recanalization Rate</th>
<th>Time Between Extracranial and Intracranial Recanalization, min</th>
<th>Good Clinical Outcome (mRS Score ≤2)</th>
<th>Intracranial Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penumbra</td>
<td>3/9 (33.3)</td>
<td>50</td>
<td>2/9 (22.2)</td>
<td>3/9 (33.3)</td>
</tr>
<tr>
<td>Solitaire</td>
<td>9/9 (100)</td>
<td>27</td>
<td>4/9 (44.4)</td>
<td>0/9 (0)</td>
</tr>
</tbody>
</table>

Values are n/N (%). mRS = modified Rankin Scale.

### Table 3

**Overview and Comparison of the Largest Studies on CAS in Acute Stroke**

<table>
<thead>
<tr>
<th>First Author (Ref. #)</th>
<th>n</th>
<th>NIHSS Score (Mean)</th>
<th>Extracranial Recanalization</th>
<th>Additional Intracranial Occlusion</th>
<th>Intracranial Recanalization</th>
<th>Overall Recanalization (Extracranial and Intracranial)</th>
<th>mRS Score at 90 Days (0–2)</th>
<th>Mortality</th>
<th>Intracranial Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jovin et al. (9)*</td>
<td>15</td>
<td>14</td>
<td>15/15 (100)</td>
<td>10/15 (66)</td>
<td>6/10 (60)</td>
<td>11/15 (73)</td>
<td>5/15 (33)</td>
<td>3/15 (20)</td>
<td>1/15 (6)</td>
</tr>
<tr>
<td>Nedeltchev et al. (10)</td>
<td>25</td>
<td>12</td>
<td>21/25 (84)</td>
<td>21/21 (100)</td>
<td>11/21 (52)</td>
<td>11/25 (44)</td>
<td>14/25 (56)</td>
<td>5/25 (21)</td>
<td>2/25 (8)</td>
</tr>
<tr>
<td>Current study</td>
<td>22</td>
<td>17</td>
<td>21/22 (95)</td>
<td>18/21 (85.7)</td>
<td>11/18 (61)</td>
<td>14/22 (63)</td>
<td>9/22 (41)</td>
<td>3/22 (13.6)</td>
<td>4/22 (18)</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>14.3</td>
<td>57/62 (91.9)</td>
<td>49/57 (86)</td>
<td>28/49 (57.1)</td>
<td>36/62 (58)</td>
<td>28/62 (45)</td>
<td>11/62 (17.7)</td>
<td>7/62 (11.3)</td>
</tr>
</tbody>
</table>

Values are n/N (%), unless otherwise indicated. *In this study, 25 patients presented but only 15 within 6 h of acute stroke symptom onset. CAS = carotid artery stenting; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale.
over, with CAS, there is an additional risk of hyperperfusion syndrome (30,31).

**Study limitations.** The first limitation is that the study is a retrospective analysis. Because acute atherosclerotic ICA occlusions presenting with severe stroke symptoms are rare, and even at high-volume stroke centers, only a few patients per year are treated interventionaly, it is difficult to perform a prospective study. The second limitation is that the study describes evolving treatment, especially over the past few years, with an enormous advancement in the field of intracranial recanalization techniques and devices.

**Conclusions**

The results of the 3 studies with CAS in acute stroke (Table 3) show a high rate of technical success (91.1%) and a satisfactory rate of favorable clinical outcome (45%). These data indicate that CAS in acute atherosclerotic extracranial ICA occlusion with severe stroke symptoms is feasible, safe, and beneficial if performed within the first 6 h.

**REFERENCES**


**Key Words:** acute stroke • carotid artery stenosis • carotid artery stenting • Penumbra • Solitaire.

**APPENDIX**

For an accompanying video, please see the online version of this article.