Stent-Assisted Endovascular Thrombolysis Versus Intravenous Thrombolysis in Internal Carotid Artery Dissection With Tandem Internal Carotid and Middle Cerebral Artery Occlusion

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Background and Purpose—Tandem internal carotid and middle cerebral artery occlusion independently predicts poor outcome after intravenous thrombolysis. Recanalization of internal carotid artery dissection by stent-assisted angioplasty has recently been proposed when anticoagulation fails to prevent a new ischemic event. We recently reported a case of tandem internal carotid and middle cerebral artery occlusion with dissection of the internal carotid artery successfully treated with endovascular stent-assisted thrombolysis.

Methods—We compared clinical outcomes in consecutive patients presenting with tandem internal carotid and middle cerebral artery occlusion with internal carotid artery dissection within 3 hours of symptom onset who were eligible for intravenous thrombolysis, treated by either endovascular stent-assisted thrombolysis or intravenous recombinant tissue-type plasminogen activator (rtPA) when an endovascular therapist was unavailable. National Institutes of Health Stroke Scale scores were obtained at baseline and after 24 hours. The modified Rankin Scale score was used to assess outcomes at 3 months. Arterial recanalization was assessed by magnetic resonance imaging.

Results—Of 10 patients screened, 6 were treated with endovascular therapy and 4 with intravenous rtPA. Before treatment, mean National Institutes of Health Stroke Scale scores were high and comparable in the 2 groups (17 and 16, respectively). In the endovascular group, all patients achieved middle cerebral artery recanalization with subsequent dramatic improvement versus only 1 patient with middle cerebral artery recanalization in the intravenous rtPA group. At 3 months, 4 patients in the endovascular group had a favorable outcome (modified Rankin Scale score=0). In the intravenous rtPA group, 3 patients had a poor outcome (modified Rankin Scale score≥3).

Conclusions—Endovascular stent-assisted thrombolysis is a promising treatment in tandem internal carotid and middle cerebral artery occlusion due to internal carotid artery dissection and compares favorably with intravenous rtPA.

(Stroke. 2007;38:2270-2274.)

Key Words: carotid artery ■ dissection ■ ischemic stroke ■ stent

Spontaneous dissection of the internal carotid artery (ICA) is 1 of the main causes of ischemic stroke in young and middle-aged patients, representing 10% to 25% of such cases. Because infarct due to dissection is mainly thromboembolic, anticoagulation has been recommended to prevent new stroke in patients with acute dissection, provided they have no contraindications. In the acute phase, intravenous recombinant tissue-type plasminogen activator (IV rtPA) given within 3 hours after onset of stroke due to dissection is reportedly safe and effective. However, published series included patients with strokes of widely varying severity and they lacked a control group, making it difficult to apply their results to patients with both dissection and tandem ICA–middle cerebral artery (MCA) (TCM) occlusion, a frequent cause of malignant brain infarction. TCM occlusion independently predicts poor outcome after IV thrombolysis. We recently reported a case with an acute TCM occlusion consecutive to a dissection that was successfully treated by stent-assisted endovascular thrombolysis. First, the stent was deployed throughout the dissection, allowing restoration of blood flow; then intra-arterial thrombolysis was performed. Since then, no controlled data have been published. The purpose of this study was to compare classic IV thrombolysis to this new procedure in patients with acute ischemic cere-

Received December 22, 2006; final revision received February 13, 2007; accepted February 20, 2007.

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Stroke is available at http://www.strokeaha.org

DOI: 10.1161/STROKEAHA.106.481093

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brovascular syndrome and TCM occlusion consecutive to ICA dissection who were eligible for IV thrombolysis.

**Patients and Methods**

**Patient Selection**

The first case of dissection with TCM occlusion was successfully revascularized and cured, so we decided to systematically consider this technique at our center for all similar patients. In this series, we included all consecutive patients entered into the database of the Bichat Stroke Centre between September 2001 and November 2006. Patients were included if they were admitted within 3 hours after symptom onset of brain infarct (BI) due to carotid dissection with TCM occlusion and if they met the criteria for IV thrombolysis. Patients were not considered candidates for IV rtPA if the following criteria were met: minor or rapidly improving symptoms; very disabling stroke: early infarct signs in more than one third of the MCA territory on computed tomography (CT) scan and/or severely impaired consciousness and/or National Institutes of Health Stroke Scale (NIHSS) score >25; uncertain time of onset; systolic blood pressure >180 mm Hg; diastolic blood pressure >85 mm Hg; or general contraindication.

**Clinical Evaluation**

Severity of neurologic deficit at admission was assessed with the NIHSS. Outcome was assessed 24 hours after stroke with the NIHSS and 90 days after stroke with the modified Rankin Scale (mRS) and NIHSS. Each patient was evaluated in the acute phase by a stroke neurologist. We considered mRS=0 to 1 as a favorable outcome, mRS 2 to 3 as a moderate outcome, and mRS ≥4 (severe disability or death) as a poor outcome.

**Imaging**

Magnetic resonance imaging (MRI) was performed with a 1.5-T whole-body system (Twinspeed, version 9.0, GE Medical Systems). Imaging study before treatment included brain MRI diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery, echoplanar T2*-susceptibility-weighted imaging and cervical MRI with T1 fat suppression, and magnetic resonance angiography. Cervical arterial dissection was based on the presence of a fresh intramural hematoma on axial cervical MRI slices. When MRI was unavailable, head CT was performed. In this case, dissection had to be confirmed by duplex ultrasound or control MRI. MRI was performed in the days after treatment in all patients and was repeated every 6 months for patients who underwent angioplasty. To evaluate arterial patency or persistent occlusion, magnetic resonance angiography and duplex ultrasound with transcranial Doppler were systematically performed in the 48 hours after the procedure and every 6 months thereafter.

**Imaging Criteria**

Initial lesion volume was assessed on the first DWI sequence and was compared with the final infarct volume on the control fluid-attenuated inversion recovery sequence. We defined 2 patterns: no infarct progression, when the final fluid-attenuated inversion recovery lesion perfectly matched the initial DWI abnormalities, and infarct progression, when the final infarct size was larger than the initial DWI lesion. Hemorrhagic transformation was evaluated on T2* susceptibility-weighted imaging. Hemorrhagic infarction type 1 (HI-1) was defined as small petechiae along the margins of the infarct, and HI-2 was defined as more confluent petechiae within the infarcted area but without space-occupying effect. Parenchymal hematoma type 1 (PH-1) was defined as hematoma in <30% of the infarcted area with some slight space-occupying effect; PH-2 was defined as dense hematoma covering >30% of the infarcted area with substantial space-occupying effect or any hemorrhagic lesion outside the infarcted area.

**Treatment**

Treatments were not randomly assigned. Patients who met the inclusion criteria were systematically allocated to the intra-arterial procedure if an endovascular therapist was available. If not, thrombolysis was performed, in which patients received 0.9 mg/kg IV rtPA according to National Institute of Neurological Disorders and Stroke guidelines. Endovascular treatment consisted of proximal ICA recanalization with self-expandable stent implantation (carotid wall stent, Boston Scientific) followed by MCA recanalization and intra-arterial thrombolysis and/or thrombectomy (the Figure). Before the procedure, a bolus of 0.25 mg/kg glycoprotein IIb/IIIa antagonist (abciximab; ReoPro, Lilly, France) was infused. After the procedure, dual antiplatelet therapy was prescribed (clopidogrel 300 mg and aspirin 250 mg just after the procedure, followed by clopidogrel and aspirin 75 mg/d for 3 months) and 1 antiplatelet drug afterward to prevent acute stent thrombosis. All procedures were performed under general anesthesia, and 5000 U heparin was given per procedure in
From September 2001, 10 patients (8 men, 2 women) admitted for acute BI due to a documented TCM occlusion consecutive to carotid dissection met the criteria for IV thrombolysis. The mean age was 46 years (range, 35 to 54 years). Six patients received endovascular therapy (patients 1 through 6), and 4 received IV thrombolysis (patients 7 through 10). The mean NIHSS score before treatment was 17 (range, 6 to 23) in the IV rtPA group and 16 (range, 12 to 20) in the endovascular group.

Time from symptom onset to MRI or CT scan varied from 20 to 170 minutes (mean, 121 minutes), and there was no difference between the 2 groups. Eight patients had MRI before treatment, all of whom had evidence of acute BI in the MCA territory on DWI but no evidence of hemorrhagic transformation (Table). Magnetic resonance angiography showed an absence of signal in the M1 segment in all cases except 1 with M2 occlusion (patient 9, IV rtPA group). Two patients had normal head CT scans, but duplex ultrasound and transcranial Doppler studies confirmed TCM occlusion (M1).

In the IV rtPA group, delay for revascularization indicates the delay between stroke onset and rtPA bolus, whereas in the endovascular group, it is the delay between stroke onset and the beginning of thrombolysis/thrombectomy.

*CT scan was performed.
†MRI was performed.


Results

Patients

From September 2001, 10 patients (8 men, 2 women) admitted for acute BI due to a documented TCM occlusion consecutive to carotid dissection met the criteria for IV thrombolysis. The mean age was 46 years (range, 35 to 54 years). Six patients received endovascular therapy (patients 1 through 6), and 4 received IV thrombolysis (patients 7 through 10). The mean NIHSS score before treatment was 17 (range, 6 to 23) in the IV rtPA group and 16 (range, 12 to 20) in the endovascular group.

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Treatment

The mean time from stroke onset to rtPA bolus was 161 minutes (range, 105 to 195 minutes) in the IV rtPA group. The mean time for revascularization, defined as the delay between stroke onset and the beginning of intra-arterial thrombectomy/thrombolysis, was 291 minutes (range, 201 to 362 minutes). All patients had stent placement; 3 needed implantation of 2 tandem self-expandable stents to cover all of the dissection. Subsequent intracranial angiography confirmed MCA occlusion. Intra-arterial rtPA (40 mg) was infused directly into the thrombus in 1 patient (patient 4), and mechanical thrombectomy with a dedicated device was performed in 5. The mean duration of the revascularization procedure was 137 minutes (range, 101 to 171 minutes).

Outcomes

The mean NIHSS score at 24 hours in the IV rtPA group was 15 (range, 3 to 20) (Table). Three of 4 patients had a severe stroke (NIHSS score ³18). In the endovascular group, the mean NIHSS score at 24 hours was 8 (range, 3 to 18), with only 1 patient having an NIHSS score of 18. The other 5 patients had a dramatic improvement (NIHSS score ≤12). The 3-month mRS and NIHSS scores were worse in the IV rtPA group. Two of 4 patients in the IV rtPA group had a poor outcome. One patient died early from a malignant cerebral
infarction, and 1 had an mRS score of 4 (NIHSS score = 16). One patient had a moderate outcome (mRS score = 3, NIHSS score = 6), and only 1 patient had a favorable outcome (mRS score = 1, NIHSS score = 1). In the endovascular group, 4 patients had a favorable outcome (mRS score = 0, NIHSS score = 0), and 2 patients had a moderate outcome with nearly full motor recovery but persistent aphasia (mRS score = 2, NIHSS scores 6 and 4).

In the IV rtPA group, 3 patients had MRI performed before and after treatment. Two had infarct progression (1 malignant cerebral infarct and 1 cortical extension) with no MCA or ICA recanalization. One had an M2 occlusion on the first MRI, and the MCA completely recanalized after thrombolysis. As a consequence, there was no BI extension. This patient had an mRS score of 1 at 3 months. One patient had MRI only after treatment. For this patient, magnetic resonance angiography showed persistence of the M1 MCA and ICA occlusion. Five of 6 patients in the endovascular group had MRI before and after treatment. Infarct size did not increase on the control MRI in 4 patients. A fifth patient had an embolic infarct in the anterior cerebral artery territory during the procedure but no cortical MCA infarct extension. Postprocedural angiography demonstrated reconstitution of the luminal diameter of the ICA in 5 of 6 patients and M1 and M2 recanalization in all patients. In 1 patient, despite antithrombotic therapy, we observed an in-stent thrombus, but the MCA remained patent. On follow-up ultrasound examination (mean follow-up, 15 months; range, 2 to 36 months), the ICA remained patent (except in 1 patient), with no in-stent restenosis. On follow-up MRI, we observed no evidence of a new BI.

Safety
None of the 10 patients had symptomatic intracranial hemorrhage. In the IV rtPA group, all patients had hemorrhagic transformation in the lentiform nucleus. Two were graded PH-1 and 2, PH-2. One had small cortical petechiae (HI-1). Despite later recanalization in the endovascular group, the rate of hemorrhagic transformation was similar. Four patients had caudate and/or lentiform nucleus hemorrhage (1 HI-2, 1 PH-1, 2 PH-2), and 2 had cortical petechiae graded PH-1. One patient had an embolic stroke and an acute stent thrombosis during the procedure.

Discussion
Several authors have proposed endovascular treatment with stent deployment for ICA dissection with high-grade stenosis or occlusion when anticoagulation fails to prevent a new ischemic event. In these cases, the MCA was patent. However, this study is the first attempt to compare outcomes of patients with acute stroke consecutive to TCM occlusion due to ICA dissection treated either by stent-assisted endovascular thrombolysis/thrombectomy or by IV rtPA thrombolysis. In our study, we used IV Ipa within 3 hours, because reports have been reassuring on the safety of this procedure regarding wall hematoma extension or other bleeding complications. We found that stent-assisted endovascular thrombolysis/thrombectomy compared favorably with IV rtPA thrombolysis. In the IV rtPA group, 3 of 4 patients were severely impaired or dead at 3 months. Conversely, in the endovascular group, 4 of 6 patients had recovered at 3 months without residual symptoms, and 2 had a nearly complete recuperation of motor sign but persistent aphasia. This better prognosis was associated with complete recanalization of M1 and M2 MCA segments with stent-assisted intra-arterial thrombolysis and/or mechanical thrombectomy; M1 recanalization was never obtained in the IV rtPA group.

This higher rate of MCA recanalization could be explained by carotid flow restoration, allowing direct access to the MCA thrombus. As a consequence, infarct size increased in the IV rtPA group in 3 of 4 cases, whereas final infarct volume matched the initial DWI lesion in 4 of 5 patients in the endovascular group (1 patient did not have an initial MRI). In the fifth patient, an ipsilateral BI occurred during the procedure in the territory of the anterior cerebral artery. Endovascular treatment could potentially extend the therapeutic window beyond 3 hours. Actually, in all cases in the endovascular group, MCA recanalization was obtained by 291 minutes. Despite this long delay, the rate of hemorrhagic transformation was similar in the 2 groups, and no patients were symptomatic. Because the stent was deployed all along the dissection, we assumed that an intimal tear (the potential source of cerebral emboli) was covered. No patients received anticoagulation after the procedure, and we did not observe recurrent stroke during follow-up.

The main limitation of this procedure is the immediate need for an experienced endovascular therapist. The number of cases of TCM occlusion due to carotid artery dissection was quite small and represented, in our stroke center, <10% of patients admitted for carotid dissection. However, we selected only patients arriving within 3 hours after stroke onset. Because we obtained recanalization later than 3 hours after symptom onset, a longer time window could be considered and evaluated in future studies. Criteria such as DWI/perfusion-weighted imaging or DWI/clinical mismatch could be useful. Despite these promising preliminary results, potential drawbacks related to the procedure must be considered. Acute complications such as transient ischemic attack, ischemic stroke, femoral or carotid dissection, and death have been reported. Other potential hazards of endovascular treatment of carotid dissection could be observed, as they were in stenting of other cases of arteriopathy. In our series, 1 embolic stroke and 1 acute in-stent thrombosis occurred in the same patient. Despite this new infarction, we observed significant neurologic improvement in this patient, probably because the MCA remained patent. Late stent thrombosis has also been reported. In our study, there was no evidences of in-stent de novo stenosis or stent thrombosis on follow-up ultrasound examination performed between 2 and 36 months later.

The small number of patients in this series is another limitation, as is the lack of randomization. However, the intra-arterial procedure was not used in the 4 patients owing to chance (the unexpected unavailability of an endovascular therapist). Furthermore, all 10 patients had the same pattern of arterial dissection with TCM occlusion and had similar initial NIHSS scores and infarct volumes on DWI. The only difference was that 1 patient in the IV rtPA group had an M2
MCA occlusion only (the 1 who had a good outcome), whereas all patients in the endovascular group had M1 occlusion, which may have favored the IV rtPA group.

In conclusion, most patients with acute cerebrovascular syndrome with TCM occlusion consecutive to ICA dissection had a poor outcome when treated with conventional IV rtPA thrombolysis, whereas most patients treated with stent-assisted endovascular thrombolysis/thrombectomy showed a dramatic improvement. Further large randomized studies are required to confirm these data.

Acknowledgment
The authors thank Sophie Rushton-Smith, PhD, who provided editorial assistance in the preparation of this manuscript.

Source of Funding
The study was funded by SOS-Attaque Cerebrale.

Disclosures
None.

References
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Stroke. 2007;38:2270-2274; originally published online June 28, 2007;
doi: 10.1161/STROKEAHA.106.481093
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/38/8/2270

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