Angioplasty after Intra-Arterial Thrombolysis for Acute Occlusion of Intracranial Arteries

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Background and Purpose—The purpose of this study was to report our experience with percutaneous transluminal angioplasty (PTA) of intracranial arteries in acute stroke patients who were resistant to intra-arterial thrombolysis alone.

Methods—PTA was performed within 6 hours from symptom onset in 13 acute stroke patients in whom no hypodensity areas were observed on initial CT. PTA was classified into 3 categories: immediate (3 patients), delayed (3 patients), and rescue (7 patients) angioplasty. Treatment results in the PTA group for 9 cases of middle cerebral artery (MCA) occlusion were compared with those in the thrombolysis alone group for 12 cases of thrombotic MCA occlusion.

Results—Technical success rates for immediate, delayed, and rescue angioplasty were 100%, 100%, and 71%, respectively, and that of angioplasty for the MCA was 100%. Ten patients (77%) showed improvement in the National Institutes of Health (NIH) stroke score after treatment. Improvement in NIH stroke scores in the PTA group for MCA occlusion was greater than that in the thrombolysis alone group (P<0.01). Nine patients (69%) had an excellent, good, or fair outcome 3 months after treatment. In 9 patients who had follow-up angiography 1 month after treatment, no restenosis or recollection was demonstrated. There were no symptomatic complications during or after treatment.

Conclusions—This limited study demonstrates the technical feasibility of angioplasty for intracranial arteries in acute ischemic stroke and suggests that angioplasty may be an effective option for improving the success rate of recanalization and preventing recollection of the MCA. The present results encourage us to perform further clinical trials in a larger number of patients to assess the efficacy of this procedure. (Stroke. 1998;29:2568-2574.)

Key Words: angioplasty • cerebral thrombosis • stroke, ischemic • thrombolytic therapy

Although the efficacy of intra-arterial thrombolytic therapy for acute ischemic stroke has been reported in several clinical studies, there is no established protocol for dealing with this therapy, and there are some limitations to this technique. It is extremely difficult to recanalize an occluded vessel with a thrombolytic agent alone when the embolus is large and/or hard, particularly if there are atherosclerotic changes in the occluded vessel. Furthermore, in acute thrombotic stroke, recollection by rethrombosis after successful thrombolysis often occurs. Because recent advances in endovascular treatment techniques for stroke patients have made it possible to perform percutaneous transluminal angioplasty (PTA) of the intracranial artery, a few reports on the usefulness of angioplasty as an adjuvant to intra-arterial thrombolysis have been published.

In a previous study, we reported on intra-arterial thrombolysis combined with PTA for acute thrombotic occlusion of the middle cerebral artery (MCA). Percutaneous transluminal coronary angioplasty in acute myocardial infarction has been classified into 4 categories: (1) immediate angioplasty, to be performed as soon as possible after thrombolysis; (2) delayed angioplasty, to be performed within several hours or a few days after thrombolysis; (3) rescue angioplasty, to be performed after failed thrombolysis; and (4) primary (direct) angioplasty, to be performed instead of thrombolysis. In this study, we report our experience with immediate, delayed, and rescue angioplasty of intracranial arteries for acute stroke patients who were resistant to intra-arterial thrombolysis alone. In addition, angiographic results, particularly recollection judged by follow-up studies, and clinical results in patients treated with PTA for MCA occlusion were compared with those in patients treated with thrombolysis alone for acute thrombotic MCA occlusion.

Materials and Methods

Between April 1989 and August 1996, 95 patients presenting with acute ischemic stroke were treated with intra-arterial thrombolytic therapy. Of this group, 13 patients were treated with PTA for acute occlusion of intracranial arteries. There were 7 women and 6 men ranging in age from 48 to 74 years (mean age, 66±8.2 years). The occluded arteries included 9 in the M1 segment of the MCA, 2 in the
internal carotid artery, and 2 in the basilar artery. Informed consent was obtained from all patients or their relatives.

Our recent inclusion criteria for intra-arterial thrombolytic therapy were as follows: (1) no apparent hypodensity areas were observed on the admission CT scan, (2) patient could be treated within 6 hours of symptom onset, (3) occluded arteries suggested by symptoms were demonstrated by cerebral angiography, and (4) patient had a good residual cerebral blood flow (CBF) value by pretreatment single-photon emission CT (SPECT) showing an ischemic regional activity (R)–to–cerebellar activity (CE) ratio (R/CE) of more than 0.35.

Our inclusion criteria for acute angioplasty were as follows: (1) residual stenosis of more than 70% immediately after thrombolysis (immediate angioplasty), (2) no recanalization by thrombolysis (rescue angioplasty), (3) symptomatic restenosis or reocclusion within several hours or a few days after thrombolysis (delayed angioplasty), and (4) contraindications to thrombolysis.

For comparison with angiographic results including reocclusion and clinical results in 9 patients with MCA occlusion, 12 patients treated with thrombolysis alone for acute thrombotic MCA occlusion were selected. The diagnosis of thrombotic stroke was based on clinical, CT, and angiographic findings. Angiographic criteria for thrombotic occlusion were good collateral circulation with retrograde filling from the anterior or posterior cerebral artery or tapered occlusion with extensive atherosclerotic changes. Embolic stroke was diagnosed according to the guidelines of the Cerebral Embolism Task Force on the basis of onset pattern, angiographic findings, and results of cardiovascular examinations such as electrocardiography and echocardiography.

CT was performed on all patients immediately after admission. When no clear hypodensity area was noted at the sites suggested by and echocardiography.

CT was obtained immediately, the next day, 1 or 2 weeks, and 1 month after treatment. Cerebral angiography was also performed the next day and 1 month after treatment. The neurological status was evaluated on admission, the next day, and 1 month after treatment according to the National Institutes of Health (NIH) Stroke Scale, which expresses the severity of neurological impairment numerically from 0 (normal) to 42. The outcome was evaluated 3 months after the onset according to the following 5-grade scale: excellent (no neurological defects were observed, and the patient had returned fully to previous daily activities); good (mild neurological defects remained, but the patient had returned partly to previous activities); fair (rehabilitation was difficult, but no assistance needed in activities of daily life); poor (assistance needed in activities of daily life); and death.

Results

The clinical, angiographic, and outcome data are summarized in Table 1. Immediate, delayed, and rescue angioplasty were performed in 3, 3, and 7 patients, respectively. Technical success rates for immediate, delayed, and rescue angioplasty were 100%, 100%, and 71%, respectively, and that of angioplasty for MCA occlusion was 100%. Delayed angioplasty was performed 48 hours after thrombolysis in patient 1, 12 hours after in patient 9, and 20 hours after in patient 13. Every patient who received rescue angioplasty for MCA occlusion had successful dilatation. In particular, 2 patients (patients 6 and 8) with cardioembolic MCA occlusion after failed thrombolysis showed complete recanalization immediately after the first dilatation of the balloon catheter without occlusion of the distal arteries. In 9 patients who had follow-up angiography 1 month later, no restenosis or reocclusion was demonstrated. Ten patients (77%) showed improvement in the NIH stroke score after treatment. Nine patients (69%) had an excellent, good, or fair outcome 3 months after treatment. In particular, all patients with MCA occlusion had complete recanalization and a relatively good outcome.

Comparison of clinical and angiographic results between the PTA and thrombolysis-alone groups is summarized in Table 2. No significant difference between these groups was observed in age, interval from symptom onset to treatment, or urokinase dose. In the thrombolysis-alone group, severe residual stenosis of the M1 segment of the MCA after treatment was found in 2 patients (90% and 95%) who had reocclusion within 24 hours. The other 2 patients with mild residual stenosis (20% and 30%) after treatment did not have reocclusion. The rates of recanalization (complete and partial) in the PTA and thrombolysis-alone groups were 100% and 83%, respectively. Changes in NIH stroke scores between the next day and baseline and between 1 month and baseline in the PTA group were much greater than those in the thrombolysis-alone group (P<0.01). Two patients (patients 10 and 11) who received rescue angioplasty for intracranial internal carotid artery bifurcation occlusion had no perfu-
Illustrative Case Reports

Immediate Angioplasty

A 51-year-old man (patient 4, Figure 1) presented with acute onset of right hemiparesis and total aphasia. CT findings were normal, and carotid angiography demonstrated complete occlusion of the proximal left M1 segment of the MCA. Intra-arterial thrombolysis with injection of 480 000 U of urokinase was performed 6 hours after symptom onset. Postthrombolysis angiography showed complete recanalization of the MCA with severe residual stenosis. The patient’s neurological symptoms showed marked improvement after thrombolysis, and she was continually heparinized for 24 hours after treatment. However, she deteriorated progressively, showing her initial symptoms 43 hours after thrombolysis. Emergency angiography 5 hours after recurrent onset revealed a higher-grade stenosis of the M1 segment than seen on the previous angiogram. A Stealth 2.0×1.0-mm balloon catheter was introduced into the M1 segment, which was dilated once at 3 atm for 20 seconds. After angioplasty, complete dilatation was obtained with neurological improvement. Follow-up angiography 1 month later demonstrated complete patency of the M1 segment. The patient had an excellent outcome.

Rescue Angioplasty

A 64-year-old woman (patient 8, Figure 3) whose past history included atrial fibrillation presented with sudden right hemiparesis and total aphasia. CT showed no abnormal density. Carotid angiography demonstrated total occlusion of the proximal left M1 segment of the MCA 5 hours after symptom onset. After infusion of 480 000 U urokinase, there was complete recanalization with residual stenosis. The patient’s neurological symptoms showed marked improvement after thrombolysis, and she was continually heparinized for 24 hours after treatment. However, she deteriorated progressively, showing her initial symptoms 43 hours after thrombolysis. Emergency angiography 5 hours after recurrent onset revealed a higher-grade stenosis of the M1 segment than seen on the previous angiogram. A Stealth 2.0×1.0-mm balloon catheter was introduced into the M1 segment, which was dilated once at 3 atm for 20 seconds. After angioplasty, complete dilatation was obtained with neurological improvement. Follow-up angiography 1 month later demonstrated complete patency of the M1 segment. The patient had an excellent outcome.
Thrombolytic therapy for acute ischemic stroke is still under investigation. The purpose of this treatment is not only to improve the neurological outcome of patients but also to avoid hemorrhagic complications. A recent controlled multi-center study demonstrated that intravenous recombinant tissue-type plasminogen activator (rtPA) was effective in the first 3 hours after symptom onset. The other major study of intravenous rtPA using the therapeutic window of 6 hours reported no evidence of efficacy. Although the therapeutic window in humans is generally believed to be the first 6 hours after symptom onset, a previous study by our group indicated a variation among different individuals. The therapeutic window for potentially salvageable ischemic tissue is likely dependent on the degree of collateral flow. Our previous studies showed that pretreatment SPECT could provide useful parameters to predict patient outcome and that it might be useful to improve patient selection for thrombolytic therapy. We believe that the evaluation of tissue reversibility should be included in the selection of appropriate patients for angioplasty in acute stroke.

Intra-arterial thrombolysis was reported to have a relatively higher recanalization rate and a lower hemorrhagic rate compared with intravenous thrombolysis. Analysis of the data from 274 patients in 10 recent studies in which intra-arterial thrombolysis was used showed a 60% recanalization rate and a 21% hemorrhage rate, whereas 4 major studies on the use of intravenous thrombolysis with angiographic control showed recanalization rates ranging from 21% to 59% and 1 major study showed a 42.8% overall hemorrhage rate and a 19.8% large parenchymal hemorrhage rate. Advantages of this approach include reliable delivery of a high concentration of thrombolytic agents at a lower dose than intravenous infusion and actual mechanical disruption of clots by the microcatheter and the micro–guidewire. However, there are several problems in intra-arterial thrombolysis. First, the efficacy of intra-arterial thrombolysis still remains unproved, so that a large, randomized, and placebo-controlled study is needed to validate the technique’s usefulness. Currently, 1 clinical trial using recombinant pro-urokinase suggested that initial data in 40 patients with MCA occlusion treated within 6 hours demonstrated recanalization rates of 57% for the pro-urokinase group compared with only 15% for the placebo group. Second, intra-arterial thrombolysis depends on rapid access to an angiographic laboratory 24 hours a day and needs to be performed by an experienced multidisciplinary team. Finally, there are some disadvantages.

### Table 2. Comparison of PTA and Thrombolysis-Alone Groups With Acute MCA Occlusion

<table>
<thead>
<tr>
<th>Group</th>
<th>PTA</th>
<th>Thrombolysis Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Age, y*</td>
<td>64±9.0</td>
<td>69±6.8</td>
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<tr>
<td>Interval, h*</td>
<td>5.3±0.74</td>
<td>4.5±1.4</td>
</tr>
<tr>
<td>Urokinase dose (×10^3 U)*</td>
<td>630±174</td>
<td>640±156</td>
</tr>
<tr>
<td>Site of occlusion</td>
<td>M1</td>
<td>9/9</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>0/3</td>
</tr>
<tr>
<td>Recanalization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Partial</td>
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<td>4</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Reocclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>NIH Stroke score†</td>
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</tr>
<tr>
<td>Baseline</td>
<td>17.6±4.1</td>
<td>15.4±5.6</td>
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<tr>
<td>Next day</td>
<td>8.8±5.6</td>
<td>11.8±7.2</td>
</tr>
<tr>
<td>1 month after treatment</td>
<td>3.5±3.2</td>
<td>5.6±4.6</td>
</tr>
<tr>
<td>Change in NIH Stroke score</td>
<td></td>
<td></td>
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<tr>
<td>Next day—baseline‡</td>
<td>8.8±2.4</td>
<td>3.6±3.8</td>
</tr>
<tr>
<td>1 month—baseline‡</td>
<td>14.0±2.2</td>
<td>9.8±4.9</td>
</tr>
<tr>
<td>1 month—next day</td>
<td>5.2±2.7</td>
<td>6.3±4.7</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
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</tr>
<tr>
<td>Good</td>
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</tr>
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<td>Poor</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*No significant difference between PTA and thrombolysis-alone groups (unpaired t test).
†National Institutes of Health Stroke Scale scores.
‡Significant difference between PTA and thrombolysis-alone groups (P<0.01, unpaired t test).

### Discussion

Thrombolytic therapy for acute ischemic stroke is still under investigation. The purpose of this treatment is not only to improve the neurological outcome of patients but also to avoid hemorrhagic complications. A recent controlled multi-center study demonstrated that intravenous recombinant tissue-type plasminogen activator (rtPA) was effective in the first 3 hours after symptom onset. The other major study of intravenous rtPA using the therapeutic window of 6 hours reported no evidence of efficacy. Although the therapeutic window in humans is generally believed to be the first 6 hours after symptom onset, a previous study by our group indicated a variation among different individuals. The therapeutic window for potentially salvageable ischemic tissue is likely dependent on the degree of collateral flow. Our previous studies showed that pretreatment SPECT could provide useful parameters to predict patient outcome and that it might be useful to improve patient selection for thrombolytic therapy. We believe that the evaluation of tissue reversibility should be included in the selection of appropriate patients for angioplasty in acute stroke.

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However, there are several problems in intra-arterial thrombolysis. First, the efficacy of intra-arterial thrombolysis still remains unproved, so that a large, randomized, and placebo-controlled study is needed to validate the technique’s usefulness. Currently, 1 clinical trial using recombinant pro-urokinase suggested that initial data in 40 patients with MCA occlusion treated within 6 hours demonstrated recanalization rates of 57% for the pro-urokinase group compared with only 15% for the placebo group. Second, intra-arterial thrombolysis depends on rapid access to an angiographic laboratory 24 hours a day and needs to be performed by an experienced multidisciplinary team. Finally, there are some disadvantages.

![Figure 1](http://stroke.ahajournals.org/). Left carotid angiograms in patient 4. A, Pretreatment angiogram shows total occlusion of the proximal M1 segment of the left MCA. B, Postthrombolysis angiogram demonstrates partial recanalization with severe stenosis of the M1 segment. C, Post–immediate angioplasty angiogram shows complete dilatation with mild dissection. D, Follow-up angiogram 1 month after treatment demonstrates complete patency of the M1 segment without dissection or restenosis.
technical problems in patients with persistent or recurrent occlusion after thrombolysis. In particular, multiple or large hardened clots are difficult to lyse with the thrombolytic agent, and vessel occlusion with hardened plaques of atherosclerotic changes is difficult to recanalize completely. Therefore, we tried to perform angioplasty for patients that were difficult to treat by intra-arterial thrombolysis alone.

Although there are several recent reports suggesting the benefit of angioplasty for the stenosis of intracranial arteries in the chronic stage,25,26 reports of angioplasty for intracranial arteries in acute ischemic stroke are still rare. Some reports suggest that PTA as an adjunct to thrombolysis for acute thrombotic MCA occlusion might be safely performed to prevent rethrombosis and reocclusion.8,9 Our study showed a high success rate for immediate or delayed angioplasty for severe residual stenosis after successful thrombolysis and demonstrated the usefulness of these procedures for preventing reocclusion. The technical feasibility of rescue angioplasty for an occluded artery after failed thrombolysis was also demonstrated. We did not try to perform direct angioplasty (without thrombolysis),27 because PTA alone might not be able to dissolve the clots or reestablish the blood flow effectively, particularly in perforating or small arteries, and the safety of this procedure had not been established at that time.

Rescue angioplasty may be applicable not only for thrombotic occlusion but also for embolic occlusion. However, it is uncertain whether rescue angioplasty should be attempted in every patient with documented failure of thrombolysis, because this procedure may not save a significant amount of ischemic tissue, considering the time delay associated with the infusion of the thrombolytic agent, recognition of failed thrombolysis, and initiation of rescue angioplasty. Furthermore, the technical success rate of rescue angioplasty is lower than that of immediate or delayed angioplasty. The application of this strategy may be suitable to improve mortality for high-risk patients.

On the other hand, rescue angioplasty after failed intravenous thrombolysis (patient 7) may be of benefit to recanalize as soon as possible the occluded artery without additional

Figure 2. Left carotid angiograms in patient 1. A, Pretreatment angiogram shows severe stenosis in the proximal M1 segment of the left MCA without filling of distal branches. B, Postthrombolysis angiogram demonstrates complete recanalization with mild stenosis of the M1 segment. C, Angiogram 2 days after treatment shows severe stenosis of the M1 segment with deterioration of neurological symptoms. D, Post–delayed angioplasty angiogram demonstrates complete dilatation of the M1 segment. E, Follow-up angiogram 1 month after treatment demonstrates complete patency of the M1 segment without dissection or restenosis.

Figure 3. Left carotid angiograms in patient 7. A, Post–intravenous thrombolysis angiogram still shows total occlusion of the proximal M1 segment of the left MCA. B, Angiogram immediately after angioplasty demonstrates a Stealth balloon catheter placed in the M1 segment with excellent filling of distal branches. C, Post–rescue angioplasty angiogram shows complete patency of the M1 segment.
infusion of the thrombolytic agent. Recently, a new strategy for the treatment of acute ischemic stroke was tried in our institution: first, intravenous rtPA thrombolysis was started during preparation for angiography after CT or during acquisition of SPECT data; and, second, intra-arterial thrombolysis using a minimum dose of urokinase with or without angioplasty was performed, if angiography demonstrated occlusion or severe residual stenosis of the vessels. We believe that this method may make it possible to shorten the duration from occlusion to recanalization of the vessel and to improve the success rate of recanalization. More experience is required to evaluate the benefits of this method.

With respect to treatment for acute MCA occlusion, our data from a small number of patients may not be able to prove the effectiveness of PTA in clinical outcome because our study is not a controlled prospective analysis. Furthermore, we think that the purpose of angioplasty should be to provide sufficient perfusion to reduce ischemic symptoms and not to achieve an angiographic cure. However, this study suggests that the improvement in NIH stroke scores in the PTA group is greater than that in the thrombolysis-alone group. Angioplasty for acute MCA occlusion may have the potential to contribute to early improvement of neurological symptoms by increasing the rate of recanalization and avoiding reocclusion. Potential technical complications related to angioplasty for intracranial arteries include dissection of the vessel wall, acute occlusion after the procedure, dissection or perforators with crushed plaque. Particularly, blind wire and catheter manipulation when rescue angioplasty is attempted may cause perforation or dissection of the vessel. Although the incidence of these complications is still unknown, it is reported to be very low in the coronary arteries. No technical complications, with deterioration of neurological symptoms, were found in this study.

There were no symptomatic hemorrhagic complications in this series. However, if early recanalization had been obtained in patient 10 or 11, these patients might have been at high risk for hemorrhage because of very low residual CBF assessed by pretreatment SPECT. At that time, we had not assigned a cutoff value for the indication of thrombolytic therapy. Because these patients might have taken a rapidly fatal course without alternative therapies, we attempted to perform angioplasty. Moreover, not all patients had successful angioplasty. A successful procedure depends on the size and hardness of the clot and the degree of kinking by atherosclerotic vessel changes. In some of our patients, the dilatation catheter could not be advanced to the stenotic lesion due to severe atherosclerotic changes. This limited study demonstrates the technical feasibility of angioplasty for intracranial arteries in acute ischemic stroke and suggests that angioplasty may be an effective option for improving the success rate of recanalization and preventing recollusion of the occluded artery, particularly the M1 segment of the MCA. Although this study is preliminary and the efficacy of this procedure should be assessed by well-designed clinical trials in a large number of patients, the present results encourage us to perform further trials in acute ischemic stroke.

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References


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