Mechanical Thrombectomy Following Intravenous Thrombolysis in the Treatment of Acute Stroke

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Background: The efficacy of intravenous thrombolytics in acute stroke is limited by low rates of recanalization of occluded arteries. Treatment with intravenous thrombolytics followed by mechanical thrombectomy is a novel approach that may increase recanalization rates without compromising time to initiation of treatment.

Objectives: To report our experience with 2 patients who received this combination therapy and outline plans for a prospective pilot study.

Design and Setting: Case studies at a university hospital.

Interventions: Patients treated with intravenous thrombolytics within 3 hours of symptom onset subsequently underwent computed tomographic angiography. If an occlusion of a proximal cerebral vessel was shown by a computed tomographic angiogram, mechanical thrombectomy was performed. Patients were observed for 1 month after treatment.

Main Outcome Measures: National Institutes of Health Stroke Scale (NIHSS) score.

Results: The computed tomographic angiography of 2 patients showed complete occlusion of the M1 branch of the middle cerebral artery following administration of intravenous thrombolytics. The NIHSS scores were 21 and 13. In both cases, blood flow through the occluded artery was restored with mechanical thrombectomy and dramatic neurologic improvement occurred. There were no complications. The NIHSS scores were 0 and 2 at 1-month follow-up.

Conclusion: Treatment with intravenous thrombolytics followed by mechanical thrombectomy may improve outcomes in acute stroke patients and a pilot safety trial is warranted.

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THE FOOD AND DRUG ADMINISTRATION'S approval of intravenous tissue plasminogen activator (IV tPA) was a major breakthrough in acute stroke therapy. Unfortunately, the majority of patients treated with IV tPA who have moderate or severe deficits at presentation do not achieve a favorable outcome. We describe 2 patients who had persistent arterial occlusion despite treatment with intravenous thrombolytics. Both underwent mechanical thrombectomy following IV thrombolytic therapy resulting in immediate clinical improvement. Based on these excellent outcomes, we propose a safety study to evaluate adjuvant mechanical thrombectomy following standard IV tPA.

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REPORT OF CASES

CASE 1

A 61-year-old woman developed acute onset of left-sided weakness and inability to speak. Her National Institutes of Health Stroke Scale (NIHSS) score was 21, with near complete left hemiparesis, left hemianopsia, and left-sided neglect. She received IV recombinant tissue plasminogen activator (alteplase) (r-tPA) at 75 minutes after symptom onset. At 120 minutes, her neurological status was unchanged and a computed tomographic angiogram (CTA) obtained at that time showed occlusion of the M1 segment of the right middle cerebral artery (MCA). This was confirmed by conventional angiography (Figure A). The occlusive thrombus was removed at 180 minutes with 2 passes of the Concentric Retriever (Concentric Medical, Mountain View, Calif). Post-treatment angiography showed restoration of flow in the distal M1 and most of the MCA circulation, but persistent nonfilling of an anterior temporal artery (Figure B). Immediately after the procedure, the left hemiparesis resolved, but mild residual dysarthria and neglect persisted (NIHSS score of 2). By the next day the patient had regained normal neuro-
logical function. Magnetic resonance images obtained at 40 hours showed an acute infarct in the right temporal lobe (Figure, C). At 1-month follow-up, her only symptom was fatigue (NIHSS score of 0; modified Rankin score of 1).

**CASE 2**

A 48-year-old woman developed sudden onset of left-sided weakness. On arrival to an outside hospital her NIHSS score was 13, with a dense left hemiparesis, dysarthria, and neglect. Because r-tPA was not available, she was treated with IV tenecteplase at 120 minutes after symptom onset and transferred to our institution. A CTA obtained at 5 hours 40 minutes showed an abrupt cutoff in the M1 segment of the right MCA. Neurologic examination results were unchanged. Conventional angiography at 6 hours and 45 minutes confirmed CTA findings (Figure, D). Two passes with the Concentric Retriever failed to recanalize the vessel. Two passes with the Neuroner (Guidant Corp, Santa Clara, Calif) achieved recanalization of the M1 at 7 hours and 45 minutes, resulting in good flow in the angular artery, but persistent slow collateral flow in several frontal opercular arteries (Figure, E). The NIHSS score had improved to 3, with only mild residual left hemiparesis and dysarthria. Magnetic resonance images at 40 hours showed an acute right basal ganglia infarct with a small area of hemorrhagic con-
version (Figure, F). At 1-month follow-up, neurological examination findings were notable for mild clumsiness and weakness of the left hand and leg (NIHSS score of 2; modified Rankin score of 1).

**COMMENT**

We report 2 cases of persistent occlusion of the main middle cerebral artery branch despite treatment with IV thrombolytics. Both patients subsequently underwent mechanical thrombectomy which led to restoration of flow and dramatic improvement of their neurological symptoms. One patient was initially treated with standard IV r-tPA, the other with tenecteplase, which is a modification of standard r-tPA. While no human data are available, animal studies suggest that tenecteplase is a more specific fibrinolytic than r-tPA, and that it is associated with somewhat faster and more complete recanalization rates.2,3

Patients with complete recanalization within 5 hours after stroke have a 4-fold increased likelihood of achieving independence compared with patients with persistent occlusion.4 Unfortunately, in up to 75% of stroke patients with an M1 MCA occlusion, recanalization is not achieved with IV r-tPA.5 Failure of recanalization is a major reason for the relatively small increased chance (absolute increase, 13%) of a favorable result in IV tPA treated patients.6 Consequently, many investigators have focused on techniques to improve recanalization rates. Promising approaches include intra-arterial tPA, continuous transcranial ultrasound, and mechanical thrombectomy. Compared with historical controls, each of these therapies increase the likelihood of restoration of blood flow by 2 to 3 times that of IV tPA alone.7-9

The main concern of mechanical thrombectomy following IV tPA is the potential for systemic and intracerebral bleeding complications. The results of the IMS trial, however, suggest that arterial catheterization following IV tPA carries an acceptable level of risk. In that trial, the use of intra-arterial tPA following IV tPA (0.6 mg/kg) led to significant catheter-related complications in only 3% of patients and the rate of symptomatic intra-cerebral hemorrhage (6.3%) was similar to that of IV tPA-treated controls.10

The results seen in the 2 patients described suggest that a pilot safety trial designed to evaluate adjunctive mechanical thrombectomy in the subgroup of acute stroke patients who do not experience clot lysis following standard IV tPA treatment may be warranted. Noninvasive imaging using CTA or magnetic resonance angiography could be used to select patients with persistent large-vessel arterial occlusion despite IV tPA. The optimal timing of imaging after the start of tPA infusion may be 45 to 60 minutes based on transcranial Doppler studies that show that the mean time to complete restoration of blood flow, if it is to occur, is 42 minutes after the beginning of tPA infusion.11 Patients with evidence of persistent major cerebral artery occlusion would be treated with mechanical thrombectomy. If safety data were promising, the combination of IV tPA and mechanical thrombectomy could subsequently be compared with IV/intra-arterial tPA or IV tPA alone in a larger trial.

In summary, adjunctive mechanical thrombectomy for stroke patients who have a persistent arterial occlusion despite IV thrombolytic therapy may lead to higher recanalization rates and improved clinical outcome. The safety of this approach should be studied prospectively.

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