Intraarterial Therapy for Acute Ischemic Strokes

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PURPOSE: To determine the safety and feasibility of intraarterial stroke therapy for acute ischemic strokes at a community-based medical center.

MATERIALS AND METHODS: This is a retrospective analysis of data gathered from consecutive stroke patients treated between June 2004 and April 2007. The following therapies were used to treat acute ischemic stroke within 6 hours of symptom onset: intraarterial thrombolytic drugs, intraarterial vasodilators, mechanical clot retrieval, intravascular stents, and angioplasty. The outcomes measured included posttherapy National Institutes of Health Stroke Score (NIHSS), neurologic function at 90 days graded according to the modified Rankin Scale (mRS), recanalization, symptomatic intracranial hemorrhage, and 90-day mortality.

RESULTS: Eighty-three patients with a median baseline NIHSS of 17 (range, 3–30) were treated with intraarterial therapy. The median posttherapy NIHSS was 5 (range, 0–33). Forty-two patients (76%) had an mRS score of 2 or less at 90 days. The recanalization rate was 76%. Five patients (6%) had symptomatic intracranial hemorrhage, and the 90-day mortality was 22%.

CONCLUSIONS: The results of this review showed that an intraarterial therapeutic approach to acute ischemic stroke was feasible at a community-based heath center and demonstrated encouraging data for outcome and safety.

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Abbreviations: MERCI = Mechanical Embolus Removal in Cerebral Ischemia, mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale, NINDS = National Institute of Neurological Disorders and Stroke, PROACT = Prolyse in Acute Cerebral Thromboembolism, TICI = Thrombolysis in Cerebral Infarction, tPA = tissue-type plasminogen activator

CURRENTLY, there are three main therapies for the treatment of acute ischemic strokes: (*a*) intravenous thrombolysis, which treats acute ischemic strokes systemically with tissue-type plasminogen activator (tPA) and is effective if administered within 3 hours of symptom onset (1); (*b*) mechanical clot retrieval; and (*c*) intraarterial thrombolysis. The latter two therapies directly target the occlusion(s) responsible for acute ischemic strokes. In 2004, the U.S. Food and Drug Administration approved the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) device (Concentric Medical, Mountain View, California) for the intraarterial retrieval of clots responsible for acute ischemic strokes. The device is for use within 8 hours of symptom onset (2). Intraarterial thrombolysis treats strokes by using thrombolytic drugs and is effective if administered within 6 hours of symptom onset (3).

No thrombolytic drug has been approved by the U.S. Food and Drug Administration for intraarterial stroke lysis, including recombinant prourokinase used in the Prolyse in Acute Cerebral Thromboembolism (PROACT) studies, but is endorsed by the Society of NeuroInterventional Surgery and the Society of Interventional Radiology following the publication of PROACT II results (4). Furthermore, its use is listed among the recommendations from the American Stroke Association as a treatment for acute ischemic strokes, stated as "intra-arterial thrombolysis is an option for treatment of selected patients who have major stroke of <6 hours' duration due to occlusions of the middle cerebral artery and who are not otherwise candidates for intravenous recombinant tPA" (5).

Because many stroke patients do not present to the emergency department within 3 hours of symptom onset, they are not candidates for intravenous recombinant tPA therapy. In fact, one study noted that the median time from symptom onset to arrival in the emergency department was between 3 and 6 hours (6). In another study, less than 25% of patients arrived within 3 hours, whereas only 3%–4% received intravenous tPA (7).

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This underutilization is especially true in areas where a limited number of treatment facilities must serve large rural populations and where the transportation of patients can take more than an hour by air. Therefore, despite the advantages of intravenous tPA (speed of initiation, availability, and lack of treatment complexity), its narrow therapeutic window makes it difficult to use on a widespread basis.

Both intraarterial thrombolysis and endovascular embolectomy allow for a longer therapeutic window and increased recanalization rates relative to intravenous thrombolysis (2,3). Specifically, the advantage of the MERCI device is its large treatment window (<8 hours) and low symptomatic intracranial hemorrhage rate (2). However, it is difficult to use when clots are located in tortuous intracranial arteries and its use carries the risk of thrombus fragmentation (2). As for intraarterial thrombolysis, the PROACT II study (3) documented favorable 90-day neurologic outcomes and a recanalization rate of 66% in treated patients versus 18% in control subjects ($P < .001$). Furthermore, the microcatheter used to administer thrombolytic drugs is smaller and more flexible than that used with the MERCI device and thus makes it easier to use in tortuous anatomy. One disadvantage of intraarterial thrombolysis versus the controls in the PROACT II study is an increased chance of symptomatic intracranial hemorrhage (3). An important benefit of both therapies is that they rely on a diagnostic cerebral angiogram to locate the occlusion and, thus, provide additional stroke information not available in intravenous tPA therapy (1,3). Finally, the recombinant prourokinase used in the PROACT studies is no longer available.

The purpose of this retrospective review was to analyze the feasibility and safety of using a combination of intraarterial therapies to treat acute ischemic strokes. By drawing from the multiple options of intraarterial thrombolysis, mechanical clot retrieval, angioplasty, and stent placement, a clinician has more information and greater flexibility in treating patients suffering from acute ischemic strokes.

MATERIALS AND METHODS

An institutional review board approved and evaluated retrospective analysis of prospectively gathered data from stroke patients treated between June 2004 and April 2007 at a single institution. The institutional review board initially approved all protocol and procedures in 2001, with revisions as new technology and terminology were available. Operative physicians received informed consent from all patients before treatment.

After initial presentation to the emergency department, all patients underwent unenhanced computed tomography (CT) and an initial stroke severity assessment. Stroke severity was measured with the National Institutes of Health Stroke Score (NIHSS), a graded neurologic examination (8–10), by a NIHSS-certified medical doctor or registered nurse. A score of 42 indicates the most severe stroke, and a score of 0 indicates no deficit (8–10). A medical doctor or a registered nurse evaluated the patient and determined an NIHSS 7–10 days after treatment or at discharge. Inclusion/exclusion criteria were based on the American Heart Association/American Stroke Association Scientific Statement: Guidelines for Early Management of Patients with Ischemic Stroke (5,11,12). It included eight absolute and 17 relative contraindications. The absolute contraindications with respect to a patient's history were as follows: no significant neurologic deficit, a stroke onset more than 5 hours before arrival at the emergency department, a history of stroke within 6 weeks or intracranial hemorrhage in the past 3 years, or a known anaphylactic reaction to contrast medium. Absolute contraindications included an unenhanced CT scan indicative of midline shift, hemorrhage, tumor or severe edema, an electrocardiogram suggestive of acute myocardial infarction, and/or an NIHSS of less than 8 or greater than 30 or no isolated severe aphasia or no complete hemianopia. The relative contraindications included aspects of the patient's clinical presentation, laboratory results, past medical history, and/or an unenhanced CT scan demonstrating a hypoattenuating defect in more than one-third of the middle cerebral artery.

Candidates for intraarterial therapy underwent diagnostic cerebral angiography by using standard angiographic techniques to determine the site of the occlusion or lesion. If no lesion was identified, then intraarterial therapy was not performed. In general, the operator used mechanical clot retrieval when thrombolysis was contraindicated or if thrombolysis failed. For example, if a clot was identified and there were no contraindications to thrombolysis, the patient received a 2,000-U bolus and a 500 U/h infusion of intravenous heparin. The protocol for heparin administration was derived from the PROACT II study (3). If the lesion was identified within 6 hours of symptom onset, a microcatheter was deployed and a 1-U bolus and a 1 U/h infusion of reteplase (Retavase; PDL BioPharma, Fremont, California) was used. It was administered proximal to the clot and laced in the clot for up to a total of 3 hours or 6 hours from symptom onset (13). After 6 hours but less than 8 hours after symptom onset or if initial intraarterial thrombolysis failed, the operator attempted mechanical clot retrieval by using the MERCI device. Failed thrombolysis was defined as no change in the clot or lesion after 1 hour. If a radiologist identified a lesion between 6 and 8 hours, then only mechanical clot retrieval was attempted. Intraarterial vasodilators, intravascular stents, and/or angioplasty were used as needed in situations of vascular stenosis and/or to gain access to clot locations. Angioplasty and stent placement were not used intracranially.

To evaluate recanalization, the patient underwent posttherapy angiography to determine a prospective Thrombolysis in Cerebral Infarction (TICI) score, where 0 = no canalization, 1 = penetration with minimal canalization, 2 = partial canalization, and 3 = complete canalization (14). The procedure was performed by one of four vascular and interventional radiologists (V.E.M., T.L.T., R.A.H., T.S.G.). If timing allowed or complexity required, an assisting physician was used. The operator made an unblinded assessment by using the TICI score. Patients underwent unenhanced CT within 24 hours of the procedure to assess intracranial bleeding.

The primary outcome, determined by a phone interview from one registered nurse with stroke training, was a