Mechanical Thrombolyis in Ischemic Stroke Attributable to Basilar Artery Occlusion as First-Line Treatment

Mauro Bergui, MD; Guido Stura, MD; Dino Daniele, MD; Paolo Cerrato, MD; Maurizio Berardino, MD; Gianni Boris Bradac, MD

Background and Purpose—To report results of mechanical disruption or retrieval of thrombus as first-line treatment in patients with stroke attributable to occlusion of the basilar artery, in particular regarding efficiency and safety.

Methods—In 12 consecutive patients with acute stroke attributable to basilar occlusion, mechanical disruption or thrombus retrieval using various loop-shaped tools was tried before eventually starting local intra-arterial thrombolysis with recombinant tissue plasminogen activator (r-tPA). Main inclusion criteria were: National Institutes of Health Stroke Scale score >8 or Glasgow Coma Scale score <12; onset or worsening of symptoms <8 hours; no hemorrhages or large hypodensities on computed tomography scan; and occlusion of the basilar artery matching clinical symptoms. Efficiency included recanalization, procedure time, and r-tPA dose; safety was defined as rate of procedure-related complications. Outcome was evaluated at 3 months.

Results—Mechanical recanalization was successful in 6 patients. A single brain infarction, possibly attributable to distal embolization, occurred. Three patients had good outcomes. In 5 of 6 remaining patients, the artery was recanalized using r-tPA. A single asymptomatic hemorrhage occurred; 3 patients had good outcomes. Procedure time and r-tPA were significantly less in patients with successful mechanical thrombolysis (43.33 minutes and 13.33 mg versus 112.33 minutes and 55.83 mg, respectively).

Conclusion—Mechanical recanalization was effective in half of the patients and at least as safe as local intra-arterial thrombolysis. It allowed to save r-tPA and time. Although the low success rate remains a limit, the excellent and quick anatomical recanalization obtained after successful procedures makes this approach promising. (Stroke. 2006;37:145-150.)

Key Words: brain stem ■ stroke ■ stroke, acute ■ thrombolytic therapy

Thrombolytic agents administered intra-arterially or intra-venously may recanalize occluded vessels responsible for ischemic stroke and improve prognosis. On the other hand, they may cause hemorrhages in ischemic lesions, eventually worsening prognosis. Strategies to avoid bleeding include not treating patients after 3 or 6 hours from onset and patients with signs of extended infarctions on computed tomography (CT) scan. In patients with stroke attributable to basilar artery occlusion, a wider time window is usually accepted because of various reasons: prognosis is supposed to be bad if untreated, in particular if consciousness disturbances are present, and strokes are frequently progressive. Late treatment leads to a greater risk of bleeding. Moreover, clots in basilar artery are frequently large, and possibly difficult to dissolve unless large doses of different drugs are administered, possibly increasing the risk of bleeding. An alternative way to recanalize vessels is mechanical action, including removal or fragmentation of the occluding material. This allows to administer lower doses of drugs, probably reducing the bleeding risk. This treatment may possibly apply to patients excluded from treatment because of the risk of bleeding, including late treatments, use of anticoagulative drugs, and presence of potential sources of bleeding. Several anecdotal cases were reported, and a recently completed multicenter trial gave promising results. An attempt to mechanically open the vessels was systematically done in a series of patients with acute stroke attributable to basilar artery occlusion. The results are presented, focusing on efficiency and safety.

Materials and Methods

Patient Selection
In January 2003, a trial called T-Stroke (“T” for Thrombolysis and Turin) was started in our department to apply local intra-arterial thrombolysis (LIT) in patients with acute ischemic stroke of anterior and posterior circulation on behalf of the ethical committee. Inclusion criteria for vertebrobasilar stroke were: (1) acute ischemic stroke with NIHSS >8 or with consciousness disturbances (Glasgow Coma Scale [GCS] <12); (2) procedure within 8 hours from onset or significant worsening (2 points of National Institutes of Health Stroke Scale [NIHSS] or 1 point of GCS); (3) <75 years of age.

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

Received July 9, 2005; final revision received August 26, 2005; accepted October 12, 2005.
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DOI: 10.1161/01.STR.0000195178.20019.de
age; (4) normal coagulation and no known risk for systemic bleeding; (5) blood pressure <180/110 mm Hg; (6) no large infarctions, hemorrhages, or significant mass effect on CT scan. Angiographic criterion was occlusion of the basilar artery matching clinical symptoms. The maximal dose of recombinant tissue plasminogen activator (rt-PA) was 80 mg. Because of the increased hemorrhagic risk of the extended time window, the protocol includes mechanical thrombolysis for 15 minutes maximum before LIT, with the goal of reducing the amount of rt-PA administered. Vessel damage, hemorrhage, and distal infarct, possibly attributable to embolisms, were considered complications of the procedure. Recanalization was defined as thrombolysis in myocardial infarction (TIMI) score of 2 or 3. Clinical outcomes were evaluated at 3 months using the modified Rankin scale (mRS).

Age, gender, presence of vascular risk factors, referral time, and NIHSS and GCS scores at the time of general anesthesia, duration of the procedure, amount of rt-PA administered, recanalization, and outcomes were recorded and compared between patients with successful and unsuccessful mechanical recanalization.

We underline that intravenous thrombolysis was not considered because it was practically unavailable in Turin, Italy, up to January 2005.

### Procedure

Mechanical reopening was tried in patients under general anesthesia after administration of 40 IU/kg heparin using a lazoo-shaped tool (tool 1: Amplatz gooseneck snare [2-mm loop]; Microvena) in the first 4 patients, a retriever (tool 2: In-Time; Boston Scientific) in the following 2, and in the remaining 6, a multiple-loops tool originally designed to treat wide-necked aneurysms (tool 3: Trispan; Boston Scientific). Microcatheter was advanced distal to the occlusion; the tool was then inserted and opened in a patent vessel distal to the occlusion and subsequently retrieved. If noting was “caught” or the artery did not recanalize, the procedure was repeated, eventually passing the occlusion site proximal to distal with the tool kept open. After 15 minutes maximum, mechanical thrombolysis was interrupted and LIT was started. Procedure time, from the beginning of selective catheterization to the final angiographic control, was recorded. After treatment, a CT scan was performed. If no hyperdense lesions or extensive hypodense infarctions were seen, 250 mg salicilate was given immediately, and low-molecular–weight heparin (0.5 mg/kg twice per day) was administered 3 hours later. If such lesions were seen, no salicilate was administered, and the dose of low-molecular–weight heparin was halved; 24 hours later, after a second CT scan, 10 mg ticlopidine twice per day and 250 mg/die salicilate were given; the dosage of low-molecular–weight heparin was progressively reduced and suspended in the following 3 days.

### Results

Of 26 consecutive patients referred for LIT from January 2003 to December 2004, 15 had stroke affecting the posterior circulation, and 12 were treated. Exclusion criteria were patent basilar artery in 2 patients and a long-standing occlusion of both vertebral arteries not allowing selective catheterization of the basilar artery in 1 patient.

Individual and group values for variables kept into account are shown in Tables 1 and 2, respectively. Briefly, mechanical thrombolysis was successful in 6 patients. Occlusion of posterior cerebral artery branches attributable to distal migration of emboli occurred in 2 patients; 1 developed an asymptomatic infarction. No hemorrhagic complications oc-

### TABLE 1. Individual Values

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Hours From Onset</th>
<th>Hours From Worsening</th>
<th>NIHSS</th>
<th>GCS</th>
<th>Basilar Occlusion Site</th>
<th>Tool</th>
<th>TIMI After Mechanical Thrombolysis</th>
<th>r-tPA Dose (min)§</th>
<th>Final TIMI</th>
<th>Procedure Time (min)§</th>
<th>Hemorrhagic Infarction</th>
<th>mRS (3 mo)</th>
<th>Cause of Ischemia</th>
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<tr>
<td>1 F</td>
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<td>0</td>
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<td>tip 1</td>
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<td>3</td>
<td>110</td>
<td>no</td>
<td>2</td>
<td>Unknown</td>
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</table>

#Hypertension, hypercholesterolemia, diabetes, and smoking; *evaluated at worsening time, when patient was placed under mechanical ventilation; §from the beginning of selective catheterization to final angiographic control.
curred. Two patients deceased; at 3 months, 1 had an mRS score of 4, and 3 had 0 to 3.

Excessively tortuous vessels, impairing selective catheterization and multiple “passing through” the thrombus, were the reason for unsuccessful mechanical thrombolysis in the remaining 6 patients. In 5 of them, LIT obtained vessel recanalization. A single patient had hemorrhage in an occipital infarction without evident clinical consequences. Two patients died. At 3 months, a single patient had an mRS score of 5; 3 had 0 to 3.

Patients with successful mechanical recanalization were significantly younger than the remaining patients (mean age 58.5; median 62.50 and 68.83; 69) and had more frequently progressive symptoms (4 of 6 and 1 of 6). Recanalization was faster (mean 43.33 minutes; median 42.5 and 112.33; 111.50) and less r-tpA was used (mean 13.33 mg; median 15 and 55.83; 60). Clinical conditions, time from onset/worsening, and outcome were not different between groups.

**Illustrative Case (Patient 5)**

A 42-year-old male had abrupt onset of left hemiparesis, worsening in the following 6 hours up to right hemiplegia, left hemiparesis with sparing of the proximal movement of the arm, skew deviation, and anarthria. CT scan was normal. Angiography demonstrated a midbasilar artery occlusion, with patent posterior communicans arteries filling the posterior cerebral arteries and the basilar tip (Figure, A and B). Tool 3 was opened in posterior cerebral artery and pulled, retrieving the thrombus. It was finally in part extracted of the patient, in part lost in the aortic arc because the 5F-guiding catheter was not large enough to allow passage of the whole embolus. Then, 5 mg of r-TPA was injected in the patent basilar artery. Final angiogram looked normal, apart from the occlusion of the right superior cerebellar artery, which was left untreated (Figure, C). Patient was awakened 48 hours later, with diplopia, mild cerebellar signs and dysarthria, minimal right hemiparesis, and dysmetria. Five days later, magnetic resonance showed “patchy” brain stem and cerebellar infarctions (Figure, D). At 3 months, the sole neurological deficit remaining was internuclear gaze palsy.

**Discussion**

Outcomes of our patients were similar to that of different series, reporting results of LIT1–5 or intravenous thrombolysis8 in patients with basilar artery occlusion, and were better than the expected natural history.6 Because selection criteria are a major determinant of the outcome, a direct comparison of the clinical result among different series is not possible.

One of the major drawbacks of treating ischemic stroke with thrombolytic drugs is the risk of causing hemorrhage by using high doses of thrombolytic agents. In this setting, management of progressive stroke may be particularly critical; thrombolytic drugs may eventually allow recovery from the most recently appeared deficits or they can stop worsening, but they cannot be used because of the older lesions. Moreover, some vessels are not recanalized because some emboli do not respond to the drug (fibrous fragment of plaques), or the maximal dose of thrombolytic agents may not be enough to dissolve a large clot. This latter problem is particularly relevant because large emboli in critical locations such as carotid bifurcation or basilar artery cause the most dramatic clinical pictures.

Mechanical disruption or retrieving of the occluding material offers some theoretical advantages over the thrombolytic treatment, possibly allowing safer and more efficient procedures. This allows a more efficient recanalization in large vessel21–23 than thrombolysis alone at the expense of an increased risk. Different techniques were suggested, efficiency usually being directly related to the amount of complications, mainly vessel rupture. The most common technique is pressure injection of saline and “getting through” the thrombus with guidewires and catheters.13,21,24 but in our experience, it has limited usefulness. Moreover, thin tools as guidewires may cause perforations.21,22 Larger tools, as we used, may reduce this risk. Different devices have been proposed, including retrievers,12,14,17–19,22 photoacoustic recanalization,20 ultrasounds,16 balloons,15,11 suction,10 coronary waterjet device,25 or an especially designed system.23 Finally, combination of thrombolytics, antiplatelets agents, and mechanical action as final resource in unsuccessful recanalization was more efficient than thrombolysis alone at the expense of an increased bleeding rate.9 A direct comparison with our experience is not

**TABLE 2. Group Values**

<table>
<thead>
<tr>
<th></th>
<th>Successful Mechanical Recanalization</th>
<th>Unsuccessful Mechanical Recanalization</th>
<th>Statistical Significance</th>
<th>Whole Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>58.50 (62.50)</td>
<td>68.83 (69.00)</td>
<td>P&lt;0.05*</td>
<td>63.67 (68.50)</td>
</tr>
<tr>
<td>Time from onset (median)</td>
<td>9.0 (7.0)</td>
<td>5.67 (4.50)</td>
<td>NS#</td>
<td>7.33 (5.50)</td>
</tr>
<tr>
<td>Time from onset/worsening (median)</td>
<td>4.67 (4.50)</td>
<td>4.82 (4.00)</td>
<td>NS#</td>
<td>4.50 (4.00)</td>
</tr>
<tr>
<td>Progressive symptoms</td>
<td>4 of 6</td>
<td>1 out of 6</td>
<td>P&lt;0.05*</td>
<td>5 of 12</td>
</tr>
<tr>
<td>Mean NIHSS (median)</td>
<td>22.10 (21.50)</td>
<td>22.60 (24)</td>
<td>NS#</td>
<td>22.42 (23)</td>
</tr>
<tr>
<td>Mean GCS (median)</td>
<td>7.30 (7.00)</td>
<td>7.67 (6.50)</td>
<td>NS#</td>
<td>7.92 (7.5)</td>
</tr>
<tr>
<td>r-TPA dose (median)</td>
<td>13.33 (15)</td>
<td>55.83 (60)</td>
<td>P&lt;0.05*</td>
<td>34.58 (22.5)</td>
</tr>
<tr>
<td>Mean procedure time (median)</td>
<td>43.33 (42.50)</td>
<td>112.33 (111.5)</td>
<td>P&lt;0.05*</td>
<td>77.83 (2.50)</td>
</tr>
<tr>
<td>mRS 0–3</td>
<td>3 of 6</td>
<td>3 of 6</td>
<td>NS*</td>
<td>6 of 12</td>
</tr>
</tbody>
</table>

#Student t test; *x² test.
possible, mainly because of the different patient selection, probably influencing vessel recanalization and outcomes.

Efficiency in vessel reopening of the sole mechanical maneuver was 50% in our series and 93% for the whole treatment; these results are among the highest reported in the literature, at the cost of no excess of complications directly related to the mechanical maneuvers.

Advantages and Limitations of the Technique
The technique was not always successful, although the learning curve showed improved results lately (5 of 6 successful procedures were done in the last 6 patients), and the limited time reserved for mechanical maneuvers may have played a role. The major advantage of the tools we used was that no special materials or equipment were required, apart from well-known materials for interventional neuroradiology. Tools 1 and 2 were difficult to navigate in cerebral vessels, and passing the occlusion more than once was the most difficult part of the mechanical approach. Attempting to retrieve something caused instability and “dropping” of the catheter. These difficulties were lesser with tool 3, which achieved 5 of 6 TIMI 2 to 3 recanalizations. After the tool passed the occlusion once, distal to proximal, multiple passing in both directions was possible in the majority of cases without using guidewires. Not to be forgotten, this device is detachable, and then it carries a significant risk of unwanted detachment of the distal portion. A second problem was the difficulty of exactly understanding where tools were placed when working into occluded and consequently not injected arteries. This problem may be partially resolved by state-of-the-art digital angiography, patients in mechanical ventilation, exact knowledge of the vascular anatomy, confidence with intracranial catheterization, and by avoiding thin tools.

A potential disadvantage of the technique is that clot, once disrupted, may migrate distally. In most of the cases, these fragments and the clot eventually remaining in the basilar artery quickly dissolved after limited injection of r-tPA. If not, because the primary goal of recanalizing basilar artery was reached, distal vessels were eventually left occluded. In our experience, thrombus frequently
underwent fragmentation during LIT; it is not rare that after a long-lasting local injection of r-tPA with limited effect on the occlusion, or after various frustrating phases of reopening and reocclusion, the behavior of the thrombus changes abruptly, leading to a quick dissolution with distal embolization. When successful, mechanical disruption obtained the same result in a few minutes.

Limitations of the Study

Our experience has many limitations, mainly on the scientific point of view. The procedure was not standardized because it was strictly operator dependent, r-tPA was given in adjunct to mechanical thrombolysis, and some mechanical maneuvers with catheters and guidewires were applied during LIT. We switched from mechanical to LIT after a limited time. Moreover, the number of patients is small, and a control group is lacking. Direct comparison of results, in particular outcomes, of patients with successful and unsuccessful mechanical recanalization and even the impact of the treatment on the final outcome, must be considered with caution because of the obvious biases. Mechanical thrombolysis allowed to save time and r-tPA, when successful, although our limited population do not allow to draw definitive results; on the other hand, a limited amount of time was lost during unsuccessful attempts. This probably means less hemorrhages and better results, but the global impact on the final outcome cannot be definitively evaluated. Our experience is limited to basilar artery, a large vessel with distal branches that may be eventually embolized with less clinical consequences. This may not apply to different anatomical districts, primarily the anterior circulation or peripheral branches. Finally, the series has the limitations and biases of all single center series.

On the other hand, we are dealing with a technique that may be used only in a few cases among the few patients referred for an experimental treatment such as LIT. Because intravenous thrombolysis is now available for our population, selection biases and further reduction of the eligible case will occur, and it will be impossible to enroll a significantly greater number of patients. For similar reasons, not even LIT in patients with basilar occlusion has been scientifically validated, although it represents an accepted treatment.1–5,9 nor will it probably be in the near future. Similar studies experience similar limitations. Smith et al involved 25 centers for 2 and half years to recruit, among 151 enrolled patients, 10 patients with vertebrobasilar occlusion. The impact of any treatment on the final outcome then could only be estimated based on previously reported series, which implies unavoidable biases.

Conclusion

Despite the above-mentioned limitations, we suggest that this technique, allowing to quickly and efficiently recanalize a significant percentage of acutely occluded vessels without significant complications may be successfully applied as first-line treatment in patients with acute stroke attributable to basilar artery occlusion.

Acknowledgments

We acknowledge Dr Marco Castelli for editorial assistance, and Dr Stefano Sales, Maria Federica Ferrio, and Marina Corsico for useful discussions.

References


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Stroke. 2006;37:145-150; originally published online December 8, 2005;
doi: 10.1161/01.STR.0000195178.20019.dc
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

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