Staged Escalation Therapy in Acute Basilar Artery Occlusion
Intravenous Thrombolysis and On-Demand Consecutive Endovascular Mechanical Thrombectomy: Preliminary Experience in 16 Patients

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Background and Purpose—The prognosis of acute basilar artery occlusion (BAO) is poor if early recanalization is not achieved. Recanalization strategies include intravenous thrombolysis (IVT) and intra-arterial thrombolysis, as well as endovascular mechanical thrombectomy (EMT). The combination of IVT with consecutive on-demand EMT may allow for early treatment initiation with high recanalization rates but has never been systematically tested in patients with BAO.

Methods—Starting in January 2006, we treated all eligible patients with acute BAO admitted to our academic stroke center or one of our cooperating community hospitals after a standardized protocol combining IVT with consecutive on-demand EMT. Inclusion criteria were: (1) presence of predefined symptoms clearly suggestive of BAO; (2) exclusion of intracerebral hemorrhage on CT scan; (3) evidence of BAO on CT angiography; (4) start of therapy within 6 hours after symptom onset; and (5) no contraindications for IVT. If CT angiography showed persistent BAO after IVT, EMT was performed.

Results—Since January 2006, 16 patients have been treated. All patients received IVT; in 7 of them, EMT became necessary because of persistent BAO. Final recanalization was achieved in 15 patients. Three months after therapy, 12 of 16 patients were still alive; 7 of them had a good outcome (modified Rankin score ≤2).

Conclusions—Our data suggest that the combination of IVT with on-demand consecutive EMT in BAO is feasible, allows for early treatment, and provides excellent recanalization rates. (Stroke. 2008;39:1496-1500.)

Key Words: basilar artery occlusion ■ mechanical thrombectomy ■ thrombolysis

Prognosis in untreated acute basilar artery occlusion (BAO) is very poor, with a mortality rate of up to 90%.1-3 If patients are treated by intra-arterial thrombolysis, mortality decreases to ≈50%.1,2,4,5 More than half of the surviving patients regain functional independency in daily life.5

Early recanalization is the most important prognostic factor for good outcome.4,6-8 However, many patients are initially admitted to community hospitals in which endovascular treatment is usually not available and secondary referral becomes necessary. Compared to patients directly admitted to specialized stroke centers, these patients have a worse outcome.9

Many consider intra-arterial thrombolysis to be the standard therapy in acute BAO.10 However, intravenous thrombolysis (IVT) may be a reasonable alternative, with recanalization rates of ≈50%.5,11 Other therapeutic strategies include the use of glycoprotein IIb/IIIa inhibitors12,13 and endovascular mechanical thrombectomy (EMT) by thrombus disruption, extraction, or aspiration.14-16 With the combination of these strategies, high recanalization rates may be achieved; however, reliable data are still lacking. Moreover, endovascular therapy is limited to specialized centers with interventional neuroradiologists and associated with a substantial time delay, especially if patients have to be transferred for treatment.9

The combination of IVT with EMT in the case of persisting vessel occlusion has been tested within the Multi MERCI (Mechanical Embolus Removal in Cerebral Ischemia) trial.17 In this prospective multicenter trial, 30 of 111 patients receiving EMT had been treated with IVT before but had not been recanalized on intravenous treatment alone. In 29 of these 30 patients, the anterior circulation was affected and only 1 patient had vertebrobasilar occlusion.17 To the best of our knowledge, the combination of IVT with EMT has never been systematically addressed in BAO.
With the aim of keeping treatment delay low and achieving maximal recanalization rates, we implemented a standardized in-house treatment protocol for all patients with documented acute BAO in 2006. This protocol provides a combination of IVT with on-demand consecutive EMT. Preliminary results after 19 months of experience are presented in this report.

**Patients and Methods**

As an academic interdisciplinary stroke center, our institution provides acute stroke treatment including EMT on a 24-hour basis. More than 20 cooperating community hospitals in the region refer patients for acute stroke treatment. These referrals are usually arranged by telephone. Some of the hospitals are connected to our center via a telemedical network that enables us to examine patients and evaluate neuroradiological images by a video conference.

Starting in January 2006, all eligible patients with acute BAO admitted to our center or one of the cooperating community hospitals were treated according to the inclusion criteria and the protocol illustrated in the Figure.

In patients primarily admitted to one of the community hospitals, IVT (0.9 mg/kg recombinant tissue plasminogen activator (rt-PA) over 1 hour, 10% as a bolus, maximum 90 mg) was started on-site followed by immediate transfer to our institution.

After IVT a further CT and CT angiography were performed to exclude hemorrhage and determine the status of the basilar artery. If occlusion persisted, EMT was performed immediately. Endovascular devices used include the Amplatz Goose Neck Snare (Microvena) and the AngioJet (Possis Medical Inc). The time to EMT was defined as the interval from symptom onset to placement of the thrombectomy device. In patients receiving EMT, recanalization was defined as basilar artery flow of TIMI II (perfusion with incomplete or slow distal branch filling) or TIMI III (full perfusion with filling of all distal branches).18 Adjunct therapy to prevent reocclusion included aspirin, intravenous heparin, and the glycoprotein IIb/IIIa inhibitor tirofiban. The choice of treatment was based on the individual assessment of the involved neurologists and neuroradiologists.

To demonstrate the extent of acute vertebo-basilar infarction, all patients received a follow-up CT or MRI including diffusion-weighted imaging 1 to 7 days after treatment.

To determine the long-term functional outcome, all patients who had survived the acute hospital phase were contacted by telephone 3 months (±2 weeks) after treatment. Functional outcome was documented using a structured interview and the modified Rankin Scale (mRS), an ordinal scale rating daily life functioning from 0 (no symptoms at all) to 6 (death). The telephone interview for determining Rankin scores had been previously validated and shown to give reliable results.19

All procedures were in accordance with our institutional guidelines. Data are presented as mean±SD.

**Results**

From January 2006 to July 2007, a total of 27 patients with radiologically confirmed BAO were treated in our center. Sixteen patients fulfilled the inclusion criteria of our protocol and were treated accordingly (Figure). In the remaining patients, the time window of 6 hours had passed (n=6) or contraindications for IVT were present (n=5).

The majority of included patients (13/16) had been primarily admitted to one of our cooperating community hospitals. After telephone contact or a telemedical video conference that confirmed eligibility, patients were immediately treated with IVT and transferred to our institution. The 3 remaining patients were directly admitted to our institution. All patients received IVT within 6 hours of symptom onset. Before treatment BAO was confirmed in all 16 patients by CT angiography (n=15) or MRA (n=1).

Clinical signs (all three required) suggesting acute basilar artery occlusion (BAO):
- reduced consciousness (GCS ≤ 14)
- oculomotor dysfunction and/or bulbar signs
- hemi- or tetraparesis and/or ataxia

Exclusion of cerebral hemorrhage on CT

Evidence of BAO on CTA

Treatment within six hours after symptom onset

IVT (0.9 mg/kg rt-PA)

Transfer to our Stroke Center (if patient was initially admitted to Community Hospital)

CT and CTA

Persisting BAO

Patient Basilar Artery

EMT

Intensive Care Unit

Figure. Inclusion criteria and treatment protocol of combined IVT with on-demand consecutive EMT.

Detailed patient characteristics and findings are presented in the Table. The mean age was 60.9 years (range, 26 to 82 years); 5 patients were female. The average dose of intravenous rt-PA was 67.1±19.8 mg. In 1 patient (patient 8) intravenous thrombolysis was stopped after 8 mg rt-PA because of a history of rectal bleeding and suspected colorectal malignancy. The average minimal score on the Glasgow Coma Scale was 7.6±3.6 (range, 3 to 14).

Time to systemic thrombolysis was 2.5±0.7 hours. After IVT, recanalization was documented in 9 patients. In the 7 patients who had not been recanalized after IVT, time to EMT was 4.6±1.2 hours. Two of the 7 patients receiving EMT were additionally treated with 20 mg intra-arterial rt-PA. EMT (± intra-arterial rt-PA) led to recanalization in 6 of the 7 patients.

In 1 patient (patient 6) with extensive cerebellar infarction, delayed secondary cerebellar hemorrhage was detected 12
hours after IVT (a CT scan 2 hours after IVT had been negative for hemorrhage). All but 1 patient had evidence of acute vertebro-basilar infarction on control CT (performed in 13 patients) or diffusion-weighted MRI (performed in 10 patients) performed 1 to 7 days after treatment. Three months after therapy, 12 of 16 patients (75%) were still alive: 7 (44%) with no or mild deficit (mRS=2), 2 (13%) with a moderate deficit (mRS=3), and 3 (19%) with a severe deficit (mRS=4 or 5).

If recanalization was achieved (15/16 patients), outcome was similar in patients who depended on EMT (n=6) compared to those with prompt recanalization after IVT (n=9): good outcome (mRS≤2) 50% versus 44%; poor outcome (mRS≥5) 33% versus 33%.

In the 11 patients who had been excluded from the treatment protocol because of delayed presentation or contraindications for IVT, outcome was rather poor. Despite endovascular therapy in most patients (8/11), more than half (6/11) died; only 1 patient reached functional independency (mRS=2). None of these patients received IVT. Mean time to endovascular treatment was 13.5±12.8 hours (range, 3 to 36 hours).
Discussion
Early recanalization is the key in the treatment of acute BAO. Endovascular approaches, such as intra-arterial thrombolysis and EMT, may provide high recanalization rates. However, their benefit is reduced by the limited availability and the substantial time delay to treatment.

IVT has become the standard treatment of acute anterior circulation stroke and is increasingly applied in community hospitals treating stroke patients. Our data suggest that the majority of patients with acute BAO are primarily admitted to these community hospitals. With IVT available on-site, it seems very reasonable to start treatment of BAO in these hospitals instead of accepting hours of treatment delay caused by transfer to a specialized stroke center.

Acute stroke treatment with rt-PA has been approved for a time window of 3 hours. However, there is growing evidence that IVT is effective up to 6 hours after symptom onset in selected stroke patients. In acute BAO, prognosis in untreated patients is extremely poor. Therefore, a more aggressive approach to recanalization therapy is justified, which may be effective and safe in selected patients up to 48 hours after symptom onset. In the majority of our patients IVT was started in community hospitals after telephone contact with our center. With the focus on safety for these patients, we defined a relatively strict time window of 6 hours in our protocol.

In our small series, a standardized combination therapy of IVT with on-demand consecutive EMT led to basilar artery recanalization in almost all and a good functional outcome in almost half of our patients. The good outcome in many of our patients is remarkable, because the majority of them were primarily admitted to a community hospital. This had been shown to be a negative prognostic factor compared to direct admission to stroke centers.

Although promising, our outcome data have to be interpreted with caution. One reason is the small number of patients. Moreover, only patients available for early treatment (within 6 hours after symptom onset) were included in our series. Other published series and meta-analyses included patients within a time window of up to 48 hours. Therefore, the short time window of 6 hours may have substantially contributed to the relatively good outcome in our series. The poor outcome in the 11 patients treated in our center but excluded from the protocol because of delayed presentation or contraindications to IVT support this assumption.

Seven patients depended on EMT. In the remaining 9 patients (56%) the basilar artery was patent after IVT. The recanalization rate of ~50% is comparable to the findings by Lindsberg et al and underscores the value of IVT in BAO. In the 7 patients with persisting BAO after IVT, EMT led to recanalization in 6, which likewise emphasizes the value of on-demand EMT in BAO.

Outcome was similar in patients who depended on EMT compared to those who did not. However, the small number of patients allows no conclusions on superiority or noninferiority of IVT or EMT. Prospective randomized multicenter trials comparing IVT, endovascular therapy, and the combination of both (as presented here) are urgently needed to define the optimal treatment for patients with acute BAO.

Complication rates were low. Only one patient with extensive brain stem and cerebellar infarction had secondary intracerebral hemorrhage after IVT. This suggests that the combination of IVT within 6 hours and consecutive on-demand EMT is reasonably safe.

Conclusion
In conclusion, our preliminary data suggest that the combination of IVT with on-demand consecutive EMT in BAO is feasible, allows for early treatment, and provides excellent recanalization rates. This concept may be particularly valuable in a cooperative setting of specialized stroke centers with interventional neuroradiologists and community hospitals with the feasibility to perform IVT. The combination of IVT and on-demand EMT may be promising enough to qualify for a treatment arm in an urgently awaited prospective randomized multicenter trial.

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Disclosures
None.

References


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