Three-Month and Long-Term Outcomes and Their Predictors in Acute Basilar Artery Occlusion Treated With Intra-Arterial Thrombolysis

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Background and Purpose—Intra-arterial thrombolysis can be used for treatment of basilar artery occlusion. Predictors of outcome before initiation of treatment are of special interest.

Methods—From 1992 to 2010, we treated 106 consecutive patients with basilar artery occlusion with intra-arterial thrombolysis. Baseline characteristics, treatment, clinical course, and 3-month and long-term outcomes (≥12 months) were assessed. Outcome parameters were vessel recanalization after treatment, complications, modified Rankin scale (mRS) score, and mortality after 3 months and in the long-term.

Results—At 3 months, clinical outcome was good (mRS score, 0–2) in 33.0% of the patients and moderate (mRS score, 3) in 11.3%. Mortality was 40.6%. Partial or complete recanalization was achieved in 69.8% of the patients, and symptomatic intracranial hemorrhage occurred in 1 patient (0.9%). Between 3-month and long-term follow-up, 22 survivors (40.8%) showed clinical improvement of at least 1 point on the mRS score, 29 (53.7%) were functionally unchanged, and 3 (5.7%) showed functional worsening (P<0.0001). Multivariate analysis identified diabetes as a predictor of poor vessel recanalization (P=0.028). Low baseline National Institutes of Health Stroke Scale score was identified as a predictor of good or moderate clinical outcome (P<0.0001) and survival (P=0.001) at 3 months, and younger age was identified as an additional predictor of survival (P=0.012). For prediction of long-term clinical outcome, age was also an independent predictor (P=0.018).

Conclusions—In our series, intra-arterial thrombolysis as treatment of basilar artery occlusion was safe. National Institutes of Health Stroke Scale score at admission and age were identified as predictors of outcome, and these predictors should be considered for treatment allocation in future randomized trials. (Stroke. 2011;42:00-00.)

Key Words: basilar artery occlusion • intra-arterial thrombolysis • outcome

Approximately 1 of 5 ischemic strokes occurs in the posterior circulation. Generally, posterior circulation strokes have a better outcome than strokes in the anterior circulation. However, among posterior circulation strokes, the outcome of basilar artery occlusion (BAO) is bleak. Fatality rates of BAO in the natural course are up to 90% and survivors usually remain handicapped.1,2 Several case series have shown that intra-arterial thrombolysis (IAT) improves the outcome, although there is a wide range of outcome and mortality. More recent studies have shown similar outcomes after intravenous thrombolysis (IVT) and similar or even better outcomes after bridging IVT and IAT. Given the lack of large randomized trials and the wide range of outcomes reported after BAO treatment, it is of clinical interest to identify predictors of treatment effects and clinical outcome. For this reason, we analyzed clinical findings, outcomes, and prognostic variables of our patients with acute BAO treated with IAT.

Patients and Methods

This study is based on the Bernese Stroke registry. Since 1992, we collected prospectively data of patients with acute ischemic stroke treated with IAT. We reported some aspects of these patients previously.3–6 All patients were examined immediately after admission by a neurologist and the neurological deficit was scored using the NIHSS score. Demographic data, time of symptom onset, and medical
history (history of coronary artery disease, atrial fibrillation, TIA, or ischemic stroke) were recorded. The following stroke risk factors were assessed: sex, hypertension, diabetes, current cigarette smoking, hypercholesterolemia, coronary heart disease, and a family history of TIA and stroke. All patients underwent a standard investigation protocol in the emergency department, including blood tests, electrocardiography, and cranial CT and/or MRI. The status of extracranial and intracranial vessels was assessed with CTA, MRA, or digital subtraction angiography. On CT scan, a hyperdense basilar artery was defined as a hyperdense vessel on noncontrast CT compared visually with the density of other unaffected vessels. IAT was performed with the consent of the patient or family members as soon as possible after CT or MRI if: (1) diagnosis of BAO was established; (2) baseline NIHSS score was ≥4 points or hemianopia was present; (3) hemorrhage on cranial CT or MRI was excluded; (4) BAO was seen on digital subtraction angiography correlated with the neurological deficit; (5) symptom duration was not >24 hours; and (6) no individual or premorbid conditions or laboratory findings advised against thrombolysis.

All patients underwent 4-vessel diagnostic digital subtraction angiography to assess the cerebral blood vessel status before IAT. The site of basilar artery occlusion was categorized according to the criteria defined by Archer et al. Collaterals were classified according to the criteria of Brandt et al. Patients were treated with intra-arterial urokinase and/or mechanical interventions. Stenting of the vertebral artery was performed in patients with vertebral artery stenosis and contralateral hypoplasia to provide access to the occluded basilar artery. Stenting of the basilar artery was performed in patients with residual severe hemodynamic impairment on control angiogram immediately after IAT, whenever it was considered feasible by the neuroradiologist.

At the end of the digital subtraction angiography, recanalization was classified according to thrombolysis in myocardial infarction (TIMI) grades. Time from symptom onset to thrombolysis, placement of microcatheter, method of thrombolysis, and urokinase dose were recorded. After IAT, all patients received 250 to 500 mg of acetylic salicylic acid intravenously but no additional antithrombotic treatment was administered according to European guidelines. Secondary preventive therapy was administered according to the TOAST criteria using ancillary investigations as necessary. Clinical-short term outcome was assessed 3 month after the stroke using the modified Rankin scale (mRS). Follow-up was performed either clinically (n=81) or by a structured telephone interview. Recurrent vascular events after hospital discharge (TIA, recurrent stroke, or myocardial infarction) were recorded. For all patients treated before November 2009 (99 of the 106 patients), long-term outcome was assessed by a structured telephone interview. Long-term data of the first 8 patients were already on record and have been published previously. A change in outcome was defined as any improvement or decline of at least 1 point on the mRS score from 3-month to long-term follow-up.

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### Table 1. Baseline Characteristics of 106 Patients With Acute Basilar Occlusion, n (%)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Age, y (SD)</td>
<td>61.6 (15.1)</td>
</tr>
<tr>
<td>Women</td>
<td>41/106 (38.7)</td>
</tr>
<tr>
<td>Vascular risk factors</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>65/105 (61.9)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>15/105 (14.3)</td>
</tr>
<tr>
<td>Smoking</td>
<td>18/105 (17.1)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>47/104 (45.2)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>17/102 (16.7)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>15/104 (14.4)</td>
</tr>
<tr>
<td>Previous transient ischemic attack</td>
<td>20/104 (19.2)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>11/106 (10.4)</td>
</tr>
<tr>
<td>Stroke etiology</td>
<td></td>
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<tr>
<td>Large artery disease</td>
<td>28/106 (26.4)</td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>32/106 (30.2)</td>
</tr>
<tr>
<td>Other determined etiology</td>
<td>13/106 (8.5)</td>
</tr>
<tr>
<td>Unknown etiology</td>
<td>37/106 (34.9)</td>
</tr>
<tr>
<td>Baseline NIHSS score, median (range)</td>
<td>18.5 (3–36)</td>
</tr>
<tr>
<td>Occlusion type of basilar artery</td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>44/106 (41.5)</td>
</tr>
<tr>
<td>Mid-basilar</td>
<td>26/106 (24.5)</td>
</tr>
<tr>
<td>Distal</td>
<td>36/106 (34.0)</td>
</tr>
<tr>
<td>Minutes from symptom onset to treatment, median (range)</td>
<td>330 (80–1472)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>Urokinase only</td>
<td>58 (54.7)</td>
</tr>
<tr>
<td>Mechanical only</td>
<td>15 (14.2)</td>
</tr>
<tr>
<td>Combined urokinase and mechanical</td>
<td>33 (31.1)</td>
</tr>
<tr>
<td>Urokinase dose, median, IU (range)</td>
<td>1 000 000 (0–1 500 000)</td>
</tr>
</tbody>
</table>

NIHSS indicates National Institutes of Stroke Scale; SD, standard deviation; IU, international units.

### Results

From May 1, 1992 to May 31, 2010, we treated 106 patients with IAT for acute BAO. Baseline characteristics are given in Table 1; 50.5% of the patients were treated within 6 hours of symptom onset and 49.5% were treated after 6 hours of symptom onset. A hyperdense basilar artery was noted in 38 of 65 patients (58.5%) examined with CT. Forty-nine patients were examined with MR (26 including diffusion-weighted and perfusion-weighted imaging; 21 (80.8%) with diffusion-perfusion mismatch). Twenty-three patients (21.7%) had an additional occlusion of a vertebral artery, 17 had occlusion of a posterior cerebral artery, 1 had occlusion of an internal carotid artery, and 2 had a BAO at 2 noncontiguous segments.
In 11 patients, a stent was deployed in the basilar (n=3) or the vertebral artery (n=8). Outcome and complications are given in Table 2.

Complete recanalization (TIMI 3) was achieved in 55 of the 106 patients, partial recanalization (TIMI 2) was achieved in 19, minimal recanalization (TIMI 1) was achieved in 10, and no recanalization (TIMI 0) was achieved in 22.

Three-month follow-up was obtained for all 95 survivors and long-term follow-up was obtained for 94 of the 99 patients (94.9%) treated ≥1 year ago. At 3 months, a recurrent stroke or TIA had occurred in 3 patients (3.2%). Median time from stroke to long-term follow-up was 37.6 months, and its range was from 1 to 11.8 years. From 3-month to long-term follow-up, another 3 patients experienced a recurrent stroke (3.2%), 22 patients (40.8%) showed clinical improvement of at least 1 point on the mRS score, and 29 (53.7%) were functionally unchanged. Three patients (5.7%) worsened, and 1 of them died. The comparison of 3-month and long-term outcomes showed significant changes (P<0.0001). Functional outcome at 3-month and long-term outcome is illustrated in Figures 1 and 2. The results of the multivariate logistic regression analysis are listed in Table 3.

In univariate analysis, lower NIHSS score on admission, absence of hypercholesterolemia and atrial fibrillation, shorter time to treatment, and the site of basilar occlusion were predictors for good or moderate clinical outcome (mRS score, 0–3) at 3 months.

In multivariate analysis, only lower NIHSS score on admission remained an independent predictor for good or moderate clinical outcome (P<0.0001). For long-term clinical outcome, younger age was identified as a predictor for mRS score 0 to 3 (P=0.018) as well. Recanalization was not included in this analysis, although it was identified as an additional independent predictor (P=0.0029) for good or moderate clinical outcome. In univariate analysis, lower NIHSS score, younger age, absence of hypertension, and the degree of collaterals were predictors for survival. In multivariate analysis, lower NIHSS score on admission and younger age were independent predictors of survival at 3-month and long-term follow-up visits (P=0.001 and P=0.012/P=0.004 and P=0.004). Recanalization was not an additional independent predictor (P=0.318). In univariate analysis, absence of diabetes, shorter time from symptom onset to treatment, and absence of previous therapy with antiplatelet agents were identified as predictors of successful recanalization. In multivariate analysis, only the absence of diabetes (P=0.028) was an independent predictor. There was a trend toward more frequent recanalization in patients with distal BAO (P=0.042).

Outcome data of patients treated between 1992 and 2003 (n=49) were compared to those treated from 2004 to 2010 (n=57). Good or moderate clinical outcome was observed in

### Table 2. Outcomes and Complications After Intra-Arterial Thrombolysis

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Recanalization TIMI 2–3</td>
<td>74/106 (69.8)</td>
</tr>
<tr>
<td>mRS score 0–1 at 3 mo/long-term</td>
<td>27/106 (25.5)/27/94 (28.7)</td>
</tr>
<tr>
<td>mRS score 0–2 at 3 mo/long-term</td>
<td>35/106 (33.0)/32/94 (34.0)</td>
</tr>
<tr>
<td>mRS score 0–3 at 3 mo/long-term</td>
<td>47/106 (44.3)/40/94 (42.6)</td>
</tr>
<tr>
<td>mRS score 4–5 at 3 mo/long-term</td>
<td>16/106 (15.1)/13/94 (13.8)</td>
</tr>
<tr>
<td>Mortality at 3 mo/long-term</td>
<td>43/106 (40.6)/41/94 (43.6)</td>
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#### Acute complications

- Symptomatic ICH: 1/106 (0.9)
- Asymptomatic ICH: 10/106 (9.4)
- Major systemic hemorrhage: 0/106 (0.0)
- Craniotomy and/or ventricular drainage: 3/105 (3.0)
- Recurrent stroke at 3 mo: 3/95 (3.2)
- Seizures: 6/105 (5.7)
- Pneumonia: 18/105 (17.1)

#### Cause of death at 3 mo

- Acute stroke: 25/43 (58.1)
- Edema: 7/43 (16.3)
- ICH: 1/43 (2.3)
- Pneumonia: 5/43 (11.6)
- Recurrent stroke: 1/43 (2.3)
- Unknown: 3/43 (7.0)

ICH indicates intracerebral hemorrhage; mRS, modified Rankin Scale; TIMI, thrombolysis in myocardial infarction.
17 patients (34.7%) of the first period and in 30 patients (52.6%) of the second period (Figure 2; \(P = 0.079\)). The survival rates did not change over time (28/49(57.1%) versus 35/57(61.4%); \(P = 0.695\)).

**Discussion**

We report the outcome of 106 patients with BAO treated with IAT in a single stroke center. At 3 months, 27 patients (25.7%) had an excellent clinical outcome (mRS score, 0–1), 35 patients (33%) had a good outcome (mRS score, 0–2), 47 patients (44.3%) had a good or moderate outcome (mRS score, 0–3), and 43 patients (40.6%) were dead. At a median long-term follow-up of 3.1 years, 27 of 94 patients (28.7%) had an excellent clinical outcome, 32 patients (34.0%) had a good outcome, 40 patients (42.6%) had a good or moderate clinical outcome, and 1 additional patient had died. From 3-month to long-term follow-up, 22 patients (40.8%) showed clinical improvement, 29 patients (53.7%) were unchanged, and 3 patients (5.7%) worsened. These data demonstrate a recovery potential beyond 3 months for many patients with BAO, especially for those with lesser handicaps at 3 months. As a result, follow-up should be extended beyond 3 months in future trials.

The present series of BAO patients was prospectively collected from 1992 to 2010. Initially, only intra-arterial urokinase was used. Gradually, techniques of mechanical recanalization evolved and the experience of the interventional neuroradiologists and potentially also the postinterventional care und patient selection improved. When the outcomes of patients treated from 1992 to 2003 were compared with those treated from 2004 to 2010, there was a trend for better outcomes in recent years (\(P = 0.079\)).

Because outcome in BAO treated with thrombolysis is highly variable, knowing predictors of outcome would help treating physicians to decide on the mode of treatment in an individual patient. In the present series, lower NIHSS score on admission and younger age were independent predictors for good or moderate clinical outcome (mRS score, 0–3). This finding is consistent with observations both in the carotid and basilar artery territories.\(^{16-19}\) In most series, successful recanalization also predicts good outcome. However, we did not include recanalization in our analysis on purpose, because recanalization will be known only after the decision for or against thrombolysis and after treatment in an individual patient. Diabetes was an independent predictor for recanalization, which is in accordance with the finding in a study of anterior circulation strokes.\(^{20}\) It may be explained by more severe atherosclerotic changes and disturbed endothelial function in diabetes. In addition, elevated levels of plasminogen activator inhibitor, which is not reversed by the standard thrombolytic therapies, may play a role in diabetic patients. A direct influence of diabetes on outcome could not be shown in our series.

Symptomatic intracerebral hemorrhage occurred in 1 patient (0.9%) only. In other series, symptomatic intracerebral hemorrhage rates after IAT of BAO range from 0% to 25% and in IVT range from 0% to 14%.\(^{21-23}\) Remarkably, the rate
of symptomatic intracerebral hemorrhage is lower in BAO compared to hemispheric stroke. Additionally, symptomatic intracerebral hemorrhage rates were higher in BAO treated with tissue plasminogen activator compared to those treated with urokinase, which might be explained by higher tissue plasminogen activator doses. Furthermore, heparin was not administered in our patients, reducing hemorrhage risk of thrombolysis. However, the reported hemorrhage rates are not comparable because of major differences of study designs and hemorrhage definitions. The European Stroke Organization guidelines recommend IAT for treatment of BAO in selected patients and IVT as an acceptable alternative.

The reports of Lindsberg et al. and the BASICS trial indicated that efficacy of IVT and IAT for treatment of BAO may be similar, and recent studies also reported good outcomes after combined intravenous/intra-arterial treatment. Figure 3 shows the functional outcome of BAO as reported in selected major series after IAT, IVT, or bridging of IVT and IAT. To date, no thrombolytic treatment modality or recanalization technique has shown any unequivocal superiority in BAO. Our series suggests that a multimodal pharmacological and mechanical approach that has been developed in recent years may be superior to IAT with urokinase alone as used in the early years of our series.

Our study has the inherent limitations of selection bias of a nonrandomized single-center study. Moreover, patient selection for treatment was made individually with bias to more severe cases. Finally, clinical follow-up was not performed by a blinded investigator.

Conclusions

In conclusion, our series shows that IAT is safe and seems to be efficacious for treatment of BAO. NIHSS score at admission and age were identified as independent predictors of outcome and should be considered for treatment allocation in future randomized trials. There is a recovery potential beyond 3 months for many patients. Thus, follow-up should be extended beyond 3 months in future trials. The question whether IAT, IVT, or bridging of IVT and IAT is the best treatment option needs to be addressed in randomized controlled trials.

Acknowledgments

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Disclosure

None.

References


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