Therapy of Acute Basilar Artery Occlusion
Intraarterial Thrombolysis Alone vs Bridging Therapy

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Background and Purpose—While intravenous recombinant tissue plasminogen activator (rt-PA) has been approved for acute stroke therapy within 3 hours, the optimum management of basilar artery occlusion (BAO) is still a matter of debate. We compared intraarterial thrombolysis with the combined bridging approach of intravenous abciximab and intraarterial thrombolysis with rt-PA (bridging therapy) in an observational, longitudinal, monocenter study.

Methods—Between 1998 and 2006, information for 106 patients with acute BAO were prospectively entered into a local database. Patients eligible for treatment received either intraarterial thrombolysis with rt-PA alone (intraarterial thrombolysis) or were treated with intravenous abciximab and intraarterial rt-PA (bridging therapy). Outcome parameters were recanalization of the basilar artery according to Trial in Myocardial Infarction criteria, survival, and reduction of severe disability and death at 3 months. Logistic regression was used to identify independent predictors for recanalization, survival, and clinical outcome.

Results—Of a total of 106 patients with confirmed BAO, 87 patients underwent subsequent angiography. Among those, 75 patients were identified who received the full treatment protocol. Patients in the bridging group had a better recanalization rate (83.7% vs 62.5%; P=0.03), a higher survival rate (58.1% vs 25%; P=0.01), and a better chance for an outcome with no or only mild to moderate disability (modified Rankin Scale score, 0–3; 34.9% vs 12.5%; P=0.02). Symptomatic intracerebral hemorrhage rates were comparable in both groups (14% in the bridging group vs 18.8%; P=0.41). Independent predictors for recanalization were age (OR, 0.95; 95% CI, 0.91–0.99), atrial fibrillation (OR, 6.53; 95% CI, 1.14–37.49), and bridging therapy (OR, 3.37; 95% CI, 1.02 to 11.18). Independent prognostic factors for outcome were Glasgow coma scale score at presentation (OR, 1.24; 95% CI, 1.03–1.45) and the combination of bridging therapy with successful recanalization (OR, 3.744; 95% CI, 1.04–13.43).

Conclusion—Bridging therapy for acute BAO with intravenous abciximab and intraarterial rt-PA appears to be safe and yields higher recanalization and improved survival rates, as well as an overall improved chance for a better outcome.

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Key Words: acute stroke • abciximab • antiplatelet agents • emergency medicine • interventional neuroradiology • neurocritical care • stents • thrombolysis • vertrobrobasilary disease

With an aging population, stroke has become one of the major causes for death and permanent disability in industrialized countries. Twenty percent of all ischemic strokes occur in the posterior circulation, with basilar artery occlusion (BAO) being the most fatal subtype. Patients with pontine, medullary, or severe cerebellar infarction frequently deteriorate and experience coma, herniation, and locked-in syndrome. Because of direct damage to the cranial nerves and autonomic centers, patients have a high early mortality rate. In patients with proven BAO, thrombolysis administered either as intravenous (IV) thrombolysis or as intraarterial thrombolysis (IAT) combined with mechanical recanalization is the treatment of choice. Because of the lack of randomized studies, the optimal treatment approach is still unclear. Regardless of the treatment, recanalization appears to be the single most important predictor for improved outcome. Probably attributable to the poor natural course, physicians favor the more aggressive approach of endovascular techniques. One of the major disadvantages of the intraarterial (IA) approach is the time loss to initiate the treatment. An attempt to overcome this disadvantage has been to combine the IV route with the IA access using the so-called bridging concept. We report the recanalization rates and the clinical outcomes of patients with BAO treated either with IA recombinant tissue plasminogen activator (rt-PA) alone or by using a bridging protocol with IV abciximab administration, subsequent angiography, and local IA fibrinolyis.

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Patients and Methods

Patient Selection
A total of 106 patients with the clinical syndrome of BAO (symptoms <24 hours) and subsequent confirmation by CT or MR angiography presented to our institution (Department of Neurology, University of Heidelberg) between January 1998 and December 2006. Data were prospectively entered into a local database, including age, sex, time of symptom onset, time to treatment, treatment specifications, baseline Glasgow coma scale (GCS) score, concomitant medication, other relevant disease, imaging data, and modified Rankin Scale (mRS) score at 90 days. All analyses were performed retrospectively using this prospectively collected dataset. All patients received an initial CT scan with CT angiography (n = 96) or MR angiography (n = 37). Subsequently, the decision for acute therapy was made by the treating physicians based on medical history, clinical presentation, and imaging information. In 18 patients no angiography was performed and no further therapeutic action was undertaken, mainly because prognosis was believed to be futile because of the following criteria: coma >3 hours, tetraplegia >6 hours, bilateral mydriasis and extinct brain stem reflexes >1 hour, and extensive infarctions seen on baseline imaging.4 One patient received IV rt-PA without subsequent angiography. All remaining patients (n = 87) underwent conventional digital subtraction angiography. Seven patients received only intravenous rt-PA after digital subtraction angiography demonstrated that IA treatment was technically not feasible (n = 7). Furthermore, in 5 patients IV bridging with abciximab was started but discontinued and IA therapy or endovascular therapy was not performed after diagnostic angiography (1 patient had recanalization after bridging, 4 patients showed extensive thrombosis, and intervention was not feasible). Thus, 75 patients remained for analysis in this study (Figure 1).

Between 1998 and 2002, patients eligible for treatment received IAT with rt-PA alone. After the publication of a pilot study by Eckert et al in 2002,3 a bridging protocol adding abciximab (initial bolus of 0.25 mg/kg body weight (BW) followed by infusion of 0.125 µg/kg BW/min over 12 hours) to the therapy was introduced to our protocol. Hence, in our study, patients received either IA rt-PA only (up to a maximum of the standard IV dose of 0.9 mg/kg; 1998–2002) or IA rt-PA in combination with IV bridging therapy with abciximab, administered immediately after diagnosis of BAO with CT angiography or MR angiography (2002–2006), resulting in a gain of time of ~45 to 60 minutes before IA treatment. Intraarterial rt-PA was stopped in both groups once recanalization was achieved. In both groups mechanical disruption of the thrombus was performed and patients with atherothrombotic occlusions who revealed major (>70%) residual stenosis after local fibrinolysis were treated with additional percutaneous transluminal angioplasty/stenting (n = 11). Only patients in the IAT group received a single bolus of 5000 IU heparin at the beginning of the intraarterial intervention. For catheter-flushing, heparin (500 IU/hour; maximum, 2000 IU) was used with in both groups. Recanalization was classified according to criteria of the Trial in Myocardial Infarction (TIMI) as follows: TIMI 0, complete occlusion of the BA; TIMI 1, partial recanalization but remnant occlusion; TIMI 2, incomplete recanalization with continuous BA patency but remnant thrombus; TIMI 3, complete recanalization. TIMI 0 and TIMI 1 were classified as recanalization failure; TIMI 2 and TIMI 3 were defined as recanalization.6

All patients had at least 1 follow-up scan (CT or MRI) within 24 hours after thrombolysis to show extent of infarction and hemorrhagic complications. Symptomatic intracerebral hemorrhage (sICH) was defined as a documented hemorrhage, temporally related to any neurological deterioration of the patient’s condition. When patients were analgesedated at the time of imaging, any substantial hemorrhage was assessed and counted if agreement by 2 independent raters was established. All patients were treated on our neurological intensive care unit according to a standard clinical pathway consistent with the recommendations of the European Stroke Initiative.7 If possible, informed consent was obtained from patients or their next of kin before treatment. The mRS was used to assess outcome at day 90 with a semistructured interview performed either by telephone or in person. According to previous comparable studies and taking the grim natural course of the disease into account, outcome was primarily dichotomized using the mRS into no or mild to moderate disability (mRS 0 to 3) and severe disability and death (mRS 4 to 6).8–10 In addition, we performed a secondary analysis using a dichotomization of mRS 0 to 2 vs 3 to 6.

Data Analysis
All statistical analyses were performed using the SPSS software package (SPSS 13.0; SPSS Inc). Baseline clinical data, recanalization rates, survival, outcome (mRS), and intracranial bleeding related to type of treatment were analyzed by Fisher exact test, Mann–Whitney test, or linear-by-linear association. Significance was accepted at the P <0.05 level. To identify independent predictive factors for recanalization, survival, and functional outcome, we performed a multivariate analysis using a binary stepwise logistic regression model. All variables showing at least a trend (P <0.1) in univariate analysis were entered into the model. In addition, age, as a known predictor, was forced in the models for survival and outcome. For all variables, probability values as well as the odds ratios and 95% CIs were determined.

Results
Baseline Characteristics
The median age of all patients was 67.5 years; 35.8% of patients were women. A summary of baseline characteristics as well as of outcome parameters of all patients are presented in Table 1. Thirty-two patients received IA therapy with rt-PA only (IAT), and 43 patients received IV bridging therapy with abciximab followed by local fibrinolysis with
rt-PA (bridging). Ten patients of the bridging group were treated with additional percutaneous transluminal angioplasty/stenting as opposed to 1 patient in the IAT group ($P = 0.02$). Doses of rt-PA were significantly different for both groups, being lower in the bridging group (40 mg vs 47.5 mg, median; $P = 0.01$). Baseline parameters, including age, sex, risk factors, GCS score at presentation, occlusion type, and time to IA treatment, did not differ significantly between the 2 groups (Table 1). However, there was a statistically nonsignificant trend toward a lower GCS score at presentation (GCS score 3 vs GCS score 5, median; $P = 0.07$) and a higher prevalence of previous cardiovascular events (56.3% vs 37.2%; $P = 0.08$) in the IAT group.

### Recanalization

The overall recanalization rate (TIMI 2 and TIMI 3) was 74.7%. Table 2 shows recanalization, outcome, and hemorrhagic complications. In the IAT group, 20 patients (62.5%) showed a successful recanalization of the BA compared to 36 patients (83.7%) in the bridging group ($P = 0.03$). Patients with percutaneous transluminal angioplasty and stenting of the vertebrobasilar system had a permanent recanalization rate of 81.8% (9 of 11 patients with TIMI 2 and TIMI 3). Results of the univariate analysis for successful recanalization are depicted in Table 3. Age, atrial fibrillation, distal occlusion of the BA (presumed cardiac embolism), and bridging therapy were significantly associated with recanalization. However, the factors that remained independent predictors for a successful recanalization in the multivariate logistic regression model were presence of atrial fibrillation (OR, 6.53; 95% CI, 1.14–37.49), bridging treatment (OR, 3.37; 95% CI, 1.02–11.18), and younger age (OR, 0.95; 95% CI, 0.91–0.99; Table 4).

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients, $n=75$</th>
<th>IAT, $n=32$</th>
<th>Bridging, $n=43$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (minimum-maximum)*</td>
<td>65 (19–86)</td>
<td>65 (19–86)</td>
<td>65 (28–83)</td>
<td>0.88</td>
</tr>
<tr>
<td>Female†</td>
<td>29 (38.7%)</td>
<td>12 (37.5%)</td>
<td>17 (39.5%)</td>
<td>0.52</td>
</tr>
<tr>
<td>Risk factors†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous cardiovascular event</td>
<td>34 (45.3%)</td>
<td>18 (56.3%)</td>
<td>16 (37.2%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36 (61.3%)</td>
<td>17 (53.1%)</td>
<td>29 (67.4%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (20%)</td>
<td>6 (18.5%)</td>
<td>9 (20.9%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>25 (33.3%)</td>
<td>10 (31.3%)</td>
<td>15 (34.9%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Hypercholesterinemia</td>
<td>12 (16%)</td>
<td>5 (15.6%)</td>
<td>7 (16.3%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Nicotine</td>
<td>9 (12%)</td>
<td>5 (15.6%)</td>
<td>4 (9.3%)</td>
<td>0.32</td>
</tr>
<tr>
<td>VA dissection</td>
<td>2 (4.7%)</td>
<td>0</td>
<td>2 (4.7%)</td>
<td>0.33</td>
</tr>
<tr>
<td>GCS at presentation, median (minimum-maximum)*</td>
<td>5 (3–15)</td>
<td>3 (3–15)</td>
<td>5 (3–13)</td>
<td>0.07</td>
</tr>
<tr>
<td>Time to IA treatment, median (minimum-maximum)*</td>
<td>5 (2–24)</td>
<td>6 (2–24)</td>
<td>5 (2–12)</td>
<td>0.24</td>
</tr>
<tr>
<td>Occlusion type of basilar artery‡</td>
<td></td>
<td></td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td>Distal</td>
<td>25 (33.3%)</td>
<td>10 (31.1%)</td>
<td>15 (34.9%)</td>
<td></td>
</tr>
<tr>
<td>Midbasilar</td>
<td>7 (9.3%)</td>
<td>4 (12.5%)</td>
<td>3 (7%)</td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>20 (26.7%)</td>
<td>10 (31.1%)</td>
<td>10 (23.3%)</td>
<td></td>
</tr>
<tr>
<td>Panocclusion†</td>
<td>23 (30.7%)</td>
<td>8 (25%)</td>
<td>15 (34.9%)</td>
<td></td>
</tr>
<tr>
<td>rt-PA Dose in mg, median (minimum-maximum)*</td>
<td>40 (5–100)</td>
<td>47.5 (10–100)</td>
<td>40 (5–60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stent§</td>
<td>11 (14.7%)</td>
<td>1 (3.1%)</td>
<td>10 (23.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Tracheotomy†</td>
<td>11 (14.7%)</td>
<td>5 (15.6%)</td>
<td>6 (13.9%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Ventilation days, median (minimum-maximum)*</td>
<td>3 (0–60)</td>
<td>2 (0–60)</td>
<td>3 (0–28)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

*Mann–Whitney test.
†Fisher exact test.
‡Linear-by-linear association.

### Table 2. Recanalization, Outcome, and Hemorrhagic Complications

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Patients, $n=75$</th>
<th>IAT, $n=32$</th>
<th>Bridging, $n=43$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recanalization*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIMI 2 and 3</td>
<td>56 (74.7%)</td>
<td>20 (62.5%)</td>
<td>36 (83.7%)</td>
<td>0.03</td>
</tr>
<tr>
<td>TIMI 1 and 0</td>
<td>19 (25.3%)</td>
<td>12 (37.5%)</td>
<td>7 (16.3%)</td>
<td></td>
</tr>
<tr>
<td>Outcome after 3 months*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS 0–3</td>
<td>19 (25.3%)</td>
<td>4 (12.5%)</td>
<td>15 (34.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td>mRS 0–2</td>
<td>10 (13.3%)</td>
<td>2 (6.3%)</td>
<td>8 (18.6%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Survival</td>
<td>33 (44%)</td>
<td>8 (25%)</td>
<td>25 (58.1%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic ICH*</td>
<td>12 (16%)</td>
<td>6 (18.8%)</td>
<td>6 (14%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Major systemic hemorrhage*</td>
<td>2 (2.7%)</td>
<td>1 (3.1%)</td>
<td>1 (2.3%)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*Fisher exact test.
Hemorrhagic Complications
The overall sICH rate was 16%, with another 2 patients experiencing major systemic bleeding (1 patient in each group). sICH occurred in 6 patients (18.8%) treated with intraarterial rt-PA only, and in 6 patients (14%) treated according to the bridging protocol. This was not a significant difference (Table 2). Doses of rt-PA in patients with sICH were also not significantly different (52.5 mg vs 40 mg, median; \( P = 0.25 \)). All patients with hemorrhagic complications died within the 3-month follow-up timeframe.

Survival and Functional Outcome
Overall, survival was 44% and an outcome with no or mild to moderate disability (mRS 0 to 3) was achieved in 25.3% of treated patients. The chance for an outcome with a mRS of 0 to 3 was significantly improved in patients treated according to the bridging protocol (Figure 2 and Table 2).

Survival increased from 25% (8 patients) in the IAT group to 58.1% (25 patients) in the bridging group (\( P < 0.01 \)). Results of the univariate analysis for survival are presented in Table 3. The presence of sICH and female gender (6 of 29 women vs 25 of 46 men survived) were negatively associated with survival. A higher GCS score at presentation, bridging therapy, recanalization, tracheotomy, and a longer period of ventilation were positively associated with survival. In the multivariate logistic regression model, a combination of bridging treatment with recanalization (OR, 6.9; 95% CI, 1.9–24.8) and bridging treatment alone (OR, 4.2; 95% CI, 1.08–16.52) independently predicted survival. Female gender remained a negative predictor (OR, 0.59; 95% CI, 0.45–0.78; Table 5).

Only 4 patients (12.5%) had an outcome of mRS 0 to 3 in the IAT group as opposed to 15 patients (34.9%) in the bridging group (\( P < 0.02 \)). The dichotomization of outcomes

Table 3. Univariate Analysis for Recanalization, Survival, and Functional Outcome

<table>
<thead>
<tr>
<th></th>
<th>Recanalization, ( P )</th>
<th>Survival, ( P )</th>
<th>Outcome (mRS 0–3), ( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>0.10</td>
<td>0.56</td>
<td>0.69</td>
</tr>
<tr>
<td>Sex†</td>
<td>0.24</td>
<td>0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Risk factors†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous cardiovascular event</td>
<td>0.16</td>
<td>0.42</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.54</td>
<td>0.36</td>
<td>0.26</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.20</td>
<td>0.11</td>
<td>0.44</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.01</td>
<td>0.23</td>
<td>0.46</td>
</tr>
<tr>
<td>Hypercholesterinemia</td>
<td>0.36</td>
<td>0.56</td>
<td>0.36</td>
</tr>
<tr>
<td>Nicotine</td>
<td>0.41</td>
<td>0.14</td>
<td>0.16</td>
</tr>
<tr>
<td>GCS at presentation*</td>
<td>0.51</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Distal BAO†</td>
<td>0.05</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>Proximal BAO†</td>
<td>0.19</td>
<td>0.11</td>
<td>0.17</td>
</tr>
<tr>
<td>Panocclusion and midbasilar†</td>
<td>0.18</td>
<td>0.25</td>
<td>0.23</td>
</tr>
<tr>
<td>Time to IA treatment*</td>
<td>0.71</td>
<td>0.83</td>
<td>0.46</td>
</tr>
<tr>
<td>rt-PA dose*</td>
<td>0.14</td>
<td>0.15</td>
<td>0.55</td>
</tr>
<tr>
<td>Bridging therapy†</td>
<td>0.04</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stent†</td>
<td>0.43</td>
<td>0.14</td>
<td>0.57</td>
</tr>
<tr>
<td>Recanalization of BAO (TIMI 2&amp;3)†</td>
<td>...</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>sICH†‡</td>
<td>...</td>
<td>&lt;0.01</td>
<td>0.02</td>
</tr>
<tr>
<td>Tracheotomy†</td>
<td>...</td>
<td>&lt;0.01</td>
<td>0.17</td>
</tr>
<tr>
<td>Ventilation days*</td>
<td>...</td>
<td>0.05</td>
<td>0.50</td>
</tr>
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</table>

*Mann–Whitney test.
†Fisher exact test.
‡sICH was not taken into multivariate analysis because all patients had a mRS of 6 after 3 months.

Table 4. Multivariate Logistic Regression Analysis: Independent Predictors for Recanalization

<table>
<thead>
<tr>
<th>Parameters Included in Model</th>
<th>( P )</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>0.03</td>
<td>6.54</td>
<td>1.14–37.49</td>
</tr>
<tr>
<td>Bridging therapy</td>
<td>0.04</td>
<td>3.37</td>
<td>1.02–11.18</td>
</tr>
<tr>
<td>Age</td>
<td>0.04</td>
<td>0.95</td>
<td>0.91–0.99</td>
</tr>
<tr>
<td>Distal BAO</td>
<td>0.49</td>
<td>1.72</td>
<td>0.36–8.16</td>
</tr>
</tbody>
</table>

Dependent Variable: Successful Recanalization (TIMI 2 and 3)

Table 5. Multivariate Logistic Regression Analysis: Independent Predictors for Survival

<table>
<thead>
<tr>
<th>Parameters Included in Model</th>
<th>( P )</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination of bridging therapy and recanalization of BAO</td>
<td>&lt;0.01</td>
<td>6.94</td>
<td>1.94–24.83</td>
</tr>
<tr>
<td>Bridging therapy</td>
<td>0.04</td>
<td>4.22</td>
<td>1.06–16.52</td>
</tr>
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<td>Female</td>
<td>0.02</td>
<td>0.19</td>
<td>0.45–0.78</td>
</tr>
<tr>
<td>GCS</td>
<td>0.06</td>
<td>1.19</td>
<td>0.99–1.423</td>
</tr>
<tr>
<td>Ventilation days</td>
<td>0.22</td>
<td>1.15</td>
<td>0.92–1.44</td>
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<tr>
<td>Tracheotomy</td>
<td>0.49</td>
<td>0.43</td>
<td>0.04–4.68</td>
</tr>
<tr>
<td>Age</td>
<td>0.75</td>
<td>1.01</td>
<td>0.96–1.06</td>
</tr>
<tr>
<td>Recanalization of BAO (TIMI 2 and 3)</td>
<td>0.74</td>
<td>4.85</td>
<td>0.89–27.36</td>
</tr>
</tbody>
</table>
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IIb/IIIa receptor inhibitors and additional percutaneous trans-
combined treatment with IA rt-PA and IV platelet glycoprotein
feasible.13–21 In a multicenter observational study it has
begun on whether to treat patients with BAO intraarterially or
recently been shown that the bridging concept, using com-
trial in patients with acute BAO ventured in Australia in
al.11 in 1988, with a survival rate of 30%. Since then,
larger case series of IA thrombolysis was published by Hacke
although better recanalization after IA therapy,
compared to other reports,4,25,26 there is a strong coherence in
with no or mild to moderate disability were the
combination of bridging therapy with successful recana-
luminal angioplasty/stenting in case of severe residual steno-
sis after IAT, might improve neurological outcome compared
to IAT with rt-PA alone.9 In this monocenter retrospective
analysis, we compared the treatment of acute BAO with IAT
alone and the combined approach of an IV glycoprotein
luminal angioplasty/stenting, recanalization was
achieved in 9 of 11 cases (81.8%). Abciximab administration
at a bolus dose of 0.25 mg/kg followed by a continuous
infusion for 12 hours rapidly produces a profound antihemo-
static effect, with blockade of 80% of platelet glycoprotein
IIb/IIIa receptors, marked reduction of platelet aggregation,
and prolongation of the bleeding time. Abciximab could
facilitate endogenous thrombolysis by reducing thrombus
growth and prevent thrombus reformation by competitive
inhibition with fibrinogen, and therefore have intrinsic recan-
alization effects. Although platelet glycoprotein IIb/IIIa in-
hibitors, according to a recent Cochrane metaanalysis,22
cannot be recommended for acute stroke therapy in general,
our findings indicate that patients with BAO might benefit
from a combined approach. Other independent predictive
factors for recanalization of BAO were atrial fibrillation and
younger age, probably because of fresher thrombus material
and less atherosclerotic vessel damage.4 Consistent with our
findings, it has been reported that cardiac embolism causes
more frequently distal BAO and is associated with higher
rates of successful recanalization.4,23,24 Other studies,9,25 how-
ever, did not report this finding.

Symptomatic bleeding complications were not increased
after bridging treatment: sICH occurred in 14% vs 18.8% and
major systemic bleeding complications occurred in 1 patient
in both groups. The rate of sICH in this series is slightly
increased compared with previous studies IAT alone,2 al-
though they are in line with the rates reported by Eckert et al.9
When sICH in addition to ischemic damage occurred, it was
fatal in all cases; hence, this variable could not be included in
multivariate analysis.

The rate of an outcome with no or only mild to moderate
disability was increased from 12.5% to 34.9% in the bridging
group and the survival rate increased from 25% to 58.9%,
respectively. Although our results tend to be worse regarding
outcome in the IAT group when compared to recent studies
and the meta-analysis from Lindsberg and Mattle,2 they are in
good concordance with findings in the comparable study by
Eckert et al.9 They found an improved rate of an outcome
with no or mild to moderate (mRS 0 to 3) from 17% to 34%.
Similarly, the mortality was reduced from 68% to 38%. It has
to be noted though that in our study, a prolonged time
window of up to 24 hours was used. Consistent predictive
factors for a better outcome in our cohort were the combina-
tion of bridging treatment with successful recanalization.
As compared to other reports,4,25,26 there is a strong coherence
in the importance of the initial severity of symptoms on out-

between mRS 0 to 2 vs 3 to 6 showed a trend but no
significant difference between the 2 groups (P=0.11); 6.25%
of patients in the IAT group and 18.6% in the bridging group
were independent at 3 months. In univariate analysis the
occurrence of a sICH was negatively associated, whereas a
higher GCS score, bridging therapy, and recanalization were
positively correlated with a better outcome. Patients who had
undergone tracheotomy and extensive ventilation periods had
a greater chance of survival but were less likely to have a
mRS of 0 to 3 at 3 months (Table 3). Independent predictors
for an outcome with no or mild to moderate disability were
the combination of bridging therapy with successful recana-
lization (OR, 3.7; 95% CI, 1.04–13.4) and a higher initial
GCS score (OR, 1.24; 95% CI, 1.03–1.44; Table 6). Comor-
bidty, time to IA treatment, stenting, as well as the amount of
tPA did not show any significant association with both
outcome measurements (Table 3).

### Discussion

BAO is the most severe form of ischemic stroke, with high
mortality and morbidity rates. Despite all advances in modern
therapy and general medical care, prognosis is still grim. To
date there is no established treatment regimen. Most national
guidelines favor endovascular thrombolysis in combination
with mechanical manipulation of the thrombus. The first
larger case series of IA thrombolysis was published by Hacke
et al11 in 1988, with a survival rate of 30%. Since then,
survival rates range between 30% and 73% in observational
studies.2 However, to date there has just been 1 randomized
trial in patients with acute BAO ventured in Australia in
199612 comparing IA thrombolysis (urokinase) with IV anti-
coagulation (heparin). The study was stopped because of low
recanalization after IAT, might improve neurological outcome compared
with rt-PA alone.9 In this monocenter retrospective

### Table 6. Multivariate Logistic Regression Analysis:
Independent Predictors for Functional Outcome

<table>
<thead>
<tr>
<th>Parameters Included in Model</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination of bridging therapy and Recanalization of BAO</td>
<td>0.04</td>
<td>3.74</td>
<td>1.04–13.42</td>
</tr>
<tr>
<td>GCS at presentation</td>
<td>&lt;0.01</td>
<td>1.24</td>
<td>1.03–1.44</td>
</tr>
<tr>
<td>Bridging therapy</td>
<td>0.12</td>
<td>3.05</td>
<td>0.73–12.61</td>
</tr>
<tr>
<td>Recanalization of BAO (TIMI 2 and 3)</td>
<td>0.17</td>
<td>4.62</td>
<td>0.52–41.28</td>
</tr>
<tr>
<td>Female</td>
<td>0.44</td>
<td>0.56</td>
<td>0.13–2.44</td>
</tr>
<tr>
<td>Age</td>
<td>0.83</td>
<td>0.99</td>
<td>0.99–1.04</td>
</tr>
</tbody>
</table>
come after BAO. Together with successful recanalization, a higher GCS score at presentation seems to be an important factor for a better outcome.27 In this context one has to notice that the IAT group in our study had a trend toward a worse GCS score at baseline. This might, in part, account for the overall better outcome in the bridging group. Female gender was negatively correlated with survival but not with outcome in total and interestingly female gender was previously described to be associated with worse outcome after stroke.28 Time to IA treatment was not an independent predictor for outcome in BAO. However, our data do not imply that treatment should be delayed. One aspect of the bridging approach was the earlier initiation of therapy until start of angiography and IAT, which hints to an influence of early treatment on better outcome. Taking the time gain by starting the IV abciximab in our study into account (≈45 min), the bridging group was overall treated significantly earlier than the IAT group. This might be a factor for the improved results in this group. Although there was a difference in the doses of rt-PA in both groups this parameter did not show a significant association with the outcome parameters and recanalization. However, there was a tendency for patients with successful recanalization and an outcome with mRS of 0 to 3 to have received less rt-PA. This is plausible because patients with treatment resistant occlusions were given higher amounts of rt-PA to reopen the vessel.

The main limitation of our analysis is the retrospective noncontrolled design leading to some inhomogeneities between both groups. Patients in the IAT group tended to have a higher rate of previous cardiovascular events and were less often treated with stenting. The more frequent application of stents in the bridging group, however, rather represents a better availability of this technique in the later years than a significant difference in the occlusion type of the BA. In addition, it has to be noted that stenting was not associated with better recanalization, improved outcome, or survival in our study (Table 3). Furthermore, our study represents a longitudinal observation of a changed treatment approach rather than a comparative trial between 2 groups. The bridging group was treated more recently, and one could argue that the observed effects are in part attributable to more practice and routine. However, IAT in our institution has been regularly performed for the past 20 years; therefore, we assume no biasing effect.4,11

In summary, we find an improved recanalization rate of BAO, a higher rate of survival, and a higher rate of outcomes with no or only mild to moderate disability without increased rates of sICH after IV bridging with abciximab. Independent predictors for better clinical outcome were bridging therapy resulting in recanalization, a higher initial GCS score, and male gender. Future randomized controlled trials comparing different recanalization techniques may shed more light onto different recanalization techniques. In hospitals with IV protocols and no access to interventional neuroradiology, treatment might be started intravenously and patients subsequently can be transferred to a comprehensive center for additional IA therapy.29

Disclosures
None.

References


Therapy of Acute Basilar Artery Occlusion: Intraarterial Thrombolysis Alone vs Bridging Therapy
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