Multimodal Recanalization Therapy in Acute Basilar Artery Occlusion
Long-Term Functional Outcome and Quality of Life

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Background and Purpose—Multimodal recanalization therapy in patients with acute basilar artery occlusion provides high recanalization rates. A substantial subset of treated patients survives with only minor or moderate functional handicap. However, long-term functional outcome and quality of life in these patients have rarely been systematically analyzed.

Methods—In this monocentric retrospective study, we analyzed mortality, long-term functional outcome (modified Rankin Scale), and quality of life (36-Item Short-Form Health Survey questionnaire) in all consecutive patients who had been treated for acute basilar artery occlusion in our institution between December 2002 and December 2009.

Results—Ninety-one patients (57 male; median age, 65 years; range, 20–89 years) were treated by multimodal recanalization therapy. This included intravenous thrombolysis (n=32) with consecutive on-demand intra-arterial therapy (n=23) or intra-arterial therapy alone (n=59). The overall recanalization rate was 89%. After a median observation time of 4.2 years (range, 0.5–7.4 years), the mortality rate was 59%. Among the 35 survivors, 26 patients (74%) had a good or moderate long-term functional outcome (modified Rankin Scale ≤3). Health-related quality of life was better than that of unselected patients with stroke. Backward stepwise logistic regression identified intravenous thrombolysis (P=0.002) and female sex (P=0.001) as predictors of favorable functional long-term outcome (modified Rankin Scale ≤3). Coma at admission (Glasgow Coma Scale ≤8) was associated with poor outcome (modified Rankin Scale ≥4; P=0.036).

Conclusions—Long-term survival is achieved in approximately 40% of patients with basilar artery occlusion treated with multimodal recanalization therapy. Approximately 75% of the survivors have a favorable functional long-term outcome with an acceptable quality of life. (Stroke. 2012;43:00-00.)

Key Words: basilar artery occlusion ■ health-related quality of life ■ intravenous thrombolysis ■ mechanical recanalization

A acute basilar artery occlusion (BAO) is associated with high mortality and poor outcome.

In the absence of data from prospective randomized trials, the optimal recanalization strategy for affected patients is still under discussion, yet the need to achieve early recanalization is well appreciated. The available therapeutic spectrum includes intravenous thrombolysis (IVT) as well as intra-arterial approaches such as intra-arterial thrombolysis (IAT) and endovascular mechanical recanalization (EMR). A prospective registry (Basilar Artery International Cooperation Study [BASICS]) was unable to show superiority of any of these treatment modalities in patients with BAO.1

So far, there are only very few studies that have analyzed functional recovery after BAO in the long term.2,3 Data on quality of life are even more limited but may be of special interest in patients with BAO because higher cognitive functions are frequently preserved despite severe motor deficits. This monocentric retrospective analysis evaluates long-term mortality, functional outcome, and health-related quality of life in a patient population with acute BAO treated by multimodal recanalization therapy.

Patients and Methods

Patient Identification
All patients with confirmed acute BAO admitted to our center between December 2002 and December 2009 were included. Acute BAO was defined as complete vascular obliteration of the basilar artery in contrast-enhanced CT angiography (CTA) and/or digital subtraction angiography in the presence of clinical signs of acute posterior circulation stroke (dysarthria, oculomotor dysfunction,
bulbar signs, motor deficits, visual deficits, impairment of consciousness). Like in the BASICS registry, the onset of persisting clinical symptoms suggestive of BAO (and not the onset of fluctuating prodromal symptoms) was used to define treatment intervals. Patients were identified from a computerized database in which basic data of all patients with BAO admitted to our center since December 2002 had been prospectively collected. Some aspects of this registry have been previously reported.4,5

Treatment
To achieve recanalization, intra-arterial therapy was regularly applied. We had no predefined time window for intra-arterial therapy. The decision to perform intra-arterial therapy was based on the interdisciplinary discussion between involved neurologists and neuroradiologists for every individual patient. In some cases patients received a bridging therapy. Up to 2005, this bridging therapy consisted of glycoprotein Ib/IIa inhibition (tirofiban) or IVT. A decision on bridging was made by the treating neurologist and the neuroradiological interventionalist for every individual patient. From 2006 bridging with IVT within a time window up to 8 hours was implemented as our first-line concept.4 Glycoprotein Ib/IIa inhibition played no further role any more. Heparin was used in a standardized rinsing solution for EMR devices during EMR recanalization therapy. In the case of IVT, bridging heparin treatment was paused for at least 24 hours. Subsequent stroke management on our neurological intensive care unit generally followed the German and European guidelines on acute stroke care valid at the time of patient admission.6,7

Data Retrieval
The following data were retrieved from medical charts: age, sex, comorbid conditions, vascular risk factors, clinical presentation, clinical course, infarct etiology and extension, modality of admission, time to intervention, details of the recanalization procedure, procedural complications, and short-term outcome including in-hospital mortality. Diagnostic workup to define infarct etiology regularly included imaging of extra- and intracranial vessels (Doppler and Duplex sonography, CTA, MR angiography), Holter electrocardiography, and transthoracic or transesophageal echocardiography. Comorbidity was quantified by the Charlson Comorbidity Index, a validated measure of pre-existing morbidity.8 Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria were applied to classify the etiology of stroke.9

Neuroradiological Analysis
Neuroradiological images of all patients were reanalyzed by experienced neuroradiologists (M.H., G.F.). Emphasis was placed on the underlying arterial pathology and the exact infarct extension. Diagnosis of vertebrobasilar infarction was made on the basis of MRI or clear evidence of infarction on CT. Recanalization after intra-arterial therapy was defined according to Thrombolysis In Myocardial Infarction (TIMI) grades as TIMI II (perfusion with incomplete or slow distal branch filling) or TIMI III (full perfusion with filling of all distal branches).10

Long-Term Follow-Up
Long-term outcome was assessed in 2010. Patients were contacted by telephone. Their clinical status was documented using a structured interview and the modified Rankin Scale (mRS).11 In addition to this telephone interview, patients were asked to answer a mailed 36-Item Short-Form Health Survey questionnaire. The 36-Item Short-Form Health Survey (SF-36) is widely used to measure health-related quality of life and has been validated for patients after stroke.12 It assesses 8 domains on physical, emotional, and mental functioning. Results were compared with historical populations of healthy German citizens and a population of nonselected patients with stroke of the International Stroke Trial 1999.13

Outcome Factors
Outcome was dichotomized in favorable (mRS ≤3) and poor (mRS ≥4). A mRS of 3 was still considered favorable in light of the often devastating functional outcome in patients with BAO. A comparable dichotomization has been used in recent trials.3 The following parameters were selected as variables in univariate analysis: age ≥65 years (with reference to the median), sex, substantial comorbidity (Charlson Index ≥3), coma at admission (Glasgow Coma Scale before therapy ≤8), direct admission versus referral from a community hospital, time to recanalization therapy, and modality of recanalization therapy (bridging, IVT, IAT, EMR).

Statistical Analysis
The statistical software package SPSS 18.0 was used. Values are given as mean±SD. For univariate analysis, the Fisher exact test was used. To identify independent variables for favorable outcome, a backward stepwise logistic regression analysis was performed including all variables with P<0.2 in univariate analysis (age, sex, Charlson Index, Glasgow Coma Scale at admission, use of IVT).

Results
Patient Characteristics
A total of 115 patients with acute BAO admitted between December 2002 and December 2009 were identified. Seventeen of these patients did not fulfill the criteria of confirmed BAO in CTA and/or digital subtraction angiography. In 7 patients recanalization was not attempted due to extensive pretreatment infarction with a grave prognosis. These patients died under palliative therapy and were not included in the analysis.

The remaining 91 patients (57 male patients [63%]) received treatment for confirmed acute BAO. Their mean age was 62.7 years (median, 65 years; range, 20–89 years). Sixty-four patients (70%) had been referred from community hospitals, 18 patients (20%) had presented directly at our emergency department, and 9 patients (10%) had already been treated in-house for other clinical conditions when BAO occurred. The mean interval between BAO and admission at our center was 5.5±4.9 hours in the case of referral from cooperating community hospitals and 2.8±2.5 hours in the case of direct admission. The distal (n=60 [66%]) and middle sections (n=53 [58%]) of the basilar artery were most frequently affected. Most patients (n=51 [56%]) presented with unisegmental BAO. In 31 patients (34%), 2 segments were affected; and in 9 patients (10%), all 3 segments. Atherosclerosis was the most frequent underlying etiology followed by cardiac embolism (Table 1). Substantial pre-existing morbidity (Charlson Index ≥3) was present in one fifth of our patients (Table 1).

Clinical Presentation
Thirty-seven patients presented with prodromal symptoms including oculomotor paresis, ataxia, paresis, and nausea. Almost all patients (89 of 91 [89%]) presented with reduced consciousness (Glasgow Coma Scale ≤14). The mean Glasgow Coma Scale was 7.7±3.7. Coma (Glasgow Coma Scale ≤8) was observed in 62 patients (68%). The mean National Institutes of Health Stroke Scale on admission was 21.7±7.8 (Table 1).

Recanalization Therapy
Forty-six patients (51%) received bridging before intra-arterial therapy. Among those, IVT was applied in 32 and tirofiban in 14 patients (Table 1). Time to IVT was 2.9±1.3
hours in the 32 patients with IVT bridging. Nine of them (28%) showed prompt recanalization of the basilar artery in posttreatment CTA or digital subtraction angiography. Accordingly, the designated intra-arterial procedure was abstained from in these patients. The remaining 82 patients received intra-arterial therapy. Time to intra-arterial therapy was 6.6 ± 5.8 hours. Intra-arterial therapy consisted of EMR alone in 34 patients (41%), IAT alone in 16 patients (20%), and a combination of EMR and IAT in 32 patients (39%). EMR devices used are specified in Table 1. In many cases, different devices were used in combination. The mean dose of intra-arterial recombinant tissue-type plasminogen activator was 41.2 ± 22.2 mg.

Overall, recanalization was achieved in 81 of 91 patients (89%). Among the 82 patients receiving intra-arterial therapy, 30 showed full (TIMI 3), 47 partial (TIMI 2), and 5 no (TIMI 0) recanalization at the end of the procedure. In 4 patients, digital subtraction angiography was not performed due to CTA evidence of complete recanalization of the basilar artery after IVT.

**Early Clinical Course and Mortality**

Almost all patients (n = 86 [95%]) showed acute infarctions in the vertebrobasilar territory on control imaging with predominance of pontine (n = 44 [48%]) and cerebellar regions (n = 51 [56%]). Thirty-six patients (40%) died during the acute hospital phase, among them all 10 patients with failed recanalization (Figure 1). In all but 2 patients, death was caused by infarction of the vertebrobasilar territory. The other 2 patients died of septic multiple organ failure.

The mean length of intensive care unit treatment was 9.5 ± 9.1 days (range, 0–42 days); the mean length of in-hospital treatment 11.6 ± 9.3 days (range, 0–42 days). Figure 2 shows the distribution of mRS scores at the end of the procedure. In 4 patients, digital subtraction angiography was not performed due to CTA evidence of complete recanalization of the basilar artery after IVT.

**Table 1. Patient Characteristics, Neuroradiological Findings, and Therapeutic Interventions**

<table>
<thead>
<tr>
<th>Basic data</th>
<th>No.</th>
<th>Percent</th>
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<tr>
<td>Age, y, mean± SD</td>
<td>62.7 ± 14.5</td>
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<tr>
<td>Male sex</td>
<td>57</td>
<td>63</td>
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<td>Referral from community hospital</td>
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<td>Time to admission, h, mean± SD</td>
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<td>Etiology</td>
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<td>Cardioembolism</td>
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<tr>
<td>Other determined etiology (inter alia vertebral artery dissection)</td>
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<td>6</td>
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<tr>
<td>Undetermined etiology</td>
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<td>13</td>
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<tr>
<td>Charlson Index ≥ 3</td>
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<tr>
<td>Clinical presentation</td>
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<tr>
<td>Coma (GCS ≤ 8)</td>
<td>62</td>
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<tr>
<td>GCS on admission, mean</td>
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<td>NIHSS on admission, mean</td>
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<tr>
<td>Perforation of intracerebral vessel during EMR</td>
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If not indicated otherwise, all percentage values refer to the total patient no. of 91.

GCS indicates Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BAO, basilar artery occlusion; IVT, intravenous thrombolysis; IAT, intra-arterial thrombolysis; EMR, endovascular mechanical recanalization.

![Figure 1](http://stroke.ahajournals.org/)
clinical recovery (mRS ≤3). Further details are given in Figure 2.

Long-Term Follow-Up and Quality of Life
After a mean observation time of 4.2 ± 2.1 years (median, 4.2 years; range, 0.5–7.4 years), 13 additional patients had died (see also Figures 1 and 2), mainly due to stroke-associated complications. Nine of these patients (69%) had a poor functional outcome (mRS 4 and 5) at 3 months. Five patients were lost to follow-up.

Among the remaining 35 long-time survivors (39%), 26 patients (74% of 35 patients) had a favorable long-term outcome (mRS 3; Figure 2). Motor deficits (54%), visual deficits (37%), and impairment of coordination (29%) were specified as the most relevant residual symptoms.

Compared with healthy age- and sex-matched control subjects, surviving patients with BAO scored moderately lower in 7 of 8 SF-36 items. Only the item bodily pain (pain) was rated similarly (Figure 3). Compared with a historical population of unselected patients with stroke of the International Stroke Trial14,15 in 1999, our patients scored moderately higher in 7 of 8 SF-36 items; the item mental health was rated similarly (Figure 3). The majority of long-term survivors lived at home and was not dependent on professional nursing care (n = 32 [91%]). Most of them (n = 28) were living with a partner or family; a few were living alone (n = 4). Only 3 surviving patients were living in a nursing home.

Asked if satisfied with their outcome, 24 patients (69%) reported full to moderate contentment and 11 patients (31%) minor or no contentment.

Prognostic Factors
All patients with failed recanalization died during the acute hospital phase due to extensive infarction. The share of patients with a favorable long-term outcome decreased with increasing time to treatment (Figure 4). None of the patients treated beyond 9 hours had a favorable long-term outcome.

Early treatment (≤3 hours) was associated with favorable outcome in univariate analysis (OR, 2.036; 95% CI, 1.211–3.425; P = 0.015). Backward stepwise logistic regression identified bridging with IVT (P = 0.002) and female sex (P = 0.001) as predictors of favorable long-term outcome (mRS ≤3). Coma at admis-
Discussion

In our study on patients with confirmed BAO, multimodal recanalization therapy provided excellent recanalization rates. However, as shown by us and others, these high recanalization rates did not guarantee good clinical outcome. In fact, only approximately 60% of our patients survived the acute hospital phase and only approximately 40% were still alive after a median follow-up period of 4.2 years. This finding is in line with previous reports on short- and long-term mortality in patients with BAO treated by IVT or IAT.

In our population, mortality was 100% in patients with failed recanalization. Additionally, outcome was poor in all patients in whom recanalization was achieved beyond 9 hours. Especially those patients who had been treated within 3 hours after symptom onset seemed to benefit from recanalization and displayed a favorable functional outcome in the long term. This underscores the necessity to not only reestablish perfusion of the vertebrobasilar territory, but also to reach it fast. A time window of 9 hours seemed to be critical in our patients. A similar observation was made in the BASICS trial, in which none of the patients with severe clinical affection had a favorable outcome if recanalization therapy was performed beyond 9 hours.

The most promising approach to provide early treatment and high recanalization rates may be the prompt initiation of IVT followed by immediate transfer and/or preparation for EMR. Indeed, preceding IVT was a strong positive predictor of favorable outcome in our patients treated by multimodal recanalization therapy. IVT may not only bridge the time to thrombectomy. It also leads to prompt recanalization in a subset of patients with BAO (28% in our population) and it may facilitate consecutive EMR. The latter was shown in a recent analysis, in which preceding IVT led to shorter EMR net intervention times in patients with proximal intracranial artery occlusion. Compared with EMR alone, pharmacological thrombolysis (IVT and/or IAT) did not seem to bear an increased risk of intracranial hemorrhage in our patients.

The most important finding of our study was the rather good long-term functional recovery and the acceptable quality of life in BAO long-term survivors. Approximately three fourths of the long-term survivors had no or only mild to moderate deficits. Almost all of them were living at home. This result may be biased by the fact that we have no information about the quality of life of the patients who had survived the first 3 months but died before the long-term follow-up telephone interview. Most of these patients had a poor functional status at 3 months. In most of these patients mortality was associated with stroke- or nursing-related complications. Both of these aspects suggest a reduced quality of life before death in this subgroup of patients. However, we still believe that an exaggerated fear to potentially “create” severely disabled survivors in the long term is not fully justified and should not withhold physicians to aggressively treat patients with BAO.

Interestingly, quality of life was better than that of unselected stroke survivors. An explanation for this difference may be the preservation of cognitive function and communicating abilities in most patients with posterior circulation stroke. Moreover, patients with posterior circulation stroke may have a decreased risk to develop depressive disorders compared with those with anterior circulation stroke. Rating of quality of life may therefore be less biased by depression in BAO survivors. However, it has to be acknowledged that the follow-up period in the International Stroke Trial population (median, 56 weeks) was shorter than that in our population (median, 219 weeks). Moreover, stroke treatment has substantially evolved over the last decade. These 2 facts may have led to an overestimation of outcome differences in the 2 populations. It would be very interesting to address the issue of long-term quality of life in patients with anterior versus posterior stroke in future studies.

Neither advanced age nor pronounced comorbidity significantly influenced long-term functional outcome in our patients with BAO. This is in contrast to recently published results and may be explained by the limited number of patients in our study. With this uncertainty, the baseline parameters age and comorbidity should not be used to generally exclude patients from recanalization therapy.

The fact that female sex appeared as a strong predictor for favorable outcome in our study is rather surprising and might reflect a chance finding due to our small population. In recent retrospective publications, women did not have a better outcome nor did they benefit more from any therapeutic strategy in posterior circulation stroke.

Our study is compromised by its nonrandomized monocentric and retrospective design and may therefore display potentially biased results. The fact that only patients with confirmed BAO in CTA and/or digital subtraction angiography have been included may have biased our IVT patient population with referral from external hospitals toward more severe cases. Like in similar studies, clinical follow-up was not performed by a blinded investigator.

Prospective trials will be necessary to define the best treatment in patients with BAO. The recently initiated BASICS trial compares IVT alone with combined IVT and endovascular therapy. Centers should be encouraged to include patients.
Conclusion

Despite multimodal recanalization therapy, mortality remains high in the acute phase of BAO. However, survivors have a 75% chance to reach a favorable functional long-term outcome, especially in the absence of coma and in the case of bridging therapy with IVT. Quality of life in these patients seems to be better than that of unselected patients with stroke.

Disclosures
None.

References

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