

Stroke

American Stroke
AssociationSM

A Division of American
Heart Association



JOURNAL OF THE AMERICAN HEART ASSOCIATION

Admission Facility Is Associated With Outcome of Basilar Artery Occlusion

Robert Müller, Thomas Pfefferkorn, Bijan Vatankhah, Thomas E. Mayer, Johannes Schenkel, Martin Dichgans, Dirk Sander and Heinrich J. Audebert

Stroke published online Feb 22, 2007;

DOI: 10.1161/01.STR.0000260089.17105.27

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214
Copyright © 2007 American Heart Association. All rights reserved. Print ISSN: 0039-2499. Online
ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://stroke.ahajournals.org>

Subscriptions: Information about subscribing to *Stroke* is online at
<http://stroke.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21202-2436. Phone 410-5280-4050. Fax: 410-528-8550. Email:
journalpermissions@lww.com

Reprints: Information about reprints can be found online at
<http://www.lww.com/static/html/reprints.html>

Admission Facility Is Associated With Outcome of Basilar Artery Occlusion

Robert Müller, MD; Thomas Pfefferkorn, MD; Bijan Vatankehah, MD; Thomas E. Mayer, MD; Johannes Schenkel, MD, MPH; Martin Dichgans, MD; Dirk Sander, MD; Heinrich J. Audebert, MD

Background and Purpose—Basilar artery occlusion (BAO) is a stroke subtype with poor prognosis, but recanalizing therapies have been reported to be effective. We investigated whether initial admission to telemedically linked general hospitals with subsequent stroke-center transfer is related to poorer outcome than direct admission to stroke centers.

Methods—All BAO cases of 3 stroke centers in Munich and 1 center in Regensburg between March 1, 2003 and December 31, 2004 were included, either if patients were directly admitted to stroke centers (n=23) or had initial admission to general hospitals of the telemedical network for integrative stroke care (TEMPiS) and secondary transfer to stroke centers (n=16). BAO was defined as angiographically (CTA, MRI or conventional angiography) confirmed occlusion of the basilar artery. Baseline parameters and therapeutic procedures were recorded. One-year follow-up was conducted prospectively.

Results—Differences in baseline parameters were not statistically significant. Time from onset to first angiography was significantly longer in patients with secondary transfer (mean: 355±93 minutes versus 222±198 minutes; $P<0.01$), mainly attributable to transfer duration (mean: 156±73 minutes). In-hospital mortality (22% versus 75%; $P<0.01$) and 1-year-mortality (30% versus 81%; $P<0.01$) were lower for patients with direct admission to stroke centers. Fifty-two percent of directly admitted patients versus 13% of patients with secondary transfer ($P=0.02$) were living at home after 1 year.

Conclusions—BAO patients who were admitted primarily to community hospitals had a worse prognosis. Patients with typical symptoms should have direct access to stroke centers, or may need bridging therapies. (*Stroke*. 2007;38:000-000.)

Key Words: basilar artery occlusion ■ interhospital transfer ■ telemedicine

Acute basilar artery occlusion (BAO) is a stroke subtype with poor prognosis. Older series demonstrated that treatment with anticoagulants alone was associated with a 75% to 91% mortality.¹ Recanalization of the basilar artery is correlated with better outcome.¹⁻³ Therefore, recanalizing therapies such as mechanical recanalization, intra-arterial or systemic thrombolysis were described to improve prognosis^{1,4} and are part of present recommendations.⁵

A recently published analysis of the Telemedical Project for integrative Stroke Care (TEMPiS) demonstrated that the diagnosis of BAO determined as most probable in telemedical assessment was often (68%) confirmed by angiography or follow-up imaging.⁶ However, the observed durations of emergency transfers were unexpectedly long.⁷

We therefore hypothesized that prognosis of patients admitted primarily to nonspecialized hospitals and then transferred to interventional stroke centers is worse than of those admitted directly to stroke centers.

Methods

The analysis includes all patients with the diagnosis of BAO, admitted directly or after interhospital transfer to 4 academic stroke centers in Munich and Regensburg between March 1st, 2003 and December 31st, 2004. All centers have specialized neurological Stroke and Intensive Care Units and offer neuroradiological diagnostics and interventional treatment at any time. BAO was defined as angiographically (CTA, MRI angiography or conventional angiography) confirmed occlusion of the basilar artery.

Baseline Data

Baseline parameters were recorded in all patients. Level of consciousness was categorized with the Best Eye Response according to the Glasgow Coma Score. Coma was determined if eyes were not opened to verbal or pain stimuli.

Patients Directly Admitted to the Academic Stroke Centers

All patients who met the criteria of BAO were included. Data collection of these patients was done prospectively in 2 centers with ongoing BAO registers and retrospectively in the other 2 centers.

Received October 23, 2006; accepted October 31, 2006.

From the Department of Neurology (R.M., J.S., H.J.A.), Klinikum Harlaching, Städtisches Klinikum München GmbH, Munich, Germany; the Department of Neurology (T.P., M.D.), Klinikum Großhadern, Ludwig-Maximilians-University Munich; the Department of Neurology (B.V.), University of Regensburg, Regensburg, Germany; the Department of Neuroradiology (T.E.M.), Klinikum Großhadern, Ludwig-Maximilians-University Munich; and the Department of Neurology (D.S.), Klinikum Rechts der Isar, Technical University Munich, Munich, Germany.

Correspondence to Dr Heinrich Audebert, Stroke Unit, Guy's and St. Thomas' Hospital NHS Trust, Lambeth Palace St, London, SE1 7EH UK. E-mail Heinrich.audebert@gstt.nhs.uk

© 2007 American Heart Association, Inc.

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

DOI: 10.1161/01.STR.0000260089.17105.27

Patients of the Community Hospitals (TEMPiS group)

The TEMPiS concept was already described in detail.⁶ In brief, 12 community hospitals without interventional facilities may present patients and their brain images by telemedical devices at any time. Obligatory indications for teleconsultation include brain stem symptoms and decreased level of consciousness.

Patients with suspected BAO were transferred from TEMPiS hospitals to the 4 stroke centers that did not provide emergency angiographic imaging and interventional stroke treatment. BAO cases were documented prospectively as they underwent telemedical examination.⁷ Duration of transfer was defined as time from start of teleconsultation until patient's arrival in the stroke center. According to the Standardized Procedures of TEMPiS, heparin or tirofiban treatment was recommended during interhospital transport.

Treatment in the Stroke Centers

BAO treatment protocols of all stroke centers included immediate heparin treatment after exclusion of intracranial hemorrhage and determination of BAO as suspected diagnosis. Decision about exact treatment was up to the stroke centers. In 3 of the centers, mechanical devices ("Merci"-retriever, "Angiojet", "Guidant Neuronet") were used in addition to intraarterial thrombolysis. All these approaches were defined as interventional treatment. Time of treatment decision was defined as time to first angiography, regardless of the type of angiography. Recanalization was assessed either directly after interventional treatment or in follow-up CT/MRI angiographies.

Complications

Intracranial hemorrhage was defined as all intracerebral or subarachnoid hemorrhages seen in follow-up CT or MRI, regardless of whether neurological deterioration was observed.

Follow-Up

Follow-up was done 1 year after the event. In patients who survived the in-hospital stay, a standardized telephone interview was conducted with the patients or their relatives. This assessment included vital status, residential status, modified Rankin Scale and Barthel Index.

For the expected severe impairment of BAO patients, good outcome was predefined as Barthel Index ≥ 60 or modified Rankin Scale ≤ 3 .

Statistical Analysis

Statistical analyses were predefined and performed with SPSS 12.0 software. For all analyses concerning patient characteristics and treatment procedures, the Mann-Whitney test was used for differences in continuous variables and the χ^2 test or Fisher exact test were used for differences in proportions. For analysis of potential outcome predictors, a stratified analysis was performed in patients who died in-hospital or survived. Statistical significance was determined at an α level of 0.05.

Ethical Issues

The patients were treated according to existing protocols of the stroke centers and the TEMPiS network. Data of patients who were not admitted to the Klinikum Munich Harlaching or to the TEMPiS hospitals were forwarded anonymously.

Results

Twenty-three patients had direct admission to the stroke centers, and 16 were primarily admitted to the community hospitals and subsequently transferred to stroke centers. In almost all patients of the TEMPiS-group, heparin ($n=6$) or tirofiban ($n=3$) or combined ($n=5$) treatment of heparin and tirofiban was started before the interhospital transport.

Baseline data, procedures and outcome of patients are listed in Table 1. No significant differences were observed in baseline data. Time to arrival in the stroke center and time to treatment decision was significantly longer in patients with primary admission to community hospitals, mainly attributed to the duration of the interhospital transfer.

Recanalization was achieved in 87% of patients treated with interventional approaches.

Bleeding Complications

No extracranial bleeding complications were observed. Intracranial hemorrhages (1 subarachnoid and 6 intracerebral hemorrhages) occurred in 7 patients of whom 4 underwent intraarterial thrombolysis alone, and 2 underwent combined mechanical removal and intraarterial thrombolysis. One patient with tirofiban pretreatment during transport had a brain stem hemorrhage after use of a mechanical device without tissue plasminogen activator.

Follow-Up

Significantly more patients with secondary transfer died in-hospital. The difference in vital status after 12 months was similar. More patients admitted directly to the stroke centers were living at home and had good outcome according to disability scores.

Associations With In-Hospital Mortality (Table 2)

Seventeen patients died in-hospital and 22 patients were discharged. In univariate analysis, only admission facility was significantly associated with in-hospital mortality. A trend for higher mortality was seen for advanced age and for a longer time to treatment decision. In patients without verbal or motor response to verbal stimuli ($n=19$), in-hospital mortality increased markedly with longer time to treatment decision. Whereas patients with shorter time to treatment decision mostly survived (mortality in first quartile: 20%; second quartile 40%), patients with longer delay died in $>50\%$ (third quartile: 60%, fourth quartile: 75%; test for trend: $P=0.09$).

Discussion

Patients who were first admitted to community hospitals and subsequently transferred to stroke centers had higher in-hospital mortality and more frequently a poor outcome compared with those with primary admission to stroke centers. Although baseline parameters and applied treatments were similar, the only statistically significant differences were seen for the times from onset to arrival in the stroke center and to treatment decision.

A major cause for the poorer outcome of patients admitted to community hospitals seems to be the delayed diagnostic work-up and treatment in this group. The importance of early treatment onset was also emphasized by Eckert et al,⁸ and the ischemic damage may be improved with early recanalization therapy as shown for systemic thrombolysis in hemispheric infarcts.⁹ In univariate analysis, a trend for poor outcome with longer time to decision was found. However, this may not completely explain the difference in outcome. Other factors

TABLE 1. Baseline Characteristics, Procedures and Outcome of Patients

	Direct Admission (n=23)	Interhospital Transfer (n=16)	P Value
Mean age in years, (SD)	67.7 (16)	63.1 (15)	
Median (range)	66.5 (40–89)	70 (27–79)	0.30
Gender female (%)	11 (48)	7 (44)	0.80
Prior stroke (%)	5 (22)	1 (6)	0.37
Artrial fibrillation (%)	7 (30)	5 (31)	0.96
Diabetes (%)	4 (17)	3 (19)	1.00
Arterial hypertension (%)	14 (61)	8 (50)	0.50
Coronary heart disease (%)	6 (26)	0 (0)	0.06
Level of consciousness (%)			
Alert	5 (22)	3 (19)	
Opens eyes with verbal commands	7 (30)	5 (31)	
Opens eyes with pain stimulus	6 (26)	3 (19)	
Doesn't open eyes with pain stimulus	5 (22)	5 (31)	0.50
Time intervals			
Prehospital time			
Mean (SD)	128 (129)	90 (62)	
Median (range)	75 (0–450)	60 (30–240)	
Onset to arrival in stroke center			0.56
Mean (SD)	128 (129)	319 (93)	
Median (range)	75 (0–450)	295 (115–465)	<0.01
Transfer duration			
Mean (SD)		156 (73)	
Median (range)		155 (50–360)	
Time to treatment decision			
Mean (SD)	222 (198)	335 (93)	
Median (range)	225 (30–750)	335 (135–525)	<0.01
Treatment in stroke centers			
None or heparin (%)	2 (9)	3 (19)	
Tirofiban (%)	1 (4)	0 (0)	
Systemic tPA (%)	0 (0)	1 (6)	
Intraarterial local tPA (%)	11 (48)	6 (38)	
Mechanical (%)	4 (17)	4 (25)	
Mechanical and tPA (%)	5 (22)	2 (12)	
Interventional treatment (%)	20 (87)	12 (75)	0.34
Recanalization	19 (83)	13 (81)	1.00
Intracranial hemorrhages	2 (9)	5 (31)	0.10
In-hospital mortality (%)	5 (22)	12 (75)	<0.01
Mortality after 12 months	7 (30)	13 (81)	<0.01
Residential status after 12 months			
At home (%)	12 (52)	2 (13)	0.02
Nursing home (%)	4 (17)	1 (6)	
Good outcome (BI ≥60) (%)	11 (48)	1 (6)	0.01
Good outcome (mRS ≤3) (%)	12 (52)	1 (6)	<0.01

tPA indicates tissue plasminogen activator; BI, Barthel Index; mRS, modified Rankin Scale.

*Interventional treatment includes intra-arterial tPA or mechanical clot removal.

TABLE 2. Stratified Analysis for In-Hospital Mortality

	Survived (n=22)	Died (n=17)	P Value
Mean age in years, (SD)	62.5 (16) 27–89	70.2 (13) 37–79	0.10
Range			
Female sex (%)	12 (55)	6 (33)	0.23
Prior stroke (%)	4 (18)	2 (12)	0.68
Artrial fibrillation (%)	5 (23)	7 (41)	0.22
Diabetes (%)	4 (18)	3 (18)	1.00
Arterial hypertension (%)	13 (59)	9 (53)	0.70
Coronary heart disease (%)	4 (18)	2 (12)	0.68
Alert (%)	5 (23)	3 (18)	
Opens eyes with verbal commands (%)	7 (32)	5 (29)	
Opens eyes with pain stimulus (%)	5 (23)	4 (24)	
Doesn't open eyes with pain stimulus (%)	5 (23)	5 (29)	0.72
Interventional treatment (%)	20 (91)	12 (71)	0.21
Time to treatment decision			
Mean (SD)	249 (201)	309 (125)	
Median (range)	155 (30–750)	315 (76–525)	0.172

such as complications of the interhospital transfer may also contribute.

Limitations

Several limitations of this analysis have to be acknowledged. The relatively small numbers of cases are consequence of the low frequency of BAO. Time estimations are a critical issue in all BAO studies because symptom onset is often stuttering and progressive¹⁰ and need of aggressive treatment may emerge only during the clinical course.

This is not a randomized trial. Hence, unknown confounders cannot be excluded, particularly, if related to prehospital management or interhospital transfer. Decisions whether patients should receive only palliative treatment before the complete diagnostic work-up might have been different. However, neurologists of stroke centers were always involved in the decisions about which patients should receive specific treatments.

Finally, different treatments were executed in the stroke centers that make direct comparisons difficult. These treatment strategies, however, were distributed similarly in both groups.

Despite these limitations, the results can be useful for clinical practice. If diagnosis of BAO is suspected in prehospital examination, patients should preferably be admitted to hospitals that provide the needed diagnostic and therapeutic resources.

Because of the critical importance of time,⁵ early start of systemic thrombolysis may be the best way to initiate therapy, particularly in telemedically equipped regional clinics. After publication of the prospective data of Lindsberg et al,³ the TEMPiS protocol for BAO was changed, accordingly. Thus, patients with a suspected BAO in the community hospitals undergo immediate CT-angiography and—in case

of confirmed vessel occlusion—receive systemic thrombolysis as a bridging therapy before the referral to stroke centers is started.

Acknowledgments

We thank all participating stroke neurologists in the stroke centers, and all TEMPiS-hospitals: Asklepios Stadtklinik Bad Tölz, Kreiskrankenhaus Burglengenfeld, Kreisklinik Cham, Klinikum Dachau, Kreisklinik Ebersberg gGmbH, Kreisklinik Eggenfelden, Klinikum Freising, Kreiskrankenhaus Kelheim, Kreisklinik Mühldorf, Kreisklinik München-Pasing, Klinikum Rosenheim, Klinikum St. Elisabeth Straubing.

Sources of Funding

TEMPiS has been supported by the Bavarian health insurance companies; Bavarian State Ministry for Employment and Social Order, Family and Women; German Stroke Foundation; and the German Federal Ministry of Research (BMBF) within the CompetenceNet Stroke.

Disclosures

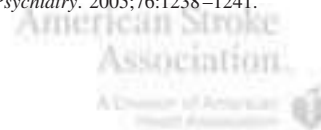
H.J.A. has received speaker's honoraria from Boehringer Ingelheim Pharma GmbH.

References

1. Hacke W, Zeumer H, Ferbert A, Bruckmann H, del Zoppo GJ. Intra-arterial thrombolytic therapy improves outcome in patients with acute vertebrobasilar occlusive disease. *Stroke*. 1988;19:1216–1222.
2. Arnold M, Nedelchev K, Schroth G, Baumgartner RW, Remonda L, Loher TJ, Stepper F, Sturzenegger M, Schuknecht B, Mattle HP. Clinical

and radiological predictors of recanalisation and outcome of 40 patients with acute basilar artery occlusion treated with intra-arterial thrombolysis. *J Neurol Neurosurg Psychiatry*. 2004;75:857–862.

3. Lindsberg PJ, Soenne L, Tatlisumak T, Roine RO, Kallela M, Happonen O, Kaste M. Long-term outcome after intravenous thrombolysis of basilar artery occlusion. *JAMA*. 2004;292:1862–1866.
4. Brandt T, von Kummer R, Muller-Kupfers M, Hacke W. Thrombolytic therapy of acute basilar artery occlusion: variables affecting recanalization and outcome. *Stroke*. 1996;27:875–881.
5. Lindsberg PJ, Mattle HP. Therapy of basilar artery occlusion: a systematic analysis comparing intra-arterial and intravenous thrombolysis. *Stroke*. 2006;37:922–928.
6. Audebert HJ, Wimmer ML, Hahn R, Schenkel J, Bogdahn U, Horn M, Haberl RL. Can telemedicine contribute to fulfill WHO Helsingborg Declaration of specialized stroke care? *Cerebrovasc Dis*. 2005;20:362–369.
7. Audebert HJ, Clarmann vC, Schenkel J, Furst A, Ziemus B, Metz C, Haberl RL. [Interhospital emergency transfers of patients after a stroke.] *Dtsch Med Wochenschr*. 2005;130:2495–2500.
8. Eckert B, Kucinski T, Pfeiffer G, Groden C, Zeumer H. Endovascular therapy of acute vertebrobasilar occlusion: early treatment onset as the most important factor. *Cerebrovasc Dis*. 2002;14:42–50.
9. Hacke W, Donnan G, Fieschi C, Kaste M, von Kummer R, Broderick JP, Brott T, Frankel M, Grotta JC, Haley EC Jr, Kwiatkowski T, Levine SR, Lewandowski C, Lu M, Lyden P, Marler JR, Patel S, Tilley BC, Albers G, Bluhmki E, Wilhelm M, Hamilton S; ATLANTIS Trials Investigators; ECASS Trials Investigators; NINDS rt-PA Study Group Investigators. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. *Lancet*. 2004;363:768–774.
10. Schonewille WJ, Algra A, Serena J, Molina CA, Kappelle LJ. Outcome in patients with basilar artery occlusion treated conventionally. *J Neurol Neurosurg Psychiatry*. 2005;76:1238–1241.



Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION

FINAL PROOF