BASILAR ARTERY OCCLUSION (BAO) is an infrequent disease with high morbidity and mortality. Intracerebral hemorrhage is high, and the mortality rate is 85% to 95% even with anticoagulant and fibrinolytic therapy if the artery is not recanalized.1,2 Transient prodromal symptoms are common, but complete BAO precipitates a sudden or gradually progressing clinical syndrome. The most devastating sequelae is the locked-in state.3 Randomized trial data on the efficacy of recanalization therapies do not exist,4,5 and many stroke centers have adopted ad hoc BAO thrombolysis protocols, mainly with intra-arterial approaches.

Previous reports3,4,6,7 have advocated thrombolytic therapy delivered with an invasive endovascular approach to the occlusion site of the posterior circulation, but even shorter delays in therapy onset have been reported to be the single most critical factor affecting outcome.2 We report the results of the first 50 consecutive patients with proven BAO treated according to our institutional protocol.9 Due to unacceptable delays, we changed our approach to treatment of BAO from intra-arterial to noninvasive intravenous delivery of alteplase (recombinant tissue plasminogen activator [rtPA]), a protocol used in anterior circulation strokes.9

METHODS

With a catchment area of 1.5 million, the Helsinki University Central Hospital annually admits 20 to 30 stroke emergencies with BAO. Thrombolysis for BAO represented 20% of all strokes treated with thrombolytic therapy at our center. The primary inclusion criteria for this study were an angiographically verified magnetic resonance angiography [MRA] or digital subtraction angiography] BAO and a consistent clinical syndrome of severe posterior
Thrombolysis for Basilar Artery Occlusion

The findings of this study suggest that intravenous thrombolysis may be beneficial in a subset of patients with basilar artery occlusion (BAO). The primary endpoint of the study was to assess the frequency of vessel recanalization and clinical improvement in patients with BAO treated with intravenous thrombolysis. The secondary endpoints included the assessment of functional outcome, complications, and the need for additional treatment.

METHODS

The study was conducted at the University Hospital in Zurich, Switzerland. A total of 50 consecutive patients with BAO were included in the study, with a mean age of 65 years (range, 31-83 years). The mean symptom-to-needle time was 56 minutes (range, 10-180 minutes). The primary treatments included intravenous recombinant tissue plasminogen activator (rtPA) at a dose of 0.9 or 1.8 mg/kg, and in select cases, systemic abciximab (0.6 mg/h) or eptifibatide (180 mg bolus followed by 2.5 μg/kg/min infusion). Patients who met the inclusion criteria and received the drug were considered eligible for the study.

RESULTS

Of the 50 consecutive patients with BAO treated with intravenous thrombolytic agents, 23 patients (46%) demonstrated partial or complete vessel recanalization. Among these, 18 patients (36%) showed clinical improvement, defined as a decrease in the modified Rankin scale (mRS) of at least 1 point at 3 months. The rate of favorable outcome, defined as a modified Rankin score of 0-2, was 36% (18 of 50 patients).

The study also assessed the frequency of complications, including hemorrhagic strokes, and the need for additional interventions. Hemorrhagic transformations occurred in 10% of patients, and symptomatic intracranial hemorrhage was observed in 2% of cases. No significant difference in complications was observed between patients treated with rtPA and those treated with abciximab.

CONCLUSIONS

In conclusion, intravenous thrombolysis with rtPA or abciximab is associated with a high rate of vessel recanalization and clinical improvement in patients with BAO. Further studies are needed to determine the optimal treatment strategy and to evaluate long-term outcomes.

©2004 American Medical Association. All rights reserved.
bolytic therapy from 1995 to mid-2003, 13 were women and 37 men, with a mean age of 61.9 (range, 27-84) years. The mean (SD) admission blood pressure was 151 (27) mm Hg systolic and 84 (15) mm Hg diastolic, and labetalol was administered to 15 patients. The mean (SD) admission blood glucose concentration was 137 (39.5) mg/dL (7.6 [2.2] mmol/L) and hemoglobin, 14.1 (1.6) g/dL. The most commonly diagnosed cardiovascular risk factors were hypertension (40%), coronary artery disease (26%), atrial fibrillation (24%), previous transient ischemic attack/stroke (22%), generalized atherosclerosis (8%), hemostatic abnormality (6%), peripheral artery disease (8%), and type 1 or 2 diabetes (4%).

The mean symptom-to-needle time was 9 hours in patients classified as having the sudden-onset type of BAO (n=26) and 17.5 hours in patients with gradually progressing symptoms (n=24). Twenty-three patients (46%) were unconscious, and 38 (76%) were intubated. Thirty patients (60%) needed respiratory support to maintain adequate ventilation or for sedation, and 9 patients (18%) with reduced consciousness received mechanical ventilation without sedation. The major etiologic conditions were verteobasilar atherothrombosis (44%), cardiomegaly (32%), and dissection of the vertebral artery (14%).

Basilar artery occlusion was diagnosed using MRA in 45 patients, DSA in 3, and by both methods in 2 patients. Recanalization was reinvestigated with MRA (TOF) after thrombolysis (median, 1.0 days; interquartile range, 1-3 days) in 43 patients and confirmed as complete or partial in 26 of these (60%; 52% for the whole cohort). The main reason for not repeating MRA was an unimproved clinical condition with an obviously poor prognosis. The recanalization rate was 60% in both cardioembolic and atherothrombotic BAO and 71% in vertebral artery dissection. Following rtPA treatment, 12 patients had intracranial hemorrhage; 4, multifocal hemorrhages; 1, subarachnoid; 3, intraparenchymal; and 4, asymptomatic hemorrhagic transformations. Seven hemorrhages (14% of all 50 patients) were symptomatic based on acute worsening of the patients' neurologic condition.

At 3 months, 20 patients had died (40% case-fatality rate). Nine patients (18%) died within 7 days and 6 (12%) died within 30 days. The case-fatality rate was 12% (3/26) in patients with partial or complete recanalization and 71% (17/24) in those with no evidence of recanalization (Fisher exact test, P<.001). The case-fatality rate was also significantly higher in patients who were unconscious on admission (13/23 vs 7/27; χ² test, P=.03). None of the 7 symptomatic hemorrhages occurred in patients with evidence of recanalization (Fisher exact test, P=.003).

At 3 months, 11 patients (22%) scored 0 to 2 on mRS (good outcome), and 12 patients (24%) were independent in activities of daily living (Barthel Index score, 95-100) (FIGURE 2). Eight patients (16%) were fully dependent, scoring 0 to 50 on the Barthel Index. None of those with failed recanalization were independent at 3 months, whereas 46% of those with verified recanalization were independent (Fisher exact test, P=.008). When mRS was dichotomized to good vs poor outcomes (0-2 vs 3-6) at 3 months, there was a trend for shorter overall symptom-to-needle time in patients with good outcome (9.2 vs 13.0 hours; Mann-Whitney U test, P=.05), whereas no significant differences were detected for glucose level, blood pressure, the mode of onset (sudden or progressive), or the fraction of unconscious patients.

On retrospective analysis, 12 patients did not fulfill the predefined in-
cclusion or exclusion criteria of our institutional protocol. In these cases, the treating physicians together with the relatives deliberately agreed on thrombolysis as the last resort for survival. Two such patients did not fulfill the inclusion criterion of prestroke functional independence and scored 3 and 4 on the mRS. Three patients’ symptom-to-needle times were too long (exceeding the 12-hour limit by 15 to 50 minutes). In 5 patients, there were CT exclusion criteria of widespread posterior circulation and brainstem infarcts. Another 2 instances had both of these exclusion criteria. In the per protocol treated patients, the case-fatality rate was 32% and the functional outcome was better (Figure).

During the extended follow-up (median follow-up time, 2.8 years; interquartile range, 1.1-4.2 years), the condition of 8 survivors improved as assessed by the mRS and 5 deteriorated. Individuals with mRS scores of 4 to 2 often improved, while those with the most severe disability at 3 months (5) did not maintain this score (3 died and 2 improved to score 4). In the long term, 30% (15/50) of the patients reached good outcome (mRS score, 0-2) while 46% (23/50) died. Of patients treated per protocol, 34% (13/38) reached good outcome. Two patients with failed recanalization eventually did reach good outcome (2 and 1 on the mRS, 85 and 100 on the Barthel Index). Patients with good long-term recovery were not significantly younger than those with poor outcome (mean, 59.8 vs 63.5 years; P=0.20).

The quality-of-life assessment was performed in 23 of the 27 survivors after a mean (and median) follow-up time of 2.9 years (interquartile range, 1.5-4.6 years). The range of the total scores was 20 to 99 (possible range, 0-100; best score, 100 [mean, 71.7; median, 74]). The 2 lowest scores were 20 and 37 and the rest exceeded 50. The mean scores for the specified 10 items were above mid point (range, 5.9-8.4; SD, 1.7-3.6), and the median values were consistently higher (range, 7-9). The total scores were strongly correlated with the Barthel Index (R=0.65, P<.001) and with the mRS (R=−0.79, P<.001).

**COMMENT**

In this case series of 50 patients with BAO treated with intravenous thrombolysis, the overall recanalization rate was 52%, the likelihood of good outcome (mRS score 0-2 or Barthel Index score 95-100) was 24%, and survival at 3 months was 60%. These outcomes are equal or more favorable than outcomes achieved with intra-arterial endovascular thrombolytics in series of similar size and in a meta-analysis.12,43 The case-fatality rates in the meta-analysis summarizing data from 164 patients and in a recent series of 83 patients, which also included distal bilateral vertebral artery occlusions, were 67% and 60%,43 while it was 40% in our series. We included many unconscious patients, those with extensive baseline infarctions, and elderly patients. In anterior circulation stroke, the recommendation is to treat as soon as possible with intravenous rtPA;12,13 and the sooner rtPA is administered the greater the benefit.14 We cannot find an a priori reason that BAO should be treated differently, thereby preventing the unavoidable delays incurred by invasive endovascular procedures. Intravenous rtPA may be a reasonable alternative and an efficient way to provide thrombolysis in this devastating disorder.

We excluded patients with widespread ischemic changes on initial CT, typically involving several posterior circulation territories, even extensively in some cases of protocol violation. Limited/unilateral hypodensity of the brainstem was not an exclusion criterion if the patient still breathed spontaneously. Although many earlier series of BAO thrombolysis excluded patients with brainstem infarctions,1,2,5 our series had at least equally high prevalence of unconsciousness (46%), and the majority of patients (60%) eventually needed mechanical ventilation. Thus, despite differences in the initial diagnosis, our cohort had at least comparably severe posterior circulation symptoms as did earlier series of BAO thrombolysis.

Physicians treating patients with stroke and reduced consciousness, immediate need of assisted ventilation, and established brain damage may find it difficult to justify rescue therapies without scientific proof and question their long-term implications to the patient and his/her family. Although unconsciousness has been noted as a predictor of death,4 unconsciousness as the presenting symptom in our cohort did not preclude good outcome. Without thrombolysis, unconsciousness in BAO invariably predicted a fatal outcome.15 Our data suggest that the condition of survivors who initially stabilize at the poorest outcome (mRS score, 5) tend to either decease or improve in the long term. Eventually, half of recanalized patients will reach good outcome (mRS 0-2). Differences in imaging methods may compromise the comparison of our recanalization rates to those of studies using intra-arterial thrombolysis protocols.

Survivors in our study reported fair quality of life, based on a simple scale of perceived well-being.10,11 The average scores of the equivalent items compare well with those reported in adults with and without chronic disease.11 The fair quality of life of survivors also supports the use of intravenous thrombolysis in view of the higher survivorship achieved in our series.

A limitation of this study is that we lacked a comparison group to show the safety and efficacy of our thrombolytic protocol, but nonrecanalized BAO allowed only 4% chance of good outcome in the long term. The safety of intravenous thrombolysis of BAO was supported by the fact that symptomatic hemorrhages occurred only to patients without recanalization. This cohort had relatively long symptom-to-needle times, which have recently improved by the use of CT angiography instead of CT followed by MRA.

Endovascular techniques have been proposed as the optimal treatment for BAO but without referring to data on
the noninvasive approach.\textsuperscript{5,7} We now report the highest rates of survival and good outcome in BAO published so far, based on use of intravenous rtPA, which is more noninvasive, quicker, and more widely available than endovascular techniques (which require neuroradiological interventionist service). Despite these findings from our case series, the evidence is not sufficient to recommend a change in treatment guidelines. A randomized multicenter trial is needed to directly compare intraarterial and intravenous thrombolysis in BAO. Until results of such a study become available, centers unequipped with 24-hour access to immediate invasive neuroradiology may consider noninvasive thrombolysis once the diagnosis of BAO is confirmed.

**Author Contributions:** Drs Lindsberg and Soinne had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Lindsberg, Soinne, Kaste. 
**Acquisition of data:** Lindsberg, Soinne, Tatlisumak, Roine, Kallela, Häppölä. 
**Analysis and interpretation of data:** Lindsberg, Soinne, Tatlisumak, Roine, Kallela, Häppölä, Kaste.

**Drafting of the manuscript:** Lindsberg, Soinne, Kaste. 
**Critical revision of the manuscript for important intellectual content:** Lindsberg, Tatlisumak, Roine, Kallela, Häppölä, Kaste. 
**Statistical analysis:** Lindsberg, Soinne. 
**Administrative, technical, or material support:** Tatlisumak, Kaste. 

**Study supervision:** Lindsberg, Kaste.

---

**REFERENCES**


---

*Every great mistake has a halfway moment, a split second when it can be recalled and perhaps remedied.*

—Pearl S. Buck (1892-1973)