Basilar artery occlusion (BAO) is a relatively infrequent but catastrophic disease with dismal natural course, carrying 85% to ≈95% mortality even during anticoagulant and fibrinolytic therapy if not recanalized.\(^1,2\) The disease also poses a diagnostic challenge because it often starts with transient nonspecific prodromal symptoms, whereas complete BAO precipitates a sudden or gradually progressing multifaceted clinical syndrome consisting of bilateral motor weaknesses, bulbar symptoms, and disturbances of the visual system, motor coordination, and balance, as reviewed recently.\(^3\) To establish firm diagnosis, vascular imaging with computed tomographic or magnetic resonance angiography or conventional angiography is necessary. The most devastating disease phenotype is the locked-in state, which has been demonstrated to be reversed by rapid recanalization.\(^4\) Because of the infrequency and the clinical variability of the disease, it has been difficult to obtain evidence-based data on the true efficacy of recanalization therapies.\(^5,6\) Instead of witnessing the natural course, some stroke centers have adopted interventional protocols to manage BAO, mostly with intra-arterial thrombolytics. In vertebrobasilar occlusive disease, numerous reports advocate local delivery of the thrombolytic agent.\(^5,7\) Several studies also found the delay in therapy onset to be a critical prognostic factor, apart from recanalization.\(^6,8\) Introduction of an intra-arterial catheter to administer thrombolytics locally may at times be difficult and time-consuming, considering the often stenosed and elongated arteriosclerotic vertebral arteries, and can increase treatment delay if considered the sole therapy mode. Therefore, some centers have adopted routinely the intravenous approach similar to that used in the anterior circulation strokes.\(^5,10\) The outcome reached with this protocol combining recombinant tissue plasminogen activator (rtPA) with heparin infusion was reported recently to be similar to that achieved with endovascular therapy\(^2,5,6\) (Figure).

Patients admitted in severe neurological condition, with reduced consciousness and already permanent brain tissue damage, pose a dilemma to emergency medical personnel who need to weigh different therapeutic options in the face of uncertain long-term prognosis. Thrombolysis might save the life, but what kind of quality of life will follow? Vertebrobasilar cerebrovascular disease may provide the most extreme physical deprivation while leaving the faculty for contemplation as good as intact. The recent analysis of the delayed-phase outcome after BAO thrombolysis suggests that on the long term, survivors who initially reach the worst functional outcome (modified Rankin Scale 5) will subsequently either decease or improve.\(^10\) Eventually, more than half of those who recanalize will acquire functional independence. Furthermore, the perceived quality of life of the survivors seems at least fair, correlating with the level of functional independence.\(^10\)

What are the risks of recanalization therapy? The rate of hemorrhagic complications in BAO thrombolysis is ≈8%, thus similar to that of rtPA therapy of anterior circulation stroke.\(^11\) Furthermore, the symptomatic hemorrhages tend to occur in patients without recanalization and poor prognosis.\(^10\) Contrary to large anterior circulation strokes, reperfusion injury and brain edema do not seem to be frequent problems in post-thrombolytic reversal of BAO. These considerations may give emergency medical personnel some latitude in therapeutic decision in favor of thrombolysis. Clearly, further work is needed to identify baseline predictors of poor outcome after thrombolysis.

“Time is brain” in the posterior circulation, as well as in the anterior territory, but available observational studies suggest that recanalization therapies for BAO can potentially benefit patients up to 24 to 36 hours after symptom onset.\(^12\) BAO as a disease can be divided into 2 clinical phenotypes: the progressing type, in which severe posterior circulation symptoms are preceded by even days of gradual deterioration of neurological function, and the sudden onset type, with dense presenting symptoms often associated with reduced consciousness. Using the intravenous route, some investigators used a protocol with a time window of 48 hours in the first disease phenotype and 12 hours in the latter.\(^10\) Although the optimal time windows for thrombolytic therapy will probably not be uniform even within these phenotypes, it would seem unjustified to apply in BAO the same time criteria as used in...
Studies with major cohort size (>40) reporting the results of thrombolytic therapy of BAO with predominantly intra-arterial and intravenous route of administration. The study by Levy et al. is a meta-analysis combining several previous studies, including the first 2. The study by Eckert et al also included bilateral vertebral occlusions. To confirm recanalization, studies used variable methodologies, which may hinder direct comparison. Furthermore, variable thrombolytic compounds were used in different studies. Note added in print: In 2004, Arnold et al. reported 58% survival and 35% good outcome in 40 patients treated intra-arterially within 12 hours of symptom onset.

The anterior circulation strokes.\textsuperscript{13} Instead, imaging methods sensitive for irreversible brain damage as well as perfusion state should be used to determine whether there still is viable brain tissue to be salvaged, no matter how long the symptom duration.\textsuperscript{12}

The mortality rates in the meta-analysis summarizing 164 patients and in a recent series of 83 patients, including distal bilateral vertebral artery occlusions,\textsuperscript{5,6} were 67% and 60%, and 40% in the recently reported series with intravenous approach.\textsuperscript{10} Although randomized controlled evidence is missing, the results of these case series studies using intravenous and intra-arterial routes of thrombolytic delivery suggest that the rates of recanalization, survival, and the likelihood of independent functional outcome are not dependent on the route of administration (Figure).\textsuperscript{1,2,5,6,9,10,14} Typically, roughly half of the patients with either route for recanalization therapy will succeed, and roughly half of those will have good outcome. In the anterior circulation, the standard recommendation is to treat ischemic stroke as soon as possible with intravenous alteplase.\textsuperscript{13} Is there an a priori physiological or biological reason for the acute occlusions in the posterior circulation to be more amenable to invasive endovascular procedures than in the anterior circulation? Based on current observational evidence, it would seem prudent to start thrombolysis with either endovascular or intravenous route as soon as possible to prevent the imminent devastating outcome.

In most stroke centers without an invasive neuroradiologist on call, the noninvasive therapy can be initiated with considerably less delay than the invasive approach. Therefore, we consider that the “jury is still out” on deciding which route of therapy is the most practical, cost-effective, and efficacious. Most likely, this decision will, after all, require a comparative randomized trial. Future study will also show the safety and efficacy of stenting or mechanical clot disruption procedures, which might benefit especially those patients with restenosis or incomplete post-thrombolytic vessel patency.\textsuperscript{15} Until such studies become available, centers unequipped with 24-hour access to immediate invasive neuroradiological expertise will do a favor to their BAO patients and their relatives by treating them noninvasively with thrombolytic therapy initiated as soon as the diagnosis is confirmed.

References


Key Words: Advances in Stroke, Basilar, Outcome, Thrombolyis