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Cerebrovascular Disorders (D Jamieson, Section Editor)

Basilar Artery Occlusion: Diagnosis and Acute Treatment

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Abstract

Purpose of review To provide the latest updates in the diagnosis, management, and prognosis in patients with basilar artery occlusion (BAO).
Recent findings The diagnosis of BAO requires a high index of suspicion among patients with sudden onset depressed level of consciousness, quadraparesis (or hemiparesis), and cranial nerve dysfunction. Computed topography with angiography is currently the diagnostic modality of choice for the diagnosis of BAO. Given the often catastrophic nature of BAO, intravenous thrombolysis combined with mechanical thrombectomy should be offered in eligible patients. Despite a lack of data from randomized clinical trials, good outcomes are possible, especially in patients without early evidence of infarction.
Summary Aggressive treatment with intravenous thrombolysis and mechanical thrombectomy should be considered in eligible patients with BAO, but there remains a dearth of information from randomized clinical trials.

Introduction

Basilar artery occlusion (BAO) is an uncommon form of ischemic stroke that is often associated with catastrophic neurological outcomes. However, with recent advancements in neuroimaging and progress in intravenous thrombolytics and endovascular therapy, we are now witnessing an era of great strides with regard to both the diagnosis and treatment of BAO. The goal of this review is to provide an overview of BAO with a particular focus on landmark studies and the most up-to-date clinical research.

Epidemiology and pathophysiology

BAO accounts for approximately 1% of all ischemic strokes, although the incidence may be increasing with time [1]. A recent population-based study of 1157 patients with large vessel occlusions from 2012 to 2015 in the USA estimated that the incidence of BAO is 4 patients per 100,000 per year [2]. In the largest prospective international registry study to date, Basilar Artery International Cooperation Study (BASICS), the average age was 63 and 37% were women [3]. Similar to ischemic stroke in general, patients with BAO often have typical vascular risk factors [3, 4]. BAO may be caused by various stroke mechanisms. In BASICS, the two most common mechanisms are cardioembolism (36%) and large artery atherosclerosis (35%), though other mechanisms such as dissection and vasculopathy account for a small percentage of cases [3, 5, 6].

Clinical features

Clinical presentation

The hallmark symptoms of BAO are (1) reduced consciousness, (2) cranial nerve dysfunction, and (3) quadriparesis. Reduced consciousness is attributed to ischemia of the reticular activating system or thalami [7]. Quadriparesis (or hemiparesis) is secondary to the affected corticospinal tracts. Cranial nerve dysfunction is due to the affected pontine and/or midbrain nuclei and/or the cranial nerves themselves. One or more of these symptoms should raise suspicion for BAO and lead to emergent brain and intracranial vessel imaging. Notably, "crossed signs" may be present and can help localize symptoms to the brainstem. The presence of ipsilateral cranial nerve involvement and contralateral hemiplegia should immediately raise concern for brainstem involvement [8]. Symptoms can be sudden onset (apoplectic) or progressive/stuttering over hours to days; classically, a stuttering progressive presentation may suggest an atherosclerotic/thrombotic origin whereas sudden onset acute symptoms are typically associated with embolic phenomenon. Notably, patients with unexplained depressed consciousness should be carefully evaluated for signs of brainstem ischemia. Any patient with unexplained depressed consciousness and evidence of cranial nerve dysfunction, weakness, or posturing should undergo emergent imaging to rule out basilar artery occlusion.

Syndromes

Two classic syndromes have been described based on the location of occlusion in the basilar artery:

1. Locked-in syndrome: Due to a mid-basilar clot at the level of the pons, this syndrome is characterized by complete quadraparesis, facial diplegia, and inability to move the eyes with sparing of vertical eye movements. In addition, consciousness is preserved [9].
2. Top of the basilar syndrome: Due to a distal basilar occlusion, this syndrome is characterized by sudden loss of consciousness due to injury to the bilateral thalami. Vision loss including cortical blindness is common due to

injury to the bilateral occipital lobes. Motor function may be preserved due to lack of injury to the corticospinal tracts [10].

Diagnostic work-up

The differential diagnosis of BAO is broad (Table 1). Given the increased availability of vessel imaging, we recommend a very low threshold to evaluate for BAO in any patient with unexplained depressed level of consciousness, or signs and symptoms of brainstem ischemia.

Diagnostic imaging modalities

Initial imaging should include a non-contrast CT and CT angiography (CTA). On non-contrast CT, a hyperdense basilar artery sign can be an indicator of BAO. In one study of 102 patients, gross visual detection of a hyperdense basilar sign had a sensitivity of 81% and a specificity of 91% [15]. Caution should be applied in over-interpreting basilar arteries in older patients who are more likely to have mural calcification which may lead to false-positives.

We recommend CTA as the initial diagnostic modality to identify BAO. CTA is quick, easy to perform, and increasingly available throughout the USA in most community and tertiary care hospitals [16] (Fig. 1). Furthermore, CTA has an excellent sensitivity compared with the gold standard, digital subtraction angiography at identifying BAO, and is cost-effective [17–19]. In addition, CTA allows for evaluation of atherosclerosis and can help differentiate a BAO due to embolus versus that due to large artery atherosclerosis.

CT and CTA can be used to evaluate the extent of early ischemia in the posterior circulation and may guide interventional decisions and help predict outcomes. The posterior circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS) allots the posterior circulation 10 points with subtraction for early ischemic changes in each affected territory, specifically 2 points for midbrain, 2 points for pons, and 1 point each for left and right thalamus, cerebellum, and PCA-territory respectively (Fig. 2) [20]. The pc-ASPECTS score has been validated to predict functional outcome in patients with BAO based on source images of CTA (and also diffusion MRI) [21, 22]. Patients with pc-ASPECTS ≥ 8 have the greatest chance of good functional

Table 1. Differential diagnoses

-Bilateral ischemic strokes
-Brainstem hemorrhage
-Subarachnoid hemorrhage
-Seizures and post-ictal state [11, 12, 13]
-Drug overdose
-Toxic-metabolic encephalopathy, particularly when the acuity of onset is unknown
-Brain mass
-Guillain Barre syndrome [14]
-Botulism
-Bickerstaff encephalitis
-Central pontine myelinolysis/osmotic demyelination syndrome

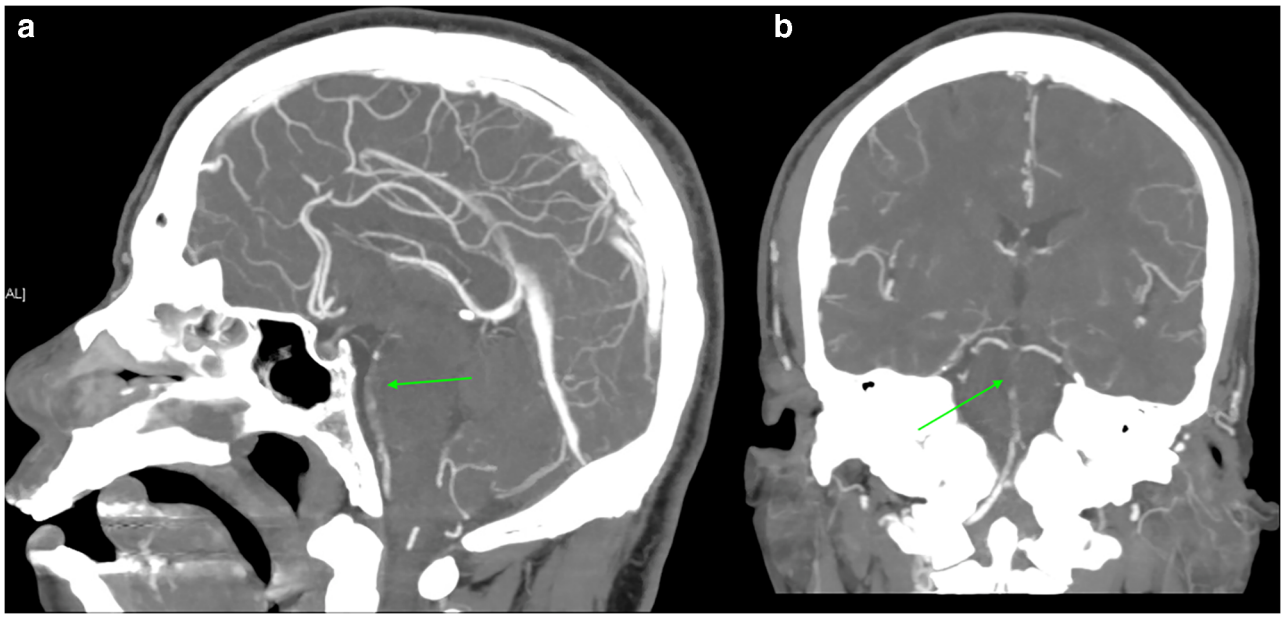

Fig. 1. Basilar artery occlusion (arrows) visualized on the CTA, sagittal (**a**) and coronal (**b**) views.

outcomes with emergent treatments including intravenous thrombolysis and mechanical thrombectomy [21–26]. Although CT perfusion has been shown to be instrumental in distinguishing which patients with ischemic strokes of the anterior circulation will benefit from mechanical thrombectomy up to 24 h after last known well [27, 28], its use in BAO is uncertain.

MRI diffusion-weighted imaging is superior to CT for evaluation of acute posterior fossa ischemia [29–31]. It is most useful as an adjunct or alternative to CT to assess the extent of injury and/or confirm the diagnosis of BAO. MRI can

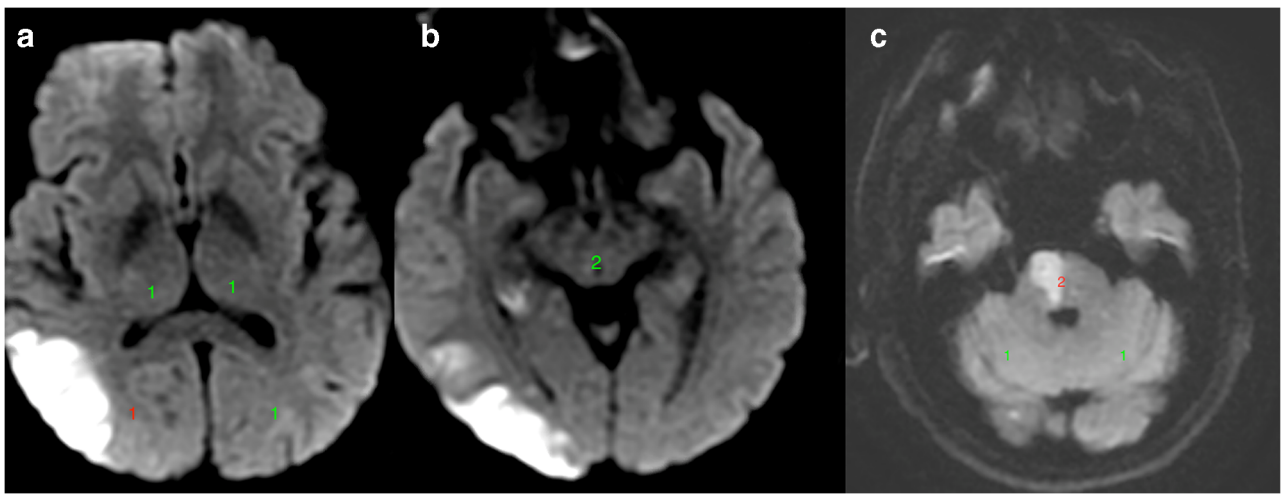

Fig. 2. Example of the posterior circulation Acute Stroke Prognosis Early CT score (pc-ASPECTS). The numbers in red represent infarcted tissue and loss of points. Conversely, the numbers in green represent preserved tissue with no loss of points. Loss of 1 point in right PCA territory with preserved bilateral thalami and left PCA territory (**a**); preserved 2 points in midbrain (**b**); loss of 2 points in pons with preserved points in bilateral cerebellum. Total pc-ASPECTS score equals 7 (**c**).

be used to calculate the pc-ASPECTS using DWI and assess the degree of DWI/FLAIR mismatch, which may suggest ischemic but not infarcted tissue, both of which may help guide decisions regarding delayed recanalization [32]. Extensive infarction may indicate poor prognosis regardless of recanalization success and conversely, patients with limited infarction (high pc-ASPECTS or significant DWI/FLAIR mismatch) are more likely to benefit from reperfusion therapy [30]. Besides pc-ASPECTS, other scoring systems have been developed to try to quantify functional outcomes using mechanical thrombectomy [32] including the brainstem DWI lesion score [33] which quantifies ischemia on a scale of 0–22; although, it is cumbersome to use. Global DWI lesion volume does not consistently correlate with severity of symptoms [34] and is not as effective at predicting outcomes as the validated scoring tools.

Overall, based on the available literature, we recommend that all patients with suspected or possible BAO undergo non-contrast CT followed by CTA. In patients with BAO beyond 6 h from last known well time, we recommend evaluating the extent of posterior circulation infarction using preferentially pc-ASPECTS or MRI DWI/FLAIR mismatch to assess potentially salvageable tissue and guide decisions regarding mechanical thrombectomy (Fig. 3).

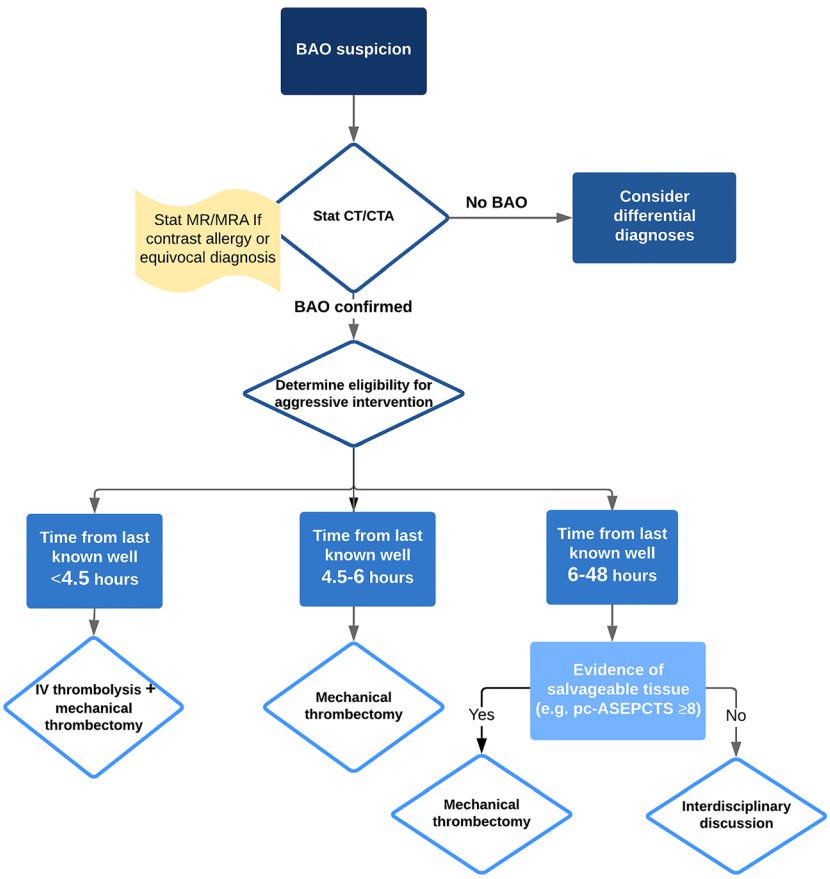

Fig. 3. Flowsheet demonstrating the acute management of patients with basilar artery occlusion (BAO).

Acute management

Unlike ischemic strokes of the anterior circulation, there is a dearth of data from randomized controlled studies evaluating the efficacy of treatments for ischemic strokes of the posterior circulation. Treatment of BAO strokes is extrapolated from studies that included either ischemic strokes of any artery or those specifically of the anterior circulation. Here we review the principles of BAO management and discuss interventions in the context of (1) antithrombotics, (2) intravenous and intra-arterial thrombolysis, and (3) mechanical thrombectomy and bridging therapy.

Antithrombotics

Antithrombotics (antiplatelet agents such as aspirin or anticoagulants such as heparin) have classically been used for less severe strokes [3, 35] or when patients with BAO are not candidates for other interventions. Data suggest that when antithrombotics are used without another more aggressive therapy (thrombolysis or mechanical thrombectomy), patients with BAO have poor outcomes. In the BASICS registry, after adjustment for National Institutes of Health Stroke Scale (NIHSS) and vascular risk factors, patients with a severe deficit had a significantly worse outcome when treated with antithrombotics alone compared with those treated with thrombolysis and/or mechanical thrombectomy [3].

Thrombolysis (intravenous and intra-arterial)

Pharmacologic thrombolysis appears to be effective at improving outcomes and reducing mortality in patients with BAO [36, 37]. Whether there is superiority of intravenous to intra-arterial thrombolysis is uncertain. It is difficult to directly compare intravenous versus intra-arterial thrombolysis using the BASICS data as their intra-arterial therapy or "IAT" group refers to both intra-arterial thrombolysis and mechanical thrombectomy. Nevertheless, patients with mild-moderate deficits had better outcomes with intravenous thrombolysis than "IAT" whereas patients with severe deficits had similar outcomes when either intravenous therapy or "IAT" was used. This difference may be explained by findings that suggest the benefit of intravenous thrombolysis depends on clot location, with the best results in those with top-of-the-basilar occlusions [38]. Given no clear superiority of intra-arterial thrombolysis over intravenous thrombolysis and the ease of administration with the latter, we recommend use of intravenous thrombolysis as the initial treatment for patients with BAO who present within 4.5 h of last known well time.

Mechanical thrombectomy and bridging therapy

Despite the lack of randomized controlled trials, systematic meta-analyses of case series and registry data indicate that mechanical thrombectomy provides the optimal potential for improved outcomes in patients with BAO [39, 40, 41•, 42]. Predictors of good outcomes among patients undergoing mechanical thrombectomy appear to have younger age (< 60), shorter time from symptom onset to recanalization, successful recanalization, absence of prior use of antithrombotic medication (i.e., individuals without concomitant vascular comorbidities), admission NIHSS < 13, better

collateral status [43–45], and lack of established infarction. Mechanical thrombectomy appears superior to intravenous thrombolysis alone; however, it is uncertain whether there is additional benefit when mechanical thrombectomy is combined with thrombolysis [3, 41•]. Nevertheless, there appears to be no evidence of increased mortality or symptomatic hemorrhage when combining mechanical thrombectomy and intravenous thrombolysis and thus, despite the unclear added benefit, given the potential for improved recanalization, easy feasibility, and low risk, intravenous thrombolysis, and mechanical thrombectomy should be offered in combination whenever possible [46, 47].

Timing of intervention

Similar to other forms of ischemic stroke, early recanalization appears to be associated with an increased likelihood of good functional outcome in patients with BAO [48]. Unlike with ischemic stroke of the anterior circulation, multiple studies of BAO have used intravenous thrombolysis up to 24 h from last known well time [49]. Notably, there was one study that suggested favorable outcomes when intravenous thrombolysis was given up to 48 h from last known well time in patients with BAO who lacked extensive baseline ischemia [23]. Hypothetically, as compared with anterior circulation strokes, strokes of the posterior circulation may be less susceptible to hemorrhagic transformation due to collateral circulation patterns and lesser infarct volume [34, 49]. While such an extended time window from last known well using intravenous thrombolysis is not the current standard of care, this study highlights the potential for improved outcomes with delayed aggressive intervention when the volume of completed posterior circulation infarction is limited and salvageable tissue is present. Similarly, data from the WAKE-UP and EXTEND trials suggest that intravenous thrombolysis may be beneficial beyond 4.5 h from last known well time in patients with strokes of the anterior circulation who have salvageable tissue [50••, 51••].

Based on the available literature, among patients with BAO, we recommend that intravenous thrombolysis be used in all patients within 4.5 h of last known well time and mechanical thrombectomy in all patients within 6 h of last known well time. In addition, intravenous thrombolysis beyond the standard 4.5 h can potentially be considered in the absence of extensive completed infarction although we favor mechanical thrombectomy in this context until more robust data is available. We recommend mechanical thrombectomy in all patients with evidence of salvageable tissue (such as that demonstrated by a pc-ASPECTS ≥ 8 or significant DWI/FLAIR mismatch) within 48 h of last known well time. In contrast, for patients with evidence of more extensive infarction/less salvageable tissue, mechanical thrombectomy within 48 h of last known well time may still be considered but should involve an interdisciplinary discussion including neurology, interventional neurology, and radiology to assess the likelihood of benefit in light of the patient's age, vascular anatomy, and medical comorbidities.

Prognosis

BAO has traditionally been a morbid disease [52]. BASICS data suggest that despite intervention, mortality or significant disability (modified Rankin

Scale 4–5) ranges from 37 to 83% [3]. However, diagnosis is often delayed and these data are prior to the advent of more modern endovascular devices and widespread use of the radiographical scoring systems. More recent data suggest that good outcomes are still possible, especially in patients with a pc-ASPECTS ≥ 8 who are offered thrombolysis or mechanical thrombectomy. In addition, younger age and shorter time to recanalization have been shown to be independent predictors of good outcome [38, 43, 44]. NIHSS on presentation does not correlate as well with disease burden and is known to be weighted toward anterior circulation stroke symptoms and is thus a less robust predictor of outcome in patients with BAO [29].

Ethical considerations

The devastating symptoms and debilitating nature of BAO raises many ethical considerations. In particular, the locked-in syndrome is a feared end result of BAO. Healthy individuals and medical professionals frequently assume the quality of life of locked-in patients to be substantially poor and not worth living [53], but in contrast to typical belief, studies have suggested that quality-of-life scores among patients with locked-in syndrome are often in the same range as in age-matched healthy individuals [54] and the request for euthanasia is infrequent [53, 54]. Nevertheless, it is reasonable to consider that this positive introspection may be a coping mechanism. Significant recovery of severe deficit such as locked-in syndrome is rare but interestingly has been documented in case report with return of ADLs, independent walking, and comprehensible speech [55].

Conclusions

BAO is a devastating entity with potentially devastating clinical outcomes. A high index of suspicion must be utilized in order to minimize delay in diagnosis. We recommend CTA as the initial imaging modality to evaluate for BAO and to help guide decisions regarding intervention. Although outcomes are generally poor, good functional outcomes are possible when intravenous thrombolysis and mechanical thrombectomy are used in patients without significant baseline ischemia.

Compliance with Ethical Standards

Conflict of Interest

Alexander E. Merkler reports a grant from American Heart Association (Grant number: 18CDA34110419), as well as a grant from Leon Levy Foundation, outside the submitted work.

Stephanie L. Buchman declares no potential conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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