



# Editorial: Challenges in Posterior Circulation Ischemic Stroke

Volker Puetz<sup>1,2\*</sup>, Daniel Strbian<sup>3</sup>, Thanh N. Nguyen<sup>4</sup> and Simon Nagel<sup>5</sup>

<sup>1</sup> Department of Neurology, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany, <sup>2</sup> Dresden Neurovascular Center, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany, <sup>3</sup> Department of Neurology and Neurosciences, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland, <sup>4</sup> Department of Neurology and Radiology, Boston Medical Center, Boston University School of Medicine, Boston, MA, United States, <sup>5</sup> Department of Neurology, Heidelberg University Hospital, Heidelberg, Germany

**Keywords:** posterior circulation stroke, basilar artery occlusion, endovascular treatment, prognosis, anatomy

## Editorial on the Research Topic

### Editorial: Challenges in Posterior Circulation Ischemic Stroke

Posterior circulation ischemic stroke comprises an estimated 15–20% of all ischemic strokes and differs from anterior circulation stroke in many ways. An acute occlusion of the basilar artery can trigger one of the most devastating ischemic stroke syndromes with reduced level of consciousness, loss of brainstem reflexes and tetraplegia. However, posterior circulation stroke is frequently difficult to diagnose clinically due to varying symptoms and signs like isolated vertigo and dizziness. Knowledge about specific brainstem symptoms and syndromes can aid early clinical recognition and thus, rapid initiation of appropriate diagnostic and therapeutic approaches (1). Due to the limited diagnostic accuracy of CT-based neuroimaging in the posterior circulation, magnetic resonance imaging is the preferred method for radiological confirmation of posterior circulation ischemia, however has limited availability and can be false-negative in the hyperacute setting (2). The anatomy of the posterior circulation is highly variable and stroke syndromes within have greater etiologic variability compared to the anterior circulation. Consequently, patients with acute posterior circulation ischemia seem to respond differently to acute revascularization therapies like intravenous thrombolysis (IVT) and endovascular therapy (EVT) (3). While mechanical thrombectomy has become the new gold standard in acute recanalization therapy for anterior circulation large vessel occlusions (aLVO), its efficacy and safety in acute basilar occlusion is still under debate despite recent completion of two randomized controlled trials (4–6). In parallel to aLVO where the Alberta Stroke Program Early CT Score (ASPECTS) identifies patients with benefit from EVT, imaging may play an important role to identify patients who benefit from such therapies in posterior circulation stroke and particularly basilar artery occlusion (7–11). Moreover, while perfusion imaging can facilitate patient selection for recanalization therapies in the anterior circulation, particularly in patients with unknown or late time-window, its role and relevance in posterior circulation ischemic stroke is currently less well-described (12, 13).

In the context of this clinical and scientific background, this Research Topic covers relevant aspects of posterior circulation ischemic stroke. Three main aspects are discussed.

First, the clinical diagnosis of posterior circulation ischemic stroke is frequently difficult due to varying and non-specific symptoms. The narrative review by Hoyer and Szabo summarizes important pitfalls in its diagnosis in the prehospital and emergency department setting, and provides strategies and approaches to improve speed and accuracy of its recognition and early management. Data on anatomical variants, i.e., bilateral vertebral hypoplasia as a potential risk factor for ischemic stroke, posterior fossa venous drainage and mechanisms of posterior circulation

## OPEN ACCESS

### Edited and reviewed by:

Jean-Claude Baron,  
University of Cambridge,  
United Kingdom

### \*Correspondence:

Volker Puetz  
volker.puetz@uniklinikum-dresden.de

### Specialty section:

This article was submitted to  
Stroke,  
a section of the journal  
Frontiers in Neurology

**Received:** 05 October 2021

**Accepted:** 18 October 2021

**Published:** 17 November 2021

### Citation:

Puetz V, Strbian D, Nguyen TN and Nagel S (2021) Editorial: Challenges in Posterior Circulation Ischemic Stroke. *Front. Neurol.* 12:789836. doi: 10.3389/fneur.2021.789836

blood flow regulation and its implications for posterior circulation stroke are detailed in the articles by Hsu et al., De Miquel, and Tamayo and Siepmann, respectively.

Second, several articles of the collection cover novel aspects of acute treatment in patients with posterior circulation ischemic stroke and particularly basilar artery occlusion. Known data for IVT in late or unknown time window mostly focus on patients with anterior circulation ischemic stroke. It is therefore reassuring that the safety and efficacy of IVT in this scenario seem similar in patients with posterior circulation ischemic stroke, as addressed in the article by Macha et al. Their findings may inform clinicians in the usage of alteplase beyond 4.5 h from symptom onset in selected patients with posterior circulation ischemic stroke. Scientifically, however, more data on this topic is needed until a general recommendation can be made.

Given the unproven benefit of EVT on improved functional outcome in patients with basilar artery occlusion, the meta-analysis by Mbroh et al. suggests that EVT in posterior circulation large vessel occlusion (pLVO) may be comparably sufficient in obtaining favorable functional outcome compared with aLVO. These findings parallel results of the recently published BASILAR registry, where patients who received EVT within 24 h after the estimated time of basilar artery occlusion had an improved chance to achieve a favorable functional outcome compared to patients who received best medical management only (14). In contrast, in the analysis of State-wide stroke registry data by Gruber et al., additional EVT was not superior compared to best medical management alone in patients with acute basilar artery occlusion. One must keep in mind that the results of the above mentioned analyses originate from non-randomized studies and are therefore limited in their informative value.

Patients with acute basilar artery occlusion who present with coma are unlikely to have a good clinical outcome. However, Ritvonen et al. demonstrate in their study that one fifth (21/103, 20.4%) of these patients can still achieve a favorable functional outcome. Moreover, recanalization and a lesser extent of early ischemic changes on neuroimaging [i.e., posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) > 8] were associated with favorable outcome in this study. These results confirm findings from a previous analysis of the BASICS registry data and underline the prognostic importance of imaging in patients with basilar artery occlusion (9, 15, 16).

As EVT is available in specialized stroke centers, patients with basilar artery occlusion are frequently transferred from remote hospitals in a drip-and-ship approach. The article by Alemseged and Campbell summarizes current data on tenecteplase as an alternative thrombolytic agent with greater fibrin specificity and longer half-life compared with alteplase in this scenario. As they recently demonstrated, tenecteplase achieved higher reperfusion rates in patients with large vessel occlusion including basilar artery occlusion (17, 18).

The effectiveness of EVT in aLVO has primarily been shown for patients with ICA or M1-segment occlusions, but is now

also frequently performed in patients with more distal (e.g., M2-segment) occlusions. Whether EVT is safe and effective in patients with posterior cerebral artery (PCA) occlusion has been analyzed in the article by Herweh et al. as a collaboration of four major stroke centers. Their main conclusion was that EVT in isolated posterior cerebral artery occlusion appears safe and at least immediately effective, however further data from prospective or randomized studies are needed, especially on the longterm outcome activities of daily living. EVT for fetal PCA thrombectomy is another posterior circulation frontier that is also being explored in patients presenting with disabling stroke (19). Lastly, Kaiser et al. show that a regular thrombus surface (defined as smoothly straight, convex, or concave) is associated with a higher chance for successful first pass reperfusion in patients with acute basilar artery occlusion which confirms previous findings in patients with aLVO (20).

Third, as outlined above, the stroke etiology in patients with basilar artery occlusion seems more heterogenous compared to aLVO. Artery-to-artery embolism and intracranial atherosclerotic disease play an important role. Characterization of such stenoses is important for acute treatment decision making and to tailor therapy in secondary stroke prevention. By using 3T high-resolution magnetic resonance imaging in patients with recent posterior circulation stroke due to intracranial vertebrobasilar atherosclerotic disease with 70–99% stenosis, Hou et al. demonstrated that intraplaque enhancement and vertebral artery involvement were associated with artery-to-artery embolism. Questions arise whether these patients may benefit from more aggressive antiplatelet regimens.

In conclusion, this issue of *Frontiers in Neurology* provides an integrated overview of the hot topics in the field of posterior circulation ischemic stroke. Emerging from the article collection is a complex picture with focus on the anatomical, clinical and pathophysiological correlates of posterior circulation stroke, acute treatment including intravenous and endovascular therapies. The studies published in this issue emphasize the need for further research to better delineate pathophysiological aspects, clinical recognition and treatment decision making in these patients, in the wake of the BASICS and BEST basilar artery occlusion trials (4, 5, 21). Stratification of patient selection by severity of disease, imaging including multimodal CT or MRI, introduction of novel thrombolytics (i.e., tenecteplase) may play an important role in modifying the natural history of posterior circulation stroke. We look forward to learning the results of this research in the future.

## AUTHOR CONTRIBUTIONS

VP drafted the manuscript. DS, TN, and SN revised the manuscript for intellectual content. All authors contributed to the article and approved the submitted version.

## REFERENCES

- Salerno A, Strambo D, Nannoni S, Dunet V, Michel P. Patterns of ischemic posterior circulation strokes: a clinical, anatomical, and radiological review. *Int J Stroke*. (2021) 2021:17474930211046758. doi: 10.1177/17474930211046758
- Saber Tehrani AS, Kattah JC, Mantokoudis G, Pula JH, Nair D, Blitz A, et al. Small strokes causing severe vertigo: frequency of false-negative MRIs and nonlacunar mechanisms. *Neurology*. (2014) 83:169–73. doi: 10.1212/WNL.0000000000000573
- Baik SH, Park HJ, Kim JH, Jang CK, Kim BM, Kim DJ. Mechanical thrombectomy in subtypes of basilar artery occlusion: relationship to recanalization rate and clinical outcome. *Radiology*. (2019) 291:730–7. doi: 10.1148/radiol.2019181924
- Liu X, Dai Q, Ye R, Zi W, Liu Y, Wang H, et al. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion (BEST): an open-label, randomised controlled trial. *Lancet Neurol*. (2020) 19:115–22. doi: 10.1016/S1474-4422(19)30395-3
- Langezaal LCM, Van Der Hoeven E, Mont'alverne FJA, De Carvalho JFF, Lima FO, Dippel DWJ, et al. Endovascular therapy for stroke due to basilar-artery occlusion. *N Engl J Med*. (2021) 384:1910–20. doi: 10.1056/NEJMoa2030297
- Nguyen TN, Strbian D. Endovascular therapy for stroke due to basilar artery occlusion: a BASIC challenge at BEST. *Stroke*. (2021) 52:3410–3. doi: 10.1161/STROKEAHA.121.035948
- Puetz V, Sylaja PN, Coutts SB, Hill MD, Dzialowski I, Mueller P, et al. Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. *Stroke*. (2008) 39:2485–90. doi: 10.1161/STROKEAHA.107.511162
- Puetz V, Dzialowski I, Hill MD, Demchuk AM. The alberta stroke program early CT score in clinical practice: what have we learned? *Int J Stroke*. (2009) 4:354–64. doi: 10.1111/j.1747-4949.2009.00337.x
- Nagel S, Herweh C, Kohrmann M, Huttner HB, Poli S, Hartmann M, et al. MRI in patients with acute basilar artery occlusion - DWI lesion scoring is an independent predictor of outcome. *Int J Stroke*. (2012) 7:282–8. doi: 10.1111/j.1747-4949.2011.00705.x
- Strbian D, Sairanen T, Silvennoinen H, Salonen O, Kaste M, Lindsberg PJ. Thrombolysis of basilar artery occlusion: impact of baseline ischemia and time. *Ann Neurol*. (2013) 73:688–94. doi: 10.1002/ana.23904
- Goyal M, Demchuk AM, Hill MD. Endovascular therapy for ischemic stroke. *N Engl J Med*. (2015) 372:2366. doi: 10.1056/NEJMoa1414905
- Pallesen LP, Gerber J, Dzialowski I, Van Der Hoeven EJ, Michel P, Pfefferkorn T, et al. Diagnostic and prognostic impact of pc-ASPECTS applied to perfusion CT in the basilar artery international cooperation study. *J Neuroimaging*. (2015) 25:384–9. doi: 10.1111/jon.12130
- Capasso R, Vallone S, Serra N, Zelent G, Verganti L, Sacchetti F, et al. Qualitative versus automatic evaluation of CT perfusion parameters in acute posterior circulation ischaemic stroke. *Neuroradiology*. (2021) 63:317–30. doi: 10.1007/s00234-020-02517-6
- Writing Group for the BG, Zi W, Qiu Z, Wu D, Li F, Liu H, et al. Assessment of endovascular treatment for acute basilar artery occlusion via a nationwide prospective registry. *J Am Med Assoc Neurol*. (2020) 77:561–73. doi: 10.1001/jamaneurol.2020.0156
- Puetz V, Khomenko A, Hill MD, Dzialowski I, Michel P, Weimar C, et al. Extent of hypoattenuation on CT angiography source images in basilar artery occlusion: prognostic value in the Basilar Artery International Cooperation Study. *Stroke*. (2011) 42:3454–9. doi: 10.1161/STROKEAHA.111.622175
- Pallesen LP, Khomenko A, Dzialowski I, Barlinn J, Barlinn K, Zerna C, et al. CT-angiography source images indicate less fatal outcome despite coma of patients in the Basilar Artery International Cooperation Study. *Int J Stroke*. (2017) 12:145–51. doi: 10.1177/1747493016669886
- Campbell BCV, Mitchell PJ, Churilov L, Yassi N, Kleinig TJ, Dowling RJ, et al. Effect of intravenous tenecteplase dose on cerebral reperfusion before thrombectomy in patients with large vessel occlusion ischemic stroke: the EXTEND-IA TNK part 2 randomized clinical trial. *J Am Med Assoc*. (2020) 323:1257–65. doi: 10.1001/jama.2020.1511
- Alemseged F, Ng FC, Williams C, Puetz V, Boulouis G, Kleinig TJ, et al. Tenecteplase vs. alteplase before endovascular therapy in basilar artery occlusion. *Neurology*. (2021) 96:e1272–7. doi: 10.1212/WNL.00000000000011520
- Abdalkader M, Sahoo A, Shulman JG, Sader E, Takahashi C, Kaliev A, et al. Acute occlusion of the fetal posterior cerebral artery: diagnosis and management paradigms. *Neuroradiol J*. (2021) 2021:19714009211019383. doi: 10.1177/19714009211019383
- Kaiser D, Laske K, Winzer R, Hadrich K, Wahl H, Krukowski P, et al. Impact of thrombus surface on first pass reperfusion in contact aspiration and stent retriever thrombectomy. *J Neurointerv Surg*. (2021) 13:221–5. doi: 10.1136/neurintsurg-2020-016194
- Puetz V, Algra A, Schonewille WJ. Trial of endovascular treatment of basilar-artery occlusion. *Reply N Engl J Med*. (2021) 385:959–60. doi: 10.1056/NEJMc2109962

**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Publisher's Note:** All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2021 Puetz, Strbian, Nguyen and Nagel. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.