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Editorial: Advances in chronic ischemic cerebrovascular disease: diagnosis and management

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Editorial on the Research Topic

[Advances in chronic ischemic cerebrovascular disease: diagnosis and management](#)

Ischemic cerebrovascular diseases relate to a variety of large vessel and small vessel angiopathies, which are common causes of ischemic stroke and cognitive dysfunction, especially in the elderly population (1–5). Although complex pathophysiological processes and high rates of morbidity make ischemic cerebrovascular diseases challenging, new clinical evidence continues to emerge for an improved understanding and treatment. Currently, basic and clinical research focuses on a variety of approaches to accelerate the understanding of the disease, improve patient care and monitoring, and, ultimately, reduce patient morbidity and mortality, with advanced neuroimaging techniques being used for biomarker development and testing in this regard (6–10). Furthermore, recent major research trajectories focused on aspects of advanced brain function, given that chronic ischemic conditions are also increasingly recognized as relevant risk factors for clinically silent brain infarctions and cognitive impairment (11–14).

Two studies of the Research Topic investigated patients with moyamoya disease (MMD) (Yu et al., Cao et al.). Specifically, MMD is a cerebrovascular disorder with typically progressive steno-occlusive disease, predominantly involving the bilateral intracranial internal carotid artery (ICA) and the proximal branches (15, 16). The disease is mainly observed in Japan, whereas the incidence in other parts of the world is rather low (15, 17, 18). The disease can entail symptoms related to brain ischemia (e.g., stroke) and/or related to compensatory mechanisms that can occur in response to ischemia (e.g., hemorrhage from fragile collateral vessels) (15, 16). In the study by Cao et al., hemodynamic abnormalities in 42 patients with MMD were examined before and after intervention by combined revascularization (i.e., surgery involving a direct superficial temporal artery-middle cerebral artery bypass and an indirect encephalo-arterio-synangiosis bypass) using intraoperative FLOW800, a specialized software utilizing indocyanine green video-angiography to analyze data and generate color delay mapping. The courses of parameters and associations between intraoperative FLOW800

and color Doppler ultrasonography (CDUS) measurements were evaluated, showing that both the intraoperatively measured delay time (i.e., the time interval between 0 and 50% of maximum fluorescence intensity for FLOW800 analysis) and rise time (i.e., the time interval between 10 and 90% of the maximum fluorescence intensity for FLOW800 analysis) substantially decreased in the recipient artery and vein (Cao et al.). Microvascular transit time from intraoperative assessment was significantly reduced after surgery, and all postoperatively collected parameters from CDUS measurements exhibited significant changes in comparison to the preoperative state (Cao et al.). Significant associations between microvascular transit time, resistance index, and pulsatility index were observed (Cao et al.). Based on the finding that hemodynamic outcomes of the donor and recipient arteries demonstrated significant changes following bypass surgery, the authors concluded that the parameter of time may be a more precise and sensitive measure of hemodynamics using the FLOW800 system (Cao et al.). Additionally, multiple hemodynamic evaluations could offer beneficial data for perioperative management in MMD (Cao et al.). In the study by Yu et al., metabolites associated with MMD were investigated by means of liquid chromatography coupled with mass spectrometry (LC-MS) to discern metabolic biomarkers in cerebrospinal fluid (CSF) samples. The patient group consisted of 16 patients with MMD, which were compared to a healthy control group of eight subjects (Yu et al.). The CSF samples were obtained during bypass surgery in the patient group and from lumbar puncture (during lumbar anesthesia) in the control group (Yu et al.). Overall, 129 differential metabolites in the CSF samples were identified when comparing the MMD patients to the healthy controls, which were associated with multiple pathways (e.g., purine metabolism and pyrimidine metabolism, among other pathways) (Yu et al.). Hence, using an LC-MS-based metabolomics approach may hold promise for enhancing the clinical diagnosis of MMD, and the identified parameters may lead to the development of novel diagnostic markers for MMD regarding the pathogenesis of the disease (Yu et al.).

Three articles published as part of the Research Topic focused on stroke regarding diagnostics or treatment (Yi et al.; Wu et al.; Wang et al.). Acute stroke is defined by an acute onset of focal neurological deficits, which can manifest due to the loss of blood supply related to ischemic or hemorrhagic stroke affecting brain territories or regions (19–21). In addition to neurological assessment, the diagnostic approach commonly includes imaging of the brain parenchyma, brain-feeding arteries, and oftentimes perfusion imaging using computed tomography (CT) or magnetic resonance imaging (MRI) (22, 23). In the study by Wang et al., a task-driven cerebral angiographic imaging (TDCAI) technique using CT perfusion images from patients with hemorrhagic or ischemic stroke was developed. Specifically, the TDCAI approach included registration and skull removal, vessel segmentation, artery-vein separation, centerline extraction, and vessel straightening as the major steps of processing (Wang et al.). The output was supplemented by diagnostic images obtained through the TDCAI approach, including CT angiography, CT venography, centerline images of the vessels of interest (i.e., ICA or Labbé vein), and straightened images

of the vessels of interest (Wang et al.). Moreover, TDCAI-CT angiography exhibited arterial architecture with greater detail (as compared to conventional imaging in 10 patients with intracranial hemorrhagic stroke and 10 patients with acute ischemic stroke), thus also visualizing small terminal branches of arteries (Wang et al.). Similarly, TDCAI-CT venography provided enhanced visualization of venous structures, clearly depicting the Labbé vein, which can be linked to hemorrhagic stroke (Wang et al.). Hence, the TDCAI technique may enable the elimination of bone and soft tissue interference, improve the segregation of cerebral venous and arterial architecture, and enable the extraction of centerlines and straightened vessels of interest to aid in assessing the outflow profiles of vessels after stroke (Wang et al.). The study by Yi et al. analyzed predictors of futile recanalization in basilar artery occlusion following endovascular treatment, which represented a *post-hoc* analysis of The Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion (ATTENTION). Specifically, ATTENTION aimed at evaluating the effects of endovascular thrombectomy in addition to best medical management compared to best medical management alone in patients with basilar artery occlusion (24). The current *post-hoc* analysis compared demographics, clinical characteristics, acute stroke workflow interval times, and imaging characteristics between futile recanalization and favorable recanalization, with favorable outcome being defined as a modified Rankin scale score of 0–3 at 90 days, successful reperfusion being defined as thrombolysis in cerebral infarction 2b and 3 on the final angiogram, and futile recanalization being defined as failure to achieve a favorable outcome despite successful reperfusion (Yi et al.). Using multivariate analyses to identify the predictors of futile recanalization, the authors showed among the 185 included patients (89 patients with futile recanalization and 96 patients with favorable recanalization) that older age and diabetes mellitus were independent predictors of futile recanalization (Yi et al.). Those two parameters may thus relate to poor outcomes in patients with acute basilar artery occlusion, but could not be directly modified in the context of emergency medical treatment (Yi et al.). In the retrospective study by Wu et al. that aimed to systematically identify risk factors for vascular complications during non-emergency endovascular treatment in patients with ICA occlusions, 92 patients were investigated using correlation analyses between intraoperative vascular complications and potential risk factors, followed by interaction analyses. The authors revealed that the use of non-neurology guide wires to open vessels and glycosylated hemoglobin (HbA1c) ≥ 6.5 mmol/L were significantly associated with vascular complications, with restricted cubic spline indicating that the higher the HbA1c level, the higher the risk of vascular complications (Wu et al.). Hence, the use of non-neurology guide wires for vessel opening may increase the risk of vascular complications, and preoperative assessment and management of HbA1c levels might help to reduce the incidence of intraoperative vascular complications (Wu et al.).

The article by Liu et al. reviewed the literature landscape regarding endovascular treatment options for intracranial ICA bifurcation region aneurysms. Yet, due to the complexity of such aneurysms and the considerable variability in contemporary

endovascular therapy techniques, the approach to the treatment of ICA bifurcation aneurysms remains challenging and non-standardized (Liu et al.). The review discusses in detail the anatomy of the ICA bifurcation region, classification schemes, natural history, and treatment approaches for ICA bifurcation region aneurysms (Liu et al.). It also reviews techniques for identifying ICA bifurcation region aneurysms, as well as the prognosis and complications of endovascular therapy for such aneurysms (Liu et al.). The authors conclude that conventional coiling seems to be the currently preferred treatment option for ICA bifurcation region aneurysms, while in selected cases, new devices such as flow diverters and woven EndoBridge devices could also be used to effectively treat ICA bifurcation region aneurysms (Liu et al.).

To conclude, this Research Topic covered a large spectrum of diagnostic and treatment aspects regarding cerebrovascular disorders, with a focus on novel diagnostic approaches and the development of potential diagnostic markers. The published studies may have the potential to facilitate improved diagnostics in patients with diseases such as MMD or hemorrhagic or ischemic stroke, and could also contribute to an improved understanding of disease (patho)physiology and characteristics. Moreover, especially diagnostic techniques that are not widely available or are emerging have been covered, and those could provide unique or complementary information when brought into context with standard diagnostic approaches using CT or MRI. Finally, more research is necessary regarding tailoring the presented procedures to clinical needs or to accelerate the transition of experimental findings to broader applications in patients. In this regard, studies using large-scale data from patients with large vessel and small vessel angiopathies and ultimately ischemic cerebrovascular diseases can help to identify common patterns from quantitative imaging related to the diagnosis, and could also help in patient phenotyping or stratification. Regarding studies published in this Research Topic on treatment options for cerebrovascular disorders, new evidence is provided for potential risk factors and predictors of clinical outcome, which

may support clinical decision-making and patient management in the future.

Author contributions

NS: Conceptualization, Project administration, Writing – original draft, Writing – review & editing. YL: Conceptualization, Project administration, Writing – original draft, Writing – review & editing. MS: Conceptualization, Project administration, Writing – original draft, Writing – review & editing.

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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.

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