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EDITORIAL (BY INVITATION)

Cerebrovascular reserve in moyamoya requires more standardization: editorial on ASL-MRI guided evaluation of multiple burr hole revascularization surgery in moyamoya disease

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Management of moyamoya arteriopathy is challenged by progressive and dynamic changes in cerebral perfusion, and non-invasive evaluation may inform indication for revascularization and technical surgical success. There are a number of surgical techniques which place vascularized tissue into close proximity with ischemic brain parenchyma, or which directly anastomose supply from the external carotid artery supply to the compromised intracranial cerebral supply.

Although revascularization surgery has been shown to reduce ischemic stroke in children and in adults with moyamoya arteriopathy, patient selection can be challenged by appropriate diagnosis of moyamoya arteriopathy versus moyamoya mimics. Native collateral formation is also possible, leading to compensated cerebral blood supply which may not require further revascularization surgery. Advances in imaging may help define the pathology and pathophysiology for an individual patient.

Lewén et al. describe a cohort of seven adults and four children in Sweden with moyamoya arteriopathy with a mixture of symptoms who were evaluated with pseudo-continuous ASL (pCASL) perfusion imaging over seven years. The patients underwent baseline and post-acetazolamide imaging to determine cerebrovascular reserve (CVR). Some patients were then treated with 10–12 burr holes, needle fenestration of the pia, and approximation of the periosteum, while others were not. There is considerable interest and debate as to the best methods to perform MRI-based perfusion and CVR imaging for patients with moyamoya arteriopathy, and Lewén et al.'s observations suggest (1) how perfusion or CVR can inform the decision to treat moyamoya with surgery and (2) how perfusion changes after multiple burr holes for moyamoya. However, there are some limitations in answering each of these questions.

Patients with symptomatic moyamoya are typically managed with revascularization if the symptoms can be referred to ischemia. While one component of this workup includes perfusion imaging, a number of other critical biomarkers indicate the diagnosis [11]. Although the field currently describes moyamoya as a specific diagnosis, the diverse genetic underpinnings of this arteriopathy remains a hidden secret given the limited ability to identify the genetic mechanism in most cases during routine clinical practice [8]. In this context, the inclusion of neurofibromatosis type I may introduce heterogeneity in the natural history and appropriate clinical decision-making [2, 10]. Accordingly, this study demonstrates some variability in the decision-making, such as participant 11, who may have an overall clinical picture suggesting a candidate for revascularization. However, there is active debate on using perfusion imaging as a surrogate biomarker in surgical decision-making until moyamoya subtypes are better defined.

Brain vasculature may recruit native collaterals to mitigate cerebral ischemia from moyamoya. This includes pial-pial leptomeningeal collaterals and extracranial-intracranial transdural collaterals [2]. These collaterals can vary depending on the patient age and the nature of the transit delay may vary accordingly. For example, we see transdural collaterals in as many as half of children with moyamoya [14]. The authors have attempted to mitigate effects of delayed arterial transit artifacts with a post-label delay of 2.5 seconds. Other groups have described using long post-labeling delays of 2 seconds up to 4 seconds [1, 5, 16]. However, this single

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strategy does not account for variability in transit from variable collateralized supply, and groups have used multi delay labeling or velocity-selective labeling to address this [6, 9].

Hypoperfusion pathology may also vary along a spectrum, with some patients having a stable baseline state but compromised ability to recruit flow when challenged, and other patients presenting in the setting of persistent compromised flow with acute stroke, misery perfusion. Similar to the studies of hemodynamics in bypass surgery for adult intracranial occlusion, challenging cerebrovascular reserve may further address the population who are not in misery perfusion but who have reduced reserve [3, 4, 12]. However, cerebrovascular reserve testing is highly variable and different assumptions limit generalizability. A number of stressors or stimuli are available, and acetazolamide presents variable dose responses that are also known to be age dependent [7]. Hypercapnia is an alternative that requires cooperation and $PaCO_2$ has a predictable relationship with cerebral blood flow, but it can be difficult to select a stimuli that elicits a sufficient $PaCO_2$ response and is clinically feasible [15]. Additional variability in the measure of perfusion introduces limitations in generalizability across institutions and limits interpretation of individual studies in the absence of normative data [13].

In this context, the authors have sought to draw general conclusions from a highly heterogeneous dataset including two different modalities of perfusion imaging, an acetazolamide challenge to measure cerebrovascular reserve, and a number of different mechanisms by which the pre- and post-intervention perfusion may be different. This heterogeneity reduces confidence in the generalized perfusion and cerebrovascular reserve changes of the cohort and points to the need of continued work to standardize perfusion imaging techniques and to gather normative datasets.

Without a robust and reliable measure of cerebrovascular reserve, the clinical application of this information in the surgical decision-making for these cases is further clouded. Separate from the typical concerns regarding size of the study population, there may be some limitations in applying the MRI data in these patients to suggest a general utility of MR perfusion or CVR in managing moyamoya arteriopathy. Fortunately, a number of other teams have studied larger populations with more optimized CVR techniques.

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Declarations

Conflict of interest The authors declare no competing interests.

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