

Short- and Long-Term MRI Assessed Hemodynamic Changes in Pediatric Moyamoya Patients After Revascularization

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Background: Cerebrovascular reserve (CVR) reflects the capacity of cerebral blood flow (CBF) to change following a vasodilation challenge. Decreased CVR is associated with a higher stroke risk in patients with cerebrovascular diseases. While revascularization can improve CVR and reduce this risk in adult patients with vasculopathy such as those with Moyamoya disease, its impact on hemodynamics in pediatric patients remains to be elucidated. Arterial spin labeling (ASL) is a quantitative MRI technique that can measure CBF, CVR, and arterial transit time (ATT) non-invasively.

Purpose: To investigate the short- and long-term changes in hemodynamics after bypass surgeries in patients with Moyamoya disease.

Study Type: Longitudinal.

Population: Forty-six patients (11 months–18 years, 28 females) with Moyamoya disease.

Field Strength/Sequence: 3-T, single- and multi-delay ASL, T1-weighted, T2-FLAIR, 3D MRA.

Assessment: Imaging was performed 2 weeks before and 1 week and 6 months after surgical intervention. Acetazolamide was employed to induce vasodilation during the imaging procedure. CBF and ATT were measured by fitting the ASL data to the general kinetic model. CVR was computed as the percentage change in CBF. The mean CBF, ATT, and CVR values were measured in the regions affected by vasculopathy.

Statistical Tests: Pre- and post-revascularization CVR, CBF, and ATT were compared for different regions of the brain. *P*-values <0.05 were considered statistically significant.

Results: ASL-derived CBF in flow territories affected by vasculopathy significantly increased after bypass by $41 \pm 31\%$ within a week. At 6 months, CBF significantly increased by $51 \pm 34\%$, CVR increased by $68 \pm 33\%$, and ATT was significantly reduced by $6.6 \pm 2.9\%$.

Data Conclusion: There may be short- and long-term improvement in the hemodynamic parameters of pediatric Moyamoya patients after bypass surgery.

Evidence Level: 4

Technical Efficacy: Stage 2

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Cerebrovascular reserve (CVR) is a hemodynamic parameter that determines the capacity to change cerebral blood flow (CBF) to meet physiological demands.¹ In this context, CVR can be measured using quantitative imaging modalities such as MRI and positron emission tomography (PET) whereby CBF is measured before and after a vasodilation

challenge in a single imaging session.^{2,3} Clinical evidence indicates that a lower CVR is associated with a higher risk for acute and recurrent strokes in patients with cerebrovascular diseases.⁴

Moyamoya disease is a chronic occlusive cerebrovascular disorder that often begins during childhood and progresses as

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the patient ages.⁵ It is characterized by severe stenosis or occlusion of the internal carotid arteries (ICA), anterior cerebral arteries (ACA), and middle cerebral arteries (MCA), and as the disease progresses, the posterior circulation can be affected as well.⁶ Networks of fragile vessels are often formed in the basal ganglia regions to compensate for the decreased blood flow caused by chronic steno-occlusion.⁷ Impaired CVR, a major factor for increased stroke risk, is a hallmark of Moyamoya disease.⁸ Therefore, external carotid-internal carotid (EC-IC) bypass surgeries, which can stabilize and restore the hemodynamics in regions affected by Moyamoya vasculopathy, are often performed in these patients.⁸ While vascular hemodynamics have been rigorously studied in adult patients with Moyamoya disease,^{9–11} data in pediatric patients are sparse because conventional perfusion imaging techniques (such as dynamic susceptibility contrast [DSC]-MRI) require the use of Gadolinium (Gd) contrast agents, that are less desirable for the pediatric population.¹²

Arterial spin labeling (ASL) is an MRI technique that enables noninvasive CBF and CVR measurements without exposure to ionizing radiation or intravenous Gd contrast agents.¹³ While pseudo-continuous ASL with a single post-labeling delay (single-PLD PCASL) is a widely used ASL technique for CBF quantification, studies have shown that ASL techniques with multiple post-labeling delays (multi-PLD PCASL) are more accurate in measuring CBF and CVR in adult patients with Moyamoya by accounting for variations in the arterial transit time (ATT).^{8,14} However, the effectiveness of multi-PLD PCASL in characterizing vascular hemodynamics in pediatric populations remains to be elucidated before and after EC-IC bypass procedures.

In this work, we aimed to investigate hemodynamic changes in pediatric Moyamoya patients after direct superficial temporal artery to middle cerebral artery (STA-MCA) bypass surgery. Specifically, we aimed to compare CBF, CVR, and ATT measured by single- and multi-PLD PCASL.

Materials and Methods

This study was approved by the local institutional review board. All participants' parents/guardians provided written informed consent.

Study Overview

We included 46 pediatric patients (18 male/28 female, between 11 months and 18 years old, median age: 13.5 years) with Moyamoya disease undergoing evaluation for STA-MCA revascularization surgery at our institution between January 2015 and January 2023. Inclusion criteria for our study were: confirmed diagnosis of Moyamoya disease (either unilateral or bilateral), 18 years or younger at the time of surgery, no other diseases affecting CBF (such as sickle cell anemia). All patients completed the initial (pre-surgery) and short-term (within 1-week post-surgery) follow-up MRI. Exclusion criteria included kidney function impairment (glomerular filtration rate < 40 mL/minute), history of brain injury, acute stroke at the time of imaging (as defined by a region of high signal on

diffusion-weighted imaging [DWI] with low signal on apparent diffusion coefficient imaging), and contraindications to MRI or acetazolamide (ACZ) administration. Patients were instructed to refrain from consuming caffeine at least 6 hours before the imaging session.¹⁵

As shown in Fig. 1a, all patients had at least 2 imaging sessions and 22 patients had 3 imaging sessions: 2 weeks before surgery (pre-surgery), 1 week after surgery (short-term post-surgery), and 6 months after surgery (long-term post-surgery). MRI procedures were conducted using 3-T MRI systems (Discovery MR 750 and SIGNA Premier, GE Healthcare, Waukesha, WI, USA). The surgical procedure for the bypass has been described in detail previously.⁹ In short, direct STA-MCA bypass was achieved by connecting the frontal or temporal branch of STA and the M4 segment of MCA near the Sylvian fissure under mild hypothermia (33–35°C). For patients with bilateral Moyamoya disease requiring bypass on both sides of the brain, two separate surgeries were performed by at least a week but less than 3 months apart. In these cases, the short-term MRI scan was performed after the second surgery.

Pre-Surgery and Long-Term Post-Surgery MRI Details

The same imaging protocols were used to measure CBF, CVR, and ATT before and at 6 months (long-term) after surgery, as shown in Fig. 1b. Specifically, single-PLD (labeling duration = 1450 msec; PLD = 1525 msec) and multi-PLD (effective labeling duration = 550 msec; 7 PLDs = 700, 1250, 1800, 2350, 2900, 3450, and 4000 msec, Hadamard labeling technique) sequences were acquired. The PCASL data were acquired before and 15 minutes after the administration of the vasodilator ACZ (Hikma Farmacêutica, Terrugem, Portugal) at a dose of 15 mg/kg of body weight (with a maximum dose of 1000 mg) over a 30-second infusion. Other MRI sequences included three-dimensional (3D) time-of-flight MR angiography (MRA), DWI, T1-weighted, and T2-weighted fluid-attenuated inversion recovery (FLAIR) structural images. The MRA was centered on the Circle of Willis covering 40 mm in the superior–inferior direction. Unlike the protocol for adult Moyamoya patients that has been previously published,¹⁴ no DSC-MRI scans were included in the pediatric protocol. The detailed scanning parameters can be found in Table S1 in the Supplemental Material.

Short-Term Post-Surgery MRI Details

Imaging protocol used at 1 week (short-term) after surgery included single-PLD (same scanner parameters as in the pre-surgery examination), MRA, DWI, T1-weighted, and T2-weighted FLAIR structural images. Since the purpose of this protocol was to assess the general outcome immediately after revascularization, multi-delay ASL was not performed and ACZ was not administered. The detailed acquisition parameters can be found in Table S1 in the Supplemental Material.

MR Hemodynamic Measurements

Values of CBF and ATT from pre- and post-vasodilation ASL data (both single- and multi-delay) were derived by fitting the ASL difference data (subtraction between label and control images) to a general kinetic model using a spatially regularized Bayesian inference technique in Bayesian Inference for Arterial Spin Labeling MRI

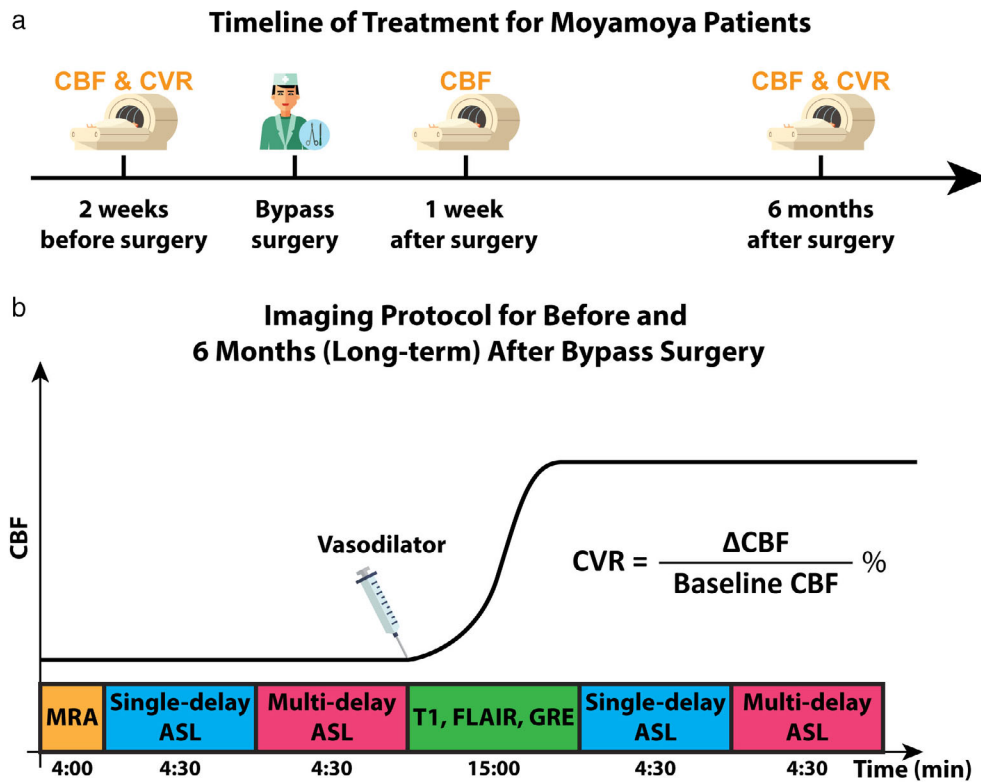


FIGURE 1: Timeline of treatment for Moyamoya patients, imaging protocols, and intra-operative hemodynamic measurements. (a) Each Moyamoya patient has three imaging sessions: 2 weeks before surgery for CBF and CVR; 1 week (short-term) after surgery for CBF only; and 6 months (long-term) after surgery for CBF and CVR. (b) In the imaging protocol for CBF and CVR measurements, single-delay and multi-delay ASL are performed before and 15 minutes after the administration of vasodilator (acetazolamide). In the imaging protocol of CBF session (1 week after surgery), only single-delay ASL is employed. Other MRI sequences include MRA, T1 and T2-FLAIR, GRE, and DWI (not shown).

(BASIL; <https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/BASIL>, version 4.0.2).^{16,17} The labeling efficiency was assumed to be 85% and a blood-brain partition coefficient of 90% for all ASL data before and after surgery was assumed.³ Partial volume effects on the edge of the brain were corrected using the erosion and extrapolation methods.¹⁸ Then, CVR was computed as the percentage change in CBF induced by the vasodilator, as shown in the equation in Fig. 1b. The CVR, CBF, and ATT maps were transformed to the Montreal Neurological Institute (MNI) 152–2 mm space to facilitate group comparison and statistical analyses using both linear and non-linear registration.¹⁹ Six flow territories (left ACA, right ACA, left MCA, right MCA, left PCA, and right PCA) were defined based on the Harvard-Oxford cortical and subcortical structural atlases.²⁰ After registration, the mean values of CBF, CVR, and ATT in each flow territory affected and unaffected by vasculopathy were computed. The grade of vasculopathy (occlusion or severe stenosis) in each patient was assessed separately using the MRA scans by two board-certified radiologists (ET with 5 years of experience and KQWY with 17 years of experience) in this work.

Statistical Analysis

Statistical tests were performed using MATLAB (Mathworks, Natick, MA, USA, version 2020b). The normality of the mean CBF, CVR, and ATT data were checked using Kolmogorov–Smirnov tests before conducting statistical analyses.²¹ They were done separately for each flow territory. Paired t-tests were performed

to compare the mean values of CVR and ATT measured by multi-PLD PCASL before and 6 months after bypass in regions affected by vasculopathy under the null hypothesis that the value of these parameters was the same. For baseline (pre-vasodilation) CBF measured by single-PLD PCASL, paired t-tests were conducted to evaluate the short- and long-term change after bypass surgeries. A *P*-value <0.05 was considered statistically significant.

Results

Patient Information

Table 1 shows the information about patients included in this study. Among the 46 patients, all of them had their short-term MRI scan after their surgery (between 4 and 14 days) and 22 of them returned for the long-term follow-up MRI after their surgery (between 135 and 279 days). The primary reason for patients not returning for follow-up was the long distance from their principal residence. Other factors included the availability of the patients and travel restriction due to the COVID-19 pandemic. The majority of the patients had severe stenosis or occlusion in the supraclinoid segment of ICA, the A1 segment of the ACA, and/or the M1 segment of the MCA, accounting for more than 95% of cases in this cohort.

TABLE 1. Patient Demographic Information and Conditions of Vasculopathy

Parameter	Value
Number of patients enrolled	46 (18 males and 28 females)
Age at the time of surgery	Median: 13.5 years Range: 11 months–18 years
Time between pre-surgery and short-term post-surgery scans	Median: 6 days Range: 4–14 days
Time between pre-surgery and long-term post-surgery scans	Median: 213 days Range: 135–279 days
Number of patients with occlusion/stenosis of the ICA	38
Number of patients with occlusion/stenosis of the ACA	13
Number of patients with occlusion/stenosis of the MCA	20
Number of patients with occlusion/stenosis of the PCA	1

ICA = internal carotid artery; ACA = anterior cerebral artery; MCA = middle cerebral artery; PCA = posterior cerebral artery.

Hemodynamic Maps

Figure 2 shows the MRA and CBF maps in a Moyamoya patient (female, 17 years) 14 days before and 1 day (short-term) after the bypass surgery. The pre-surgery MRA showed occlusion of the supraclinoid segment of the right ICA and stenosis of the A1 segment of the right ACA. After bypass, the circulation of the right hemisphere was chiefly supplied by the right STA through the STA-MCA graft. Before bypass, CBF measured by single-PLD PCASL in the affected regions (right hemisphere) was significantly lower than in the unaffected regions (left hemisphere). After bypass surgery, the right hemispheric CBF increased and was similar to the CBF of the left (unaffected) hemisphere.

Figure 3 shows the MRA and hemodynamic maps computed from multi-PLD PCASL data in a Moyamoya patient (female, 17 years, same patient as in Fig. 2) 14 days before and 7 months after bypass. The STA-MCA graft showed a patent bypass supplying the circulation of the right hemisphere. Before bypass, low CVR in the right hemisphere was

present. Regions with vascular steal (negative CVR values) were present in the right hemisphere, indicating blood re-directed to the unaffected side, and further decreasing CBF in the right hemisphere after the vasodilator challenge. After bypass, CVR in the affected (right) hemisphere improved. Comparing the CVR of the right hemisphere before and after bypass, the values were restored toward the normal level on the left hemisphere, but still remained decreased compared with the left hemisphere. In addition, delayed ATT can be seen in the affected (right) hemisphere pre- and post-vasodilation caused by the occlusion and stenosis before bypass. After bypass, ATT in the affected (right) hemisphere decreased while still higher than in the unaffected (left) hemisphere.

Baseline CBF Changes After Bypass

Figure 4 shows the pre-vasodilation CBF change after bypass surgery. Overall, the CBF in the affected regions increased significantly after bypass, with the long-term CBF increase revealing a marginally higher effect size than the short-term change (by $51 \pm 34\%$ and $41 \pm 31\%$, respectively). In the unaffected regions, CBF remained unchanged for both short- and long-term comparisons after bypass surgery ($P = 0.71$ and 0.18 , respectively).

CVR and ATT Changes After Bypass

Figure 5 shows the long-term hemodynamic changes in CVR and ATT measured by multi-PLD PCASL before and 6 months after bypass surgery. Overall, CVR increased significantly and ATT decreased significantly after bypass surgery in regions affected by vasculopathy. Specifically, the mean CVR values of the cohort increased by an average of $68 \pm 33\%$ after bypass. Furthermore, the CVR in regions without vasculopathy (unaffected regions) demonstrated no significant changes ($P = 0.88$). Bypass surgery reduced the mean ATT of the cohort by an average of $6.6 \pm 2.9\%$ before vasodilation and $10.7 \pm 3.5\%$ after vasodilation (comparison between blue and red boxes in Fig. 5b). Before bypass surgery, mean ATT did not show significant changes after vasodilation in these regions ($P = 0.16$, comparison between values in blue boxes in Fig. 5b). After bypass surgery, however, the mean ATT of the cohort decreased significantly by an average of $6.1 \pm 2.7\%$ after vasodilation (comparison between values in red boxes in Fig. 5b).

Discussion

In this work, we investigated the short- and long-term hemodynamic changes in 46 pediatric Moyamoya patients after bypass surgery using single- and multi-PLD PCASL. The primary findings of our work include: 1) CBF and CVR in regions affected by vasculopathy increased significantly after bypass surgery in pediatric Moyamoya patients; 2) transit

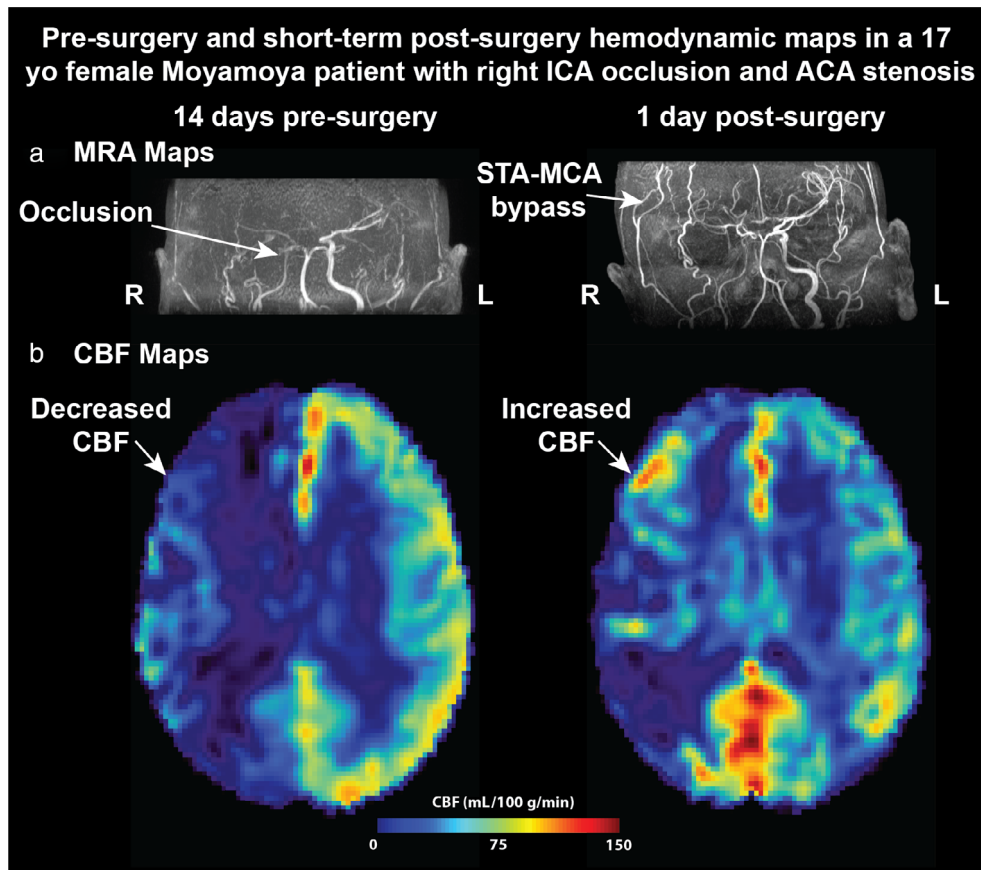


FIGURE 2: Pre-surgery and short-term post-surgery hemodynamic maps in a Moyamoya patient (17 years, female) with right ICA occlusion and ACA stenosis. (a) MRA images (acquired 14 days before bypass surgery) show occlusion at the supraclinoid segment of the right ICA and moderate stenosis of the A1 segment of the right ACA. Post-surgery MRA (acquired 1 day after bypass) shows a successful bypass at the STA-MCA graft. (b) Before bypass, CBF of the right hemisphere was significantly lower than the left. After surgery, CBF of the right hemisphere increased due to direct STA-MCA revascularization.

delay measured by multi-PLD PCASL reduced significantly after bypass surgery.

Baseline CBF in regions affected by vasculopathy increased significantly short- and long-term after bypass surgery. The improvement in baseline CBF implied restored delivery of essential nutrients and oxygen for brain tissues through the STA-MCA graft. Such changes agree with previous observations where CBF in pediatric Moyamoya patients increased significantly at least 6 months after bypass.²² Similar to our study, single-PLD PCASL was applied to evaluate CBF pre- and post-surgery due to its availability and robustness.²³ The assessment of short-term CBF changes in our study here provides new information about pediatric hemodynamics after bypass surgery. Previously, Antonucci et al reported that CBF in adult Moyamoya patients did not show significant changes after bypass surgery when assessed by xenon-enhanced computed tomography (CT) perfusion.⁴ The discrepancy between their results and ours may be due to the difference between imaging modalities and hemodynamic response between adults and children.⁴ In general, CBF derived by ASL can be measured directly from the MRI data using model-fitting techniques with a high

reproducibility on single-PLD PCASL, as has been reported previously.²⁴ Xenon-enhanced CT perfusion, however, relies on integrating a CT scanner and a xenon inhalation device to enable CBF quantification,²⁵ which is less desirable in pediatric patients than the fully noninvasive ASL technique. In terms of the different hemodynamic responses to neurosurgery in adults and children, although no direct comparison in CBF between these two groups was made in our study, previous work reported a slightly higher modified Rankin scale in pediatric than adult patients after neurosurgeries.²⁶ Such findings may explain the CBF improvement seen in pediatric patients reported here. Nevertheless, a systematic comparison in vascular hemodynamics is needed to elucidate whether there is a different response in pediatric and adult Moyamoya patients after bypass.

Comparing the CVR values in regions affected by vasculopathy, we demonstrated that CVR measured by multi-PLD PCASL improved significantly after revascularization. These results indicated a higher capacity for CBF to increase in a vasodilation challenge, presumably leading to a reduced risk for strokes. Similar findings have been reported in a pediatric Moyamoya cohort using single-PLD PCASL, whereby

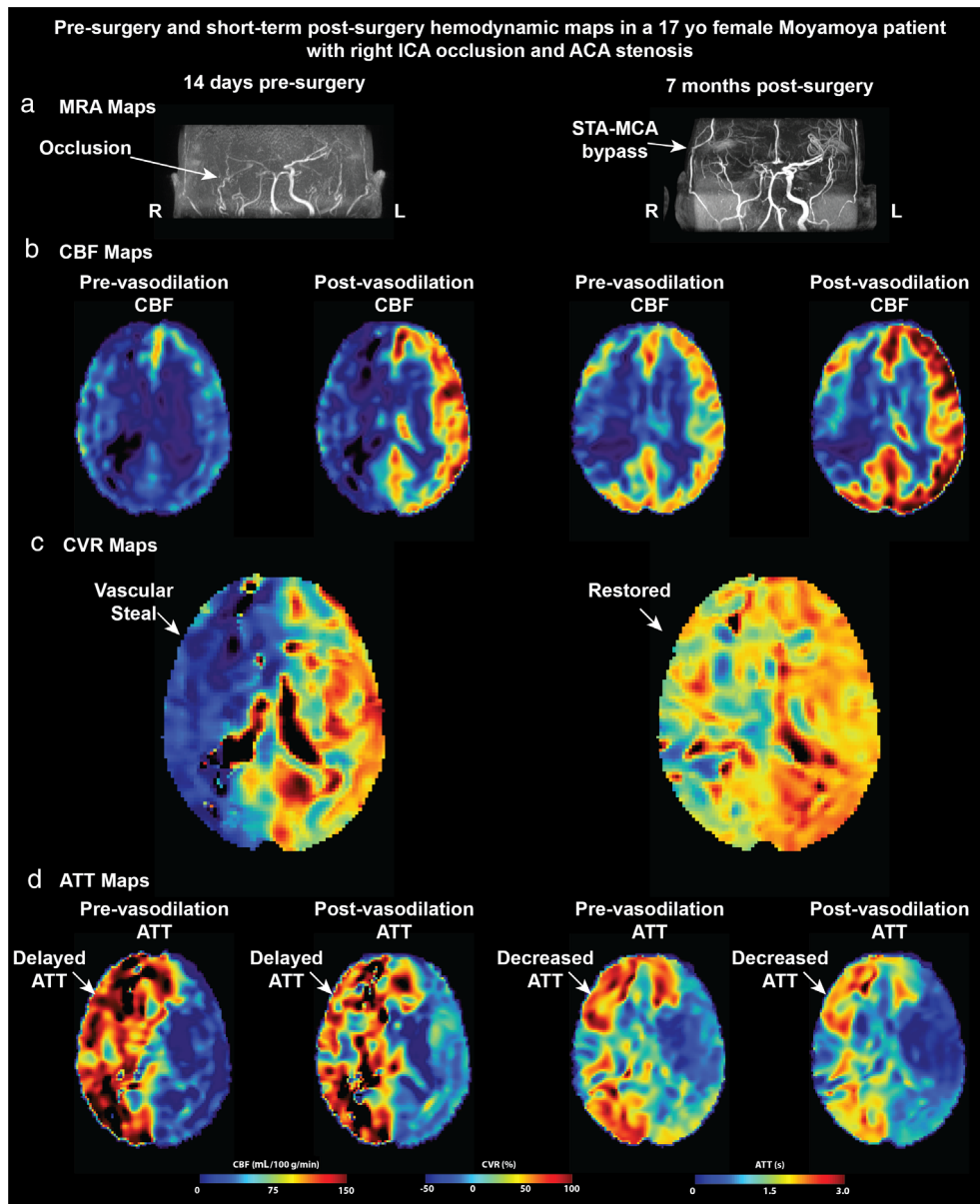


FIGURE 3: Pre-surgery and long-term post-surgery hemodynamic maps in a Moyamoya patient (17 years, female) with right ICA occlusion and ACA stenosis. (a) Seven months after the bypass, the STA-MCA graft continued to demonstrate restored circulation to the right hemisphere. (b) Before bypass, poor CBF augmentation in the right hemisphere can be seen post-vasodilation. After bypass, CBF augmentation in the right hemisphere improved. (c) Before bypass, vascular steal (inferred by negative CVR values) can be seen in the right hemisphere due to vasculopathy. After bypass, CVR in the affected (right) hemisphere was restored toward the level on the unaffected (left) hemisphere. (d) Before bypass, delayed ATT can be seen in the affected (right) hemisphere pre- and post-vasodilation. After bypass, ATT in the affected (right) hemisphere decreased while still higher than the unaffected (left) hemisphere.

the mean CVR increased by 36% after bypass.²² In the present study, we observed a significant increase in CVR. Such differences in effect size (the amount of CVR change after bypass) may also be explained by the different ASL techniques adopted. In contrast to the standard single-PLD PCASL technique, the multi-PLD PCASL techniques employed in our Moyamoya protocol have been shown to detect a larger CBF increase after vasodilation and demonstrated better agreement with the reference standard as given by the ¹⁵O-water PET perfusion technique.^{3,8} Furthermore,

since multi-PLD PCASL can measure both CBF and ATT at the same time, the improved CBF and CVR can also be indirectly explained by the reduced ATT. Unlike the multi-PLD PCASL with five PLDs that we adopted in our adult Moyamoya protocol,¹⁴ we modified our ASL technique by using seven PLDs to compensate for the rapid flow often observed in the pediatric population.²⁷ Based on the CVR, CBF, and ATT results, we conclude that bypass may considerably enhance the vascular hemodynamics in pediatric Moyamoya patients and that multi-PLD ASL may be the

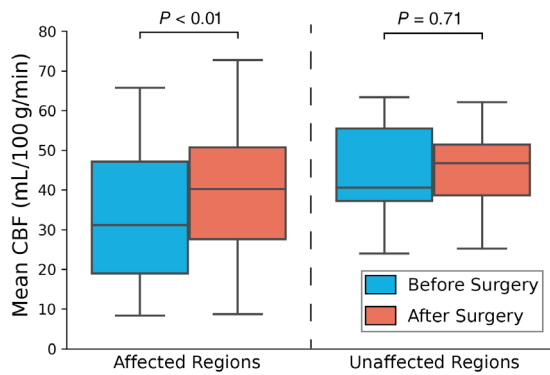
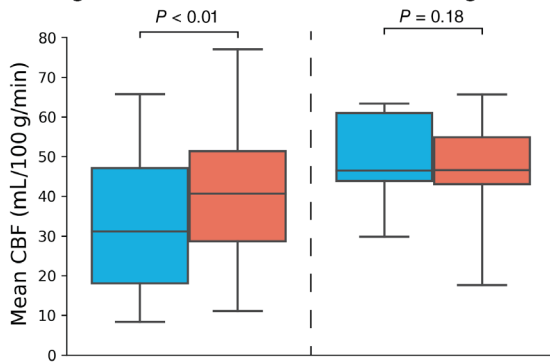
Baseline CBF Change Before and After Bypass Surgery**a Short-term (Within 1 Week) CBF Change (n=46)****b Long-term (After 6 Months) CBF Change (n=22)**

FIGURE 4: Short- and long-term baseline CBF changes after bypass surgery. (a) CBF measured by single-PLD PCASL increased significantly after bypass surgery in regions affected by vasculopathy while remaining unchanged in unaffected regions. (b) Similar to the short-term changes, CBF in the affected regions increased significantly while no significant differences were observed in the unaffected regions. Note that the long-term results were derived from a smaller sample size than the short-term results due to patient drop-out. Each box plot indicates, from top to bottom, the maximum, 75th, 50th, 25th percentiles, and minimum.

preferred imaging modality to evaluate cerebral hemodynamics in these patients.

Apart from ASL, blood oxygenation level dependent (BOLD) functional MRI (fMRI) has been applied to characterize vascular reactivity in pediatric patients with cerebrovascular diseases.²⁸ Both breath-holding and hypercapnic gas challenges can induce vasodilation to alter vascular hemodynamics.²⁹ For example, a pilot study revealed a mean cerebrovascular reactivity of 12% in eight pediatric patients with Moyamoya disease using breath-holding and BOLD fMRI.³⁰ Similarly, another study found that by using BOLD fMRI, the cerebrovascular reactivity in Moyamoya patients who underwent bypass surgery was significantly higher than in the patients without surgery.³¹ Despite BOLD fMRI being an alternative method to assess cerebrovascular reactivity, the fundamental difference between using ASL and BOLD lies in the hemodynamic values of interest for clinical decision making. Since our work focused on the vascular reserve reflected

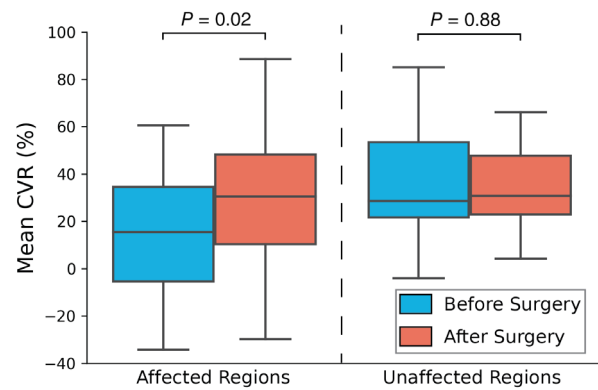
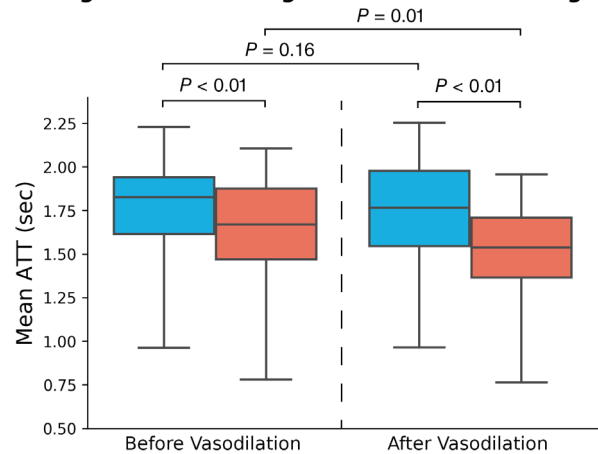
a Long-term CVR Change Before and After Surgery**b Long-term ATT Change Before and After Surgery**

FIGURE 5: Long-term hemodynamic changes after bypass surgery. (a) Mean CVR measured multi-PLD PCASL increased significantly after bypass surgery. The CVR in the unaffected regions showed no significant changes after bypass surgery ($P = 0.16$). (b) Bypass surgery caused mean ATT in the affected regions to decrease significantly before and after vasodilation conditions. Before bypass surgery, mean ATT showed no significant changes after vasodilation. By contrast, surgery ATT reduced significantly after vasodilation in the post-surgery condition. Each box plot indicates, from top to bottom, the maximum, 75th, 50th, 25th percentiles, and minimum.

by CBF change, we employed ASL as the imaging modality to measure perfusion and CVR directly. On the contrary, BOLD signal arises from a variety of hemodynamic responses including CBF, CBV, and oxygenation,^{32,33} which may complicate the interpretation of the BOLD data. Another advantage of ASL is its ability to measure CBF and CVR,^{13,34} allowing direct comparison in data collected from different time points, such as the pre-surgery and post-surgery cases in this work.

A key advantage of multi-PLD PCASL is its ability to measure ATT without the need for MR contrast agents,³⁵ making it a favorable modality for pediatric neuroimaging applications. Previously, we demonstrated a significant reduction in ATT after vasodilation in patients with Moyamoya disease before bypass surgery using similar imaging

protocols.^{8,36} In the present study, the reduction in ATT after bypass surgery implied that revascularization improved blood circulation in regions affected by vasculopathy to be restored toward normal levels. The results of our study also encompass the assessment of transit time in different physiological conditions (such as pre- and post-vasodilation) in pediatric patients with cerebrovascular diseases. Specifically, the ATT in the affected regions after bypass declined significantly after the administration of ACZ, which indirectly reflected an improved response to the vasodilation challenge. These data complement our previous findings in adult Moyamoya patients¹⁴ that multi-PLD PCASL can be applied as a noninvasive surrogate for evaluating transit delay and circulation for Moyamoya patients of all ages. Unlike conventional MR perfusion techniques (such as DSC-MRI) that rely on the administration of Gd-based contrast agents, multi-PLD PCASL uses magnetically labeled blood water as an endogenous tracer that is freely diffusible across the blood–brain barrier.³⁷ Furthermore, since ATT measured by multi-PLD PCASL indicates the time for the blood to travel from the labeling plane to the tissue of interest, it can be directly compared in longitudinal studies. The comparison of ATT across cohorts (such as between pediatric and adult patients) and among different ASL techniques (such as between pulsed and continuous ASL) should be conducted with care because the location of the labeling plane and the labeling technique can affect the measurements of ATT.³⁷ Standardization of the methodology behind multi-PLD PCASL would facilitate research in this area. An open question is the relationship between imaging markers and the neurological improvements of Moyamoya patients after revascularization. This may be addressed by elucidating the correlation between hemodynamic parameters (such as CBF and CVR) and neurological outcomes (such as Modified Rankin Scale) in future studies.

Limitations

One limitation is that the short-term CBF changes were assessed using the single-PLD PCASL sequence, which might be less accurate than the multi-PLD PCASL technique. Since all short-term MR scans were performed before patients were discharged, single-PLD PCASL was the only ASL technique available on the inpatient MRI scanners in our hospital. Additionally, the patient retention rate was moderately low—22 out of 46 (48%) patients completed the long-term imaging session 6 months after revascularization, leading to the possibility of population bias. This was due to the unavailability of local imaging facilities near the patients' residence and the inconvenience of traveling from their primary residence to our hospital. For example, five patients lived outside the country where this study was performed, and the COVID-19 pandemic also interrupted long-distance travel for patients to return for follow-up scans. Improving the accessibility of advanced perfusion imaging techniques to

sites beyond tertiary referral centers would improve the timely assessment of vascular hemodynamics after bypass. Furthermore, although having a third reader to evaluate the vasculopathy in each patient might improve the consistency of the interpretation of the imaging data, only two pediatric neuroradiologists were available in this study.

Conclusion

In this work, we investigated the short- and long-term vascular hemodynamic changes in pediatric Moyamoya patients after bypass surgery using ASL. In regions affected by vasculopathy, increases in both CVR and CBF and decreases in transit time may be identified after revascularization using multi-PLD PCASL.

Author Contributions

Moss Y. Zhao: Conceptualization, methodology, investigation, writing, funding acquisition. Elizabeth Tong: Conceptualization, investigation, writing, resources. Rui Duarte Armindo: Methodology, data curation. Ates Fettahoglu: Data curation. Jason Choi: Methodology. Jacob Bagley: Methodology. Kristen W. Yeom: Supervision. Michael E. Moseley: Supervision, manuscript editing. Gary K. Steinberg: Supervision, manuscript editing. Greg Zaharchuk: Supervision, manuscript editing, funding acquisition.

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