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Cerebrovascular Autoregulation in Pediatric Moyamoya Disease

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Abstract

Background—Moyamoya syndrome carries a high risk of cerebral ischemia, and impaired cerebrovascular autoregulation may play a critical role. Autoregulation indices derived from near-infrared spectroscopy (NIRS) may clarify hemodynamic goals that conform to the limits of autoregulation.

Objectives—The aims of this pilot study were to determine whether the NIRS-derived indices could identify blood pressure ranges that optimize autoregulation and whether autoregulatory function differs between anatomic sides in patients with unilateral vasculopathy.

Methods—Pediatric patients undergoing indirect surgical revascularization for moyamoya were enrolled sequentially. NIRS-derived autoregulation indices, the cerebral oximetry index (COx) and the hemoglobin volume index (HVx), were calculated intraoperatively and postoperatively to measure autoregulatory function. The 5-mmHg ranges of optimal mean arterial blood pressure (MAP_{OPT}) with best autoregulation and the lower limit of autoregulation (LLA) were identified.

Results—Of seven enrolled patients (aged 2–16 years), six had intraoperative and postoperative autoregulation monitoring and one had only intraoperative monitoring. Intraoperative MAP_{OPT} was identified in six (86%) of seven patients with median values of 60–80 mmHg. Intraoperative LLA was identified in three (43%) patients at 55–65 mmHg. Postoperative MAP_{OPT} was identified in six (100%) of six patients with median values of 70–90 mmHg. Patients with unilateral disease had higher intraoperative HVx ($p=0.012$) on the side with vasculopathy.

Conclusions—NIRS-derived indices may identify hemodynamic goals that optimize autoregulation in pediatric moyamoya.

Keywords

Pediatric; neurosurgery; moyamoya; cerebrovascular; autoregulation

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Introduction

Moyamoya disease, a rare disorder that predominantly affects Asians (1) and Asian-Americans (2), and moyamoya syndrome involve progressive steno-occlusive changes in the internal carotid arteries and main branches with compensatory formation of a fine vascular network (3,4). The disorder is more common in females than in males (5). Patients with moyamoya are at high risk of perioperative cerebral ischemic events (6) or hyperperfusion injury (7) with surgical revascularization. One factor that may be critical to this increased risk is the propensity toward altered cerebral blood flow (CBF) autoregulation (6,8,9). Cerebrovascular autoregulation maintains relatively constant CBF across changes in perfusion pressure and prevents cerebral ischemia from pressure-passive CBF. The blood pressure limits of autoregulation are unknown in pediatric patients, and these limits may vary according to age and disease severity. The risk of impaired autoregulation may be even greater in pediatric patients with moyamoya disease than in adults (8). The incidence of perioperative ischemic complications has ranged from 5% to 20% in large contemporary surgical series of moyamoya patients (6,10). Clinical monitoring methods that reduce the risk of cerebral ischemia in patients with moyamoya have not been identified. Intraoperative electroencephalography monitoring does not predict perioperative ischemic events in those with the disease (11). Although intraoperative CBF has been measured by laser-Doppler flowmetry (12), jugular bulb oxygen saturation measurements (13), and micro-Doppler ultrasonography (14), these techniques are not routinely used in clinical practice. Improved monitoring methods and a better understanding of preventable events that contribute to the risk of perioperative cerebral ischemia are needed in this vulnerable population.

Continuous autoregulation monitoring could enable clinicians to target a blood pressure range that maximizes autoregulatory function and avoids pressure-passive CBF. Traditional techniques utilize transcranial Doppler and intracranial pressure (ICP) monitors (15,16). However, these methods are not standard during moyamoya revascularization. To address this need, we developed autoregulation indices derived from cerebral near-infrared spectroscopy (NIRS): the cerebral oximetry index (COx) and hemoglobin volume index (HVx). COx represents the relationship between cerebral oximetry and mean arterial blood pressure (MAP). The theory behind COx is based on the assumption that changes in tissue oxygen saturation are proportional to changes in CBF over brief periods with steady cerebral metabolic rate (17,18). HVx represents the relationship between relative tissue hemoglobin (rTHb; a surrogate measure of cerebral blood volume [CBV] obtained by NIRS) and MAP. HVx is based on the assumption that autoregulatory vasodilation and vasoconstriction produce changes in CBV that are proportional to changes in rTHb (19). The indices are calculated by a correlation coefficient between cerebral oximetry (for COx) or rTHb (for HVx) and MAP. When autoregulation is functional, cerebral oxygen saturation and rTHb are either not correlated or negatively correlated to MAP, yielding near-zero or negative index values. When autoregulation becomes impaired, cerebral oxygen saturation and rTHb positively correlate to MAP, resulting in positive indices (17,19) (Figure 1).

The objectives of this pilot study were to determine whether the NIRS-derived autoregulation indices could identify blood pressure ranges that optimize autoregulation intraoperatively and postoperatively in children with moyamoya and whether autoregulatory function differs between anatomic sides in patients with unilateral moyamoya. Autoregulation measures included the range of MAP with most robust autoregulation, the lower limit of autoregulation (LLA), and mean COx and HVx during the intraoperative and postoperative periods.

Methods

This study was approved by the Johns Hopkins University IRB, which waived the requirement for written informed consent. Between January 2011 and February 2012, pediatric patients with moyamoya were sequentially enrolled for autoregulation monitoring during indirect surgical revascularization and postoperatively overnight in the pediatric intensive care unit (PICU). All patients were admitted the night before surgery and started on 1.25–1.5 times maintenance IV hydration and continued aspirin therapy (81 mg/day), a preoperative practice that has been described previously (20). As per standard anesthesia practice at our institution, invasive arterial blood pressure cannulae were placed, and self-adhesive cerebral oximetry probes (INVOS; Covidien, Boulder, CO) were placed bilaterally on the patients' foreheads. A bedside, laptop computer was connected to the patient's blood pressure monitor and cerebral oximeter. MAP (GE Marquette, Garnerville, NY) and NIRS signals were synchronously sampled at 100 Hz and processed with an analog-to-digital converter (DT9804, Data Translation, Marlboro, MA) and bedside computer using ICM+ software (Cambridge Enterprises, Cambridge, UK) as previously described (17–19,21–24). Artifacts in the NIRS and MAP signals (e.g., arterial line flushes and arterial blood gas sampling) were removed manually, and data comprising less than 1% of the recording period were excluded as an additional measure to remove signal artifacts (25).

Time-integrated, 10-s mean values of MAP, cerebral oximetry, and rTHb were recorded as a low-pass filtering step to remove oscillations from pulse and respiratory frequencies. Consecutive, paired 10-s averaged values from 300 s duration were used for each index calculation, thereby incorporating 30 data points for each index (24). COx was calculated with a continuous, moving Pearson correlation coefficient between MAP and cerebral oximetry (17,18,22,23). HVx was similarly calculated with a correlation coefficient between MAP and rTHb (19,22,23). Calculations for COx and HVx were updated every 10 s to incorporate MAP and cerebral oximetry or rTHb data from the preceding 300 s in overlapping windows. This method resulted in 360 COx calculations and 360 HVx calculations per hour.

COx and HVx are continuous variables that range from –1 to +1. When autoregulation is functional, the indices are negative or near zero because MAP and CBF (for COx) or MAP and CBV (for HVx) are either not correlated or negatively correlated. When MAP decreases below the LLA and autoregulation becomes impaired, the indices become increasingly more positive and approach +1 because MAP and CBF or CBV are positively correlated. Average index values were sorted into 5-mmHg bins of MAP to generate bar graphs.

The optimal MAP (MAP_{OPT}) was identified as the bin with the most negative COx or HVx value (nadir) when the graph showed increasing index values as MAP deviated from this nadir (26). (Figure 1) MAP_{OPT} represents the 5-mmHg range of MAP in which autoregulation and vasoreactivity are most responsive to changes in perfusion pressure. The LLA was identified as the MAP bin with COx = 0.5 or HVx = 0.3 when the graph showed increasing index values as MAP decreased (Figures 2 and 3). The threshold for COx in identifying the LLA was based on a cardiopulmonary bypass study that compared transcranial Doppler measurements of CBF velocity to COx (24). The HVx threshold for identifying the LLA was determined by a study in swine that compared laser-Doppler measurements of CBF to HVx (19). Two physicians experienced with the NIRS-derived autoregulation monitors independently interpreted the autoregulation indices.

The treating clinicians determined all clinical management, including blood pressure and ventilator management, laboratory measurements, and anesthetic technique. Clinicians could view the blood pressure and cerebral oximetry readings, but they were blinded to the

autoregulation indices. Continuous end-tidal CO₂ (ETCO₂) and intraoperative esophageal or rectal temperatures were monitored. These data were electronically retrieved from the electronic anesthetic record (Metavision v 5.45.58, Hanover, Germany) in intervals of 1–5 min. Postoperative axillary temperatures were measured in hourly intervals in the PICU. Patients were followed for ischemic events during their hospital stay and for one month postoperatively in the outpatient setting.

Data were analyzed and graphs generated with STATA (v11.1), SigmaPlot (v11.2), and GraphPad Prism (v5.03, GraphPad Software, Inc.). Data are shown as means with standard deviations or medians with interquartile ranges when appropriate. Differences were considered statistically significant if $p < 0.05$. Intraoperative MAP, regional cerebral oxygen saturation (rSO₂), temperature, and ETCO₂ were analyzed as means of 1-min intervals. Postoperative MAP and rSO₂ were analyzed as means of 3-min intervals. MAP, rSO₂, ETCO₂, temperature, PaCO₂, and hemoglobin were compared with repeated measures one-way ANOVA and Student Newman-Keuls multiple comparison tests. In patients with unilateral moyamoya, mean COx and HVx of affected and unaffected sides were compared by paired t-tests.

Results

Seven female patients (aged 2–16 years) were enrolled. Intraoperative autoregulation was monitored in all patients, but postoperative monitoring was possible only in six because one patient removed her arterial blood pressure catheter. All patients were extubated in the operating room, and no patient received blood transfusions. The preoperative angiographic findings, Suzuki grades of disease severity (27), and procedures are described in Table 1.

All patients received anesthesia with isoflurane, opiates, and neuromuscular blockade. Three patients received midazolam. The patients' intraoperative MAP (76 ± 13 mmHg), right rSO₂ ($83 \pm 11\%$), and left rSO₂ ($86 \pm 11\%$) did not statistically differ as time progressed under anesthesia. The patients' intraoperative temperature increased significantly with time (mean $36.9 \pm 0.7^\circ\text{C}$, range 35.0°C – 38.4°C for the entire intraoperative period; $p < 0.001$), and ETCO₂ was higher after induction than for the remainder of anesthesia (mean 38 ± 3 mmHg, range 27–64 mmHg for the entire intraoperative period; $p < 0.001$). Intraoperative PaCO₂ (mean 38 ± 3 mmHg, range 32–44 mmHg) and hemoglobin levels (mean 10.5 ± 1.6 g/dL, range 7.8–13.5 g/dL) were not statistically different among the six patients who had intraoperative laboratory measurements.

Agreement on identifying MAP_{OPT} and LLA was 100% between the physicians who interpreted the indices. Intraoperative MAP_{OPT} was identified on at least one side in six (86%) of seven patients by COx and in six (86%) of seven patients by HVx (Table 2). Intraoperative LLA was identified on at least one side by COx in three (43%) of seven patients and by HVx in two (29%) of seven patients (Table 3). Patients with unilateral disease had higher intraoperative HVx ($p = 0.012$) and COx ($p = 0.172$) on the side with vasculopathy (Figure 4). There were no statistical differences in HVx or COx between the right or left sides in patients with bilateral disease ($p = 0.883$ for HVx; $p = 0.743$ for COx).

During the postoperative period, MAP decreased significantly with time (mean 80 ± 10 mmHg, range 58–111 mmHg for the entire monitoring period; $p < 0.001$). There were no statistically significant differences in left rSO₂ ($73 \pm 7\%$; $p = 0.945$). A statistical difference was detected in the right rSO₂ values over time ($75 \pm 8\%$; $p = 0.026$) because of a difference between two 3-min intervals ($p < 0.001$) out of a total of 307 intervals. Temperature in the PICU increased significantly with time (mean $37.1 \pm 0.6^\circ\text{C}$, range 35.1 – 39.1°C for the entire monitoring period; $p = 0.002$). Postoperative MAP_{OPT} was identified on at least one side in

six (100%) of six patients by both COx and HVx (Table 2). No patient had identifiable LLAs postoperatively.

No complications were associated with the autoregulation monitoring. One patient (patient 2) experienced several transient ischemic attacks (TIAs) on postoperative days 4–9. This patient had a history of preoperative bilateral strokes and diabetes mellitus. Postoperatively, she experienced transient episodes of aphasia and dysphagia, all of which were self-limited and responded to IV hydration. No patient experienced a fixed neurologic deficit during the 1-month follow-up period.

Discussion

This study demonstrates that autoregulation monitoring with the NIRS-derived COx and HVx indices can identify hemodynamic goals that conform to the limits of autoregulation during surgical revascularization and postoperative recovery in children with moyamoya. The indices identified the blood pressure range with optimal autoregulatory function in more than 80% of patients during surgery and in all patients during postoperative recovery. Furthermore, the index measurements suggest that autoregulation was worse on the side with vasculopathy in patients with unilateral moyamoya.

The purpose of this pilot study was to determine the feasibility of NIRS autoregulation monitoring in pediatric patients with moyamoya. We are planning future studies that will correlate the NIRS-derived indices to transcranial Doppler measurements of CBF during moyamoya revascularization. COx already has been shown to correlate to CBF velocity measurements obtained with transcranial Doppler during cardiopulmonary bypass (21), and HVx has been shown to correlate to an ICP-derived measure of vascular reactivity in patients with traumatic brain injuries (26) and to transcranial Doppler during cardiopulmonary bypass (28). We also have demonstrated that both COx and HVx correlate to laser Doppler measurements of cerebral red blood cell flux in a piglet model (17-19,22,23).

In patients with unilateral moyamoya, the higher intraoperative HVx and COx on the side with vasculopathy suggests that autoregulation was worse on the affected side. The surgical procedures performed in this study do not provide direct revascularization, so the decrease in HVx and COx postoperatively cannot be attributed to the operation. We can surmise that autoregulation during anesthesia is worse in the diseased vasculature, but this speculation requires future studies.

Identifying MAP_{OPT} with the NIRS-derived indices may provide a more rational target for blood pressure management in children at risk of cerebral ischemia than the ill-defined goal of maintaining a patient's "baseline" blood pressure. Moyamoya patients are at high risk of ischemic stroke, intracranial hemorrhage, TIAs, and hyperperfusion injury (7). Maintaining CBF autoregulation is of utmost importance. After revascularization procedures, hypertension can cause bleeding, and hypotension can result in graft thrombosis (29). Patients with preoperative histories of TIAs already have compromised CBF and are at increased risk of perioperative ischemic events. Furthermore, children with moyamoya are at higher risk of impaired autoregulation than are adults (8). Thus, precise blood pressure control is critical in this population.

Maintaining blood pressure within a range that optimizes autoregulation has been associated with improved outcomes in adults at risk of cerebral ischemia. For instance, minimizing the time spent below the optimal cerebral perfusion pressure (CPP) with maximal autoregulatory function (CPP_{OPT}) was associated with improved outcomes in adults with aneurysmal subarachnoid hemorrhages (30). In adults with traumatic brain injuries,

mortality was associated with greater deviation in CPP below CPP_{OPT} , severe disability was associated with greater deviation in CPP above CPP_{OPT} , and the best outcome was associated with the least deviation in CPP from CPP_{OPT} (31).

The ideal blood pressure range in pediatric moyamoya is unknown and may vary by patient age and disease severity. The general consensus among anesthesia guidelines is to maintain CPP at or above baseline and to raise the blood pressure to a high-normal range for revascularization techniques (29). However, ICP is not routinely monitored in this patient population, so CPP cannot be calculated. Obtaining a reliable baseline blood pressure can be difficult in pediatric patients. Thus, the NIRS autoregulation indices may be useful for clarifying neuroprotective hemodynamic goals in this population. Future studies with a larger sample size, correlation of the indices to transcranial Doppler measurements, and correlation of the autoregulation measurements to neurologic outcomes are indicated.

MAP_{OPT} and LLA were not identifiable in some patients. In our study, identification of MAP_{OPT} required a clear nadir in COx or HVx with increasing index values as MAP deviated from this nadir, plus independent interpretation of the index bar graphs with agreement between two physicians. Even with these relatively strict criteria, COx and HVx each identified MAP_{OPT} in 86% of patients intraoperatively and in 100% of patients in the PICU. One patient who did not have an identifiable MAP_{OPT} by COx did have an identifiable MAP_{OPT} by HVx . Another patient did not have a MAP_{OPT} by HVx but did have one by COx . In the situations where MAP_{OPT} was not identified, the requirement for a consistent increase in index values as MAP deviated from the nadir was not met. We used stringent criteria with this conservative approach to identify MAP_{OPT} because blood pressure norms and the limits of autoregulation in pediatric moyamoya are unknown.

LLA was not identified in some patients because COx or HVx did not exceed 0.5 or 0.3, respectively. It is possible that these patients' blood pressures did not become low enough to cross the LLA. Because this was an observational study, blood pressure was not intentionally manipulated, and purposely lowering a patient's blood pressure would be unsafe. Therefore, we suggest that using MAP_{OPT} as a neuroprotective hemodynamic goal would be more useful than trying to identify the LLA.

The blood pressure limits of autoregulation in pediatric patients with and without neurologic disease are unknown. Methods of examining autoregulation include monitoring during spontaneous changes in blood pressure (as in this study) or intentionally manipulating blood pressure. Vavilala et al. (32) measured changes in CBF with transcranial Doppler during phenylephrine infusion in healthy children under general anesthesia. If a patient's LLA was not evident during the period of blood pressure manipulation, the investigators used the patient's baseline MAP as the LLA. Although the investigators reported no differences in the LLA by age, LLA did vary within each age group. Our measured intraoperative LLAs of 55 – 65 mmHg were consistent with the range of LLA reported by Vavilala et al. (32) MAP_{OPT} has not been studied in healthy children with spontaneous variation in blood pressure. In children resuscitated from cardiac arrest, MAP_{OPT} has a linear and statistically significant relationship with age (unpublished data). In this small pilot study, we were unable to correlate LLA and MAP_{OPT} to age.

All patients were anesthetized with isoflurane and opiates. However, we did not monitor anesthetic depth. Isoflurane impairs autoregulation in a dose-dependent manner (33), resulting in a narrowed blood pressure range that supports autoregulation. Even though the blood pressure limits that conform to autoregulation may shift during anesthesia, CBF maintains some degree of pressure reactivity along the autoregulatory plateau, which permits the identification of MAP_{OPT} during general anesthesia with isoflurane (28). We

have also demonstrated that both COx and HVx identify the LLA during isoflurane anesthesia as accurately as do transcranial Doppler and laser-Doppler measurements of CBF (22-24,28). The fact that the NIRS-derived indices identified MAP_{OPT} and LLA in this study verified the intraoperative utility of these monitors in pediatric moyamoya. Moreover, the risk of pressure-passive CBF may increase as the vascular abnormalities become more severe. In this small pilot study, we were unable to correlate autoregulation to disease severity or Suzuki grade (27).

A limitation of the NIRS-derived indices is the restricted sampling of regional measurements from the frontal cortex, which is not the site of revascularization. However, since moyamoya affects the internal carotid artery terminus, both the anterior and middle cerebral arteries on one side tend to be diseased, as seen in our series of angiographic findings (Table 1). Because NIRS monitoring is not technically feasible directly in the surgical field, we used frontal cortex monitoring as the best surrogate determination of the CBF of interest. We suggest that guiding blood pressure management with COx and HVx monitoring combined with good clinical judgement is preferable to no monitoring in light of the risks of cerebral ischemia in this patient population.

Conclusions

Autoregulation monitoring with the NIRS-derived indices identified the blood pressure range with optimal autoregulatory function during neurosurgery and postoperative recovery in children with moyamoya. In patients with unilateral moyamoya, the index measurements suggested that autoregulatory function was worse on the side with vasculopathy. Future validation of the indices is needed for comparison against more direct measures of CBF. Future studies that correlate autoregulation measurements to neurologic outcomes are also indicated. This pilot study suggests that NIRS-derived measures of autoregulation could become useful clinical monitors to clarify neuroprotective hemodynamic goals in pediatric moyamoya.

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Figure 1.

Calculation of the hemoglobin volume index (HVx) in an 11-year-old girl with bilateral moyamoya (patient 2). (A, B) When mean arterial blood pressure (MAP) was approximately 60–90 mmHg intraoperatively, MAP and cerebral blood volume (CBV, or the relative total hemoglobin [rTHb] measured by near-infrared spectroscopy) were positively correlated. This positive correlation yielded an HVx value of 0.46, indicating pressure-passive vascular reactivity with impaired autoregulation. The linear regression line is illustrated ($E[Y] = 112.0 + 0.08X$; 95% confidence interval for slope: 0.07, 0.10; $p < 0.0001$). (C, D) In the same patient, when MAP was 90 mmHg in the postoperative period, MAP and CBV were negatively correlated. This negative correlation resulted in an HVx value of -0.26 , indicating pressure-reactive vascular reactivity with functional autoregulation. The linear regression line is illustrated ($E[Y] = 195.9 - 0.39X$; 95% confidence interval for slope: $-0.56, -0.21$; $p < 0.0001$). (E) HVx monitoring for 8 h during surgery and postoperatively is shown. Mean values of HVx were sorted into 5-mmHg bins of MAP. HVx became higher when MAP was < 90 mmHg, indicating that autoregulation was more impaired at lower blood pressures. When MAP was 90 mmHg, HVx decreased with improving autoregulation. Autoregulation was most robust at a MAP of 95 mmHg, as indicated by the nadir in HVx. Data in panels B and D are shown with linear regression lines and 95% confidence intervals. Data in panel E are shown as means $\pm$ SD.

Figure 2.

Patient 1 was a 16-year-old girl with unilateral moyamoya. (A) Magnetic resonance angiography revealed right internal carotid artery stenosis with attenuation of the right middle cerebral artery. (B) MRI diffusion-weighted image of the brain showed an ischemic stroke 2 months prior to revascularization surgery. (C) Mean intraoperative values of COx were placed into 5-mmHg bins of mean arterial blood pressure (MAP). On the affected side (right), COx indicated a lower limit of autoregulation (LLA; defined as COx $\geq$ 0.5) at the MAP bin 60 mmHg (solid arrow). An LLA was not detected on the unaffected (left) side, although COx increased as MAP decreased, suggesting worsening autoregulation with lower MAP. Optimal MAP, the blood pressure at which autoregulation was most functional (COx nadir), was at 95 mmHg (open arrows) on both sides. The fact that COx values across blood pressures were higher overall on the affected side than on the unaffected side suggests that autoregulation was more impaired on the side with diseased vasculature. A.U., arbitrary unit.

Figure 3.

Patient 2 was an 11-year-old girl with bilateral moyamoya. (A) Cerebral angiography showed occlusion of the terminal right and left internal carotid arteries. (B) MRI diffusion-weighted image of the brain showed preoperative strokes in the right anterior cerebral artery, middle cerebral artery, and posterior cerebral artery watershed distributions. (C) Mean intraoperative values of COx were placed into 5-mmHg bins of mean arterial blood pressure (MAP). COx detected different optimal MAP values on each side. The optimal MAP was 95 mmHg on the right and 85 mmHg on the left (open arrows). Left-sided COx indicated an LLA at 60 mmHg (solid arrow), whereas an LLA could not be detected on the right. The fact that COx values were higher on the left side than on the right at all blood pressures suggests that autoregulation was more impaired on the left side. COx increased as MAP decreased, suggesting that autoregulation worsened with lower blood pressures. A.U., arbitrary unit.

Figure 4.

In the four patients with unilateral moyamoya, autoregulatory function differed during surgery between the unaffected side and the side with vasculopathy as measured by the autoregulation indices. (A) During the intraoperative period, the cerebral oximetry (COx) and hemoglobin volume (HVx) indices (mean $\pm$ SEM) were higher on the side with vasculopathy, suggesting more impaired autoregulation ($p=0.172$ for COx; $*p=0.012$ for HVx). (B) In the postoperative period, COx and HVx were similar, suggesting similar autoregulatory function between affected and unaffected sides ($p=0.850$ for COx; $p=0.612$ for HVx).

Table 1

Clinical characteristics of the patients.

Patient	Age (y)	Preoperative angiographic findings	Surgical procedure	Preoperative comorbidities	Suzuki grade(27)
1	16	Unilateral moyamoya with right ICA supraclinoid stenosis. Normal left MCA flow with collateral vessel formation to the left ACA distribution.	Right pial synangiosis	<ul style="list-style-type: none"> Prior right MCA territory strokes Trisomy 21 Repaired esophageal atresia 	2
2	11	Bilateral moyamoya with occlusion of terminal right and left ICAs.	Bilateral pial synangiosis	<ul style="list-style-type: none"> Prior strokes in right ACA, MCA, and PCA watershed distributions Encephalomalacia Diabetes mellitus type I 	5
3	8	Bilateral moyamoya with ICA and ACA terminal occlusions. This patient had revascularization of the MCA territories from prior bilateral pial synangiosis, but she had persistent ACA distribution TIAs.	Bilateral encephalogalectomy synangiosis in the ACA territory	<ul style="list-style-type: none"> Prior bilateral pial synangiosis Recurrent TIAs Seizures 	3
4	2	Bilateral moyamoya with distal ICA and basilar tip occlusions.	Bilateral pial synangiosis	<ul style="list-style-type: none"> Prior bilateral strokes Neurofibromatosis type I eizures 	3
5	5	Unilateral moyamoya with left MCA occlusion.	Left pial synangiosis	<ul style="list-style-type: none"> Neurofibromatosis type I Asthma 	4
6	6	Unilateral moyamoya with right ICA distal occlusion. Left, 2–3 mm anterior choroidal aneurysm.	Right pial synangiosis	<ul style="list-style-type: none"> Prior bilateral ACA-MCA watershed strokes Sickle cell disease (hemoglobin SS) Obstructive sleep apnea 	3
7	9	Unilateral moyamoya with left ACA, MCA, and PCA stenosis.	Left pial synangiosis	<ul style="list-style-type: none"> Prior left MCA and ACA territory strokes Encephalomalacia Diabetes mellitus type I Hypothyroidism 	3

ACA, anterior cerebral artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; TIA, transient ischemic attack.

Table 2

Intraoperative and postoperative optimal mean arterial blood pressures (MAP_{OPT}) determined by the cerebral oximetry (COx) and hemoglobin volume (HVx) indices.

Measurement side	Intraoperative (n = 7)		Postoperative (n = 6)	
	MAP _{OPT} (mmHg; median [IQR])	No. of patients with identifiable MAP _{OPT}	MAP _{OPT} (mmHg; median [IQR])	No. of patients with identifiable MAP _{OPT}
Bilateral disease				
Right COx	70 (60, 95)	3	90 (85, 90)	2
Left COx	75 (70, 85)	3	80 (70, 85)	2
Right HVx	70 (60, 95)	3	80 (80, 85)	2
Left HVx	80 (60, 85)	3	80 (75, 85)	2
Unilateral disease				
COx on diseased side	65 (60, 95)	3	80 (70, 90)	4
COx on unaffected side	60 (40, 95)	3	80 (70, 85)	4
HVx on diseased side	60 (60, 65)	2	70 (70, 80)	4
HVx on unaffected side	65 (60, 95)	3	80 (70, 85)	4

IQR, Interquartile range.

Table 3

Intraoperative mean arterial blood pressure lower limit of autoregulation (LLA) determined by the cerebral oximetry (COx) and hemoglobin volume (HVx) indices.

Patient	Age (y)	Moyamoya location	LLA (mmHg)	Identifying index
1	16	Unilateral	Diseased side: 60 Unaffected side: 60	COx and HVx
2	11	Bilateral	Left: 60 Right: 65	COx and HVx
5	5	Unilateral	Diseased side: 55 Unaffected side: None identified	COx