



## OPEN ACCESS

## EDITED BY

Teodor Svedung Wettervik,  
Uppsala University, Sweden

## REVIEWED BY

Yu Lei,  
Fudan University, China  
Stefan Yu Bögli,  
Cambridge University Hospitals,  
United Kingdom

## \*CORRESPONDENCE

Lan Yao  
✉ yaolan@pkuih.edu.cn

†These authors share first authorship

RECEIVED 30 May 2023

ACCEPTED 24 August 2023

PUBLISHED 21 September 2023

## CITATION

Chen X, Qin X, Wang J, Wang R, Guo X and Yao L (2023) Effect of cerebral oxygen saturation monitoring in patients undergoing superficial temporal anterior-middle cerebral artery anastomosis for ischemic Moyamoya disease: a prospective cohort study. *Front. Neurol.* 14:1226455. doi: 10.3389/fneur.2023.1226455

## COPYRIGHT

© 2023 Chen, Qin, Wang, Wang, Guo and Yao. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

# Effect of cerebral oxygen saturation monitoring in patients undergoing superficial temporal anterior-middle cerebral artery anastomosis for ischemic Moyamoya disease: a prospective cohort study

Xuanling Chen<sup>1†</sup>, Xuwei Qin<sup>1†</sup>, Jing Wang<sup>2</sup>, Rong Wang<sup>3</sup>, Xiangyang Guo<sup>4</sup> and Lan Yao<sup>1\*</sup>

<sup>1</sup>Department of Anesthesiology, Peking University International Hospital, Beijing, China, <sup>2</sup>Department of Neurosurgery, Peking University International Hospital, Beijing, China, <sup>3</sup>Department of Neurosurgery, Tiantan Hospital, Capital Medical University, Beijing, China, <sup>4</sup>Department of Anesthesiology, Peking University Third Hospital, Beijing, China

**Objective:** Regional cerebral oxygen saturation (rSO<sub>2</sub>) is linked with blood pressure. This study evaluated the influence of perioperative rSO<sub>2</sub> monitoring on the prognosis of ischemic Moyamoya disease (MMD) patients undergoing anastomosis surgery.

**Methods:** In this prospective cohort, patients with unilateral ischemic MMD of Suzuki stage  $\geq 3$  were included. The decision of rSO<sub>2</sub> was made by the clinician and the patient. The rSO<sub>2</sub> group maintained intraoperative rSO<sub>2</sub> levels through the modulation of blood pressure, inhaled oxygen concentration, carbon dioxide in arterial blood, and red blood cell transfusion. The non-rSO<sub>2</sub> group used conventional anesthesia practices. Perioperative mean arterial pressure (MAP), rSO<sub>2</sub> values, neurological complications, and postoperative results were assessed.

**Results:** A total of 75 eligible patients were categorized into a rSO<sub>2</sub> monitoring group ( $n = 30$ ) and a non-rSO<sub>2</sub> monitoring group ( $n = 45$ ). For the rSO<sub>2</sub> group, the preoperative rSO<sub>2</sub> was significantly lower on the affected side ( $P < 0.05$ ). After anastomosis, this value notably increased ( $P = 0.01$ ). A moderate relationship was observed between perioperative rSO<sub>2</sub> and MAP before, during, and after surgery, with correlation coefficients ( $r$ ) of 0.536, 0.502, and 0.592 ( $P < 0.05$ ). Post-surgery MAP levels differed between the groups, with the rSO<sub>2</sub> group showing decreased levels compared to pre-surgery and the non-rSO<sub>2</sub> group displaying elevated levels. Notably, the rSO<sub>2</sub> group reported shorter hospitalizations and decreased neurological complications. Patients with a hypertension history found postoperative MAP influencing hospital stay duration.

**Conclusion:** Perioperative rSO<sub>2</sub> surveillance enhanced cerebral perfusion and minimized postoperative complications in ischemic MMD patients. Thus, rSO<sub>2</sub> monitoring is advocated for MMD patients undergoing vascular anastomosis.

## KEYWORDS

ischemic MMD, superficial temporal artery-middle cerebral artery anastomosis, regional cerebral oxygen saturation (rSO<sub>2</sub>), anesthesia management, mean arterial pressure

## 1. Introduction

Moyamoya disease (MMD) is a chronic vascular brain disorder marked by progressive stenosis or occlusion of crucial cerebral arteries. Its clinical presentation is varied, including epilepsy, cognitive dysfunction, headache, and cerebral ischemia (1). The disease affects 1.14 out of 100,000 people in China (2), with women being twice as susceptible as men (3). It typically presents in children at ~5 years of age and adults in their 40s (4).

Surgery is the predominant treatment for MMD (5), with the superficial temporal anterior-middle cerebral arterial anastomosis being the standard approach for ischemic MMD (6). This surgery promotes blood supply from the unaffected parietal branch of the superficial temporal artery to the ischemic brain hemisphere (7), enhancing perfusion and setting up collateral circulation (8). However, perioperative complications such as cerebral hemorrhage and infarction remain a concern. It is essential to balance oxygen supply and demand in the brain's affected area during the perioperative period and swiftly address intraoperative cerebral hypoxia to prevent stroke (9). Traditionally, anesthesiologists have relied on experience for perioperative management, using preoperative mean arterial pressure (MAP), partial pressure of carbon dioxide in arterial blood (PaCO<sub>2</sub>), and other cerebral perfusion indicators. The perioperative MAP should be kept roughly 10% above the preoperative level to boost cerebral perfusion during vascular anastomosis (10). However, post-anastomosis, the affected brain region's blood flow can surge, risking vessel rupture and hemorrhage (11). Notably, if the empirical systolic blood pressure remains under 130 mmHg post-surgery and postoperative brain tissue perfusion is not improved (12), it fails to ameliorate the affected side's cerebral tissue perfusion. This can lead to complications such as hyperperfusion syndrome (CHS) (13), cerebral hemorrhage (14), and infarction (15). Thus, managing blood pressure is paramount during the perioperative phase (16).

Regional cerebral oxygen saturation (rSO<sub>2</sub>) offers non-invasive, real-time monitoring of local cerebral blood perfusion. It has been employed in various surgeries, including cardiac, orthopedic, and neurosurgery, displaying remarkable accuracy in gauging oxygen saturation and minimizing postoperative neurological complications (17). Prior research indicates that rSO<sub>2</sub> reliably represents cerebral perfusion in MMD patients and can predict postoperative outcomes such as delirium, cerebrovascular reactive delirium (18), and CHS (19, 20). However, the utilization of rSO<sub>2</sub> for perioperative blood pressure monitoring in MMD patients remains under-explored (1).

This study aimed to assess the impact of rSO<sub>2</sub> monitoring in MMD patients undergoing unilateral superficial temporal artery to middle cerebral artery branch anastomosis.

## 2. Methods

### 2.1. Study design and surgical procedure

#### 2.1.1 Study design and participants

This prospective cohort study included 110 patients with ischemic MMD who underwent direct anastomosis

between the superficial temporal artery and the middle cerebral arterial branch for the first time between January 2019 and July 2021 in the Neurosurgery Department of Peking University International Hospital. The ethics committee of the university approved the study, and all patients provided signed informed consent for their participation.

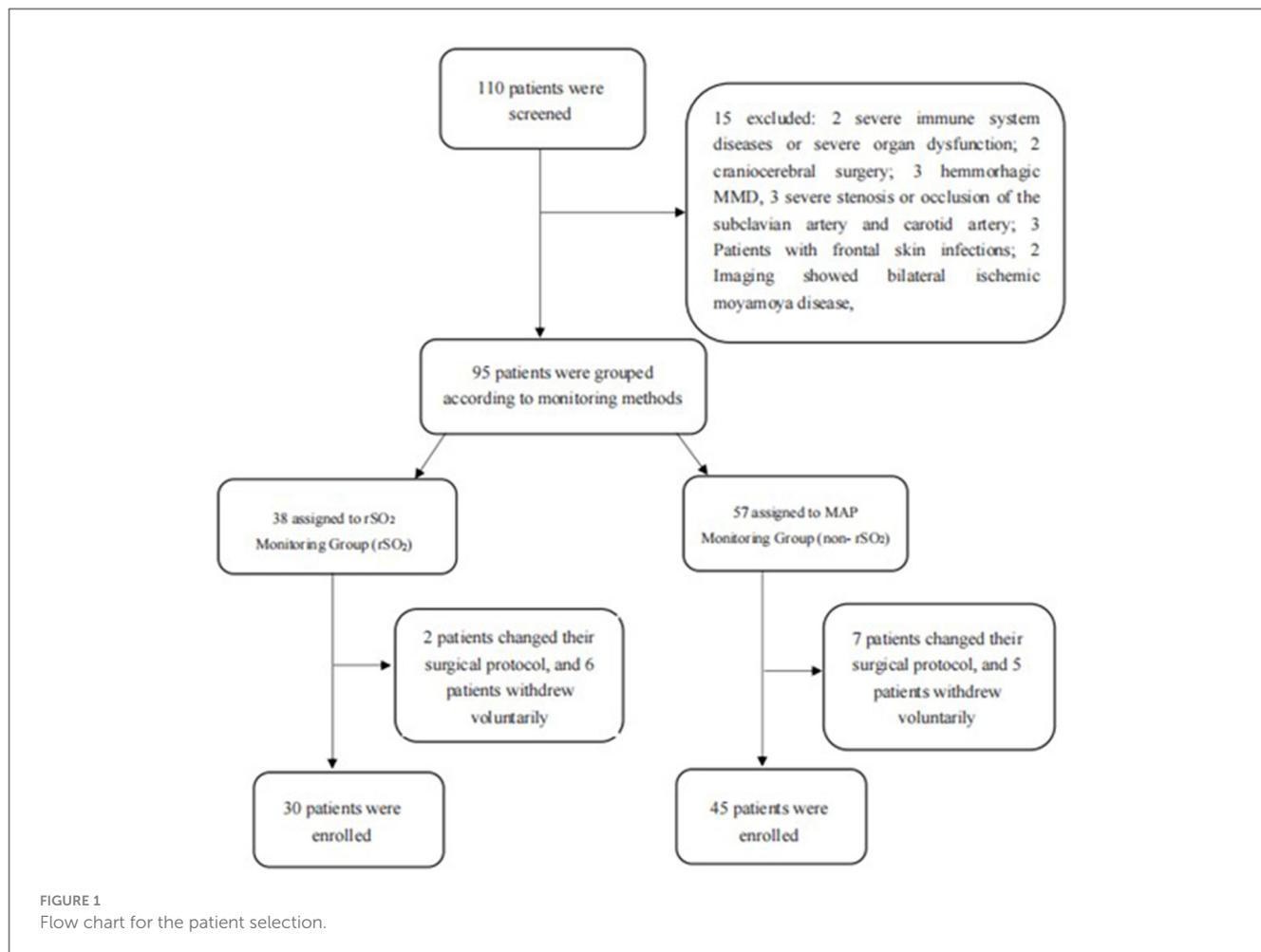
The inclusion criteria were as follows: (1) patients with unilateral ischemic MMD seen on cerebral angiography; (2) patients without intracranial space-occupying lesions, cerebral hemorrhage, aneurysms, massive cerebral infarction, and other related diseases detected on CT imaging; (3) patients aged between 18 and 65 years and with any gender; (4) patients with ASA physical status classification scores of I and II; (5) patients with the Suzuki staging of  $\geq 3$  calculated on digital subtraction angiography (DSA) and the score of Mini-mental State Examination (MMSE) of  $>24$  points; and (6) patients who furnished signed informed consent. The exclusion criteria were as follows: (1) patients who experienced severe immune system diseases or severe organ dysfunction, such as heart, liver, and kidney dysfunctions; (2) patients who underwent prior craniocerebral surgery; (3) patients with hemorrhagic MMD; (4) patients who had severe stenosis or occlusion of the subclavian artery and carotid artery; (5) patients with frontal skin infections in which the measuring of rSO<sub>2</sub> could not have been done; (6) patients with bilateral ischemic MMD; and (7) changed surgical protocol or patients who withdrew voluntarily.

Seventy-five patients were included in the study analysis. The decision was made by the clinician and the participants whether monitoring of rSO<sub>2</sub> is needed or not. The participants were divided into two groups according to whether rSO<sub>2</sub> was monitored or not: the rSO<sub>2</sub> monitoring group (the rSO<sub>2</sub> group) and the non-rSO<sub>2</sub> monitoring group (the non-rSO<sub>2</sub> group).

### 2.2. Anesthesia and monitoring methods

#### 2.2.1. Anesthesia protocol

Midazolam at a dosage of 0.02 mg/kg, propofol at a dosage of 1.5 mg/kg, sufentanil at a dosage of 0.4  $\mu$ g/kg, and rocuronium at a dosage of 1 mg/kg were used for inducing anesthesia in both groups. When the bispectral index (BIS) reached 40–60 (the electrode was placed on the forehead contralateral side), endotracheal intubation and mechanical ventilation were connected. The end-tidal expiratory carbon dioxide pressure (PetCO<sub>2</sub>) was maintained between 35 and 45 mmHg by adjusting tidal volume and respiratory rate, and the inhaled oxygen concentration was adjusted to 60%. Anesthesia was maintained by intravenous infusion of propofol at the rate of 3–4 mg/(kg·h), remifentanil at the rate of 0.1–0.2  $\mu$ g/(kg·min), continuous inhalation of sevoflurane at a percentage concentration of 0.8%–1.0%, and BIS was maintained between 40 and 60. During the operative procedure, rocuronium was given intravenously, and 10  $\mu$ g sufentanil was given at the time of suturing the scalp. After completion of the scalp suture, all anesthetic drugs were withdrawn.



### 2.2.2. Monitoring of blood pressure and medications for blood pressure adjustment

Fluid access was established, and the Allen test was negative on the right/left hand. Subsequently, the radial artery puncture catheterization was performed, and the MAP (intraoperative MAP), ECG, SPO<sub>2</sub>, body temperature, and BIS were determined. The rSO<sub>2</sub> (Medtronic 5100C, America) was monitored in the rSO<sub>2</sub> group. In the rSO<sub>2</sub> group, rSO<sub>2</sub> and MAP were monitored 1 day before surgery in the ward. The same trained anesthesiologist performed all rSO<sub>2</sub> monitoring and postoperative follow-up. Method of rSO<sub>2</sub> monitoring: alcohol was applied to the forehead for sterilization and dehydration. Then, patches for measuring rSO<sub>2</sub> were placed on the forehead 1 cm away from the middle of the forehead and 1–2 cm above the eyebrow arch, and the rSO<sub>2</sub> monitor was connected. The baseline rSO<sub>2</sub> values were calibrated and monitored continuously for 3 h after stabilization of values for 5 min. MAP was measured from the right upper limb, with an interval of 5 min, and monitored for 3 h. The monitoring was performed on alternate days after entering the operating room. During surgery, blood pressure was adjusted in the rSO<sub>2</sub> group with the observation of rSO<sub>2</sub>. The objective of monitoring rSO<sub>2</sub> was to maintain no more than a 20% decrease in the baseline value or no

more than a 55% decrease in the baseline absolute value during surgery.

When the rSO<sub>2</sub> was lower than this level, the following treatment measures were adopted (21): (1) The connection and position of the rSO<sub>2</sub> patch were checked; (2) The blood pressure was increased; (3) The concentration of inhaled O<sub>2</sub> was raised; (4) If the above treatment measures did not improve the rSO<sub>2</sub>, blood gas was analyzed, and if anemia was present (<80 g/L), 2–4 U suspended red blood cells were transfused based on the oxygen saturation. The rSO<sub>2</sub> was monitored for three consecutive days following the surgery. On D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub>, all data were collected by the same anesthesiologist. In the non-rSO<sub>2</sub> group, the anesthesiologist maintained the MAP before vascular anastomosis ~10% above the baseline value of the preoperative MAP. The intraoperative MAP was collected by the monitor. If the blood pressure decreased during the operation, ephedrine of 3–6 mg intravenously was administered to achieve the blood pressure rapidly, and also, noradrenaline was continuously administered to maintain the target blood pressure level. The endotracheal cannula was removed after the patient recovered from anesthesia, and the patient returned to the ward. For three consecutive days after surgery (D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub>), patients in both groups were

continuously monitored for 8 h (8 am to 4 pm) based on MAP or rSO<sub>2</sub>.

## 2.3. Indicators that determine the outcome

### 2.3.1. Outcome indicators

The perioperative period (22) is referred to 7 days before surgery to 7 days after surgery. The outcome indicators were the postoperative cerebral hemorrhage, cerebral infarction, and incidence of CHS in the two groups.

The clinical manifestations of cerebral hemorrhage and CHS were similar, such as postoperative headache, seizure, and focal neurological deficit. (1) Diagnosis of cerebral hemorrhage: new intracranial blood was seen on a postoperative craniocerebral CT scan. (2) Diagnosis of CHS: (a) The diagnosis was done by observation of local neurological dysfunction and epilepsy. (b) CT/MRI perfusion imaging and SPECT scans showed that blood perfusion at the bypass site increased from the lowest value before surgery to the highest value after surgery and was locally clustered. (c) The diagnosis was performed by excluding local muscle swelling and compression (23). (3) Diagnosis of cerebral infarction: postoperative craniocerebral CT or MRI images showed new cerebral ischemic lesions. All patients received an MRI for outcome evaluation. The postoperative complications of all patients were analyzed by the same senior neurosurgeon and radiologist.

## 2.4. Data source and evaluation

Data were obtained from the medical records, anesthesia information system, and rSO<sub>2</sub> monitors of Peking University International Hospital. The general characteristics of 75 patients were collected, and operation time and MAP values were recorded for the preoperative period (3 h on the day before the surgery), intraoperative period (from the time when the skin was incised to the time of the end of suturing), postoperative period (from the end of the surgery to the time when leaving the surgery room), and postoperative three consecutive days (D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub>). Hemoglobin content from the blood gas analysis before and after surgery was recorded for the two groups. The perioperative rSO<sub>2</sub> mean values (D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub>) were recorded in the rSO<sub>2</sub> group. The data of cerebral infarction, CHS, cerebral hemorrhage, reoperation, and death were recorded from the postoperative period to the time of discharge.

## 2.5. Statistical analyses

SPSS version 20.0 statistical software was used to analyze the data. The Shapiro–Wilk test evaluated the normal distribution. The measurement data were expressed as mean ± standard deviation (mean ± SD). If they did not fit the normal distribution, the quartile method M (P25 and P75) was used. The intra-group comparison

was performed by *t*-test and repeated measure analysis of variance between the two groups. For comparing the measurement data between groups, repeated measurement analysis of variance was used for complex conditions. The least significant difference (LSD) method was used for the comparison between the groups and the Kruskal–Wallis H method was used for testing if the application conditions were not met. Counting data were expressed as frequencies and percentages and compared using the chi-square tests. The Kolmogorov–Smirnov test was used to evaluate the data distribution. The Pearson method was used for correlation analysis. An alpha value of 0.05 and a *P*-value of <0.05 were considered to be statistically significant differences.

## 3. Results

### 3.1. The flow chart for the selection of patients

In this study, 110 patients were enrolled, and 15 patients were excluded due to severe immune system diseases or severe organ dysfunction (*n* = 2), craniocerebral surgery (*n* = 2), hemorrhagic MMD (*n* = 3), severe stenosis or occlusion of the subclavian artery and carotid artery (*n* = 3), frontal skin infections (*n* = 3), and bilateral ischemic Moyamoya disease. Finally, 95 patients were screened and divided into the rSO<sub>2</sub> group (*n* = 38) and the non-rSO<sub>2</sub> group (*n* = 57) according to whether the rSO<sub>2</sub> was monitored or not. In the rSO<sub>2</sub> group, the surgical protocol was changed in two patients, and six patients withdrew voluntarily from the study. In the non-rSO<sub>2</sub> group, the surgical protocol was modified in seven patients, and five patients withdrew voluntarily from the study. Finally, 38 patients were included in the rSO<sub>2</sub> group and 45 in the non-rSO<sub>2</sub> group. The flow chart for the selection of patients is shown in Figure 1.

### 3.2. General characteristics of patients

Seventy-five patients were included in the analysis, and all underwent direct anastomosis of the unilateral superficial temporal artery and middle cerebral arterial branch. The mean age of the patients in the rSO<sub>2</sub> group was 47.33 ± 7.52 years, and the preoperative MAP was 97.28 ± 11.67 mmHg. The mean age of the patients in the non-rSO<sub>2</sub> group was 46.30 ± 7.80 years, and the preoperative MAP was 98.57 ± 9.92 mmHg. A statistical difference in the general characteristics of patients was found between the two groups, except for gender (*P* > 0.05), as shown in Table 1.

### 3.3. Multiple factors influencing the length of stay (multi-factor analysis)

The length of stay in the rSO<sub>2</sub> group was 7.73 ± 2.23 days and in the non-rSO<sub>2</sub> group was 9.04 ± 2.68 days with a statistically significant difference (*P* = 0.03). The length of stay in the two groups was correlated to rSO<sub>2</sub> monitoring, history of hypertension, preoperative PaCO<sub>2</sub>,

TABLE 1 General characteristics of patients in both groups.

Parameters	rSO <sub>2</sub> group (n = 30)	Non-rSO <sub>2</sub> group (n = 45)	P-value
Age (mean ± SD), years	46.30 ± 7.80	47.33 ± 7.52	0.567
<b>Sex</b>			
Male, n (%)	19 (63.33)	11 (24.44)	0.000
Female, n (%)	11 (36.67)	34 (75.56)	
BMI (mean ± SD), kg/m <sup>2</sup>	26.22 ± 3.01	26.09 ± 2.20	0.821
Operation time (mean ± SD), min	275.97 ± 22.30	272.76 ± 33.97	0.650
<b>Operative side</b>			
Left	13 (43.33)	18 (40)	0.774
Right	17 (56.67)	27 (60)	
MAP (mean ± SD), mm Hg	98.57 ± 9.92	97.28 ± 11.67	0.620
<b>Arterial systolic blood pressure, n (%)</b>			
100–140 mmHg (1)	16 (53.33)	21 (46.67)	0.572
141–180 mmHg (2)	14 (46.67)	24 (53.33)	
Heart rate (mean ± SD), bpm	77.90 ± 8.66	78.04 ± 9.69	0.948
SpO <sub>2</sub> (mean ± SD), %	98.93 ± 1.59	98.78 ± 1.53	0.673
PaO <sub>2</sub> (mean ± SD), mm Hg	86.33 ± 5.14	84.60 ± 4.32	0.119
PaCO <sub>2</sub> (mean ± SD), mm Hg	36.79 ± 2.59	36.50 ± 3.49	0.701
Hb (before surgery; mean ± SD), g/dl	117.27 ± 14.04	117.00 ± 10.83	0.926
Hb (after surgery; mean ± SD), g/dl	114.63 ± 13.75	112.33 ± 18.73	0.566

preoperative Hb, time of surgery, postoperative MAP D<sub>1</sub>, MAP D<sub>2</sub>, MAP D<sub>3</sub>, and preoperative PaO<sub>2</sub>. Utilizing the rSO<sub>2</sub> monitored could have shortened the length of stay ( $P = 0.042$ ). Patients with a history of hypertension, postoperative MAP D<sub>1</sub>, MAP D<sub>2</sub>, and MAP D<sub>3</sub> affected the length of stay, and the rest were not significantly correlated, as shown in Table 2.

### 3.4. Perioperative mean arterial pressure

No significant difference in preoperative MAP was found between the two groups perioperatively ( $P = 0.62$ ). Within the rSO<sub>2</sub> group, the intraoperative MAP and postoperative MAP decreased significantly compared to the preoperative MAP ( $P < 0.01$ ). Within the non-rSO<sub>2</sub> group, the intraoperative and postoperative MAPs differed significantly from the preoperative MAP ( $P = 0.00$ ), as shown in Table 3.

### 3.5. Perioperative rSO<sub>2</sub>

The preoperative rSO<sub>2</sub> in the rSO<sub>2</sub> group was significantly lower on the affected side than on the healthy side ( $P = 0.00$ ). The rSO<sub>2</sub> of the affected side was higher than that of the healthy side after vascular anastomosis, and the difference was statistically significant ( $P = 0.01$ ). The rSO<sub>2</sub> on the affected side was higher than that on the same side before surgery ( $P < 0.05$ ).

The rSO<sub>2</sub> of D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub> on the affected side were significantly higher than those on the healthy side for 3 days after surgery ( $P < 0.01$ ; Table 4).

### 3.6. Relationship between rSO<sub>2</sub> and MAP during the perioperative period

The mean value of rSO<sub>2</sub> showed a moderately positive correlation to the corresponding MAP before, during, and after surgery, and the correlation coefficients ( $r$ ) were 0.536, 0.502, and 0.592, respectively ( $P < 0.05$ ), as shown in Figures 2A–C.

### 3.7. Neurological complications

One case had CHS (3.3%), and one case experienced cerebral hemorrhage (3.3%) in the rSO<sub>2</sub> group between the time after surgery and the time of discharge. Two cases had cerebral hemorrhage (4.4%), and 10 cases had CHS (33.3%) in the non-rSO<sub>2</sub> group. No cerebral infarction, reoperation, or death occurred in the two groups. Fisher's test showed that neurological complication in the rSO<sub>2</sub> group were significantly less than those in the non-rSO<sub>2</sub> group ( $P = 0.036$ ).

### 3.8. Logistic regression analysis of complications, use of rSO<sub>2</sub>, and blood pressure at different time periods.

Postoperative complications such as CHS and cerebral hemorrhage in patients with ischemic MMD were correlated with rSO<sub>2</sub> and the management of MAP during and for three consecutive days after surgery (D<sub>1</sub>, D<sub>2</sub>, and D<sub>3</sub>;  $P < 0.05$ ), as shown in Table 5.

## 4. Discussion

Blood pressure is regulated to ensure good cerebral perfusion when the brain region is affected. However, blood pressure cannot directly reflect the blood perfusion in encephalopathy, which may be an indirect indicator (24). The rSO<sub>2</sub> is the measure of blood oxygen saturation in local tissues, including the brain tissue, and is monitored non-invasively.

Many previous studies (4, 25–27) found that frequent intraoperative monitoring of rSO<sub>2</sub> had a certain predictive value of intraoperative cerebral ischemia and postoperative neurological complications. Samra et al. (28) found that when rSO<sub>2</sub> was reduced

TABLE 2 Multivariate analysis for the length of stay.

Parameters	B-value	t-value	P-value	95.0% confidence interval of B	
				Lower limit	Upper limit
Use of rSO <sub>2</sub> or not	-1.233	-2.068	0.042	-2.423	-0.044
History of hypertension	1.286	2.186	0.032	0.112	2.460
Preoperative PaCO <sub>2</sub>	0.03	0.39	0.696	0.89	1.2
Preoperative Hb	0.002	0.094	0.925	0.96	1.04
Time of surgery	0.004	0.46	0.645	0	0.31
<b>Postoperative</b>					
MAP D <sub>1</sub>	-0.057	-2.108	0.035	0.9	1
MAP D <sub>2</sub>	-0.064	-2.375	0.018	0.89	0.99
MAP D <sub>3</sub>	-0.099	-2.774	0.006	0.84	0.97
Preoperative PaO <sub>2</sub>	0.081	1.539	0.124	0.98	1.2

TABLE 3 Comparison of MAP of perioperative periods between the rSO<sub>2</sub> group and the non-rSO<sub>2</sub> group (mean ± SD).

Parameters	rSO <sub>2</sub> (n = 30)	non-rSO <sub>2</sub> (n = 45)	t-value	P-value
Preoperative MAP	98.57 ± 9.92	97.28 ± 11.67	-0.498	0.620
Intraoperative MAP	91.00 ± 9.22	102.26 ± 7.21	5.922	0.000
Postoperative MAP	93.53 ± 6.90	104.05 ± 8.22	5.779	0.000
MAP D <sub>1</sub>	94.76 ± 8.99	99.45 ± 10.70	1.980	0.002
MAP D <sub>2</sub>	93.99 ± 9.59	100.12 ± 10.45	2.564	0.012
MAP D <sub>3</sub>	93.81 ± 7.76	99.75 ± 8.11	3.159	0.002

by <20% of the baseline value, the occurrence of postoperative neurological complications was significantly reduced, and the rSO<sub>2</sub> level had high sensitivity (80%) and specificity (82.2%) in predicting neurological complications.

The patients in the rSO<sub>2</sub> group were monitored for rSO<sub>2</sub> on the day before surgery, and the rSO<sub>2</sub> value on the affected side was lower than that on the healthy side, suggesting that vascular lesions could have led to abnormal cerebral perfusion. The sensitivity of rSO<sub>2</sub> level in monitoring cerebral perfusion had another viewpoint. The results of the present study showed a moderate positive correlation between perioperative rSO<sub>2</sub> and MAP, which suggests that empirical blood pressure management is necessary. In a normal population with conditions of reasonable blood volume, no serious cardiac dysfunction, and no serious anemia, the improvement of cerebral perfusion can be achieved by adjusting the patient's blood pressure using only vasoactive drugs. However, in patients with ischemic MMD, it might not be beneficial to simply elevate blood pressure due to the fragile vascular mass. At this point, an individualized blood pressure regulation program may be more appropriate for such patients when cerebral perfusion decreases and rSO<sub>2</sub> decreases. In addition to increasing blood pressure, cerebral perfusion in the affected area of the brain can also be improved through comprehensive treatments, such as increasing inhaled O<sub>2</sub> concentration, adjusting PaCO<sub>2</sub>, and transfusing red blood cells (29) to reduce the incidence of CHS and cerebral hemorrhage caused by the elevated blood pressure.

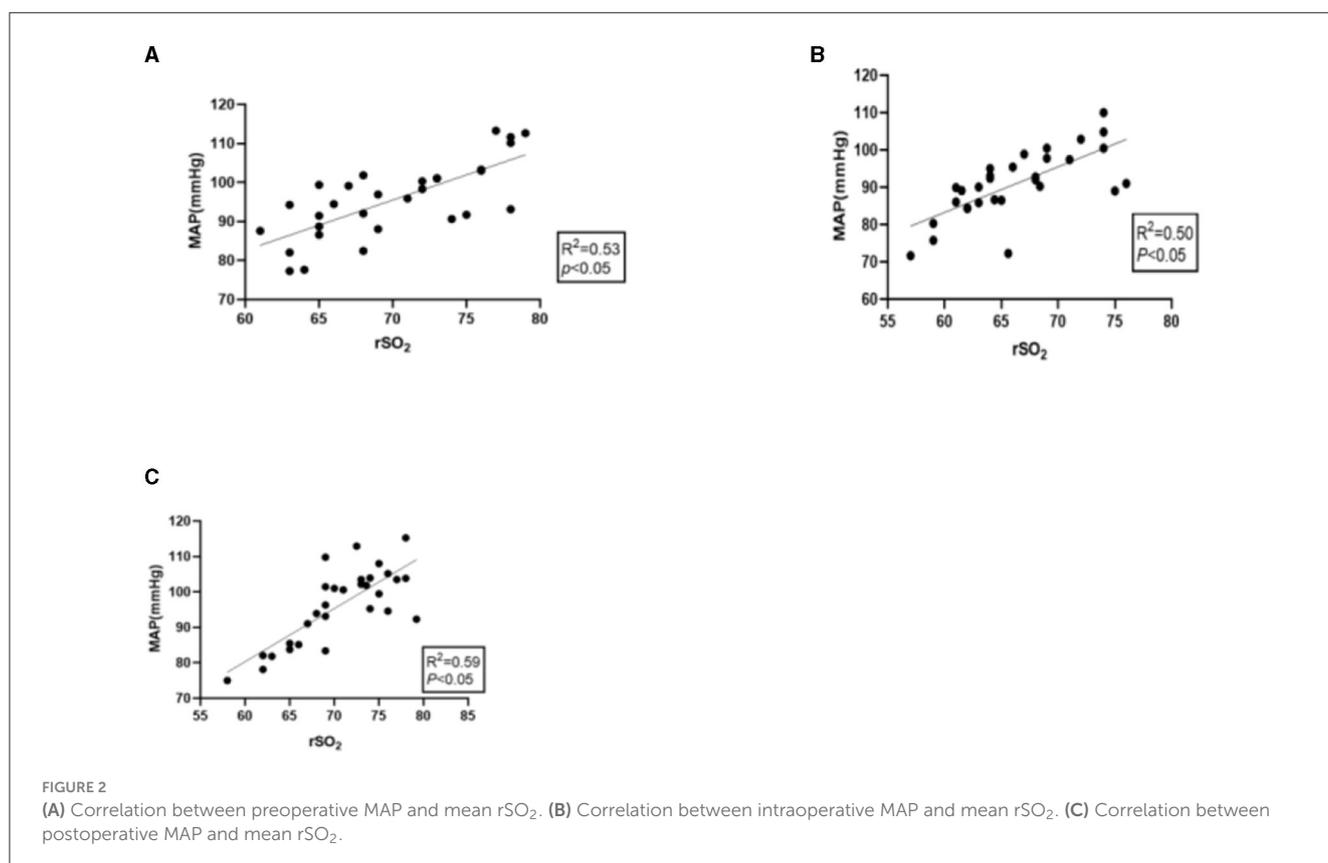
After vascular anastomoses, rSO<sub>2</sub> on the affected side increased even more than that on the healthy side, demonstrating that blood from the superficial temporal artery on the affected side entered the cerebral ischemic area and improved the cerebral tissue blood perfusion. The rSO<sub>2</sub> was monitored continuously for 3 days after surgery in the rSO<sub>2</sub> group, and the value of rSO<sub>2</sub> on the diseased side was similar to the value at the time of vascular opening after vascular anastomosis, which may have been due to the poor compensatory capacity of cerebral vessels in the affected area, the increased cerebral blood flow shunt, and the ischemic area reaching a new equilibrium point after a certain period. The rSO<sub>2</sub> value could reflect the cerebral perfusion on the affected side in real-time and let the anesthesiologist adjust accordingly, which could reduce the occurrence of postoperative neurological complications, ensuring surgical benefit, and improving the postoperative outcome of patients (all patients in the rSO<sub>2</sub> group received an intraoperative reduction of BP due to the rSO<sub>2</sub> measurement). The results of He et al. (29) show that the length of hospital stay in the non-rSO<sub>2</sub> group was longer than that in the rSO<sub>2</sub> group, which was consistent with our result of multivariate analysis. We also found that the length of stay of MMD patients was related to hypertension, so controlling the patients' blood pressure might have a positive effect on reducing the length of stay.

Complications such as CHS syndrome and cerebral hemorrhage were low in this study, which is a decrease compared to previous studies (30, 31). The empirical method of maintaining

TABLE 4 Comparison of the rSO<sub>2</sub> between the affected side and the healthy side in the rSO<sub>2</sub> group at each time of the perioperative period (mean ± SD).

Parameters	Healthy side (n = 30)	Affected side (n = 30)	t-value	P-value
Preoperative rSO <sub>2</sub>	66.87 ± 7.82	61.77 ± 7.84*	5.391	0.000
Intraoperative rSO <sub>2</sub>	69.13 ± 6.34	71.48 ± 6.10*	-2.670	0.012
Postoperative rSO <sub>2</sub>	71.07 ± 7.12	71.87 ± 8.47	-0.582	0.565
rSO <sub>2</sub> D <sub>1</sub>	68.87 ± 5.16	73.03 ± 5.64	3.358	0.002
rSO <sub>2</sub> D <sub>2</sub>	68.67 ± 5.45	75.21 ± 4.50	5.052	0.000
rSO <sub>2</sub> D <sub>3</sub>	69.20 ± 5.94	75.09 ± 3.84	4.771	0.000

\*Statistical significance difference.



blood pressure ~10% above the preoperative MAP before vascular anastomosis could not better provide cerebral perfusion on the affected side, even with the occurrence of cerebral perfusion syndrome and cerebral hemorrhage after the opening of the artery clamp, which was similar to the outcome of some study (11, 32). Blood pressure management should be individualized to reduce the occurrence of complications (32). Through logistic regression analysis, we found that rSO<sub>2</sub> and perioperative BP control were directly correlated with postoperative neurological complications, and the BP in the rSO<sub>2</sub> group was significantly lower than that in the non-rSO<sub>2</sub> group, and the complications were also fewer as well. This finding suggested that intervention using rSO<sub>2</sub> monitoring could assist to detect and adjust in cerebral perfusion and oxygen supply in real-time, leading to an improved prognosis for patients, as well as a shorter hospital stay, which was consistent with the results of Li et al. (33).

This study had a small sample size, and short-term follow-up and the postoperative BP management and treatment of patients in the rSO<sub>2</sub> group were adjusted by the surgeon according to the value of rSO<sub>2</sub>. Unfortunately, we did not collect the specific management methods.

Moreover, since no monitoring of rSO<sub>2</sub> was performed in the non-rSO<sub>2</sub> group, no comparison of the brain oxygenation itself can be made thus putting in question whether the reduced number of complications and shorter length of stay were due to better oxygenation or purely due to the lower BP, requiring a more rigorous study design analyzing a larger sample of patients and longer follow-up to confirm or negate the value of rSO<sub>2</sub> monitoring.

The current study outcome found that the intraoperative use of rSO<sub>2</sub> monitoring was associated with a positive impact on the quality of recovery of patients after vascular reconstruction for ischemic MMD.

TABLE 5 Multivariate logistic regression analysis of MMD postoperative complications with rSO<sub>2</sub> and MAP at different time periods.

Parameters	B	T	Sig	B 95% (CI)	
				Upper Limit	Lower Limit
rSO <sub>2</sub> monitoring	0.075	1.97	0.049	1	1.16
Preoperative MAP	0.09	2.495	0.013	1.02	1.17
Intraoperative MAP	0.113	2.723	0.006	1.03	1.21
Postoperative MAP	0.117	3.016	0.003	1.04	1.21
MAP D <sub>1</sub>	0.259	3.605	<0.001	1.13	1.49
MAP D <sub>2</sub>	0.193	3.701	<0.001	1.09	1.34
MAP D <sub>3</sub>	0.200	3.493	<0.001	1.09	1.37

In conclusion, during the surgical procedure in patients undergoing superficial temporal anterior-middle cerebral arterial branch anastomosis for ischemic MMD, the application of MAP and rSO<sub>2</sub> monitoring reduced the MAP of patients during the middle and early postoperative period and was associated with the occurrence of postoperative neurological complications compared with the patients who had only MAP detection. It is recommended to monitor rSO<sub>2</sub> as a routine procedure for patients with ischemic MMD undergoing bypass surgery, which would benefit the patients.

## Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

## Ethics statement

The studies involving humans were approved by the institutional review Committee of Peking University International Hospital approved the study (KYSQ2019-058-01). The studies were conducted in accordance with the local legislation and institutional

requirements. The participants provided their written informed consent to participate in this study.

## Author contributions

XC and XQ collected the clinical data and drafted the manuscript. JW analyzed and interpreted the data. RW and LY critically revised the important knowledge content. XG and JW analyzed the data statistically. All authors read and approved the manuscript.

## Funding

This study was supported by the National Natural Science Foundation of China (NSFC # 82171887).

## Acknowledgments

The authors thank RW and JW for their support in data collection during the second multiple-valve operation.

## 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.

## References

- Zhang X, Xiao W, Zhang Q, Xia D, Gao P, Su J, et al. Progression in Moyamoya disease: clinical features, neuroimaging evaluation, and treatment. *Curr Neuropharmacol.* (2022) 20:292–308. doi: 10.2174/1570159X19666210716114016
- Zhang D, Huang L, Huang Z, Zhou Q, Yang X, Gu H, et al. Epidemiology of Moyamoya disease in China: a nationwide hospital-based study. *Lancet Reg Health West Pac.* (2022) 11:100331. doi: 10.1016/j.lanwpc.2021.100331
- Shang S, Zhou D, Ya J, Li S, Yang Q, Ding Y, et al. Progress in Moyamoya disease. *Neurosurg Rev.* (2020) 43:371–82. doi: 10.1007/s10143-018-0994-5
- Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. *N Engl J Med.* (2009) 360:1226–37. doi: 10.1056/NEJMra0804622
- Smith ER, Scott RM. Surgical management of moyamoya syndrome. *Skull Base.* (2005) 15:15–26. doi: 10.1055/s-2005-868160
- Ando T, Shimada Y, Fujiwara S, Yoshida K, Kobayashi M, Kubo Y, et al. Revascularisation surgery improves cognition in adult patients with moyamoya disease. *J Neurol Neurosurg Psychiatry.* (2020) 91:332–4. doi: 10.1136/jnnp-2019-321069
- Smith ER, Scott RM. Progression of disease in unilateral moyamoya syndrome. *Neurosurg Focus.* (2008) 24:E17. doi: 10.3171/FOC/2008/24/2/E17
- Mayeku J, Lopez-Gonzalez MA. Current surgical options for Moyamoya disease. *Cureus.* (2020) 12:e11332. doi: 10.7759/cureus.11332
- Suzuki J, Takaku A. Cerebrovascular “moyamoya” disease. Disease showing abnormal net-like vessels in base of brain. *Arch Neurol.* (1969) 20:288–99. doi: 10.1001/archneur.1969.00480090076012
- Parray T, Martin TW, Siddiqui S. Moyamoya disease: a review of the disease and anesthetic management. *J Neurosurg Anesthesiol.* (2011) 23:100–9. doi: 10.1097/ANA.0b013e3181f84fac
- Li Sh, Yu Rg, He F, Qiu PL, Fiu W. Influencing factors of regional cerebral oxygen saturation during cardiopulmonary bypass. *Shanghai Med J.* (2016) 39:202–7.
- Thudium M, Ellerkmann RK, Heinze I, Hilbert T. Relative cerebral hyperperfusion during cardiopulmonary bypass is associated with risk for

- postoperative delirium: a cross-sectional cohort study. *BMC Anesthesiol.* (2019) 19:35. doi: 10.1186/s12871-019-0705-y
13. Yu J, Zhang J, Li J, Zhang J, Chen J. Cerebral hyperperfusion syndrome after revascularization surgery in patients with moyamoya disease: systematic review and meta-analysis. *World Neurosurg.* (2020) 135:357–66. doi: 10.1016/j.wneu.2019.11.065
14. Tokairin K, Kazumata K, Uchino H, Ito M, Ono K, Tatezawa R, et al. Postoperative intracerebral hemorrhage after bypass surgery in adult Moyamoya disease: profiles and clinical associations. *World Neurosurg.* (2018) 120:e593–600. doi: 10.1016/j.wneu.2018.08.132
15. Cho H, Jo KI, Yu J, Yeon JY, Hong SC, Kim JS. Low flow velocity in the middle cerebral artery predicting infarction after bypass surgery in adult Moyamoya disease. *J Neurosurg.* (2017) 126:1573–7. doi: 10.3171/2016.3.JNS152256
16. Funaki T, Takahashi JC, Houkin K, Kuroda S, Takeuchi S, Fujimura M, et al. Angiographic features of hemorrhagic Moyamoya disease with high recurrence risk: a supplementary analysis of the Japan Adult Moyamoya Trial. *J Neurosurg.* (2018) 128:777–84. doi: 10.3171/2016.11.JNS161650
17. Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults. *Cochrane Database Syst Rev.* (2018) 1:CD010947. doi: 10.1002/14651858.CD010947.pub2
18. Han C, Gao TX, Zhang HD, Ma W, Li Y, Li B, et al. Wavelet analysis of cerebral oxygenation signal measured by near-infrared spectroscopy in Moyamoya disease. *World Neurosurg.* (2023) 172:e12–8. doi: 10.1016/j.wneu.2022.10.074
19. Wang X, Feng K, Liu H, Liu Y, Ye M, Zhao G, et al. Regional cerebral oxygen saturation and postoperative delirium in endovascular surgery: a prospective cohort study. *Trials.* (2019) 20:504. doi: 10.1186/s13063-019-3586-y
20. Iwaki K, Takagishi S, Arimura K, Murata M, Chiba T, Nishimura A, et al. A novel hyperspectral imaging system for intraoperative prediction of cerebral hyperperfusion syndrome after superficial temporal artery-middle cerebral artery anastomosis in patients with Moyamoya disease. *Cerebrovasc Dis.* (2021) 50:208–15. doi: 10.1159/000513289
21. Ito K, Ookawara S, Ueda Y, Miyazawa H, Uchida T, Kofuji M, et al. Cerebral oxygenation improvement is associated with hemoglobin increase after hemodialysis initiation. *Int J Artif Organs.* (2020) 43:695–700. doi: 10.1177/0391398820910751
22. Pinto BB, Chew M, Buse GL, Walder B. The concept of peri-operative medicine to prevent major adverse events and improve outcome in surgical patients: a narrative review. *Eur J Anaesthesiol.* (2019) 36:889–903. doi: 10.1097/EJA.0000000000001067
23. Wang S, Han J, Cheng L, Li N. Risk factors and preventive measures of cerebral hyperperfusion syndrome after carotid artery interventional therapy. *Exp Ther Med.* (2017) 14:2517–20. doi: 10.3892/etm.2017.4796
24. Zhang Y, Bao X-Y, Duan L, Yang W-Z, Li D-S, Zhang Z-S, et al. Encephaloduroarteriosynangiosis for pediatric Moyamoya disease: long-term follow-up of 100 cases at a single center. *J Neurosurg Pediatr.* (2018) 22:173–80. doi: 10.3171/2018.2.PEDS17591
25. Cura Z, Oc B, Arun O, Oc M, Duman I, Duman A. Effects of sevoflurane and propofol anesthesia on cerebral oxygenation in patients undergoing carotid endarterectomy. *Turk Neurosurg.* (2022) 32:76–82. doi: 10.5137/1019-5149.JTN.33776-21.2
26. Juliana N, Abu Yazit NA, Kadiman S, Hafidz KM, Azmani S, Teng NIMF, et al. Intraoperative cerebral oximetry in open heart surgeries reduced postoperative complications: a retrospective study. *PLoS ONE.* (2021) 16:e0251157. doi: 10.1371/journal.pone.0251157
27. Zugni N, Guadrini L, Rasulo F. Noninvasive neuromonitoring in the operating room and its role in the prevention of delirium. *Best Pract Res Clin Anaesthesiol.* (2021) 35:191–206. doi: 10.1016/j.bpa.2020.09.006
28. Samra SK, Dy EA, Welch K, Dorje P, Zelenock GB, Stanley JC. Evaluation of a cerebral oximeter as a monitor of cerebral ischemia during carotid endarterectomy. *Anesthesiology.* (2000) 93:964–770. doi: 10.1097/0000542-200010000-00015
29. He S, Duan R, Liu Z, Ye X, Yuan L, Li T, et al. Characteristics of cognitive impairment in adult asymptomatic moyamoya disease. *BMC Neurol.* (2020) 20:322. doi: 10.1186/s12883-020-01898-8
30. Zhang Y, Tan J, Li P, Zhang X, Yang Y, Liu Y, et al. The perioperative application of continuous cerebral autoregulation monitoring for cerebral protection in elderly patients. *Ann Palliat Med.* (2021) 10:4582–892. doi: 10.21037/apm-21-707
31. Ding L, Chen DX, Li Q. Effects of electroencephalography and regional cerebral oxygen saturation monitoring on perioperative neurocognitive disorders: a systematic review and meta-analysis. *BMC Anesthesiol.* (2020) 20:254. doi: 10.1186/s12871-020-01163-y
32. Shi Z, Wu L, Wang Y, Zhang H, Yang Y, Hang C. Risk factors of postoperative cerebral hyperperfusion syndrome and its relationship with clinical prognosis in adult patients with moyamoya disease. *Chin Neurosurg J.* (2023) 9:10. doi: 10.1186/s41016-023-00321-8
33. Li C, Zhang N, Yu S, Xu Y, Yao Y, Zeng M, et al. Individualized perioperative blood pressure management for adult Moyamoya disease: experience from 186 consecutive procedures. *J Stroke Cerebrovasc Dis.* (2021) 30:105413. doi: 10.1016/j.jstrokecerebrovasdis.2020.105413