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ABO blood types may affect transient neurological events after surgical revascularization in patients with moyamoya disease: a retrospective single center study

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Abstract

Background Moyamoya disease (MMD) is a cerebrovascular disease with unknown cause. Patients with MMD disease usually experience transient neurological events (TNEs) after revascularization surgery. This retrospective single-center study was aimed to explore the risk factors of postoperative TNEs after surgical revascularization in patients with MMD.

Methods We selected 324 patients who underwent surgical revascularization between January 2017 and September 2022 in our center. The perioperative characteristics of the patients were recorded and the outcome was TNEs after surgery. An analysis of risk factors contributing to postoperative TNEs by using logistic regression model.

Results Three hundred twelve patients were enrolled, and the incidence of postoperative TNEs was 34% in our study. Males were more likely to suffer from postoperative TNEs (OR = 2.344, p = 0.002). Preoperative ischemic presentation (OR = 1.849, p = 0.048) and intraoperative hypotension (OR = 2.332, p = 0.002) were associated with postoperative TNEs. Compared to patients with blood type O, patients with blood type A (OR = 2.325, p = 0.028), B (OR = 2.239, p = 0.027) and AB (OR = 2.938, p = 0.019) had a significantly higher incidence of postoperative TNEs. A risk prediction model for postoperative TNEs was established, and the established risk prediction area under the receiver operating characteristic curve (ROC) of the model was 0.741.

Conclusions Males, preoperative ischemic presentation and intraoperative hypotension were associated with postoperative TNEs. We also found a possible link between postoperative TNEs and ABO blood types after surgical revascularization for moyamoya patients.

Keywords Moyamoya Disease, ABO blood types, Postoperative transient neurological events

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Background

Moyamoya disease (MMD) is a cerebrovascular disease with unknown cause. It is characterized by occlusion of the end and main branches of the internal carotid artery and often presents as intracranial hemorrhage, transient ischemic attacks or seizures [1, 2]. Compared with other treatments, surgical revascularization is the most effective treatment for MMD [3]. However, postoperative transient neurological events (TNEs) are usually occurred after surgical revascularization for MMD. Previous studies have indicated that the incidence of postoperative TNEs ranges from 15–67.1% [4, 5].

Postoperative complications are closely related to operation and anesthesia. Perioperative factors can affect intracranial hemodynamics in MMD patients, leading to new neurological complications in some patients after surgery [6]. The ABO blood group system is one of the most important systems known in humans that is used in clinical transfusion [7]. Previous research has shown that ABO blood types are correlated with many clinical conditions, including pain perception, diverse cancers, and cardiovascular diseases [8-10]. In a study [11] on the relationship between ABO blood type and delayed cerebral ischemia onset after aneurysmal subarachnoid hemorrhage, Researchers have found that blood type may be associated with cerebral vasospasm. Bypass vessels vasospasm can affect the perfusion of brain tissue and may lead to the occurrence of postoperative TNEs in patients with moyamoya disease. However, the relationship between blood type and TNEs after revascularization surgery for patients with MMD has not been reported. The aim of this retrospective single-center study was to identify the risk factors of postoperative TNEs after surgical revascularization in patients with MMD.

Materials and methods

Ethics and patients

This study was permitted by the Clinical Research Ethics Committee of The First Affiliated Hospital of University of Science and Technology of China, Anhui, China (2022-RE-352, Chairperson Prof. Zuojun Shen). Due to the non-interventional study design, the Institutional Review Board of The First Affiliated Hospital of University of Science and Technology of China waived the need for written informed consent from participants. This study was performed in accordance with the Declaration of Helsinki and with the STROBE Statement. The revascularization surgery was performed by the same neurosurgeon in our center between January 2017 and September 2022. Only patients with a confirmed diagnosis of MMD by preoperative diagnostic cerebral angiography were included in this study. We retrospectively reviewed the medical records of patients with Moyamoya disease older than 18 years who underwent a combined bypass of superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis and encephalo-duro-arterio-synangiosis. Patients with missing data were excluded from the study.

Methods and data acquisition

After entering the room, the patient underwent invasive arterial pressure measurement. All patients underwent general anesthesia with midazolam (0.02 mg/kg), etomidate (0.2 mg/kg), sufentanil (0.5 µg/kg), and cisatracurium (0.2 mg/kg) for induction and propofol (6 to 8 mg/ kg/h), remifentanil (0.1–0.3 µg/kg/min) and sevoflurane (up to 0.5MAC) for maintenance. During the operation, the blood pressure was maintained above the preoperatively measured blood pressure (vasoactive drugs were used when necessary). A normal CO2 level (35-45 mm Hg) was maintained throughout surgery. Data were obtained by retrospectively reviewing records maintained in our institution. Patient demographic information, preoperative comorbidities, clinical features, preoperative imaging, preoperative laboratory data, intraoperative factors, postoperative results and laboratory data were recorded. The outcome was the occurrence of postoperative TNEs. The evaluation period for TNEs was the first 24 h postoperatively. Postoperative TNEs were defined as the appearance of transient neurological symptoms (lasting<24 h) as previous literature [12, 13]. The episodes of neurological dysfunction as follows: (1) no sign of cerebral infarction or acute cerebral hemorrage in radiological images; (2) any reversible neurological defects (e.g., number) recognized subjectively by the patients; (3) any reversible neurological defects (e.g., hemiparesis, dysarthria) observed objectively by the doctors.

Postoperative management and clinical follow-up

After extubation, patients were transferred to the neurosurgery intensive care unit (NICU). After the operation, blood pressure was maintained at the baseline level. Postoperative CT scan was routinely performed to identify hemorrhagic or infarction on the first postoperative day. Perform head CT-CTA assessment on patients with postoperative TNEs to rule out hemorrhagic events and confirm bypass patency. All patients should avoid the occurrence of hypovolemia and hypotension, and aspirin was administered for patients with ischemic-type MMD at the first day after surgery. Patients were given improve circulation drugs and resisting vasospasm drugs to relieve the symptoms of postoperative TNEs. Patients were clinically evaluated at discharge and after three months follow-up. Clinical follow up angiography was conducted 3 months postoperatively to evaluate the patency of the bypass vessel.

Statistical analysis

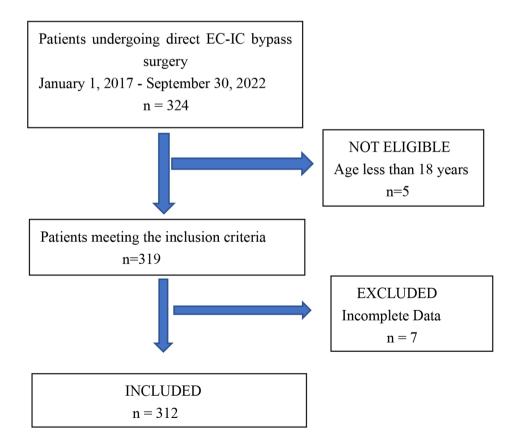
The normal distribution test was checked in the continuous variables using Shapiro test. Continuous variables are expressed as the mean±SD, and categorical variables are reported as counts with percentages. T-test or Mann-Whitney test was used to test for differences between continuous variables. Chi-square test or Fisher's exact test was used to compare the proportions of categorical variables between groups. Based on various predictive variables, univariate and multivariable logistic regressions were performed with postoperative TNEs as the outcome variable. A predictor variable was included in the multivariable model if p < 0.15. Statistically significant differences between groups were indicated by a P value<0.05. The receiver operating characteristic (ROC) curve and the area under the curve (AUC) were calculated.

All significance tests were two-sided and p value less than 0.05 was considered as statistically significant. Tukey method was used for post-hoc multiple comparisons testing when needed. SAS version 9.4 (SAS Institute Inc.) was used for all analyses.

Results

Three hundred twenty-four patients who underwent unilateral surgical revascularization were included in this study, and 12 patients were excluded (Fig. 1). The incidence of postoperative TNEs was 34% (n=106). Table 1 shows the perioperative characteristics of the patients in each group. There was significantly statistical difference between the two groups in the age, proportion of male patients, preoperative hemoglobin, fasting blood glucose, preoperative stroke, onset symptoms, intraoperative hypotension (relative decrease in systolic blood pressure more than 20% from baseline) and postoperative hemoglobin (p < 0.05).

In the regression model with TNEs as the outcome, only age, sex, fasting blood glucose, stroke status, blood type, onset symptoms, intraoperative hypotension and angiographic Suzuki grade were included in the final multivariate logistic regression. Males were more likely to suffer from postoperative TNEs (OR=2.344,95% CI, 1.387, 3.961; p=0.002). Preoperative ischemic presentation (OR=1.849,95% CI, 1.005, 3.400; p=0.048) and intraoperative hypotension (OR=2.332, 95% CI, 1.350,4.030; p=0.002) were associated with postoperative TNEs. Compared to patients with blood type O, patients with blood type B (OR=2.239, 95% CI, 1.095, 4.580;



Variable		Transient Neurologica	l Events	p	
	All Patients n = 312	Yes, n = 106	No, n = 206		
Age (y)	45.11±9.96	43.14±9.83	46.13±9.89)	0.0119*	
Male, n (%)	145(46.47)	63(59.43)	82(39.81)	0.001*	
Body mass index (kg/m2)	24.2 ± 2.85	24.24 ± 2.96	24.19±2.81	0.8849	
Preoperative platelets(10^9/L)	190.13±56.59	184.79 ± 54.09	192.88±57.76	0.2325	
Preoperative Hemoglobin (g/dL)	129.32±14.18	132.68 ± 14.57	127.59±13.69	0.0026*	
Preoperative NA+(mmol/L)	141.4±1.94	141.47 ± 1.92	141.36 ± 1.95	0.6434	
Fasting blood glucose(mmol/L)	4.86 ± 0.88	4.73 ± 0.74	4.93 ± 0.94	0.0376*	
Comorbidities, n (%)					
Hypertension	112 (35.9)	33 (31.13)	79 (38.35)	0.2081	
Diabetes	19 (6.09)	4 (3.77)	15 (7.28)	0.2198	
Stroke	39 (12.5)	19 (17.92)	20 (9.71)	0.0377*	
Blood types, n (%)				0.0591	
0	82 (26.28)	18 (16.98)	64 (31.07)		
A	86 (27.56)	33 (31.13)	53 (25.73)		
В	103 (33.01)	38 (35.85)	65 (31.55)		
AB	41 (13.14)	17 (16.04)	24 (11.65)		
Preoperative albumin(g/L)	40 ± 2.86	40.23 ± 2.99	39.88 ± 2.79	0.3008	
Onset symptoms, n (%)				0.0463*	
Ischemic	77(24.68)	35(33.02) 42(20.39)			
Hemorrhagic	50 (16.03)	14 (13.21)	36(17.48)		
Others	185 (59.29)	57(53.77) 128 (62.13)			
Intraoperative hypotension, n (%)	103(33.01)	45(42.45)	58(28.16)	0.0120*	
Angiographic Suzuki Grade [#] , n (%)				0.0897	
Grade III	73 (23.4)	31 (29.25)	42 (20.39)		
Grade IV	64 (20.51)	26 (24.53)	38 (18.45)		
Grade V	118 (37.82)	34 (32.08)	84 (40.78)		
Grade VI	57 (18.27)	15 (14.15)	42 (20.39)		
Duration of surgery(min)	341.34 ± 53.15	342.87 ± 53.66	340.55 ± 53	0.7163	
Duration of anesthesia(min)	387.43 ± 52.39	388.84 ± 50.69	386.7 ± 53.35	0.7337	
Infusion volume(ml)	4186.25 ± 1014.65	4191.98±1090.68	4183.3 ± 975.98	0.9431	
Postoperative Hemoglobin(g/dL)	111.58 ± 14.26	114.44±14.16	110.1 ± 14.11	0.0106*	
Postoperative platelets(10^9/L)	185.04 ± 50.96	185.35 ± 51.09	184.87 ± 51.02	0.938	
Postoperative albumin(g/L)	33.13±3.1	33.48±3.34	32.95 ± 2.97	0.1508	

Table 1 Perioperative Characteristics of Patients with and without Postoperative	VEs (Transient Neurological Events)
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Note: [#] Suzuki Grading System: Grade I: narrowing of ICA apex; grade II: initiation of moyamoya collaterals; grade III: progressive ICA stenosis with intensifification of moyamoya-associated collaterals; grade IV: development of ECA collaterals; grade V: intensifification of ECA collaterals and reduction of moyamoya-associated vessels; grade VI: total occlusion of ICA and disappearance of moyamoya-associated collaterals. * Indicates *P*<0.05

p=0.027), AB (OR=2.938, 95% CI,1.197, 7.212; p=0.019) and A (OR=2.325, 95% CI, 1.096, 4.933; p=0.028) had a significantly higher incidence of postoperative TNEs (Table 2). Blood types were still an independent risk factor for predicting postoperative TNEs with AUC=0.741 (Fig. 2).

Discussion

Transient neurological events are commonly observed after surgical revascularization for MMD patients [14]. Previous studies have shown that these events will last for 7–10 days, which will increase the duration of hospitalization and the healthcare-related cost [15, 16]. However, the cause of TNEs in patients with MMD undergoing bypass surgery is still unclear. Our data show that gender, preoperative ischemic presentation, intraoperative hypotension and blood types were the risk factors of postoperative TNEs after revascularization surgery for MMD patients. Males were more likely to suffer from postoperative TNEs in our study. The relationship between gender and postoperative neurological events in patients with MMD was unclear. Study [17] has shown that female was independent risk factors for postoperative TNEs. However, A study has found that there is no gender difference in postoperative neurological outcomes in MMD [18]. A possible explanation for this may be related to different sex ratios of the selected research subjects. The presence of transient ischemic attack [19] and preoperative ischemic presentation [20] were identified as predictors of postoperative neurological outcomes, and our results

Risk factors	Univariate logistic regres	sion	Multivariable logistic reg	ression
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Age	0.970(0.947, 0.994)	0.013	0.979 (0.953, 1.006)	0.112
Male	2.215 (1.374, 3.571)	0.001	2.344(1.387, 3.961)	0.002*
BMI	1.006 (0.927, 1.092)	0.884		
Preoperative platelets	0.997 (0.993, 1.002)	0.232		
Preoperative Hemoglobin	1.026 (1.009, 1.044)	0.003		
Preoperative NA+	1.029 (0.912, 1.162)	0.642		
Fasting blood glucose	0.711 (0.499, 1.011)	0.058	0.715(0.498, 1.026)	0.068
Comorbidities				
Hypertension	0.727 (0.442, 1.196)	0.209		
Diabetes	0.499 (0.161, 1.544)	0.228		
Stroke	2.031 (1.031, 3.999)	0.040	2.010 (0.917, 4.404)	0.081
Blood types				
0	Reference		Reference	
A	2.214 (1.122, 4.370)	0.022	2.325 (1.096, 4.933)	0.028*
В	2.079 (1.076, 4.016)	0.029	2.239 (1.095, 4.580)	0.027*
AB	2.519 (1.118, 5.673)	0.026	2.938 (1.197, 7.212)	0.019*
Preoperative albumin	1.044 (0.962, 1.134)	0.301		
Onset symptoms				
Others	Reference		Reference	
Hemorrhagic	0.873 (0.437, 1.744)	0.701	1.024(0.484,2.167)	0.950
Ischemic	1.871(1.084, 3.232)	0.025	1.849(1.005, 3.400)	0.048*
Intraoperative hypotension	3.194(1.955, 5.218)	0.012	2.332(1.350, 4.030)	0.002*
Angiographic Suzuki Grade				
Grade III	Reference		Reference	
Grade IV	0.927 (0.469, 1.832)	0.827	1.247 (0.589,2.640)	0.563
Grade V	0.548 (0.297, 1.011)	0.054	0.552 (0.280,1.088)	0.086
Grade VI	0.484 (0.229, 1.025)	0.058	0.484 (0.214,1.098)	0.083
Duration of surgery	1.001 (0.996, 1.005)	0.715		
Duration of anesthesia	1.001 (0.996, 1.005)	0.733		
Infusion volume	1 (1, 1)	0.943		
Postoperative hemoglobin	1.022 (1.005, 1.039)	0.012		
Postoperative platelets	1 (0.996, 1.005)	0.938		
Postoperative albumin	1.057 (0.98, 1.14)	0.151		

Table 2	Logistic Regr	ession Ana	lysis for (Dccurrence of	Postoperative TNEs
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* Indicates P<0.05

were consistent with these research conclusions. Patients with the presence of transient ischemic attack were sensitive to intraoperative hemodynamic fluctuations, leading to the occurrence of postoperative TNEs.

Although study [21] has shown that the effect of intraoperative hypotension on perioperative stroke is unclear. Some studies [22, 23] have shown that intraoperative hypotension can be harmful to cerebral blood flow (CBF). Patients with moyamoya disease may be more sensitive to changes in CBF [24]. Intraoperative hypotension can aggravate insufficient cerebral microcirculation perfusion. The occurrence of intraoperative hypotension may lead to transient neurological events. Study has shown that intraoperative blood pressure fluctuations were independent risk factors for postoperative infarction after revascularization surgery in patients with moyamoya disease [25]. we also found intraoperative hypertension was associated with postoperative TNEs. There is no universal definition of intraoperative hypotension. We defined hypotension as a 20% reduction from baseline, study [26] suggested that this may be more appropriate for patients with chronic hypertension. Although our definition of hypotension is applicable to most patients, relative hypotension in few patients may be underrecognized.

Our study found a correlation between ABO blood type and the incidence of TNEs after surgical revascularization in patients with moyamoya disease. The incidence of TNEs in patients with blood type O was obviously lower than that in patients with blood type A, B or AB in our study. Studies have shown that non-O blood type individuals have increased risks of peripheral vascular disease, venous thrombosis, coronary heart disease, cancer, and ischemic stroke [27–31]. Differences in platelets, endothelial cells and coagulation factors among patients

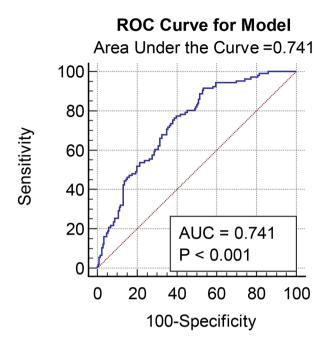


Fig. 2 ROC curve of postoperative TNEs risk prediction model

with different blood types may be the cause of this phenomenon [32, 33].

Genetic factors may be the reason that blood type is related to the incidence of postoperative TNEs. ABO blood groups are determined by the ABO gene [34]. As a genetic marker, the ABO blood group antigen is inherited and expressed in a wide variety of human cells and tissues, such as platelets, endothelial cells and sensory neurons [35, 36]. Some studies [37, 38] have shown that peripheral vasospasm is related to increased levels of VIII factor. Compared with other blood types, plasma levels of von Willebrand factor (vWF) and factor VIII were significantly decreased in patients with blood type O [39]. Low levels of factor VIII and vWF might be the reason for the relatively low incidence of postoperative TNEs after surgical revascularization for MMD patients with blood type O.

Nitric oxide (NO) regulates regional cerebral blood flow and correlates with the occurrence of ischemia [40, 41]. Studies [42] have shown that the reduction of contents of NO can inhibit endothelium-dependent vasodilatation function, leading to cerebral vasospasm. Nitric oxide (NO) regulates regional cerebral blood flow and correlates with the occurrence of ischemia [40, 41]. Studies [42] have shown that the reduction of contents of NO can inhibit endothelium-dependent vasodilatation function, leading to cerebral vasospasm. Local cortical hyperperfusion and watershed shift caused by vasospasm after surgical revascularization might be the cause of postoperative TNEs [43, 44]. NO may play a role in regulating the occurrence of vasospasm after revascularization surgery for MMD. Individuals with blood type B or AB were significantly less responsive to NO than individuals with blood type O or A [45]. NO reaction may be another reason for the relatively low incidence of TNEs in patients with blood type O compared with others.

There were several limitations in our study. First, our study was based on single center results, so selection bias is possible. Second, the study included an unequal distribution of patients with different blood types, which may have affected the results. Third, although many clinical factors were recorded in our study, the changes of postoperative blood pressure and other unknown confounders were not analyzed in this study. Last, Hemodynamic studies were mandatory to discuss TNEs after revascularization surgery for MMD. It remains uncertain which types of hemodynamic changes (hyperperfusion, hypoperfusion, watershed shift, and so on) result from ABO blood type. Further studies are required to verify which hemodynamic changes are affected by ABO blood type after surgical revascularization for Moyamoya disease.

Conclusion

The incidence of postoperative TNEs was 34% in our study. Males, preoperative ischemic presentation, intraoperative hypotension were risk factors for postoperative TNEs. We also found a possible link between postoperative TNEs and ABO blood types after surgical revascularization for moyamoya patients.

Abbreviations

MMD TNEs	Moyamoya disease transient neurological events
ROC curve	receiver operating characteristic curve
STA-MCA	superficial temporal artery-middle cerebral artery
NICU	neurosurgery intensive care unit
CBF	cerebral blood flow
NO	Nitric oxide
BMI	body mass index
SD	standard deviation

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Author contributions

MPQ and MRD were responsible for designed this study and collected the data. MPQ and MMH was responsible for study execution and manuscript writing. JL and FK revised it critically. All authors have read and approved the final version of the manuscript.

Funding

Not applicable.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was permitted by the Clinical Research Ethics Committee of The First Affiliated Hospital of University of Science and Technology of China, Anhui, China (2022-RE-352, Chairperson Prof. Zuojun Shen). Due to the non-interventional study design, the Institutional Review Board of The First Affiliated Hospital of University of Science and Technology of China waived the need for written informed consent from participants. This study was performed in accordance with the Declaration of Helsinki and with the STROBE Statement.

Consent for publication

Not applicable.

Competing interests

We declare that we have no conflicts of interest to this work.

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