

## Clinical Article

# Ischemic Complications Occurring in the Contralateral Hemisphere after Surgical Treatment of Adults with Moyamoya Disease

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**Objective :** Direct revascularization surgery is regarded as the most effective method of treatment of adults with moyamoya disease. These patients, however, have a higher risk of perioperative ischemic complications than do patients with atherosclerotic stroke, and are at risk for ischemic complications in the hemisphere contralateral to the one operated on. We investigated the incidence and risk factors for ischemic stroke in the contralateral hemisphere after surgical treatment of adults with moyamoya disease.

**Methods :** We retrospectively reviewed the medical records and results of neuroimaging studies on 79 hemispheres of 73 consecutive patients with adult moyamoya disease (mean±SD age, 37.96±11.27 years; range, 18-62 years) who underwent direct bypass surgery over 6 years.

**Results :** Ischemic complications occurred in 4 of 79 (5.1%) contralateral hemispheres, one with Suzuki stage 3 and three with Suzuki stage 4. Three patients showed posterior cerebral artery (PCA) involvement by moyamoya vessels. Advanced stage of moyamoya disease (Suzuki stages 4/5/6;  $p=0.001$ ), PCA involvement ( $p=0.001$ ) and postoperative hypotension (mean arterial blood pressure <80% of preoperative mean arterial blood pressure) on the first ( $p<0.0001$ ) and second ( $p=0.003$ ) days after surgery were significantly correlated with postoperative contralateral ischemic complications.

**Conclusion :** In patients with advanced moyamoya disease and involvement of the PCA, intentional hypotension can result in ischemic stroke in the hemisphere contralateral to the one operated on. Careful control of perioperative blood pressure is crucial for good surgical results.

**Key Words :** Cerebral revascularization · Complications · Moyamoya diseases · Perioperative period.

## INTRODUCTION

Moyamoya disease is a chronic, occlusive cerebrovascular disease of unknown etiology, characterized by bilateral steno-occlusive changes at the terminal portion of the internal carotid artery and an abnormal vascular network at the base of the brain<sup>15</sup>. Because surgical revascularization prevents further cerebral ischemic attacks by improving cerebral blood flow (CBF), superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis with or without indirect bypass is generally used as the standard surgical treatment for adults with moyamoya disease<sup>1,4,8,12</sup>. Despite the benefits of surgical treatment, however, the incidence of perioperative ischemic complications is higher in patients undergoing surgery for moyamoya disease (3-31%)

than in those undergoing any other type of cerebrovascular surgery<sup>3,5,9,13</sup>. Also, in contrast to other cerebrovascular diseases, ischemic stroke in the hemisphere contralateral to the one operated on is not rare, occurring in about 3% to 14% of patients<sup>3,6,7</sup>. Despite reports of its incidence, the causes of this complication have not been described. We assessed the incidence of this complication in 79 hemispheres of 73 adult patients with moyamoya disease that underwent surgery over the past 6 years, as well as the risk factors associated with this complication.

## MATERIALS AND METHODS

### Patients

This study included 79 hemispheres of 73 consecutive adults with moyamoya disease that underwent direct bypass surgery, performed by a single surgeon, from April 2004 to August 2009. We reviewed their medical records and post-surgical neuroimaging results. We enrolled patients with symptomatic episodes in spite of maximal medical therapy, with compromised cerebral hemodynamic reserve as demonstrated by single photon emission computed tomography (SPECT), and lack of major

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medical comorbidity.

## Interventions

The neurologic state of the patients was assessed by neurologists and their radiologic findings, including computed tomography (CT), transfemoral cerebral angiography (TFCA) and magnetic resonance image (MRI), were interpreted by neuro-radiologists and a neurosurgeon.

Preoperative TFCA, including bilateral internal carotid artery (ICA), bilateral external carotid artery, and vertebral artery injection, was performed to evaluate donor vessels, collateral circulation, moyamoya vessels and recipient vessels. SPECT with and without acetazolamide challenge to assess for loss of cerebrovascular reserve capacity was performed. TFCA was performed to evaluate postoperative bypass patency, extent of revascularization, and regression of moyamoya vessels. Postoperative SPECT was used to assess improvement in baseline perfusion and hemodynamic reserve.

For a least 1 week preoperatively, patients were discontinued from aspirin and other antiplatelet medications. All patients were placed under general anesthesia using a combination of isoflurane and intravenous agents. Before middle cerebral artery (MCA) occlusion for bypass graft, patients were administered an intravenous bolus of 250-300 mg thiopental. After surgery, patients were kept overnight in the intensive care unit with strict blood pressure control, usually a mean arterial blood pressure (MABP) between 80 and 100 mm Hg. Patients were administered a loading dose of 300 mg aspirin on the day after surgery, followed by a maintenance dose of 100 mg. Patients were clinically evaluated every day after surgery and were examined by a neurologist 1, 6, and 18 months after discharge. Cerebral angiography was performed 1 week after surgery and cerebral perfusion after 6 months. Surgical morbidity was defined as newly developed neurological deficits lasting 7 days or longer after revascularization surgery, correlated with findings on MRI or CT imaging.

## Analysis of risk factors

To investigate the risk factors for contralateral ischemic complications after revascularization surgery, we analyzed the peri-

operative factors of each revascularization procedure. Patients were divided into two groups, one with and one without postoperative contralateral ischemic complications. All statistical analyses were performed using the SPSS program (version 12.0; SPSS, Inc., Chicago, IL, USA). Categorical variables were compared using Pearson's chi-square tests or Fisher exact tests, where appropriate. Continuous variables were reported as means±standard deviations and compared using independent Student t-tests or Mann-Whitney U-tests. A probability less than 0.05 was considered statistically significant.

## RESULTS

Over the past six years, 79 hemispheres of 76 patients underwent direct anastomosis (STA-MCA bypass) with or without indirect methods. Of these 79 hemispheres, 9 (11.4%) showed postoperative ischemic complications, 5 in the ipsilateral hemisphere and four in the contralateral hemisphere.

Table 1 summarize the clinical characteristics of the four patients with postoperative contralateral ischemic complications. All four had ischemic symptoms, with low density areas observed on preoperative CT scans. Preoperative angiography showed that one patient had Suzuki stage 3 and three had Suzuki stage 4. SPECT showed moderately decreased perfusion of the MCA territory with or without perfusion defects, and mild to moderately decreased perfusion reserve of the anterior cerebral artery (ACA), in all patients. All four patients underwent STA-MCA bypass surgery with or without indirect surgery. Postoperative ischemic complication in the contralateral hemisphere occurred from the 1 day after surgery to 2 days after surgery.

The occurrence of these ischemic complications did not correlate with sex, age, body mass index, preoperative low density on CT, urine output during the operation, hematocrit reduction, hemoglobin reduction or perioperative hypocapnia or hypercapnia (Table 2).

When we compared patients with and without postoperative contralateral ischemic complications, we found that these ischemic complications were related with advanced stage of moyamoya disease (Suzuki stages 4 and 5;  $p=0.001$ ), involvement of the posterior cerebral artery (PCA) ( $p=0.001$ ) and postoperative hy-

**Table 1.** Characteristics of patients with postoperative contralateral ischemic complications

Case	Age	Sex	Preop Suzuki stage	PCA involvement	Onset/Infarction area	Cause of infarction	Preop MABP	Intraop MABP	POD #1 MABP	POD #2 MABP
1	40	M	4	+	POD 2/left P	Inappropriate blood pressure control	117.33	66.67	90.00	86.67
2	31	M	4	+	POD 2/right F, P, O	Inappropriate blood pressure control	109.00	66.67	85.33	80.33
3	31	F	4	+	POD 2/right F	Induced hypotension for treatment of brain swelling	99.33	60.00	73.00	69.00
4	45	F	3	-	POD 1/right T, P, O	Inappropriate blood pressure control	114.67	60.00	71.33	83.67

MABP : mean arterial blood pressure, PCA : posterior cerebral artery, POD : postoperative day, F : frontal, T : temporal, P : parietal, O : occipital

**Table 2.** Risk factors for postoperative contralateral ischemic complications

	No. of hemispheres		p value
	Without complications (n=75)	With complications (n=4)	
Sex (female : male)	49 : 26	2 : 2	NA
Age	39.93±11.48	36.75±6.95	NA
BMI	25.06±3.21	23.61±0.79	NA
Preoperative LDA on CT	41	4	NA
Urine output (mL/min)	3.64±1.86	5.17±2.52	NA
Down of Hb (g/dL)	1.58±1.40	2.50±1.06	NA
Down of Hct (%)	4.46±3.77	7.95±2.79	NA
Operation time (min)	385.6±81.1	451.75±19.63	NA
Intraoperative hypocapnia/hypercapnia	19	0	NA
Postoperative hypocapnia/hypercapnia	34	2	NA

BMI : body mass index, LDA : low density area, CT : computed tomography, Hb : Hemoglobin, Hct : hematocrit, hypocapnia : PCO2 <35 mm Hg, hypercapnia : PCO2 >45 mm Hg

**Table 3.** Risk factors for postoperative contralateral ischemic complications

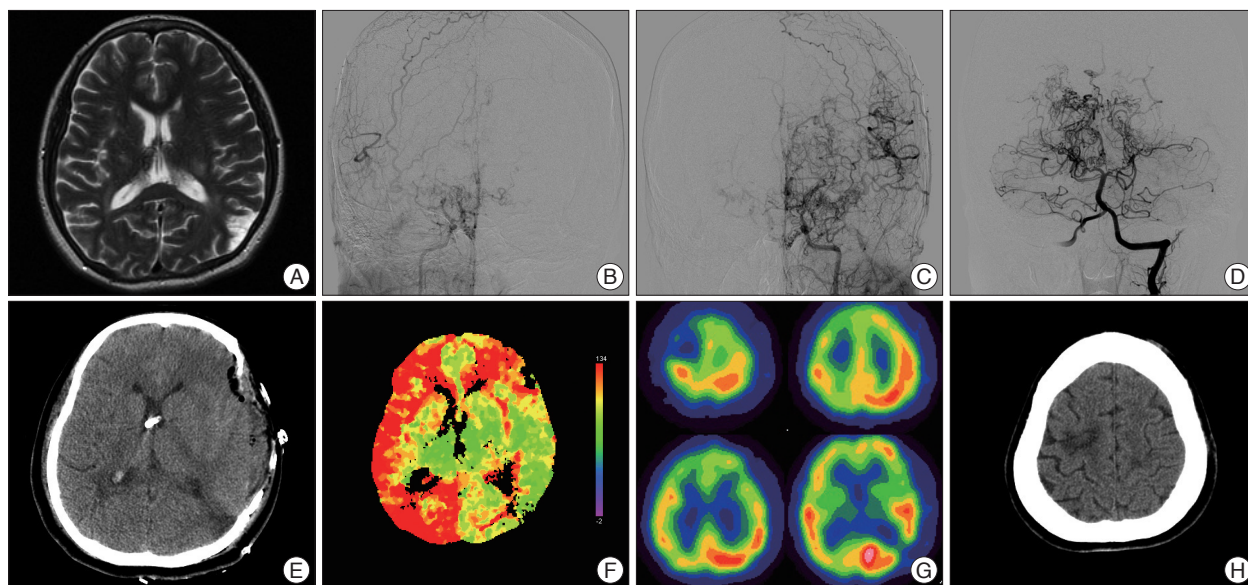
	No. of hemispheres		p value
	Without complications (n=75)	With complications (n=4)	
Suzuki stage			0.001
I/II/III	0/12/51	0/0/1	
IV/V/VI	12/0/0	3/0/0	
PCA involvement	3	3	0.001
Intraoperative MABP down (>20%)	72	4	NA
POD #1 MABP down (>20%)	8	4	0.0001
POD #2 MABP down (>20%)	16	4	0.003

PCA : posterior cerebral artery, POD : postoperative day, MABP : mean arterial blood pressure

potension (mean arterial blood pressure <80% of preoperative MABP) on the first ( $p < 0.0001$ ) and second ( $p = 0.003$ ) days after surgery (Table 3).

**Case illustration**

This patient was admitted to our department due to right leg weakness (grade 4). MRI showed chronic infarction in the frontal white matter, corona radiata, and left parietal lobe (Fig. 1A). Magnetic resonance angiography and conventional angiography showed occlusion at the distal ICA on both sides and occlusion of both PCAs at the level of the P2/P3 junction (Fig. 1B, C and D). SPECT and MRI showed decreased perfusion of the right MCA and PCA territory and a perfusion defect in the left temporo-occipital cortex due to previous infarction. The patient underwent STA-MCA bypass with encephaloduroarteriomyosinangiosis (EDAMS) operation in the left hemisphere. Release of the vessel clamp used for cross clamping of the M4 segment after successful STA-MCA anastomosis resulted in sudden brain swelling with cor-



**Fig. 1.** A : T2 weighted MRI showing an old infarction in the left temporo-occipital cortex. B, C and D : Preoperative angiography showing findings typical of moyamoya disease with involvement of bilateral PCA. E : Immediate postoperative CT scan showing neither focal hematoma nor acute infarction on the operated hemisphere. An extraventricular drainage catheter was placed on the frontal horn of the lateral ventricle. F : TTP image of the perfusion CT showing improvements in delayed time on the left compared with the right hemisphere after STA-MCA bypass with encephalomyoarteriosynangiosis. G : Follow-up SPECT 9 days after surgery showing perfusion defects in the right frontal cortex and right ACA-MCA watershed zone due to a newly developed infarction. H : Non-enhanced CT scan showing focal low density on the left frontal area, the same area of the left frontal cortex. MRI : magnetic resonance image, PCA : posterior cerebral artery, CT : computed tomography, STA : superficial temporal artery, SPECT : single photon emission computed tomography, ACA : anterior cerebral artery, MCA : middle cerebral artery.

tical subarachnoid hemorrhage. There was no visible bleeding site on the exposed cerebral cortex, and brain swelling was controlled by placing extraventricular drainage at the frontal cortex, draining the subarachnoid hemorrhage through multiple arachnoid incisions over the cerebral cortex, and reducing blood pressure to below the normal range. Even with copious saline irrigation through the arachnoid incision, however, we could not identify a visible bleeding site and the operation was completed by EDAMS operation with temporalis muscle flap. Immediate postoperative CT scan showed no evidence of focal hematoma or acute infarction on the operated hemisphere (Fig. 1E), and time-to-peak image of the perfusion CT after direct bypass showed improvement of the delayed time on the left compared with the right side (Fig. 1F). Since sudden brain swelling with subarachnoid hemorrhage after direct bypass surgery is indicative of hyperperfusion syndrome, the patient was treated with strict blood pressure control. Two days after the operation, the patient worsened neurologically to a slightly stuporous level of consciousness and left motor power decreased to grade 2. Follow-up SPECT showed a perfusion defect on the right frontal cortex and a watershed zone on the right ACA-MCA due to a newly developed infarction (Fig. 1G). A CT scan performed 1 month later showed infarction on the right ACA territory (Fig. 1H). The patient recovered after treatment but experienced weakness in the left leg.

## DISCUSSION

Perioperative ischemic complications are more common in patients with moyamoya disease than in patients with other cerebrovascular occlusive diseases<sup>5,9</sup>, with ischemic complications in the hemisphere contralateral to that operated on regarded as unique to moyamoya disease.

In general, the risk factors for perioperative ischemic complications in patients with moyamoya disease include hypotension, hypocapnia, preoperative low density areas on neuroimaging, perioperative hypovolemia, reduction in the hematocrit, and history of cerebrovascular disorder<sup>10,14</sup>. The relationship between these risk factors and ischemic complications is likely due to reduced cerebral blood flow and lack of cerebral autoregulation<sup>2,16</sup>. Less is known, however, about ischemic complications occurring in the contralateral hemisphere.

We found that advanced stages of moyamoya disease (Suzuki stage 4/5), involvement of the PCA and postoperative hypotension on the first and second days after surgery were significant risk factors for the postoperative development of contralateral ischemic complications.

Our finding that PCA involvement was a risk factor for postoperative contralateral ischemic complications was not surprising because, in patients with advanced stage moyamoya disease, the PCA is one component of collateral blood flow source, along with the leptomeningeal collateral circulation. In these patients, cerebral hemodynamics is impaired, with stress, such

as surgery, inducing ischemic complications. Although direct bypass graft can maintain operative-side CBF, contralateral CBF could not keep up with the demand, resulting in ischemic complications.

We found that intraoperative hypotension was common, occurring in 73 of 79 (92.4%) hemispheres, but it did not independently affect the occurrence of postoperative ischemic complications. In contrast, postoperative hypotension was a significant risk factor for postoperative ischemic complications. While the absolute blood pressure was not important, the relative blood pressure, compared with preoperative level, was. Patient 1 had a preoperative blood pressure of 156/98 mm Hg and an MABP of 117.33 mm Hg. After revascularization, however, this patient's systolic blood pressure was maintained at 120-130 mm Hg to prevent hyperperfusion, resulting in MABPs on the first and second days after surgery of 90.00 mm Hg and 86.67 mm Hg, respectively. Although these MABP values were lower than this patient's preoperative MABP, it was maintained at a normal or slightly subnormal value. In the other three patients with postoperative ischemic complications, their systolic blood pressure was maintained at 107-130 mm Hg and their MABPs at 69.0-85.3 mm Hg. Thus, despite their blood pressures being normal to subnormal, they experienced postoperative contralateral ischemic complications. These findings indicate the importance of maintaining a patient's postoperative blood pressure as near as possible to that patient's preoperative blood pressure. Although MABP reduction was more common during than after surgery, it was not associated with postoperative complications. This may be due to protective effects of anesthesia on the brain and the lower demand for cerebral metabolism during surgery<sup>11,12</sup>. Upon awakening, cerebral blood flow returns to normal, making the patients more prone to hypotension. Thus, a small postoperative reduction in MABP may lead to postoperative complications.

## CONCLUSION

Postoperative hypotension in patients with advanced stage moyamoya disease and PCA involvement may result in ischemic complications to the contralateral hemisphere. Careful preoperative management of blood pressure is important in preventing these ischemic complications.

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