

Research Article

Analysis of Cerebral Perfusion and Vascular Reserve after Combined Revascularization for Moyamoya Disease

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Ischemic Stroke: A Cerebrovascular Accident

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Abstract

Background and purpose: Moyamoya disease is a progressive occlusive disease of the cerebral arteries. Various vascular reconstruction surgeries have been reported, but the most appropriate procedure remains unclear. We have preferred to perform a combined direct and indirect bypass to the Rolandic region to prevent ischemic stroke. The purpose of this study was to evaluate the surgical results of our method using cerebral blood flow (CBF) from single photon emission computed tomography (SPECT).

Methods: This study examined 29 hemispheres in 21 patients (6 males, 15 females; mean age, 33.25 ± 19.26 years; range, 9-67 years). All patients underwent combined vascular reconstruction using a superficial temporal artery (STA)-middle cerebral artery (MCA) anastomosis and encephaloduromyosynangiosis. Regional CBF (rCBF) and cerebrovascular reserve (CVR) were measured using N-isopropyl-p-[123 I]-iodoamphetamine (123 I-IMP) SPECT before and after the procedure.

Results: Postoperatively, 28 direct bypasses were patent, but one became occluded within 3 months after surgery. Preoperative symptoms completely resolved in all except one case. Three months postoperatively, improvement of rCBF at rest was not evident in the ipsilateral frontal lobe after surgery, but CVR was widely and significantly improved in the frontal lobe involving the motor cortex (preoperative CVR, $-1.1 \pm 16.1\%$; postoperative CVR, $14.3 \pm 19.7\%$, $p < 0.001$) and premotor area (preoperative CVR, $-2.14 \pm 15.9\%$; postoperative CVR, $10.2 \pm 15.9\%$, $p < 0.001$).

Conclusions: Our combined direct and indirect bypass effectively reduced ischemic symptoms of moyamoya disease and increased CVR. The possibility that transient ischemic attack was more strongly affected by CVR than by CBF was suggested.

Keywords

- Moyamoya disease
- Combined revascularization
- Single photon emission computed tomography
- Cerebral blood flow

ABBREVIATIONS

SPECT: Single Photon Emission Computed Tomography; **Cbf:** Cerebral Blood Flow; **Rcbf:** Regional Cerebral Blood Flow; **Cvr:** Cerebral Vascular Reserve; **123 I-imp:** N-Isopropyl-P-[123 I]-Iodoamphetamine; **Sta:** Superficial Temporal Artery; **Mca:** Superficial Temporal Artery; **Mri:** Magnetic Resonance Imaging; **3d-Cta:** Three Dimension-Computed Tomographic Angiography; **Icga:** Indocyanine Green Fluorescence Videoangiography; **Acz:** Acetazolamide; **Dtarg:** Dual Table Autoradiographic; **Qspect:** Quantitative Spect; **3d-Srt:** Three-Dimensional Stereotactic Roi Template; **Roi:** Region Of Interest; **Ich** Intracerebral

Hemorrhage; **Ems:** Encephalomyosynangiosis; **Eds:** Encephalodurosynangiosis; **Eas:** Encephaloarteriosynangiosis; **Edams:** Encephaloduroarteriomyosynangiosis; **Tia:** Transient Ischemic Attack; **Aca:** Anterior Cerebral Artery; **Pca:** Posterior Cerebral Artery

INTRODUCTION

Moyamoya disease is a cerebrovascular disease characterized by progressive stenosis of the terminal portion of the internal carotid artery, proximal portion of the anterior cerebral artery and middle cerebral artery (MCA) [1]. Two patterns of onset are known: ischemic attacks; and hemorrhagic attacks [2].

No effective medical treatment for moyamoya disease has yet been identified. However, surgical revascularization has been validated, particularly for patients with ischemic symptoms. Many efficient surgical procedures have been reported, including direct and indirect revascularization [3-12]. We have been performing surgery applying a combination of both direct and indirect revascularizations. This procedure has two characteristics. One is the place of the direct revascularization, which is constructed mainly in the precentral sulcus, with the aim of preventing postoperative paralysis as the first priority. The other is the use of thin temporalis muscle for indirect anastomoses. Indirect bypass involves both dura mater turned under the skull and temporalis muscle torn into thin sheets to prevent brain compression. We report herein the clinical outcomes of this technique using cerebral perfusion and vascular reserve capacity as measured by N-isopropyl-p-[¹²³I]-iodoamphetamine (¹²³I-IMP) single photon emission computed tomography (SPECT).

MATERIALS AND METHODS

Methods

The medical charts of consecutive patients who underwent the combined direct and indirect bypass surgery after being diagnosed with moyamoya disease at our institution between January 2009 and August 2013 were retrospectively reviewed. Clinical diagnosis of moyamoya disease was accomplished using the criteria proposed by the Research Committee on Spontaneous Occlusion of the Circle of Willis (moyamoya disease) in Japan [13]. Both definite and probable cases were included. Patients with Suzuki stage VI moyamoya [1] were excluded from this study. Cerebral angiography, magnetic resonance imaging (MRI) and ¹²³I-IMP-SPECT were performed preoperatively for all patients. Surgical reconstruction, which involved direct and indirect bypass, was performed in the same manner for all patients. Patency of the direct bypass was examined on three-dimensional computed tomographic angiography (3D-CTA) on the day after surgery and on MRI at both 1 week and 3 months postoperatively. In addition, ¹²³I-IMP-SPECT was performed 3 months after surgery for postoperative evaluation of cerebral perfusion. Clinical outcomes were evaluated at 3 months postoperatively and then every year thereafter, and classified as: 1) no further attack, no ischemic attacks observed postoperatively; 2) improvement, symptoms still observed but at decreased frequency or severity; 3) no change, no new symptoms in patients who had no symptoms previously; or 4) worsened, appearance of new symptoms or increased frequency of ischemic attack.

Surgical reconstruction procedure

Our surgical procedure consisted of direct and indirect bypass, i. e. , anastomosis of superficial temporal artery (STA) to MCA with encephaloduromyosynangiosis. Our standardized direct bypass procedures were as follows. The parietal branch of the STA was dissected out about 7-8 cm from the scalp after making a linear skin incision just over the course of the vessel. A curvilinear frontotemporal skin flap was made, including the temporal fascia. Temporalis muscle was cut and dissected from the skull in the same fashion as the skin flap. The frontal branch of the STA was preserved to maintain blood supply to both the

scalp and the indirect bypass in the future. Craniotomy was performed to expose the precentral gyrus in the microscopic surgical field. Although the size of craniotomy varied depending on the anatomical variation of the parietal branch, a 6'6-cm craniotomy was usually performed. Dural opening was made to allow for triangular dural flap. The cortical surface in the central or precentral sulcus was inspected and an adequate M4 artery in the area was chosen as a donor. After preparation of the anastomosis on the brain surface, the distal end of the parietal branch was cut and cleaned. An STA-MCA anastomosis was then completed in side-to-end fashion. The anastomosis was tested for patency with both intraoperative indocyanine green fluorescence videoangiography (ICGA) and using an ultrasonic blood flow meter. After direct arterial reconstruction, an indirect bypass was constructed. The arachnoid membrane was opened widely over the brain surface. The triangular dural flap described above was turned under from the craniotomy edge and laid directly on the cortical surface. Temporalis muscle was torn into two thin pieces, then the thin muscle sheet was placed on the brain surface in which the direct bypass had already been constructed. Closure was performed in the usual method using the other thin muscle sheet.

SPECT procedure

Quantitative regional cerebral blood flow (rCBF) and cerebrovascular reserve (CVR) in response to acetazolamide (ACZ) challenge were evaluated using a dual-table autoradiographic quantitative SPECT method with ¹²³I-IMP, as previously described in detail [14-16]. All patients were scanned on a gamma camera imaging system (Symba T6 SPECT/CT Imaging System; Siemens, Germany) for 60 min. Before SPECT was performed, an intravenous line was inserted. Each patient received the first intravenous injection of 111 MBq of ¹²³I-IMP while lying in prone at the beginning of the examination. One gram of ACZ was injected 20 min later, and a second injection of 111 MBq of ¹²³I-IMP was made 30 min after the first ¹²³I-IMP injection.

Assessment of rCBF

Values of rCBF were calculated using a 3-dimensional stereotactic region of interest (ROI) template (3D-SRT; Fuji Film RI Pharma, Japan) [17]. Twelve ROIs, including the motor cortex, were placed in each cerebral hemisphere using 3D-SRT.

The rCBF of the motor cortex and premotor area at rest and under ACZ challenge were compared between pre- and postoperative states. In addition, CVR was calculated according to the following equation:

$$\text{CVR} = (\text{rCBF after ACZ challenge} - \text{rCBF at rest}) / \text{rCBF at rest} \times 100$$

Statistical analysis

All values are expressed as mean \pm standard deviation. Continuous data between before and after surgery were compared using paired t-tests. The Wilcoxon signed-rank test was used for comparison of CVR data. Values of $P < 0.05$ were considered statistically significant.

RESULTS

Twenty-nine hemispheres in 21 patients (6 males, 15 females; mean age, 33.25 ± 19.26 years; range, 9-67 years) were included in this study (Table 1). The initial pattern of onset was transient ischemic attack (TIA) in 9 patients, cerebral infarction in 5, syncope in 1, epilepsy in 1, and intracerebral hemorrhage (ICH) in 1; 4 patients remained asymptomatic prior to diagnosis. Preoperative Suzuki angiographic stage was stage II in 2 hemispheres, stage III in 17, stage IV in 6 and stage V in 4. Surgical reconstruction was performed in all 29 hemispheres. Postoperatively, 28 direct bypasses remained patent throughout follow-up up to 3 months, but the remaining bypass (Case 9) became occluded within 3 months. Significant complications due to reconstruction surgery, such as ischemic or hemorrhagic stroke, were not observed in any patients. Ten of the 11 symptomatic patients with TIA, epilepsy or syncope showed complete resolution of symptoms after surgery, and frequency of TIA was markedly decreased in the remaining 1 patient. Six patients with a history of cerebral infarction or ICH did not experience any kind of postoperative stroke. The 4 patients with asymptomatic moyamoya disease remained asymptomatic after surgery. No ischemic or hemorrhagic stroke has been recognized after surgery in any of the 29 hemispheres during follow-up (mean, 25.4 ± 15.2 months; range, 3-57 months).

In the SPECT study, rCBF at rest in the motor cortex before and after reconstruction surgery was 25.8 ± 4.0 ml/100 g/min and 26.4 ± 4.7 ml/100 g/min, respectively. In the premotor area before and after reconstruction surgery, rCBF was 29.5 ± 4.3 ml/100 g/min and 30.1 ± 5.5 ml/100 g/min (Figure 1). No significant differences in rCBF at rest were seen between pre- and postoperatively. On the other hand, rCBF under ACZ challenge in the motor cortex before and after reconstruction surgery was 25.4 ± 5.8 ml/100 g/min and 30.3 ± 8.1 ml/100 g/min, respectively. In the premotor area before and after reconstruction surgery, rCBF was 28.9 ± 6.7 ml/100 g/min and 32.7 ± 7.6 ml/100 g/min (Figure 2). A significant difference in rCBF under ACZ challenge ($p < 0.001$ in motor cortex; $p = 0.006$ in premotor area) was seen between pre- and postoperatively. CVR in the motor cortex before and after reconstruction surgery was -1.1 ± 16.1% and 14.3 ± 19.7%, respectively. CVR in the premotor area before and after reconstruction surgery was -2.14 ± 15.9% and 10.2 ± 15.9%, respectively (Figure 3). A significant increase in CVR was seen after vascular reconstruction ($p < 0.001$ in both areas).

DISCUSSION

Various vascular reconstruction techniques have been reported for patients with moyamoya disease [3-12]. Those

Table 1: Clinical Characteristics of All Cases.

Case No.	Age	Sex	Suzuki's stage	Surgical Side	Initial Onset	Clinical Outcome
1	9	M	4	R	TIA	Improvement
		M	4	L		
2	27	F	3	L	TIA	No further attack
		F	3	R		
3	67	F	4	R	incidental	No change
4	54	F	3	R	incidental	No change
5	57	F	3	L	TIA	No further attack
6	13	M	3	R	incidental	No change
7	59	F	3	R	cerebral infarction	No further attack
8	31	F	3	R	epilepsy	No further attack
9	34	F	3	L	TIA	No further attack
		F	3	R		
10	39	F	3	R	TIA	No further attack
11	45	F	3	R	TIA	No further attack
		F	3	L		
12	48	F	2	R	TIA	No further attack
		F	3	L		
13	39	M	5	R	ICH	No further attack
14	37	M	2	R	cerebral infarction	No further attack
15	44	F	5	R	cerebral infarction	No further attack
		F	5	L		
16	55	F	4	L	cerebral infarction	No further attack
		F	5	R		
17	20	F	3	R	syncope	No further attack
		F	3	L		
18	50	F	3	L	TIA	No further attack
19	53	F	4	R	incidental	No change
20	38	M	4	R	cerebral infarction	No further attack
21	10	F	3	L	TIA	No further attack

TIA indicate transient ischemic attack; M, male; F, female; R, right; L, left

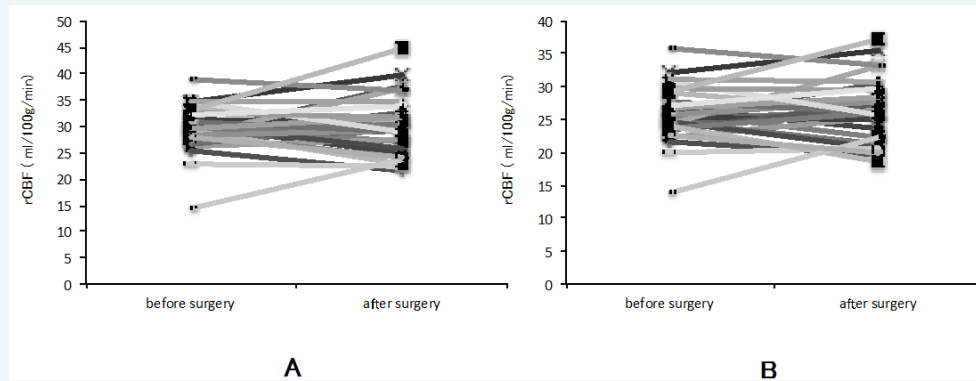


Figure 1 Regional cerebral blood flow (rCBF) at rest before and after surgery in the motor cortex (A) and in the premotor area (B).

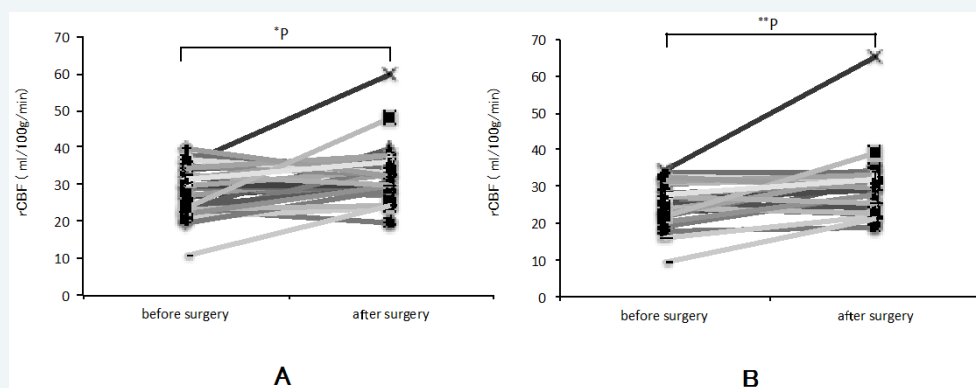


Figure 2 Regional cerebral blood flow (rCBF) in response to acetazolamide (ACZ) challenge before and after surgery in the motor cortex (A) and in the premotor area (B) (* $P < 0.001$, ** $P = 0.006$).

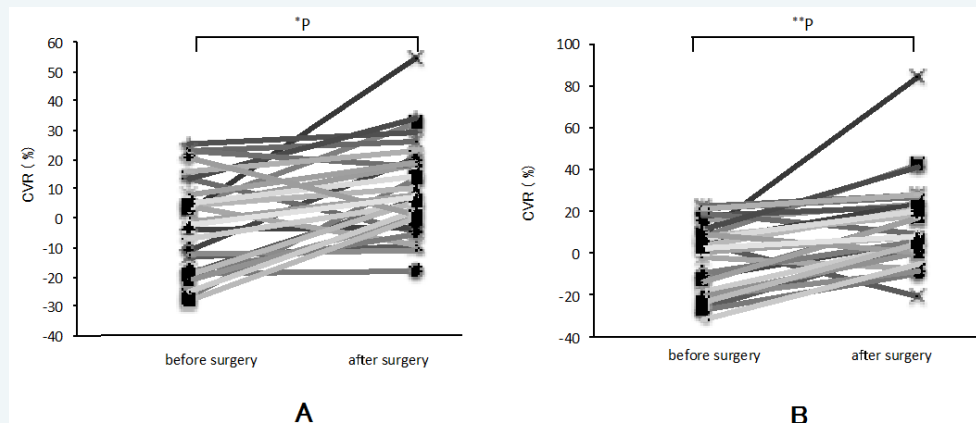


Figure 3 Cerebral vascular reserve (CVR) before and after surgery in the motor cortex (A) and in the premotor area (B) (* $P < 0.001$; ** $P < 0.001$).

surgical methods can be grouped into three main categories: direct revascularization; indirect revascularization; and combined revascularization. Direct bypass is considered to have the benefit of immediately supplying new blood to the ischemic area, and prevent perioperative stroke [5,6]. On the other hand, indirect bypass including encephalomyosynangiosis (EMS), encephalodurosynangiosis (EDS), encephaloarteriosynangiosis (EAS), and their combined bypass also aims to form a new bridging arterial supply that takes a long time to construct. However, no data yet support what kind of revascularization

procedure is optimal for the treatment of moyamoya disease. Combined direct-indirect revascularization procedures have grown in popularity due to their reliability and success in moyamoya patients [8]. Matsushima et al. first reported the usefulness of a combined bypass procedure [3]. They divided patients into two groups, and performed STA-MCA bypass with either EMS or encephaloduroarteriomyosynangiosis (EDAMS). Complete resolution of presenting symptoms was recognized in only 3 of 13 hemispheres after encephaloduroarteriosynangiosis (EDAS), whereas all hemispheres showed absence of

neurological symptoms after STA-MCA bypass with encephalomyoarteriosynangiosis (EMAS). Mizoi et al. also reported surgical results of combined revascularization involving direct STA-MCA bypass and EMS [4]. Twenty-seven of 30 patients experienced resolution of presenting symptoms after the surgery. The authors identified a significant difference in surgical procedure between direct and indirect bypasses, based on differences in the existing vasculature depending on age. Our bypass surgery was conducted with the primary aim of improving rCBF in the motor area, and almost all patients experienced complete resolution of symptoms. Only one patient showed their preoperative symptoms postoperatively, but the frequency of TIA was dramatically diminished in that case. Our results thus appear comparable or superior to those reported previously [5,9,10].

SPECT is a useful modality for evaluating of rCBF and CVR, which can be calculated after intravenous administration of a vasodilator. Many reports of moyamoya patients have described decreased rCBF and CVR that can be improved by vascular reconstruction surgery [10-12]. Touho et al. reported rCBF and CVR in response to ACZ challenge after vascular reconstruction using combined bypass surgery (STA-MCA anastomosis with EMS or other indirect bypass) [9]. They showed improvements to both rCBF and CBV after the surgery. However, the area of improvement was restricted to within the MCA territory. Cerebral perfusion in the territory of both the anterior cerebral artery (ACA) and posterior cerebral artery (PCA) remained poor. The authors described indirect bypass which composed of tissue such as omentum could be a potential treatment of choice for ischemia in the territory of the ACA and PCA. Young et al. described the utility of postoperative CVR measured using ACZ challenge as a predictor of clinical outcomes [12]. Patients with preserved CVR on postoperative SPECT experienced more favorable clinical outcomes compared to those with decreased CVR. In the present study, significant increases in rCBF at rest were not recognized in the MCA territory. However, rCBF after administration of vasodilator and CVR were significantly improved. Decreased reactivity to ACZ is thought to be due to decreases in CVR capacity and vasodilation at rest, which occurs to compensate for proximal stenosis [9]. The present results suggest that our procedure could contribute to rises in rCBF velocity and vasoconstriction at rest for moyamoya patients. TIA in patients with moyamoya disease was thought to be caused not by the rCBF decrease itself, but rather by loss of CVR.

CONCLUSION

Hemodynamic impairment was recognized in patients with moyamoya disease. Our combined direct and indirect surgical reconstruction contributed to the resolution of presenting symptoms, particularly TIA. Cerebral perfusion study using SPECT showed significant improvements in postoperative CVR in the ipsilateral frontal lobe, including the motor cortex, although rCBF at rest in the same area was unchanged. Long-term follow-up study is needed to evaluate whether this vascular reconstruction procedure can reduce the risk of further stroke.

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