Late (5–20 years) outcomes after STA-MCA anastomosis and encephalo-duro-myo-arterio-pericranial synangiosis in patients with moyamoya disease

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OBJECTIVE Surgical revascularization is known to reduce the incidence of further ischemic and hemorrhagic events in patients with moyamoya disease, but the majority of previous studies report only short-term (< 5 years) outcomes. Therefore, in this study the authors aimed to evaluate late (5–20 years) outcomes of moyamoya patients after superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis and indirect bypass (encephalo-duro-myo-arterio-pericranial synangiosis [EDMAPS]).

METHODS Cumulative incidences of late morbidity/mortality and disease progression were evaluated among 93 patients who underwent STA-MCA anastomosis and EDMAPS. All of the patients were prospectively followed up for longer than 5 years postsurgery (10.5 ± 4.4 years). There were 35 pediatric and 58 adult patients. Initial presentation included transient ischemic attack/ischemic stroke in 80 patients and hemorrhagic stroke in 10 patients, and 3 patients were asymptomatic. Surgery was performed in a total of 141 hemispheres. Follow-up MRI/MRA was performed within a 6- or 12-month interval during the follow-up periods.

RESULTS During the follow-up periods, 92/93 patients were free from any stroke or death, but 1 patient had a recurrence of hemorrhagic stroke (0.10% per patient-year). Disease progression occurred in the territory of the contralateral carotid or posterior cerebral artery (PCA) in 19 hemispheres of 15 patients (1.5% per patient-year). The interval between initial surgery and disease progression varied widely, from 0.5 to 15 years. Repeat bypass surgery for the anterior and posterior circulation resolved ischemic attacks in all 10 patients.

CONCLUSIONS The study results indicate that STA-MCA anastomosis and EDMAPS would be the best choice to prevent further ischemic and hemorrhagic stroke for longer than 10 years on the basis of the demonstrated widespread improvement in cerebral hemodynamics in both the MCA and ACA territories in the study patients. However, after 10 years postsurgery regular follow-up is essential to detect disease progression in the territory of the contralateral carotid artery and PCA and prevent late cerebrovascular events.

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KEYWORDS moyamoya disease; late outcome; combined bypass; disease progression; vascular disorders

MOYAMOYA disease often causes ischemic and/or hemorrhagic events in both children and adults. Radiologically, the terminal portion of the internal carotid artery (ICA) and its main branches within the circle of Willis show progressive occlusion associated

with the formation of a fine vascular network (moyamoya vessels) at the base of the brain.^{20,35} Most pediatric moyamoya patients suffer transient ischemic attack (TIA) and/or ischemic stroke due to persistent cerebral ischemia in the territory of the involved arteries. On the other hand, a

ABBREVIATIONS CBF = cerebral blood flow; CVR = cerebral blood reactivity; EDAS = encephalo-duro-arterio-synangiosis; EDMAPS = encephalo-duro-myo-arterio-pericranial synangiosis; EDPS = encephalo-duro-pericranio-synangiosis; EMS = encephalo-myo-synangiosis; ICA = internal carotid artery; MCA = middle cerebral artery; mRS = modified Rankin Scale; PCA = posterior cerebral artery; STA = superficial temporal artery; TIA = transient ischemic attack.

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significant number of adult patients are known to develop hemorrhagic stroke.²⁰ It is widely recognized that surgical revascularization improves cerebral blood flow (CBF) and metabolism and reduces the incidence of further ischemic and hemorrhagic events.^{16,19,22,28,29} Previously, three types of surgical procedures have been reported for moyamoya disease: direct, indirect, and combined bypass. Direct bypass procedures such as superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis are known to quickly improve CBF and reduce ischemic attacks after surgery. Indirect bypass induces spontaneous angiogenesis between the brain surface and vascularized donor tissues such as the dura matter and temporal muscle. Combined bypass includes both procedures.^{19,20} However, each surgical procedure is known to improve patient outcomes. For example, indirect bypass increases the incidence of perioperative ischemic events because of the lack of surgical collaterals just after surgery, and direct or combined bypass improves cerebral hemodynamics just after surgery.¹³ Furthermore, surgery through a small craniotomy centered on the temporoparietal region is closely related to poor intellectual outcome in pediatric moyamoya disease patients because of persistent cerebral ischemia in the frontal lobe, even after surgery.²¹ Furthermore, a majority of surgical procedures are targeted to the MCA territory, but it is also important to revascularize the ACA territory in order to resolve sudden spontaneous falls, known as drop attacks, and preserve intellectual function in both pediatric and adult patients with moyamoya disease.^{11,22} For these purposes, some reports have recommended STA-ACA anastomosis to improve hemodynamic compromise in the ACA territory, but this procedure is still challenging because of the small caliber and fragility of the recipient vessels. Dissection of a longer graft of the STA may also cause delayed wound healing or scalp necrosis.¹⁴

To further improve long-term outcomes in moyamoya patients, we developed a novel indirect bypass procedure, encephalo-duro-myo-arterio-pericranial synangiosis (EDMAPS). In this procedure, the frontal pericranium is used as donor tissue to widely cover the frontal lobe and improve cerebral hemodynamics in both the MCA and ACA territories. As reported previously, we performed STA-MCA anastomosis and EDMAPS in a total of 123 hemispheres of 75 patients (28 children and 47 adults).²² The incidences of mortality and morbidity were 0% and 5.7%, respectively. Follow-up blood flow studies clearly showed that the procedures were effective in improving CBF and reactivity to acetazolamide in both the MCA and ACA territories. During a mean period of 67 months, the annual risk of cerebrovascular events during the follow-up periods was 0% in pediatric patients. Only 1 adult patient developed a cerebral infarction in the occipital lobe because of disease progression in the PCA (annual risk, 0.4% per year). Clinical results after STA-MCA anastomosis and EDMAPS were considered better than those after previously reported procedures.^{2,5,6,10,27,32} Therefore, we reported EDMAPS to be an “ultimate” indirect bypass.²²

However, most previous studies have evaluated only short-term (< 5 years) outcomes after surgery, including our previous study. As a result, before we undertook this investigation the impact of the EDMAPS indirect bypass

procedure on long-term (> 5 years) outcomes was unknown. We believe that therapeutic benefits of surgical treatment of moyamoya should be assessed for a much longer time, because a majority of surgically treated patients are children or young adults. In addition, few studies have evaluated disease progression in the nonoperated hemispheres and the posterior cerebral artery (PCA) for an extended postsurgical time period. Therefore, in this study we aimed to evaluate the long-term (5–20 years) clinical and radiological outcomes after STA-MCA anastomosis and EDMAPS for moyamoya patients.

Methods

Patients

This study was approved by the local institutional review board, and informed consent was obtained from all participants or their legal representatives. This study included a total of 105 patients who underwent STA-MCA anastomosis and EDMAPS for moyamoya disease at Toyama University Hospital or Hokkaido University Hospital between April 1998 and August 2014. All patients fulfilled the radiological criteria for the diagnosis of moyamoya disease set by the Research Committee on Moyamoya Disease established by the Ministry of Health, Labor and Welfare of Japan.³⁴ Patients with secondary moyamoya syndrome associated with underlying disorders such as trisomy 21 and neurofibromatosis type 1 were excluded from this study.

Surgical revascularization was performed in 157 hemispheres of the 105 patients. Of these, 4 patients suffered major ischemic or hemorrhagic stroke within 30 days after surgery (3.8% per patient or 2.5% per surgery) and were excluded from the study. Another 8 patients (7.6%) were lost during follow-up within 5 years after surgery mainly because they moved to a new address. The remaining 93 patients (88.6%) were prospectively followed up for 5 years or longer after surgery and their outcomes were precisely analyzed in this study.

Preoperative Examinations

The following examinations were performed in all patients: plain CT, MRI, MRA, cerebral angiography, and SPECT/PET. Using a 1.5- or 3.0-Tesla MR apparatus, multisequence MRI and 3D time-of-flight (3D-TOF) MRA were performed, including T1-, T2-, T2*- and diffusion-weighted images and FLAIR imaging. Using ¹²³I-iodoamphetamine SPECT or ¹⁵O-gas PET, CBF and cerebral blood reactivity (CVR) were quantitatively measured before and after intravenous injection of acetazolamide.²³

Surgical Indication

In ischemic-type moyamoya disease, reduced CVR in response to acetazolamide was considered a key finding to identify a critical decrease of cerebral perfusion pressure in the involved hemispheres.²² In hemorrhagic-type moyamoya disease, surgical revascularization was indicated in both hemispheres on the basis of the criteria used in the Japan Adult Moyamoya (JAM) Trial.³⁰ Surgical revascularization was indicated for asymptomatic patients when their angiographical stage was markedly advanced in as-

sociation with dense cerebral ischemia or silent microbleeds increased in number during the follow-up period.¹⁸

Perioperative Management

All patients received an extracellular fluid intravenous drip (500–1000 ml) overnight prior to surgery to prevent dehydration-induced ischemic stroke during and after surgery. During and following the induction of general anesthesia, systolic blood pressure was kept between 100 and 120 mm Hg, and PaCO₂ was strictly maintained around 40 mm Hg.²²

Using SPECT, we qualitatively measured CBF immediately after surgery and 2 days and 7 days postsurgery to promptly detect postoperative hyperperfusion. Blood pressure was controlled at a level up to 20% lower than usual when the operated hemisphere was judged as having hyperperfusion.³⁸

Surgical Procedures

STA-MCA anastomosis and EDMAPS were performed as described previously, with minor modifications.²² Following the induction of general anesthesia, the patients were placed in the supine position with the head fixed with a 3-point fixation device. The course of the STA was detected using a Doppler ultrasound probe. The hair was partially shaved, and a skin incision was made along the course of the main trunk and parietal branch of the STA. These were dissected from the surrounding tissues under a surgical microscope and were kept patent. Then, the scalp flap was reflected laterally, and the frontal branch of the STA was also carefully dissected. The galeal tissue over the frontal branch of the STA was repaired with absorbable surgical sutures to prevent delay of wound healing.

The vascularized frontal pericranium was then prepared for subsequent encephalo-pericranio-synangiosis (EPS) using the cranium periosteum and the overlying loose areolar layer. Then, a vascularized flap of temporal muscle was prepared for encephalo-myo-synangiosis (EMS). A standard frontotemporal craniotomy extending into the frontal area was performed, preserving the middle meningeal artery (MMA).⁹ The dura was incised and rolled back by preserving the main branches of the MMA.

An STA-MCA single or double end-to-side anastomosis was then performed using 10-0 or 11-0 nylon threads on the brain surface. The authors preferred 11-0 nylon threads for pediatric patients younger than 10 years. Procedures were performed very carefully, which was important to create a successful STA-MCA anastomosis because the diameters of the recipient vessels were very small (0.4–1.0 mm) and their walls were very thin. Blue dye was put onto the surface of the cut ends of the donor and recipient vessels to enable their clear visualization.¹⁵ A green silicone sheet was inserted beneath the recipient vessel for the same purpose. Usually, 12 to 16 interrupted sutures were made to complete the STA-MCA anastomosis, and 20–30 minutes was required for recipient vessel clamping. ICG (indocyanine green) videoangiography was performed to confirm the patency of the STA-MCA anastomosis during surgery.

Encephalo-duro-synangiosis (EDS) was performed by

turning the dural flaps inward toward the epi-arachnoid space to facilitate the development of surgical collaterals between the outer surface of the dura and the brain. Then, the dural window was covered with both the temporal muscle and pericranial flap. Cranioplasty was performed as usual, using titanium plates, but absorbable fixation plates were employed for pediatric patients younger than 10 years to avoid disturbing the normal growth of the skull. The wound was closed in a layer-by-layer fashion. The total operation time ranged from 5 to 6 hours.

Follow-Up

All patients were prospectively checked at an outpatient clinic for a mean of 10.5 ± 4.4 years (range 5–20 years). MRI and MRA were repeated every 6 or 12 months. In this study, the primary endpoint was any ischemic or hemorrhagic stroke during the follow-up period. TIA with fresh cerebral infarction on diffusion-weighted MRI was considered an ischemic stroke even if clinically transient neurological deficits resolved within 24 hours after the onset. The secondary endpoint was disease progression during the follow-up periods.

Results

In this study we aimed to evaluate late (longer than 5 years) outcome in 93 moyamoya patients who underwent STA-MCA anastomosis and EDMAPS. Of these 93 patients, 35 were pediatric (age < 18 years) and 58 were adult patients. There were 29 male and 65 female patients. The mean $\pm$ SD age for all patients was 30.0 ± 19.0 years (range 1–70 years). The clinical diagnosis included TIA or ischemic stroke in 80 patients, hemorrhagic stroke in 10, and asymptomatic in 3 patients. Precise data are presented in Table 1.

Clinical Outcome

STA-MCA anastomosis and EDMAPS were performed on 141 hemispheres of 93 patients. There was no mortality. During perioperative periods, a total of 19 complications occurred (13.5%), including ischemic stroke ($n = 5$), symptomatic hyperperfusion ($n = 6$), transient cheiro-oral syndrome ($n = 5$), and delay of wound healing ($n = 3$). Of 5 cases of ischemic stroke, 1 case occurred before surgery in a 1-year-old patient. Ischemic stroke-related neurological deficits were mild but persisted in 3 of 5 cases for longer than 30 days. Symptomatic hyperperfusion resolved within 7 days after surgery in all 6 cases. Transient cheiro-oral syndrome disappeared within 3 weeks after surgery in all patients.³⁴ Wound healing delay occurred in 3 cases but did not require additional surgery. Therefore, the incidence of 30-day morbidity was 2.1% (3/141).

During follow-up periods, none of the patients developed ischemic stroke, but 1 patient (1.1%) experienced hemorrhagic stroke. At initial presentation, this 49-year-old male patient developed intracerebral hemorrhage in the left temporal lobe and a diagnosis of unilateral moyamoya disease was made. The patient underwent STA-MCA double anastomosis and EDMAPS on the left side. His clinical course was good, but he suffered rebleeding in the left putamen associated with intraventricular hema-

TABLE 1. Summary of 93 patients who were followed up for at least 5 years after STA-MCA anastomosis and EDMAPS for moyamoya disease

	Pediatric Group	Adult Group	Total
No. of patients	35	58	93
No. of treated hemispheres	54	87	141
Age, yrs	8.8 ± 3.8	42.3 ± 12.0	30.0 ± 19.0
Sex			
Male	15	14	29
Female	20	44	64
Initial diagnosis			
TIA	7	35	42
Ischemic stroke	28	10	38
Hemorrhagic stroke	0	10	10
Asymptomatic	0	3	3
Comorbidity			
Hypertension	0 (0%)	12 (20.7%)	12 (12.9%)
Hyperlipidemia	0 (0%)	8 (13.8%)	8 (8.6%)
Diabetes	0 (0%)	3 (5.2%)	3 (3.2%)
Smoking	0 (0%)	7 (12.1%)	7 (7.5%)
Baseline mRS score	0.31 ± 0.76	0.31 ± 0.73	0.31 ± 0.74
Suzuki stage			
3	15	18	33
4	12	23	35
5	7	12	19
6	1	5	6
Preop disease period, mos	4.2 ± 2.6	8.0 ± 7.2	6.3 ± 4.0
Follow-up, yrs	10.9 ± 4.8	10.2 ± 4.3	10.5 ± 4.4

Values are presented as number of patients or mean ± SD unless otherwise indicated.

toma 9.5 years after surgery. Therefore, the risk of any stroke after STA-MCA anastomosis and EDMAPS was 0.10% per patient-year. At the last follow-up, modified Rankin Scale (mRS) scores were graded as 0 in 80 patients, 1 in 8 patients, 2 in 2, 3 in 2, and 4 in 1 patient. The mean mRS for all 93 patients changed from 0.32 ± 0.74 at initial presentation to 0.24 ± 0.70 at the last follow-up. There was no significant change between the two periods.

Radiological Outcome

Repeated MRA revealed disease progression in 19 hemispheres (13.5%) of 15 patients (16.1%) during a mean of 10.5 years (Table 2). Therefore, the annual risk of disease progression was 1.5% per patient-year. Female predominance was observed (11/15). The clinical diagnosis at initial presentation was TIA or ischemic stroke in 14 of the 15 patients, with 1 patient asymptomatic.

Disease progression was observed in the contralateral ICA in 9 patients who underwent STA-MCA anastomosis and EDMAPS on the unilateral hemisphere at initial presentation. Of these, 7 patients were younger than 20 years. Disease progression in the contralateral ICA occurred within 5 years after initial surgery in 6 patients

and caused TIA in 7 of 9 patients. STA-MCA anastomosis and EDMAPS were performed on the contralateral hemisphere in 7 of 9 patients. All of these patients remained free from any cerebrovascular events at the time of this report.

As shown in Table 2, disease progression in the PCA was observed in 11 hemispheres of 8 patients. Their age varied widely, from 1 to 52 years. The timing of disease progression after initial surgery also widely differed among these patients, varying from 0.5 to 15 years (mean 5.4 ± 4.4 years). Disease progression occurred in the bilateral PCAs of 3/8 patients or in both the contralateral ICA and unilateral PCA in 2/8 patients. Transient neurological symptoms such as homonymous hemianopsia were recorded in 6 hemispheres of 8 patients. Of these, indirect bypass (encephalo-duro-pericranio-synangiosis [EDPS]) was performed in 4 hemispheres of 4 patients because the acceptable recipient artery could not be found in the operative field. After additional surgery, all 4 patients experienced no cerebrovascular events.

Discussion

Late Clinical Outcomes

According to previous reports by us and other investigators, surgical revascularization has substantially improved short-term to midterm (< 5 years) outcomes in patients with moyamoya disease. However, a period of 5 or 6 years is too short to fully assess the benefits of bypass surgery for moyamoya disease, because most of the patients are children or young adults and have a much longer lifetime after surgery than before. As the results of the present study clearly indicate, treatment with STA-MCA anastomosis and EDMAPS may lead to satisfactory outcomes in both pediatric and adult patients with moyamoya disease. During the follow-up period of the current study, which ranged from 5 to 20 years (mean 10.5 years), 92 of 93 patients (98.9%) were free from any stroke and death, although 1 patient experienced rebleeding in the ipsilateral hemisphere 9.5 years postsurgery (0.10% per patient-year).

Recently, two Japanese groups have published their long-term (> 10 years) outcome results in a large cohort of surgically treated children with moyamoya disease. Namely, Mukawa et al. (2012) surveyed 14.3-year outcomes after indirect bypass (encephalo-duro-arterio-synangiosis [EDAS]) in 172 pediatric patients. In about 80% of patients the results were graded as good functional outcome (mRS score 0–2). Of the 172 patients, however, 6 developed ischemic (n = 3) or hemorrhagic (n = 9) stroke at 8–22 years after EDAS. Based on these results, the risk of stroke in this large cohort at 10, 20, and 30 years post-EDAS was 0.8%, 6.3%, and 10.0%, respectively.³¹ Funaki et al. (2014) also evaluated the 18.1-year outcome after STA-MCA anastomosis and EMS in 56 pediatric patients and found that 4 of 56 patients developed ischemic (n = 1) or hemorrhagic (n = 4) stroke at 2–20 years postsurgery. The 10-, 20-, and 30-year cumulative risks of stroke were 1.8%, 7.3%, and 13.1%, respectively.⁴ Therefore, STA-MCA anastomosis and EDMAPS may lead to better long-term (> 5 years) outcomes for pediatric patients than EDAS or STA-MCA anastomosis combined with EMS.

TABLE 2. Summary of 15 patients who showed disease progression after STA-MCA anastomosis and EDMAPS

Case No.	Age at Presentation, yrs	Sex	Initial Presentation	Initial Op	Disease Progression				
					Contralateral ICA		PCA		
					Symptoms	Repeat Bypass	Symptoms	Repeat Bypass	1st Op to 1st Progression, yrs
1	1	M	Ischemic stroke	Lt STA-MCA + EDMAPS, Rt STA-MCA + EDMAPS			TIA	Rt EDPS	0.5
2	4	F	Ischemic stroke	Rt STA-MCA + EDMAPS			TIA	Rt EDPS	1
3	7	M	TIA	Rt STA-MCA + EDMAPS	TIA	Lt STA-MCA + EDMAPS			5
4	8	F	TIA	Lt STA-MCA + EDMAPS, Rt STA-MCA + EDMAPS			None	None	15
5	8	F	TIA	Lt STA-MCA + EDMAPS	None	None	None	None	6
6	8	F	TIA	Lt STA-MCA + EDMAPS	TIA	Rt STA-MCA + EDMAPS	TIA	Lt EDPS	1
7	11	M	TIA	Rt STA-MCA + EDMAPS	TIA	Lt STA-MCA + EDMAPS			1
8	11	F	TIA	Lt STA-MCA + EDMAPS	None	None	None	None	7
9	12	F	TIA	Lt STA-MCA + EDMAPS	TIA	Rt STA-MCA + EDMAPS			2
10	19	F	TIA	Lt STA-MCA + EDMAPS	TIA	Rt STA-MCA + EDMAPS			0.7
11	35	F	TIA	Lt STA-MCA + EDMAPS	TIA	Rt STA-MCA + EDMAPS			7
12	38	F	TIA	Lt STA-MCA + EDMAPS, Rt STA-MCA + EDMAPS			TIA		8
13	47	F	Ischemic stroke	Rt STA-MCA + EDMAPS	TIA	Lt STA-MCA + EDMAPS	TIA	Rt EDPS	1.5
14	49	F	Asymptomatic	Lt STA-MCA + EDMAPS			None	None	7
15	52	M	TIA	Lt STA-MCA + EDMAPS, Rt STA-MCA + EDMAPS			None	None	8

"None" in the "Symptoms" column means that the patients did not develop any cerebrovascular events in spite of disease progression. "None" in the "Repeat Bypass" column means that the patients did not undergo repeat bypass because of the lack of cerebrovascular events in spite of disease progression.

However, further study is essential to follow up these pediatric patients for a longer time period extending to adulthood.

On the other hand, there are almost no reports of study results for long-term (> 10 years) outcomes in adult moyamoya patients who underwent bypass surgery, although many reports of clinical results during 5- to 6-year follow-up periods have been published. Only Bao et al. (2018) performed EDAS for 145 adult patients and followed them up for approximately 12 years. These authors reported 1-, 5-, and 10-year estimated cumulative stroke rates of 2.1%, 6.8%, and 8.9%, respectively. Bao et al. concluded that bilateral involvement was a common significant factor in any strokes and that hypertension was a risk factor for ischemic strokes during follow-up.¹ The values reported by Bao et al. were somewhat larger than those of the present study. Therefore, the present study is to our knowledge the first to clearly show that STA-MCA anastomosis and EDMAPS may also lead to the best long-term (> 5 years) outcomes reported to date for adult patients with moyamoya disease.

Late Radiological Outcome and Repeat Bypass

Previously, we analyzed the findings on serial MRA in adult patients and reported that disease progression occurred in 15 of 86 nonoperated hemispheres (17.4%), or in 15 of 63 patients (23.8%), during the first 6 years after bypass surgery.²⁴ The present study clearly shows that moyamoya patients are exposed to the risk for disease progression even thereafter, and thus it should be recognized that disease progression is likely to occur during at least the first 15 years after surgery.

In the present study, disease progression occurred in the contralateral ICA territory in 9 patients during the follow-up period. Most of them (7/9) were younger than 20 years and showed disease progression within 5 years after the initial surgery. These findings are supported by previous reports. Namely, Yeon et al. (2011) reported that contralateral progression occurred in 8 of 45 children (17.8%) with unilateral moyamoya disease within 3 years of initial diagnosis. All of these patients were younger than 9 years.³⁹ Park et al. (2011) also reported that 20 of 34 pediatric patients (58.8%) with unilateral moyamoya disease experienced contralateral progression within approximately 3 years.³³

In our study, disease progression in the PCA occurred in 11 hemispheres of 8 patients. The features of PCA progression largely differed from those of contralateral progression. The age of the study patients varied from 1 to 52 years at initial presentation, and there was very wide variation in the timing of disease progression, from 0.5 to 15 years after initial surgery. About half (6/11) of the PCA lesions caused TIA. There are few reports regarding disease progression in the PCA in surgically treated moyamoya patients during long-term follow-up periods. However, it should be noted that occlusive arterial lesions progressed in both carotid and PCA territories.²⁴ Huang et al. (2009) reported that occlusive lesions in the PCA progressed on 18/38 sides (47.4%) after surgical revascularization for anterior circulation.¹² Lee et al. (2013) found that 29/166 sides (17%) showed PCA disease progression in pediatric moyamoya

disease patients during a mean follow-up period of 8.3 years. The mean timing of disease progression after the initial surgery was 4.9 years, with the latest onset at 10.8 years.²⁶ Based on these observations, we should recognize that disease progression in the PCA is not as rare as was previously considered. Furthermore, occlusive lesions in the PCA may be key factors leading to hemorrhagic stroke in adult moyamoya disease.³ Therefore, we should be aware that disease progression in the PCA may occur in a delayed fashion, and we should follow up moyamoya patients for longer than 10 years after bypass surgery in order not to miss disease progression in the PCA, which carries the potential risk for TIA or ischemic or hemorrhagic stroke.

In this study, repeat bypass surgery was indicated when ischemic symptoms were severe due to dense cerebral ischemia in the territory of the contralateral ICA (n = 7) or PCA (n = 4). For the former, STA-MCA anastomosis combined with EDMAPS was performed. For the latter, however, only an indirect bypass procedure (EDPS) was performed because of the lack of an acceptable recipient artery. Recently, several reported studies have demonstrated the feasibility and beneficial effects of repeat bypass for both the anterior and posterior circulation.^{8,17,25,36,37} Hayashi et al. (2009) reported 3 patients with moyamoya disease who underwent occipital artery (OA) to PCA anastomosis and indirect bypass because of disease progression in the PCA.⁷ Lee et al. (2014) also performed indirect bypass onto the PCA territory for 41 children with delayed PCA insufficiency, and these authors observed that this treatment yielded good clinical outcomes.²⁵ We also performed OA-MCA (n = 3) or OA-PCA anastomosis (n = 8) combined with indirect bypass in patients who showed disease progression in the PCA after surgical revascularization for the anterior circulation.¹⁷ Furthermore, we very recently reported that repeat bypass is feasible and very effective for both the carotid and PCA territories on the basis of our experience in 20 patients with refractory moyamoya disease.³⁷

Conclusions

STA-MCA anastomosis and ultimate indirect bypass (EDMAPS) may be one of the best choices of surgical treatment to prevent further cerebrovascular events for longer than 10 years in moyamoya patients by widely providing surgical collaterals to both the MCA and ACA territories. However, regular follow-up should be planned for longer than 10 years postsurgery to identify disease progression in the territory of the contralateral carotid artery and PCA and prevent late cerebrovascular events. Repeat bypass surgery is feasible and effective to resolve ischemic attacks in both carotid and PCA territories.

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Disclosures

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Author Contributions

Conception and design: Kuroda. Acquisition of data: Kuroda, Nakayama, Yamamoto, Kashiwazaki, Uchino, Saito, Hori, Akioka, Kuwayama. Analysis and interpretation of data: Kuroda. Drafting the article: Kuroda. Critically revising the article: Kuroda. Reviewed submitted version of manuscript: Kuroda. Approved the final version of the manuscript on behalf of all authors: Kuroda. Study supervision: Houkin.

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