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CLINICAL ARTICLE

Long-term follow-up results in 142 adult patients with moyamoya disease according to management modality

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Abstract

Background To clarify the most beneficial treatment of the management modality based on our experience with adult moyamoya disease (MMD).

Methods From 1998 to 2010, clinical results of 142 patients (ischemic, 98; hemorrhagic, 44) with adult MMD were investigated according to management modality. Revascularization surgery (direct, indirect, and combined bypass) was performed in 124 patients. We observed the clinical course of 18 patients who were treated conservatively. Clinical outcome, angiographic features, hemodynamic change, and incidence of recurrent stroke were investigated pre- and postoperatively.

Results In patients with ischemic MMD, direct and combined bypasses were more effective treatments to prevent recurrent ischemic stroke than indirect bypass surgery ($P<0.05$). In patients with hemorrhagic MMD, rebleeding was less likely to occur in patients who had undergone bypass surgery. However, no significant difference was observed in the rebleeding rate between patients with and without revascularization surgery ($P>0.05$). An angiogram after bypass surgery comparing the extent of revascularization and reduction of moyamoya vessels in patients treated with direct, indirect, and combined bypass showed a significant difference ($P<0.05$) in favor of direct and combined bypass. Postoperative angiographic changes and SPECT results demonstrated significant statistical correlation ($P<0.05$).

Conclusion Revascularization surgery was effective in further ischemic stroke prevention to a statistically significant extent. Direct and combined bypasses were more effective to prevent recurrent ischemic stroke than indirect bypass. However, there is still no clear evidence that revascularization surgery significantly prevents rebleeding in adult MMD patients. More significant angiographic changes were observed in direct and combined bypasses compared with indirect bypass.

Keywords Adult moyamoya disease · Bypass surgery · Intracranial hemorrhage · Revascularization

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Introduction

Moyamoya disease, as first described in the Japanese medical literature in 1957 by Takeuchi and Shimizu, is a rare, cerebrovascular disorder characterized by idiopathic, progressive occlusion of bilateral supraclinoidal internal carotid arteries and the development of an extensive basal cerebral collateral vascular network [35, 36]. Moyamoya disease can be divided into two clinical entities: juvenile- and adult-onset types [11, 34]. Adult patients' clinical features are much different from those seen in juvenile patients. Most juvenile patients develop ischemic events in all stages of MMD, whereas the hemorrhagic event is prevalent among adults [34, 40].

The incidence of disease progression in adult MMD is much higher than recognized before [8, 17, 22, 33, 37]. Therefore, symptomatic adult MMD should be treated as soon as possible, similar to juvenile MMD. Based on previous reports, revascularization surgery has been shown to improve clinical symptoms and reduce the incidence of subsequent ischemic stroke in pediatric patients [16, 18, 19, 24]. There is some controversy regarding the prevention of recurrent hemorrhagic events in adult MMD [1, 13, 14, 28, 31, 40]. We have used many surgical techniques to enhance cerebral revascularization in adult patients with MMD: direct revascularization via the superficial temporal artery (STA)–middle cerebral artery (MCA) anastomosis, indirect bypass surgery such as encephaloduroarteriosynangiosis (EDAS), encephalomyosynangiosis (EMS), encephaloduroarteriogaleosynangiosis (EDAGS), and a combined STA-MCA anastomosis with EDAGS surgery using an inverted STA-galeal flap (GF) and STA-galeal pedicle (GP).

We present a retrospective analysis of adults with MMD admitted and treated at our institution during the last 13 years. We aimed to clarify the most beneficial treatment for preventing recurrent stroke in symptomatic adult MMD patients. In addition we investigated which surgical modality was associated with postoperative angiographic change and SPECT results.

Clinical material and methods

Patient selection, inclusion criteria, and operative procedure

From 1998 to 2010, 169 patients were diagnosed with adult MMD (≥18 years of age) and admitted and treated at our institution. In this study, we retrospectively analyzed records of 142 patients who were followed up for over 1 year, from onset until 2010.

All patients had ischemic or hemorrhagic symptoms. The diagnosis of MMD was made based on angiography according to published guidelines [9]. All patients presenting ischemic and hemorrhagic symptoms were evaluated with computed tomography (CT), computed tomographic perfusion (CTP), magnetic resonance imaging (MRI) including diffusion-weighted imaging (DWI), and fluid attenuated inversed recovery (FLAIR) imaging to assess the overall stroke burden. Preoperative 6-vessel angiography was performed in all patients to determine disease severity and to evaluate the presence of the superficial temporal artery (STA). Preoperative angiographic staging was performed based on Suzuki's angiographic criteria [35]. All patients underwent a cerebral blood flow analysis using single-photon emission computed tomography (SPECT) studies with an acetazolamide (Diamox) challenge preoperatively.

Bypass surgery was indicated for (1) symptomatic patients, e.g., those with transient ischemic attack (TIA), cerebral ischemia, and hemorrhage; (2) patients with impaired cerebral blood flow (CBF) and cerebral reserve capacity on acetazolamide SPECT. In patients with conservative treatment, their neurological status was inadequate for bypass surgery because of major cerebral infarction or a large amount of hemorrhage. Some patients refused revascularization surgery because of their mild symptoms. We included those patients who were available for over 1 year of follow-up. We did not operate on asymptomatic patients with a normal hemodynamic study. Revascularization surgery was performed more than 1 month after the onset of initial hemorrhage or infarction. In patients with symptoms of transient ischemic attack (TIA), revascularization surgery was performed as soon as possible to prevent a secondary ischemic attack.

In this series, revascularization surgery for MMD was divided into three categories: direct bypass, indirect bypass, and combined bypass. Direct bypass procedures include only STA-MCA anastomosis [18]. If a suitable recipient artery could not be found during surgery, indirect surgery was performed instead of the STA-MCA bypass. We performed EDAGS, EDAMS, or EMS as indirect methods [10, 32]. Combined bypass surgery was performed by direct STA-MCA anastomosis, and EDAGS was performed using inverted STA-GF/GP [20].

Clinical and radiological data

Clinical and radiological data were reviewed for the following characteristics: demographics, surgical modalities, clinical outcome, recurrence of ischemic and hemorrhagic stroke after bypass, postoperative angiographic change, and cerebral blood flow (CBF) change by SPECT. Each patient's clinical status was assessed pre- and postoperatively using the modified Rankin Disability Scale (mRDS) [39]. Recurrence of ischemic and hemorrhagic attack was confirmed using CT or MRI scanning. Postoperative angiographic change was evaluated according to the extent of revascularization and changes in moyamoya vessels observed on a postoperative angiogram obtained 6–12 months after surgery. The change of moyamoya vessels was determined if the number of moyamoya vessels decreased or did not change compared with the preoperative angiogram. We measured the revascularization area and area of MCA territory in the capillary phase of the lateral view in the external carotid angiogram (Fig. 1). We calculated the relative percentage of the revascularization area compared to the area of the MCA territory [4]. The revascularization area was measured on a PACS workstation (Marosis, Marotech, Korea) using its free-hand region of interest measurement tools. The postoperative angiographic change was categorized into good, moderate, and poor groups. If the extent of revascularization area supplied by the surgical bypass covered more than two thirds (66%) of the middle cerebral artery (MCA) distribution and the number of moyamoya vessels decreased, the change was classified as "good." If the extent of the revascularization area covered between one third (33%) and two thirds (65%) of the MCA distribution and the number of moyamoya vessels decreased, the change was determined to be "moderate." If the aforementioned criteria were not met or there were no changes, the angiographic change was determined to be "poor." These data were calculated by a neurosurgical resident who was not involved in the surgery. We checked those areas twice and gained the mean to reduce the error.

Basal and acetazolamide-challenged brain perfusion SPECT was performed to evaluate CBF pre- and postoperatively. Routine postoperative evaluation with SPECT was accomplished 3–6 months after surgical treatment. The postoperative CBF was compared with the preoperative value. We classified

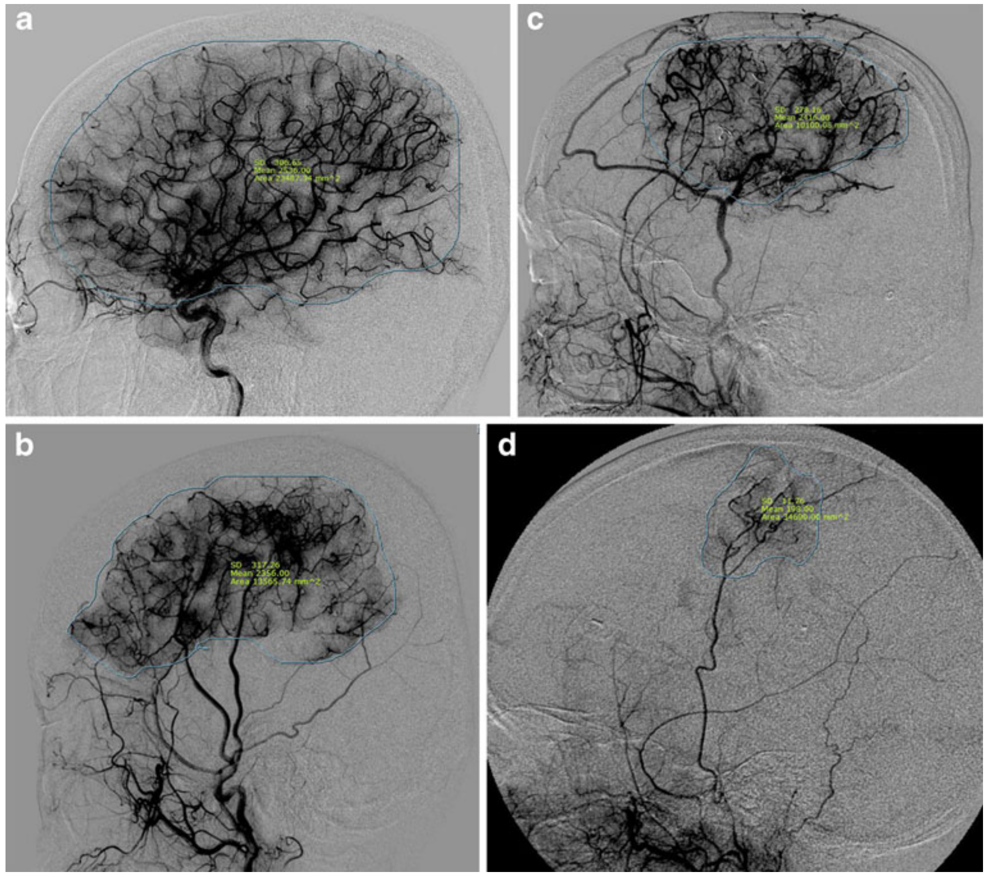

Fig. 1 Classification of the extent of revascularization demonstrated on the postoperative external carotid angiograms in patients with revascularization surgery. The capillary phase of the angiographic lateral image shows (**a**) the area of the MCA territory. The extent of revascularization (**b**) covered more than two-thirds of the MCA distribution; (**c**) between two-thirds and one-third of the MCA; and (**d**) was slight or none

SPECT results into three categories as follows: improved, unchanged, and worsened. Improved, unchanged, and worsened definitions are based on radiological readings. We also investigated the correlation between postoperative angiographic change and SPECT results.

Clinical outcomes were assessed by a neurosurgeon (T-G Lee), who did not participate in the bypass surgery, and radiological data were reviewed by a neuroradiologist who was unaware of the clinical results. All SPECT data were interpreted by a nuclear medicine doctor who was not involved in the surgery.

Statistical analysis

The incidence of hemorrhagic or ischemic events, demographic data, the angiographic revascularization at the operated sites, and the effect of revascularization surgery were analyzed using the chi-square test according to treatment modality. The change in clinical status (mRDS) was analyzed using the Wilcoxon signed-rank test according to treatment modality. Correlations between the angiographic change, postoperative SPECT results, and incidence of recurrence stroke were analyzed using linear-by-linear association. Stroke-free time from recurrent hemorrhagic and ischemic stroke were estimated using the Kaplan-Meier product-limit method. The log-rank test was applied to evaluate differences between two or more hemorrhage- and ischemia-free time curves. SPSS software (version 15.0, 2006; SPSS, Inc., Chicago, IL, USA) was used, and probability values <0.05 were considered statistically significant.

Results

Among the 142 adult patients with MMD, 147 hemispheres of 124 adult MMD patients underwent revascularization surgery (103 hemispheres of 89 ischemic MMD patients, 44 hemispheres of 35 hemorrhagic MMD patients), and 18 patients were treated conservatively. Table 1 summarizes the general demographic features of the patients. Among the 18 patients with conservative treatment, 4 refused bypass surgery because of their mild neurological symptoms, and 6 patients refused bypass surgery for other reasons (such as financial problems, etc.). Eight patients could not undergo bypass surgery because of their poor neurological status. Of these patients, three underwent decompressive surgery. No significant differences were observed for age, gender, or length of follow-up period among patients when grouped according to treatment modalities in this series. Weakness was the most common symptom. A significant difference was observed in the initial RDS score between patients with ischemic and hemorrhagic MMD ($P<0.05$). Six-vessel angiography was performed preoperatively in all patients, and the predominant angiographic finding was

Table 1 Demographic characteristics in patients

	Ischemic (bypass) group	Hemorrhagic (bypass) group	Conservative group	p-value
Number of patients	89	35	18	
Number of treated hemispheres	103	44		
Age, mean ± SD, year†	38.7±12.3	43.1±10	41.5±9.6	NS
Sex (male/ female, %)	32/57, 59.8%	15/20, 75%	7/11, 63.6%	NS
Symptom at presentation				
	TIA: 30	Mental change: 16	Mental change: 6	
	Paresis: 59	Paresis: 19	Paresis: 12	
RDS at presentation				<0.05
0-1	16 (17.9%)	0 (0%)	1 (5.6%)	
2	23 (25.9%)	3 (6.8%)	6 (33.3%)	
3	34 (38.3%)	24 (54.5%)	7 (38.9%)	
4	16 (17.9%)	14 (31.9%)	3 (16.7%)	
5	0 (0%)	3 (6.8%)	1 (5.5%)	
Suzuki grade				
1	0	0	0	
2	2	1	1	
3	44	13	10	
4	38	19	6	
5	5	2	1	
6	0	0	0	
Mode of treatment				
Direct bypass	18	9		
Indirect bypass	50	18		
Combined bypass	21	8		
Follow-up period (months)†	56.4±26.2	55 ±19.2	54.1±15	NS

NS Not statistically significant

†Values are expressed as means ± standard deviation

RDS Rankin Disability Scale

disease progression to stages III and IV. The follow-up duration ranged from 12 to 112 months (mean, 54.5 months). During the follow-up period, 23 (15.6%) of 147 hemispheres presented recurrent stroke (ischemic events, 14 patients; hemorrhagic events, 9 patients) after revascularization surgery. In 18 patients treated conservatively, 10 (55.6%) experienced recurrent stroke (ischemic events, 6 patients; hemorrhagic events, 4 patients). After the second ischemic and hemorrhagic events, 20 of 33 patients (60.6%) experienced worsening of their clinical symptoms. Poor prognosis was seen in patients with recurrent hemorrhagic events. Of the 13 patients who experienced recurrent intracranial hemorrhage, 5 (38.4%) died, 4 (30.8%) deteriorated to a persistent vegetative state, and 4 (30.8 %) were severely disabled.

Recurrent stroke events and final clinical status in patients with ischemic MMD

Follow-up periods ranged from 12 to 112 months (mean, 56.2 months). A total of 103 hemispheres of 89 patients were treated surgically, and 9 patients were treated conservatively. Fourteen patients had bilateral bypass surgeries, and 75 patients had unilateral bypass surgery. The incidence of recurrent stroke events for each treatment modality is presented in Table 2. Seventeen (16.5%) of 103 hemispheres had recurrent stroke events (ischemic events, 14 patients; hemorrhagic events, 3 patients) after revascularization surgery, whereas 6 of 9 patients (66.7%) who underwent conservative treatment presented with recurrent ischemic stroke. The incidence of recurrent stroke in patients who underwent direct and combined bypass surgery was significantly lower ($P<0.05$, χ^2-test) than that in patients treated with indirect bypass or conservative treatment. Kaplan-Meier plots demonstrated that patients who underwent revascularization surgery had significantly longer stroke-free times ($P<0.05$) than patients who were treated conservatively (Fig. 2). Significant improvement in the RDS score was seen after surgery ($P<0.05$, χ^2-test), but no improvement was observed in patients who were treated conservatively. However, no significant difference was observed according to the bypass method.

Recurrent stoke events and final clinical status in patients with hemorrhagic MMD

Follow-up periods ranged from 12 to 105 months (mean, 55.4 months). A total of 44 hemispheres of 35 patients were

Table 2 Clinical outcomes of the 98 patients with ischemic MMD stratified by treatment

	Surgical treatment			Conservative treatment
	Direct bypass	Indirect bypass	Combined bypass	
Number of patients	18	50	21	9
Number of treated hemispheres	25	55	23	9
Patient's age (years, mean)	41.8	38.2	37.4	39.1
Sex (male/female)	9/9	18/32	5/16	4/5
Patients with improved RDS	13 (72.2%)	29 (58%)	15 (71.4%)	2 (22.2%)
Follow-up periods (months)	54.8	59.6	56.5	50.9
Patients with recurrent stroke*	2 (8.0%)	14 (25.5%)	1 (4.3%)	6 (66.7%)
Stroke* free times†	78.5±8.8	71.5±6.6	87.1±11.4	31.2±4.6

*Rebleeding or ischemic event

†Values are expressed as means ± standard deviation

RDS Rankin Disability Scale

surgically treated, and 9 patients were treated conservatively. Nine patients had bilateral bypass surgeries, and 26 patients had unilateral bypass surgery. The incidences of recurrent hemorrhagic events for each treatment modality are presented in Table 3. Six (15.9%) of 44 hemispheres had recurrent hemorrhagic events after revascularization surgery. In contrast, four (44.4%) of nine patients who were treated conservatively experienced recurrent hemorrhagic events. However, the incidence of recurrent hemorrhagic events in patients who underwent revascularization surgery tended to be lower than that in patients treated conservatively, but no significant difference was observed ($P>0.05$, χ^2-test). No significant difference was found between the bypass methods. Kaplan-Meier plots demonstrated that patients who underwent revascularization surgery remained stroke-free longer than those treated conservatively (Table. 3). However, no statistical difference ($P>0.05$) was observed between patients who underwent revascularization surgery and patients who were treated conservatively (Fig. 3). Significant improvement was observed in the RDS score after revascularization surgery ($P<0.05$, χ^2-test). No improvement was seen in patients with conservative treatment.

Angiographic changes and SPECT analysis

Postoperative angiograms were obtained for 138 hemispheres in 114 patients with revascularization surgery, and postoperative SPECT was done in 111 patients. Table 4 shows the results. Among the 138 hemispheres, good angiographic change was

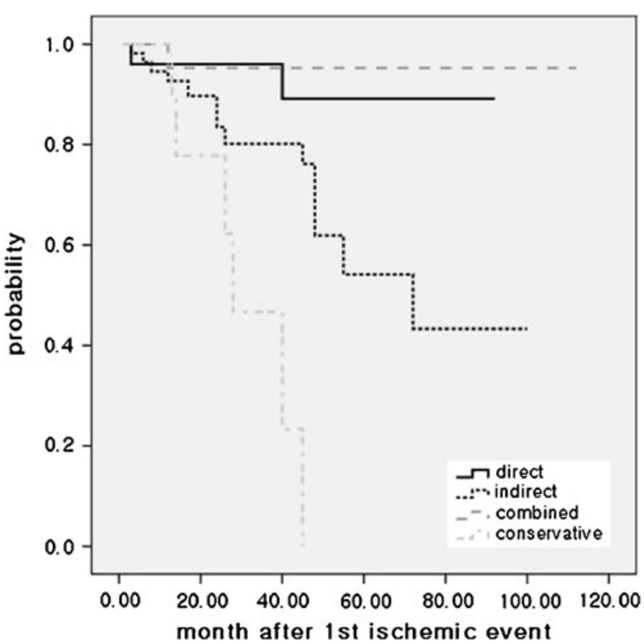

Fig. 2 Kaplan-Meier plots of hemorrhagic and stroke-free time demonstrated that patients who underwent revascularization surgery had significantly longer stroke-free times than those treated conservatively ($P<0.05$)

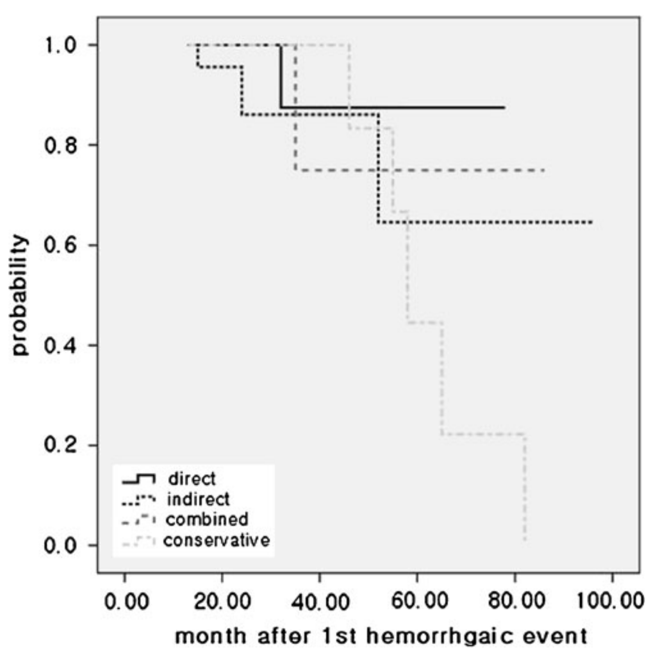

Fig. 3 Kaplan-Meier plots of stroke-free time demonstrated that patients who underwent revascularization surgery tended to have longer stroke-free times than those treated conservatively, but no statistical difference was observed ($P>0.05$)

Table 3 Clinical outcomes of the 44 patients with hemorrhagic MMD stratified by treatment

	Surgical treatment			Conservative treatment
	Direct bypass	Indirect bypass	Combined bypass	
Number of patients	9	18	8	9
Number of treated hemispheres	11	23	10	0
Patient's age (years, mean)	46.2	41.5	47	49.9
Sex (male/female)	4/5	7/11	4/4	3/6
Patients with improved RDS	6 (66.7%)	11 (61.1%)	5 (62.5%)	2 (22.2%)
Follow-up period (months)	51.2	56.4	55.8	59.6
Patients with recurrent stroke*	1 (9.1%)	4 (17.3%)	1 (10%)	4 (44.4%)
Stroke* free times†	70.3±7.5	77.4±5.8	81.1±9.6	41.8±3.7

*Rebleeding or ischemic event

†Values are expressed as means ± standard deviation

RDS Rankin Disability Scale

found in seven hemispheres (23.3%) with direct bypass, in eight (10.4%) with indirect bypass, and in nine (29%) with combined bypass. More significant angiographic changes were observed in patients who underwent direct and combined bypasses compared to those in patients who underwent indirect bypass ($P<0.05$, χ^2-test).

Correlation between the postoperative angiographic changes and stroke recurrence was investigated (Table 5). Statistical analysis between the angiographic change and recurrent ischemic events demonstrated significant statistical correlation (P-value=0.036, linear-by-linear association). However, no statistical correlation was observed between the angiographic change and rebleeding (p-value=0.426, linear-by-linear association).

We also investigated postoperative SPECT results and compared them with the angiographic changes. Table 6 shows the postoperative SPECT results. Statistical analysis between the angiographic changes and SPECT result demonstrated significant statistical correlation. This result shows that the angiographic changes are well correlated with CBF change (p-value=0.001, linear-by-linear association).

Discussion

Moyamoya disease has been recognized as a devastating condition and has a specific pattern of age distribution in adults and children, with a higher incidence in childhood [34, 40]. The clinical symptoms of MMD relate directly to abnormal vasculature. The incidence of hemorrhage is reported to exceed 60% in adults, whereas it is only 10% in children [30]. The reason why intracranial hemorrhage frequently occurs in adult patients is unclear. The difference in the presenting symptoms between juvenile and adult patients may reflect the differences in cerebral hemodynamics and metabolism [15, 23, 28]. The clinical presentations of patients in this study were slightly different from those in other reports. In the present study, patients with ischemic symptoms were more predominant than those with hemorrhagic symptoms [ischemic symptoms, 98 patients (69%), hemorrhagic symptom, 44 patients (31%)]. It is true that hemorrhagic MMD is more predominant in adult patients compared to pediatric patients. However, in our study, ischemic MMD was more predominant than hemorrhagic MMD for several reasons. This study was limited to a single institution in Gyung-gi Province, and the number of cases was small and limited; thus, referral and selection bias could not be excluded. Additionally, with recent advances in neuroradiological diagnostic modalities, including MR angiography and three-dimensional CT angiography, the diagnosis of adult MMD has become more frequent, and these diagnostic tools are now used more easily in an outpatient setting than in the past. Furthermore, MMD is detected earlier before hemorrhagic attacks occur [3].

Regardless of whether patients initially experienced an ischemic attack or an intracranial hemorrhage, a secondary ischemic or hemorrhagic attack may have occurred during the

Table 4 Angiographic change of the 138 hemispheres with revascularization surgery

Angiographic change	Number of treated hemispheres (n=138)			
	Direct (n=30)*	Indirect (n=77)	Combined (n=31)*	Total
Good	7 (23.3%)	8 (10.4%)	9 (29%)	24 (17.4%)
Moderate	18 (60%)	28 (36.4%)	17 (54.9%)	63 (45.7%)
Poor	5 (16.7%)	41 (53.2%)	5 (16.1%)	51 (36.9%)

* Significant angiographic changes observed in direct and combined bypass ($P<0.05$)

Table 5 Correlation between postoperative angiographic change and incidence of recurrent stroke event

Angiographic change	Recurrent stroke events		
	Ischemic events (n=14)*	Hemorrhagic events (n=9)	Total (n=23)
Good	0 (0 %)	3 (33.3%)	3 (13.1%)
Moderate	5 (35.7%)	2 (22.2%)	7 (30.4%)
Poor	9 (64.3%)	4 (44.5%)	13 (56.5%)

* Significant correlation was observed between angiographic change and recurrent ischemic event ($P<0.05$)

follow-up period. Therefore, patients with MMD should be treated with the aim of preventing recurrent ischemic or hemorrhagic attacks. Although direct, indirect, or combined direct and indirect bypass has been utilized in patients with MMD, especially with ischemic MMD, it is unclear what the best treatment is for preventing recurrent hemorrhage or ischemic events in adult MMD patients [1, 13, 14, 28, 31]. Direct and combined bypasses provide an immediate increase of the blood supply to the ischemic brain compared to indirect bypass, and favorable results have been reported [10, 18, 20, 27]. However, direct bypass has some considerable drawbacks; it is difficult to find both good donor and recipient arteries of sufficient caliber in some patients with moyamoya disease, and some complications are related to direct bypass surgery, such as symptomatic hyperperfusion, cerebral infarction, intracerebral hemorrhage, or even death [7, 12, 16, 27, 38]. In contrast, indirect bypass is generally considered easier, safer, and less invasive than direct bypass, and is more feasible in patients with inadequate recipient or donor artery grafts [24, 25]. Although it has low rates of perioperative complications, formation of collateral vessels takes longer, and during this time, recurrent episodes of stroke attack can still be expected to develop [16, 38]. In our series, a total of 23 (15.6%) stroke cases occurred among 147 hemispheres after revascularization surgery. This was similar to other studies where the rates of recurrent stroke range from 5-31% [5, 27, 40]. In patients with ischemic MMD, the incidence of future stoke events in patients who underwent direct and combined bypass surgery was significantly lower than that in patients treated with indirect bypass or conservative treatment. Moreover, the stroke-free time of patients who underwent revascularization surgery was also longer than that of patients treated conservatively ($P<0.05$). From these results, direct and combined bypasses appear to be effective to prevent recurrent stroke, especially ischemic events, because these bypasses provide immediate improvement of CBF as compared with indirect bypass, which can require several weeks to form collateral vessels [2, 10].

Table 6 Postoperative SPECT results of the 111 patients with revascularization surgery

Angiographic change	Postoperative SPECT results (n=111)		
	Improved (n=53)	Unchanged (n=43)	Worsened (n=15)
Good	15 (28.3%)	4 (9.3%)	1 (6.7%)
Moderate	27 (50.9%)	19 (44.2%)	4 (26.7%)
Poor	11 (20.8%)	20 (46.5%)	10 (66.6%)

* Significant correlation was observed between angiographic changes and SPECT results ($P<0.05$)

In hemorrhagic MMD, recurrent hemorrhagic events tended to be lower in patients who underwent revascularization surgery (15.9%) than in patients who were treated conservatively (44.4%), but no significant difference was observed. No statistical difference in hemorrhagic stroke recurrence was observed among surgical modalities. Even with a long-term follow-up of 13 years in this study, no correlation was observed between hemorrhagic stroke recurrence and surgical method. A major cause of this lack of correlation was that the area for investigation was limited to a single institution, which further narrowed the already limited number of cases. Also, sampling error may affect the results because the number of direct/combined bypasses was relatively small (11/10 cases) compared with indirect bypasses (23 cases). Another postulated cause was that even though direct and combined bypasses provide an immediate increase in the blood supply to the brain and favorable results have been reported [10, 18, 29], this direct anastomosis alone does not promote long-lasting filling of the MCA, which is presumably due to progression of the occlusive process with involvement of the recipient artery in MMD [2, 29]. These findings supported the results of our study, which did not show significant statistical differences among the three surgical procedures with respect to hemorrhagic stroke recurrence.

In this study, we investigated whether the extent of revascularization was influenced by the surgical modality. The extent of revascularization does not mean the whole hemodynamic status, but rather the degree of angiogenesis because the hemodynamic status was influenced by the collateral circulation. The results showed that the extent of revascularization was significantly greater in patients treated with direct and combined bypass surgery than in those treated with indirect revascularization surgery. The reason why indirect bypass was not as effective in adult cases is unclear. The extent of the postoperative collateral circulation seemed to be limited in indirect bypasses because the operative field was usually made along the course of the parietal branch of the STA compared with the combined bypass, which covered the widest surgical field for revascularization.

Some authors reported on the cerebral hemodynamics after bypass with SPECT and showed good correlation between clinical outcome and CBF/vasomotor reactivity [6, 27]. SPECT is considered to be very useful for visualizing not only the CBF, but also the cerebral vascular reservoir (CVR). However, the surgical effect does not always improve the CBF and CVR on the treated side [26]. In our study, the correlation between the angiographic changes and postoperative SPECT results was analyzed, and statistical significance was observed (P-value=0.001, linear-by-linear association). These results may reflect the significant correlation between the decrease in the number of moyamoya vessels and a recovery of vascular reactivity via newly formed angiogenesis after bypass surgery. However, further study is needed to clarify this.

We were also curious about the correlation between the postoperative angiographic change and stroke recurrence. Although there was statistical correlation between the angiographic change and recurrent ischemic event, no statistical correlation was observed for hemorrhagic stroke recurrence. Kobayashi et al. reported that the second bleeding episode was frequently characterized by a change in hemisphere and the type of bleeding that occurred, as observed on CT scans [21]. This result suggests that recurrent hemorrhage does not result from a breakdown of a specific weak point, but from diffuse vulnerability of collateral vessels adjacent to the lateral ventricle, and unpredictability is thought to be one of the main reasons that the efficacy of bypass surgery has still not been clarified. Therefore, it seems too early to conclude that good angiographic change equates with a reduced number of recurrent hemorrhagic events.

There are some limitations to our study. First, it was not a prospective and controlled study. There may have been a potential bias in patient selection and demographics. Referral and selection bias cannot be excluded from this single-institution study. Secondly, we did not choose a constant period of time after the bypass surgery to analyze the angiographic and clinical outcomes. This made our results slightly difficult to compare with different treatment modalities. Additionally, there were no strict indications in which a bypass was performed in individual cases. In the initial years, our institution's policy was to perform an indirect bypass for these patients. Currently, as more studies demonstrate the efficacy of direct and combined bypass and more surgical expertise is available, we try to perform direct or combined bypass on adult-onset MMD patients. Indirect bypass is performed only as a salvage surgical procedure if there is no proper recipient artery for a STA–MCA bypass.

Conclusion

The usefulness of direct and combined bypasses in patients with ischemic MMD for preventing recurrent stroke, especially ischemic events, was statistically confirmed in this study. However, there is still no clear evidence that revascularization surgery prevents rebleeding in patients with hemorrhagic MMD to a significant extent. We statistically confirmed that both direct and combined bypasses were much more effective for achieving a good extent of revascularization and decrease of moyamoya vessels than an indirect bypass. The extent of revascularization was well correlated with the CBF change of SPECT. Although statistical analysis between the extent of revascularization and ischemic stroke recurrence demonstrated significant statistical correlation, no statistical correlation was observed in hemorrhagic stroke recurrence. Therefore, it seems too early to conclude that good revascularization equates with a reduced number of recurrences of hemorrhagic events. A long-term prospective study of a large number of patients with hemorrhagic moyamoya disease is required to determine whether bypass surgery prevents rebleeding.

Conflict of interest None.

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Comment

This is a valuable contribution to the literature in that the study provides high-quality, rigorous follow-up of a large patient sample. It provides potentially important data to guide the choice of bypass (direct/combined vs. indirect). This is achieved by correlating the treatment with an evaluation of the clinical and imaging outcomes, and provides comparative evidence as to the clinical value of direct/combined, indirect, and conservative management. A caveat remains that this is a retrospective study in which the treatments were not randomly allocated. Nonetheless, it is of significant interest to those who treat patients with adult moyamoya disease.

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