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Long-Term Outcomes After Combined Revascularization Surgery in Adult Moyamoya Disease

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***Background and Purpose*—**The surgical outcomes of adult moyamoya disease are rarely reported. We aimed to evaluate the long-term outcomes of combined revascularization surgery in patients with adult moyamoya disease.

***Methods*—**Combined revascularization surgery consisting of superficial temporal artery–middle cerebral artery anastomosis with encephalodurogaleosynangiosis was performed on 77 hemispheres in 60 patients. Clinical, angiographic, and hemodynamic states were evaluated retrospectively using quantitative methods preoperatively and postoperatively in the short-term (≈6 months) and long-term (≈5 years) periods. The mean clinical follow-up duration was 71.0±10.1 months (range, 60–104 months).

***Results*—**Clinical status improved until 6 months after surgery and remained stable thereafter, as assessed by the Karnofsky Performance Scale and modified Rankin Scale. The revascularization area relative to supratentorial area significantly increased in the long-term period compared with that in the short-term period (54.8% versus 44.2%; $P<0.001$). Cerebral blood flow in the territory of the middle cerebral artery improved in the short-term period compared with that in the preoperative period (68.7 versus 59.1; considering blood flow of the pons as 50; $P<0.001$) and thereafter became stable (65.5 in the long term; $P=0.219$). The annual risks of symptomatic hemorrhage and infarction were 0.4% and 0.2%, respectively, in the operated hemispheres.

***Conclusions*—**Combined revascularization surgery resulted in satisfactory long-term improvement in clinical, angiographic, and hemodynamic states and prevention of recurrent stroke. **(*Stroke*. 2014;45:3025-3031.)**

Key Words: adult ■ assessment, outcomes ■ combined revascularization surgery ■ moyamoya disease

Moyamoya disease (MMD) is an idiopathic and progressively occlusive disease of the bilateral internal carotid arteries with characteristic abnormal vascular networks.[1] Although the pathogenesis is not yet known, revascularization surgery has shown satisfactory results in pediatric and adult MMD.[2–21] Indirect revascularization surgeries, such as encephaloduroarteriosynangiosis and other variants, are generally accepted as standard for pediatric MMD.[3,4,7,9,12] In adult MMD, however, there is still controversy about the effectiveness of some types of revascularization surgeries because there have been no randomized studies to compare the efficacy of surgical techniques, and several retrospective studies have been conducted with various age ranges, small numbers of patients, short-term follow-up, and no standardization of surgical techniques.[5–7,10,12,15,16,18,20–22] We aimed to quantitatively evaluate the long-term outcomes of combined revascularization for patients with adult MMD in our institute in terms of clinical, angiographic, and hemodynamic states.

Methods

Patient Selection

Between 2004 and 2008, combined revascularization surgery was performed on 86 hemispheres in 69 consecutive patients with adult MMD by a single surgeon (J.E.K.). Among them, 77 hemispheres from 60 patients were used in this study because 9 patients did not reach follow-up duration of ≥5 years. Medical data were collected prospectively according to our protocol and reviewed retrospectively under approval of the institutional review board. The inclusion criteria were as follows: (1) patients treated by combined revascularization surgery, aged ≥18 years; (2) compatibility with the diagnostic criteria for MMD[23]; (3) recurrent ischemic symptoms including transient ischemic attack and cerebral infarction, predominantly in the middle cerebral artery territory; (4) significant decrease in basal perfusion and reservoir capacity by brain single photon emission computed tomography (SPECT); and (5) clinical follow-up duration of ≥5 years among patients treated between 2004 and 2008. The patients are generally scheduled to undergo postoperative follow-up 6 months (short-term period) and 5 years (long-term period) after surgery.

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Surgical Procedures

Combined revascularization surgery consisted of direct (anastomosis between the superficial temporal artery and cortical branch of the middle cerebral artery) and indirect (encephalodurogaleosynangiosis) surgeries. Detailed technique and perioperative management are presented in Method I in the online-only Data Supplement. The laterality of the operated hemispheres was the right side for 37 hemispheres and the left side for 40 hemispheres.

Clinicoradiological Evaluation

Baseline characteristics are summarized in Table 1. The types of hemorrhagic presentation consisted of intracerebral hemorrhage in the basal ganglia with or without intraventricular hemorrhage in 4 patients. Although they initially presented with hemorrhage, they underwent an operation because of the concomitant ischemic symptoms and hemodynamic compromise on brain SPECT. In addition, seizure, involuntary movement, and headache were identified in 8 (10.4%), 7 (9.1%; limb-shaking feature in 4 patients, dyskinesia in 3), and 24 (31.2%) of all patients, respectively.

Clinical status was evaluated using the modified Rankin Scale[24] and Karnofsky Performance Scale[25] at the initial visit, discharge, within 3 to 6 months after surgery, and during the last follow-up period. The mean duration of clinical follow-up was 71.0±10.1 months (range, 60–104 months).

Brain MRI and computed tomography were performed to evaluate the status of the brain parenchyma at the scheduled periods and when neurological status declined.

Cerebral hyperperfusion syndrome was evaluated separately with perioperative morbidity and mortality. Symptomatic cerebral hyperperfusion syndrome was diagnosed when transient neurological deterioration occurred after surgery and the hyperperfusion area on SPECT corresponded well to the neurological deficits, with no sign of acute infarction or hemorrhage.[26]

Angiographic Evaluation

Cerebral angiography was generally performed preoperatively (within 1 month) and postoperatively (immediate, short-term and long-term follow-up). Angiographic stages were evaluated according to the report by Suzuki and Kodama[1] (Table 1; Table I in the online-only Data Supplement). Immediate postoperative angiography was performed to check the patency of the direct anastomosis within 2 weeks after surgery. Short-term (5–12 months after surgery) and long-term (51 months or more) follow-up angiographies were performed to evaluate the postoperative status of revascularization.

Table 1. Baseline Characteristics

Hemispheres/patients	77/60
Women/men	41/19
Age, y	36.9±10.7 (18–56)
Bilateral:unilateral type	42:18
Familial type	9 (15.0)
Initial presentations*	
Ischemia	77 (100)
Transient ischemic attack	64 (83.1)
Infarction	45 (58.4)
Hemorrhage	4 (5.2)
Initial Suzuki angiographic stage*	
2	6 (7.8)
3	56 (72.7)
4	15 (19.5)

Data are number of patients (%) and mean±SD (range) for continuous variables.

*Number of symptomatic hemispheres (%).

The revascularization area (RA) was measured on follow-up cerebral angiography using MAROSIS PACS systems (INFINITT, Seoul, Korea). The relative RA was calculated as follows: relative RA (%)=RA/supratentorial area×100, which was used to compare the status of revascularization in the short-term and long-term follow-up periods. The details of the measurement are described in Figure I in the online-only Data Supplement.

Hemodynamic Evaluation

Brain SPECT was used to determine the need for surgical revascularization and to evaluate the postoperative hemodynamic status. Preoperative basal and acetazolamide (Diamox)-challenged SPECT with 99mTc-hexamethylpropyleneamine oxime were accomplished within 2 months before the operation. Postoperative follow-up was performed in the short-term (5–12 months after surgery) and long-term (≥54 months) periods.

Semiquantitative analysis of cerebral blood flow (CBF) on SPECT was conducted in the same manner as in a previous report.[27] Cerebrovascular reserve was calculated as follows: $(CBF_{acetazolamide} - CBF_{basal})/CBF_{basal} \times 100$. $CBF_{acetazolamide}$ represents a value acquired on acetazolamide-challenged SPECT and CBF_{basal} represents a value on basal SPECT. A detailed protocol is described in Method II in the online-only Data Supplement.

Statistical Analysis

Continuous variables were presented as the mean±SD. Paired *t* tests were performed to compare the angiographic and hemodynamic states in patients who had consecutive follow-ups with cerebral angiography and SPECT, preoperatively and postoperatively (both short term and long term). Pearson correlation test was used to identify correlations between cerebrovascular reserve and any postoperative events. The annual risk of symptomatic infarction or hemorrhage in the ipsilateral hemispheres after revascularization surgery was calculated with a person-year method, and the event-free survival rate was evaluated using the Kaplan–Meier method. The end point was the occurrence of stroke and last follow-up (censored). $P<0.05$ was considered to be statistically significant. All of the statistical analyses were performed using SPSS 19.0 software (IBM SPSS Inc, Chicago, IL).

Results

Clinicoradiological Outcomes

Clinical states at each period are presented in Figure 1. Clinical status continued to improve postoperatively and became stable 6 months after surgery until the last period. The mean preoperative Karnofsky Performance Scale and modified Rankin Scale were 81.1±6.7 (range, 60–90) and 1.5±0.6 (range, 1–3), respectively. The mean Karnofsky Performance Scale and modified Rankin Scale in the last period were 96.2±8.4 (range, 40–100) and 0.4±0.7 (range, 0–5), respectively. Comparing the clinical states of 60 patients between the preoperative and last follow-up, 58 (96.6%) improved, 1 (1.7%) was unchanged, and 1 (1.7%) worsened. Two patients improved after surgery but returned to the preoperative status or worse because of the basal ganglia infarction and hemorrhage on the ipsilateral side of the operation during follow-up.

Among the 64 hemispheres in patients initially presenting with transient ischemic attack, the same types of transient ischemic attacks persisted in 15 (23.4%) patients within 3 months after surgery, 10 (15.6%) within 6 months, and 8 (12.5%) within the final period. Three (37.5%) of 8 patients with an initial seizure presentation infrequently experienced the same symptoms until the last period. Involuntary movement in 7 patients completely

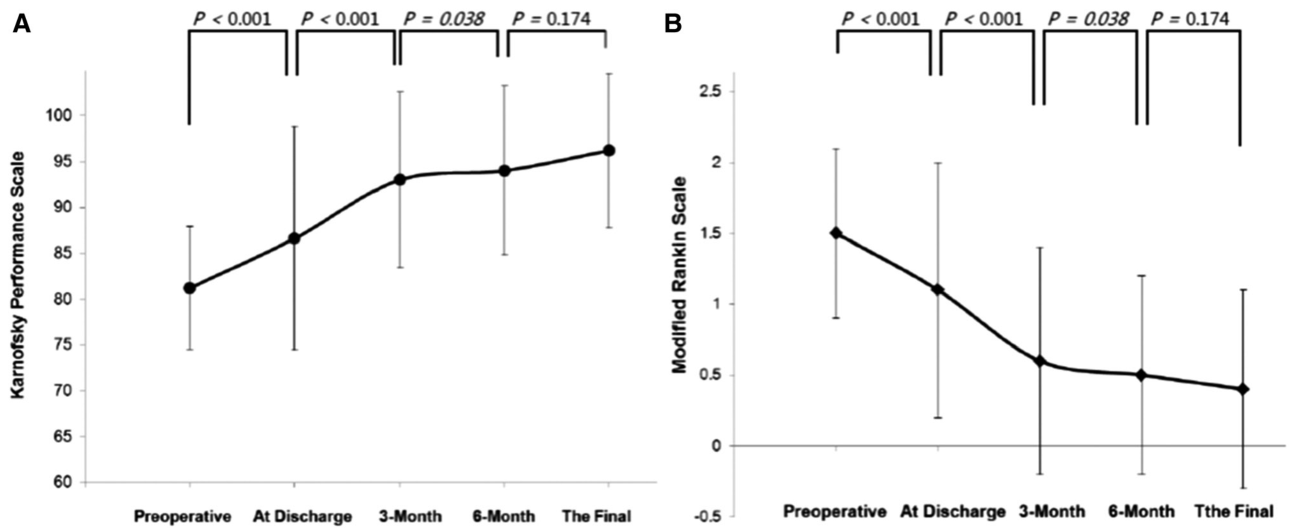

Figure 1. Comparison of clinical status at each period with Karnofsky Performance Scale (**A**) and modified Rankin Scale (**B**).

disappeared within 3 months after surgery. There was 1 patient with a new occurrence of partial seizure corresponding to the operated hemisphere.

Perioperative complications included asymptomatic subgaleal hemorrhage in 4 hemispheres (5.2%), infarction in 10 (13.0%), transient seizure in 2 (2.6%), and wound infection in 1 (1.3%). Among the 10 infarction cases, 3 patients (3.9%) had permanent neurological deficits. Symptomatic cerebral hyperperfusion syndrome was identified during 23 operations (29.9%), in which 21 patients experienced transient neurological deficits without any parenchymal lesion and 2 patients demonstrated an intracerebral hemorrhage on the same side of the operated hemisphere (including 1 patient with permanent neurological symptoms). Finally, the mortality rate was zero, and the permanent morbidity rate was 5.2% per operation (4 of 77 operations) and 6.7% per person (4 of 60 patients).

Angiographic Outcomes

The angiographic outcomes are summarized in Table 2. The consecutive follow-up for the short-term and long-term angiographies were available for 61 (79.2%) of 77 hemispheres. The relative RA significantly increased by the long-term follow-up compared with the short-term

Table 2. Angiographic and Hemodynamic Outcomes

	Preoperative	Short Term	Long Term
Angiographic outcomes			
Hemispheres	...	61 (79.2)	61 (79.2)
Relative revascularization area,* %	...	44.2±15.9 (12.3 to 76.7)	54.8±18.7 (10.3 to 88.6)
Follow-up duration, mo	...	6.8±1.3 (5 to 12)	62.9±5.7 (51 to 81)
Hemodynamic outcomes			
Hemispheres	57 (74.0)	57 (74.0)	57 (74.0)
Cerebral blood flow†			
Basal‡	59.1±12.1 (43.5 to 88.7)	68.7±13.4 (36.1 to 113.8)	65.5±17.2 (50.2 to 108.3)
Acetazolamide challenged§	55.7±7.6 (44.1 to 79.4)	70.8±14.8 (37.2 to 104.7)	68.3±19.5 (49.4 to 106.8)
Cerebrovascular reserve,‖ %	−4.3±8.5 (−31.7 to 13.1)	4.7±27.1 (−59.5 to 99.9)	0.0±0.1 (−0.2 to 0.2)
Follow-up duration, mo	...	7.0±1.6 (5 to 12)	63.7±6.1 (54 to 81)

Data are number of hemispheres (%) and mean±SD (range) for continuous variables. All the comparison analyses were performed with a paired *t* test.

*$P<0.001$ between short-term and long-term relative revascularization areas.

†Cerebral blood flow in the territory of middle cerebral artery, with a blood flow of the pons as a control of 50.

‡$P<0.001$ between preoperative and short-term cerebral blood flows; $P=0.219$ between short term and long term; and $P<0.001$ between preoperative and long term.

§$P<0.001$ between preoperative and short-term cerebral blood flows; $P=0.641$ between short term and long term; and $P<0.001$ between preoperative and long term.

‖$P=0.015$ between preoperative and short-term cerebrovascular reserve; $P=0.214$ between short term and long term; and $P<0.001$ between preoperative and long term.

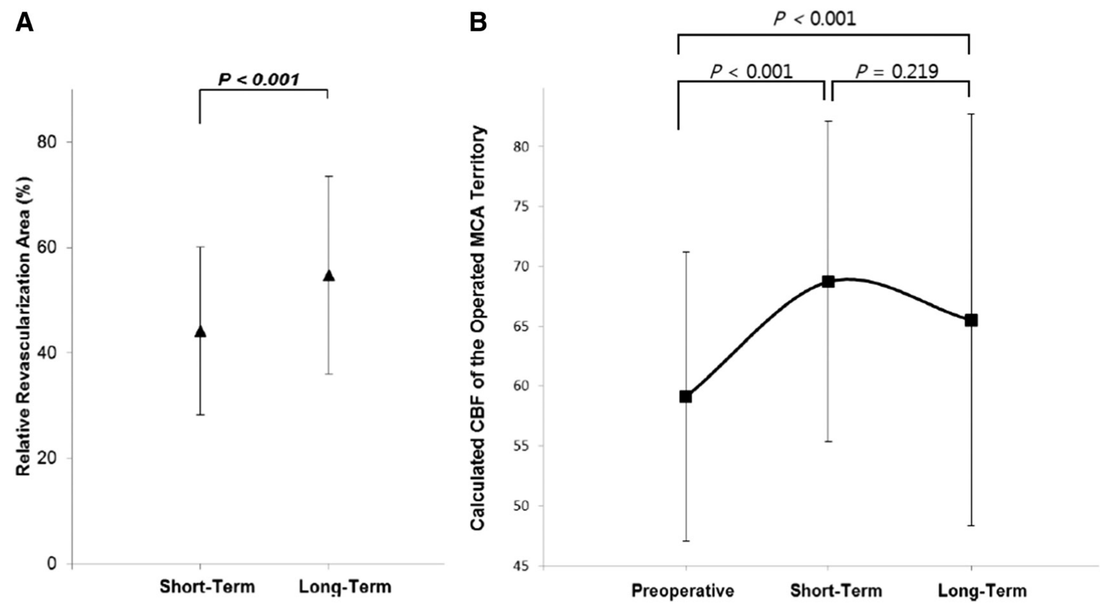

Figure 2. Comparison of relative revascularization areas in the short-term and long-term follow-up periods (**A**). Comparison of cerebral blood flows (CBFs) at the territory of middle cerebral artery (MCA) in the operated hemispheres at each period (**B**).

follow-up (P<0.001; Figure 2A). The Suzuki grade during the follow-up is presented in Table I in the online-only Data Supplement.

Immediate, short-term, and long-term angiographic follow-ups were available in 77 (100%), 71 (92.2%), and 67 (87.0%) hemispheres, respectively. The patency of the direct anastomosis was 96.1% (74 of 77 sites) at the immediate check-up, 94.4% (67 of 71) in the short term, and 76.1% (51 of 67) in the long term. As demonstrated in Figure 3 and Figures II to IV in the online-only Data Supplement, the contribution of direct and indirect revascularizations in the 61 hemispheres with consecutive short-term and long-term angiography showed various shifting patterns over time.

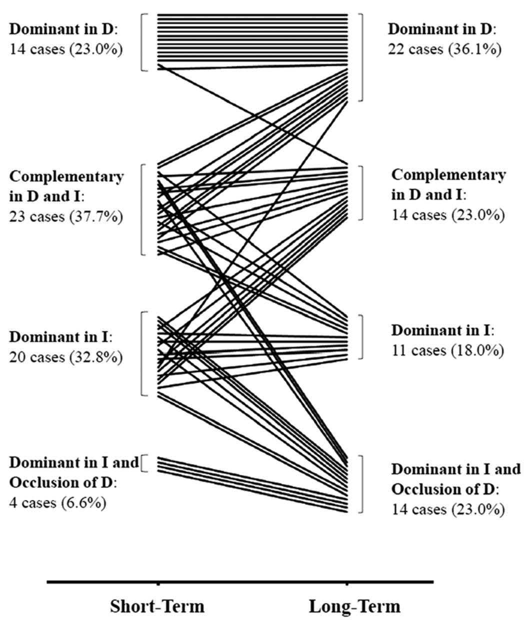

Figure 3. Contribution of direct (D) and indirect (I) revascularizations in the short-term and long-term periods with visual evaluation on cerebral angiography. Dominant contribution means more than two thirds of whole revascularization area; complementary means contribution of revascularization between one third and two thirds as well as different areas of responsibility.

Hemodynamic Outcomes

Semiquantitative analyses of brain perfusion SPECT data are displayed in Table 2. The consecutive follow-up for short-term and long-term SPECT was available in 57 (74.0%) cases. The mean CBF in the middle cerebral artery territory significantly improved in the short term compared with the preoperative test (P<0.001; Figure 2B), and the mean CBF became stable thereafter (P=0.219). The same pattern was also observed in the cerebrovascular reserve in the middle cerebral artery territory at each period (P=0.015 between the preoperative and short-term periods; P=0.214 between the short-term and long-term periods). For the correlation analyses between the preoperative cerebrovascular reserve and any postoperative events, there was no statistical significance (P=0.624 for cerebral hyperperfusion syndrome; P=0.542 for postoperative infarction).

Stroke Risk During Follow-Up

There were 2 hemorrhagic events and 1 infarction during the follow-up after surgery. Two hemorrhagic events in each hemisphere (a subarachnoid hemorrhage 3 months after surgery and a basal ganglia intracerebral hemorrhage with intraventricular hemorrhage at 87 months) and 1 thalamic infarction (at 21 months) occurred in the ipsilateral hemisphere of the operation. Therefore, the annual rates of symptomatic hemorrhage and infarction in the operated hemispheres were 0.4% per person-year and 0.2%, respectively. In addition, the 5-year event-free survival rates for symptomatic hemorrhage and infarction ipsilateral to the operated hemispheres were all 98.7% (Figure 4). There was no new case of transient ischemic attack after surgery.

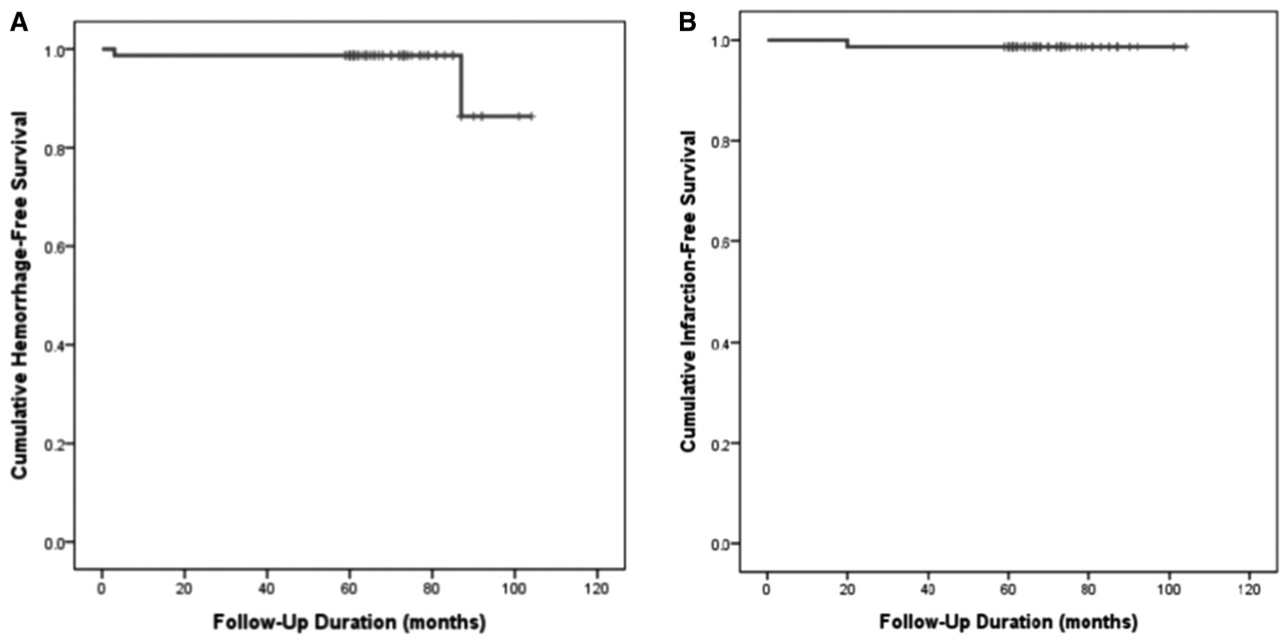

Figure 4. Kaplan–Meier survival curves of hemorrhage (**A**) and infarction (**B**).

Discussion

In this study, 77 hemispheres in 60 patients were treated with combined revascularization surgery, and the majority was followed up for ≥5 years in terms of clinical, angiographic, and hemodynamic parameters. Clinical and hemodynamic states progressively improved until 6 months after surgery and remained stable thereafter. Meanwhile, angiographic revascularization continued to increase until the last follow-up. The annual risks of symptomatic hemorrhage and infarction ipsilateral to the operated hemispheres were 0.4% and 0.2%, respectively. To our knowledge, this study included the largest number of patients with adult MMD treated using the same combined revascularization surgery technique with a long-term follow-up and quantitative analyses of clinical, angiographic, and hemodynamic states. Our results may reinforce the previous knowledge about the effect of combined revascularization surgery on improvement in patient status and the prevention of stroke recurrence.

Identifying which type of surgical technique is the most effective has been the center of controversy in adult MMD; however, there is no definitive evidence for each technique thus far. There have been 5 comparative studies of combined and indirect revascularization surgery.[6,10,12,14,18] Four of the studies revealed no difference in clinical outcomes[6,10,12,14] despite the angiographic superiority of combined surgery.[10,12,14] In some studies on indirect surgery for adult MMD,[5,13,16,22] satisfactory angiographic revascularization reaches 76% to 100% of cases,[5,16,22] and the 5-year cumulative risk of recurrent stroke ranges from 6% to 15%.[11,13,16] However, there is no report of combined surgery alone for adult MMD. The obstacles to make a conclusion about the best choice of surgical technique include a limited number of retrospective studies with small sample sizes, difficulties in systemic reviews and meta-analyses because of the differences in baseline characteristics, poorly described surgical techniques, follow-up duration (generally short), and analytic methods. Although our study addressed the outcomes of combined surgery alone, the long-term surgical outcomes seem to be satisfactory in terms of a low risk of recurrent stroke and good clinical status. Further studies may provide concrete evidence for the superiority of a certain surgical technique if we could perform the indirect revascularization surgery for patients with at least similar conditions as those receiving combined surgery.

Direct revascularization surgery is thought to provide immediate flow augmentation by the anastomosis between extracranial and intracranial vessels. Meanwhile, indirect surgery is considered to require ≈3 months for neoangiogenesis between vascularized extracranial tissues and brain cortex,[6,11] and neoangiogenesis after indirect surgery has been suggested to be poorer in adults than in pediatric MMD.[12] However, recent reports showed satisfactory angiographic and clinical outcomes of indirect surgery for adult MMD[5,6,14,16] or a significant role in the formation of an anastomosis between indirect pedicles and brain cortex after combined bypass surgery.[20]According to our analysis, the RA continued to widen, and indirect and direct revascularization each played an important role in collateral formation although the contribution patterns for direct and indirect revascularizations were different. Thus, the following can be speculated. Direct revascularization could play its role at the early phase after surgery; thereafter, direct revascularization may maintain its dominant role for collateralization, or as parts of the distal cerebral vessels progressively become occluded (compartmentation), some direct revascularization may slowly regress partly or on the whole. Then indirect revascularization would replace the areas in which blood flow could not reach via direct bypass. In that sense, combined surgery is considered to be the most effective technique.

In this study, the RA continuously increased during the follow-up, whereas hemodynamic status became stable 6 months after surgery. This result is thought to be because of the time difference between the formation of revascularization and the regression of the major cerebral arteries and abnormal moyamoya vessels. This disappearance of the abnormal moyamoya vessels and occlusive changes in the distal internal carotid artery are known to accelerate after surgery.[28] Our hypothesis is as follows: during the short-term period, surgical revascularization rapidly augments the CBF, meanwhile abnormal basal perforators and major cerebral arteries slowly start to regress after reaching a certain period (at least ≈6 months after surgery), the increase in CBF caused by revascularization and decrease in CBF by the disappearance of abnormal perforators and occlusion of major arteries become equilibrated, and the hemodynamic status remains stable.

According to Hallemeier et al[2] and Chiu et al,[13] the 5-year stroke risk between the operation and observation groups was 15% to 17% versus 20% to 27%. The annual risks of symptomatic hemorrhage and infarction were 0.4% and 0.2%, respectively, and the 5-year stroke-free survival rate of hemorrhage and infarction was 98.7% after surgery in this study. In our recent report addressing the natural clinical course in hemodynamically stable patients,[29] the annual stroke risk in adult MMD with an ischemic presentation was 4.2% (3.0% ischemic stroke, 1.2% hemorrhagic stroke), and the 5-year stroke risk was 17%. Considering that the patients surgically treated were more hemodynamically unstable than those who were conservatively treated, the stroke risk in patients recruited in this study would have been higher if they had not undergone surgery. Therefore, combined revascularization surgery is thought to be effective in preventing ischemic and hemorrhagic strokes.

This study has some limitations. First, this study examined a small number of patients. However, this study is thought to be significant because MMD itself is rare, and long-term follow-up is not easy in terms of clinical, angiographic, and hemodynamic states. Second, a selection bias may exist in this retrospective study. However, most consecutive patients underwent surgery by a single surgeon, and most of them were followed up. Third, the RA and supratentorial area were estimated on 2-dimensional angiographic images, although the brain surface is not flat but curved. Exact methods should be devised. Fourth, surgical outcomes were mainly evaluated with a focus on clinical, hemodynamic, and angiographic states. Because quality of life has recently become an important consideration in patients with MMD,[3,30] further study is needed about the cognitive and behavioral states in adult MMD.

In conclusion, combined revascularization surgery achieved satisfactory long-term outcomes in terms of clinical, angiographic, and hemodynamic states. In addition, this technique showed a protective effect on stroke recurrence. Given that direct revascularization requires expert surgical skill and experience, and recent reports of indirect surgery showed favorable results, future comparative studies of combined, direct, and indirect surgical techniques under similar conditions are expected to provide evidence on the best treatment, or alternative treatment choices, for patients with adult MMD.

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Disclosures

None.

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ONLINE SUPPLEMENT

Long-term Outcomes after Combined Revascularization Surgery in Adult Moyamoya Disease

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Supplemental Methods

Supplemental Method I. Surgical Procedures.

Combined revascularization surgery was finally decided under the following situations for the patients who basically met the inclusion criteria mentioned in the Methods: (1) When the patients presented with symptoms other than acute infarction and hemorrhage, we performed surgery as soon as possible; (2) When they presented with acute infarction, we managed them for at least 3 weeks after the event. Confirming that the patients clinically become stable and hemodynamic status on follow-up SPECT is still unstable, we finally decided to perform surgery; (3) When they presented with acute hemorrhage, we managed them until the hemorrhage nearly resolved and the hemorrhage-related problems, such as hydrocephalus and mass effect were treated. Hemodynamic status was re-evaluated again, and we finally decide to perform surgery to improve the hemodynamic status.

Surgery was performed under general anesthesia with intravenous propofol and remifentanil. During the operation, the arterial P_{CO2} was maintained between 35 and 40 mmHg, and mild hypothermia of about 34℃ and systolic blood pressure around 120 mmHg were induced. Antiepileptic drug was perioperatively administered. Postoperative pain was controlled with patient-controlled analgesia system containing fentanyl and ketorolac. Mean postoperative arterial blood pressure was maintained at the preoperative level ± 20%, and normovolemia was kept.

Combined revascularization surgery consisted of direct (anastomosis between the superficial temporal artery and cortical branch of MCA) and indirect (encephalo-duro-galeo-synangiosis) surgeries. Surgical technique of direct anastomosis was the same as in the previous report.[1] Indirect revascularization surgery was performed to cover the exposed brain cortex. A large bone flap (approximately 10 x 8 cm) and galeal flap were prepared. Incised dura mater was infolded into the subdural space, preserving the meningeal artery, and the arachnoid membrane was incised along the sulci containing the arteries. The laterality of operated hemispheres was the right side in 37 hemispheres and the left side in 40 hemispheres.

Supplemental Method II. Hemodynamic Evaluation

Semiquantitative analysis of cerebral blood flow (CBF) on brain single photon emission computed tomography (SPECT) was conducted with the same manner in the previous report.[2] Spatial normalization of different SPECT data into standard SPECT templates was done with SPM99 software (Institute of Neurology, University of College of London, London, UK) implemented in MATLAB 5.3 (The MathWorks, Natick, Mass., USA). Using a statistical probabilistic anatomic map of International Consortium of Brain Mapping, specific voxels of interest were evaluated. The average value of voxels of the pons was used as a control CBF of 50. CBF of the cerebellum was not considered as a control because of the diaschisis of cerebellum in bilateral progression of moyamoya disease. Average CBFs of middle cerebral artery territory in each SPECT images were obtained using proportional scaling.

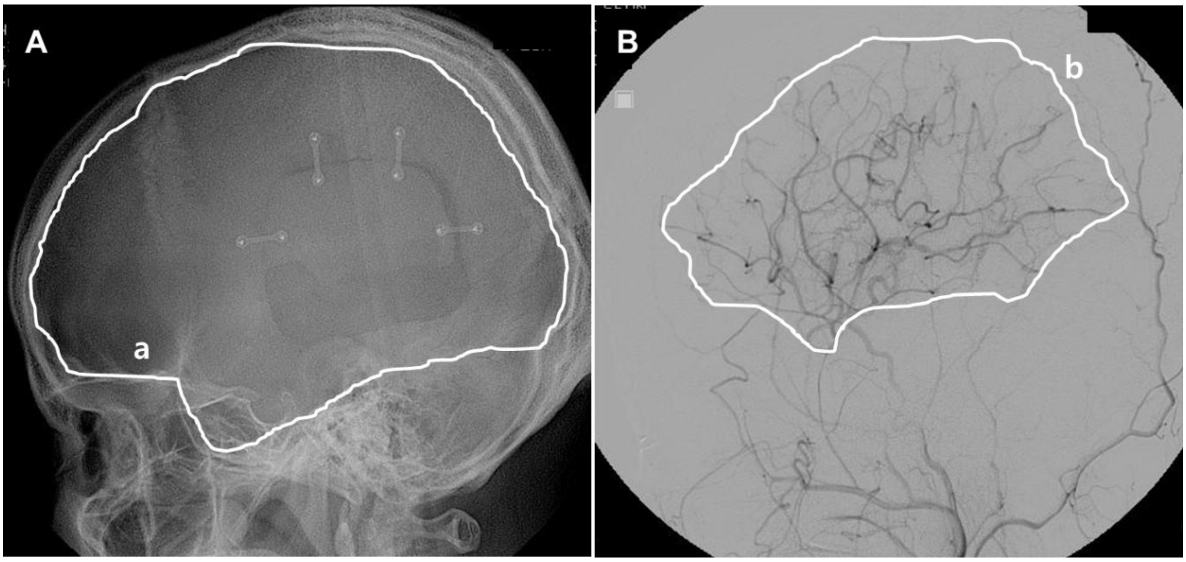
Supplemental Tables

Supplemental Table I. Comparison of the Suzuki grade during the follow-up.[3]

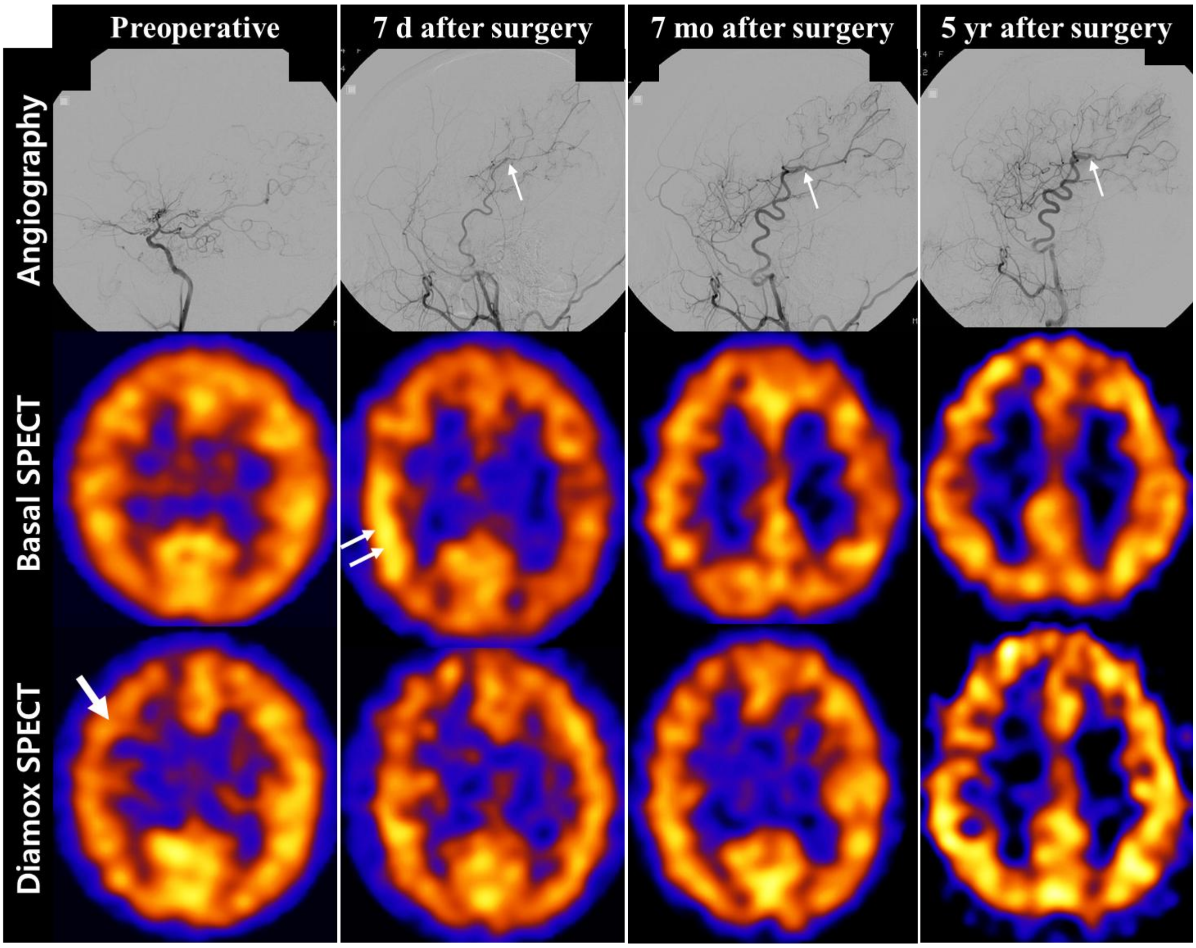
Suzuki Grade	Preoperative	Short-term	Long-term
1	0	0	0
2	5 (8.2)	1 (1.6)	0
3	44 (72.1)	20 (32.8)	10 (16.4)
4	12 (19.7)	35 (57.4)	39 (63.9)
5	0	5 (8.2)	11 (18.0)
6	0	0	1 (1.7)

Data are no. of hemispheres (%) among a total of 61 hemispheres which were consecutively followed up with cerebral angiography, preoperatively, in the short-term and long-term periods after surgery.

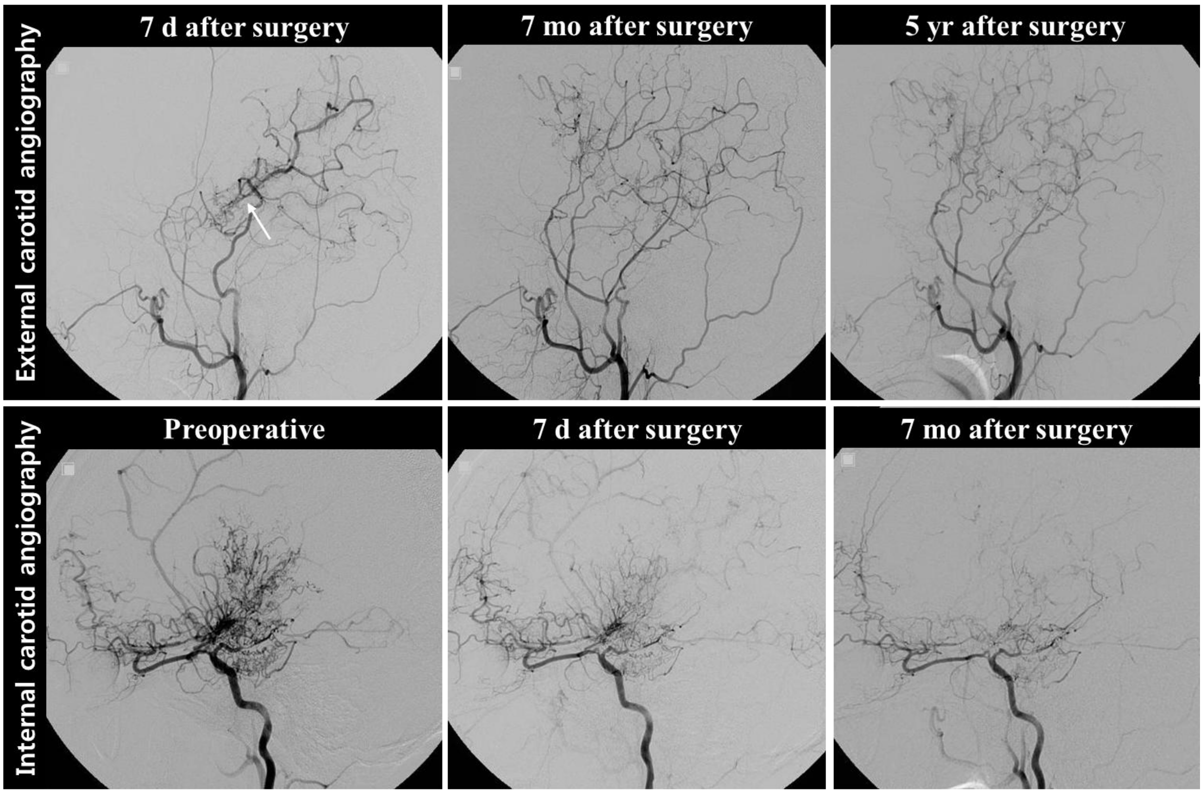
Supplemental Figures



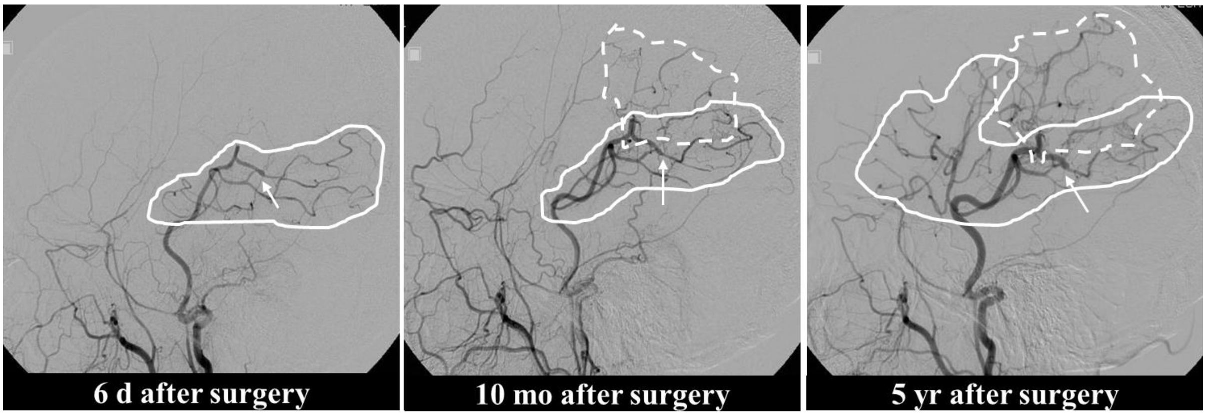
Supplemental Figure I. Supratentorial area (a) was measured on the bone setting of a lateral angiographic image, referencing capillary phase of the same lateral angiographic image (A). Then, revascularization area (RA; b) was drawn along the margin of revascularized area on the same lateral angiographic image with capillary phase (B) and calculated as follows: relative RA (%) = RA / supratentorial area (b / a) x 100.[4] All areas were repeatedly measured 3 times and each area was determined with the mean value of them.



Supplemental Figure II. A representative case of dominant contribution of the direct revascularization. A patient presented with a left side motor TIA which well corresponded to the SPECT findings of the decrease in reservoir at the right frontal lobe (thick arrow; first left column). Seven days after right-sided combined revascularization surgery, small area of direct revascularization (thin arrow) was identified on cerebral angiography, and slight hyperperfusion (double arrows) was found on SPECT (second left column). Revascularization area of direct bypass continued to increase and reservoir capacity at right frontal lobe was nearly normalized 7 months and 5 years after surgery (third and fourth left columns).



Supplemental Figure III. A representative case of dominant contribution of the indirect revascularization. Direct revascularization (arrow) was identified on the 7th day angiography, however, it was found to be occluded and indirect revascularization became dominant on the 7-month and 5-year angiography. Abnormal basal moyamoya vessels slowly regressed, which was demonstrated on 7-day and 7-month angiography, compared to the preoperative imaging.



Supplemental Figure IV. A representative case of complementary contribution of the direct and indirect revascularizations. Direct revascularization area (a solid line) was mainly limited in the temporo-occipital area on the 6-day and 10-month angiography, and it was extended to the frontal branches on the 5-year angiography. Meanwhile, indirect revascularization area (a dotted line) continued to develop and take charge of the parietal area to which blood supply was not reached via direct bypass pedicle.

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