Effect of direct arterial bypass on the prevention of future stroke in patients with the hemorrhagic variety of moyamoya disease

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Object. The authors evaluated the effects of superficial temporal artery–middle cerebral artery (STA–MCA) bypass in the prevention of future stroke, including rebleeding or an ischemic event, in patients suffering from hemorrhagic moyamoya disease by comparing this method with indirect bypass and conservative treatment.

Methods. Twenty-two patients who had hemorrhagic moyamoya disease but no aneurysm comprised the study group. These patients' clinical charts were examined with respect to their treatment and clinical course after an initial hemorrhagic episode. The mean age of the patients was 43 years and the follow-up period ranged from 0.8 to 15.1 years, with a mean of 8 years. Eleven patients (50%) were conservatively treated. Among the 11 patients who were surgically treated, STA–MCA bypass was performed in six patients (27%) and encephaloduroarterio-synangiosis (EDAS) in the other five patients (23%). Nine patients (41%) presented with an ischemic or rebleeding event during the follow-up period. The incidence of future stroke events in patients who had undergone an STA–MCA bypass was significantly lower (p < 0.05) than that in patients who had been treated conservatively or with EDAS. Kaplan–Meier plots comparing stroke-free times in patients treated with direct bypass and those in patients who conservatively or with indirect bypass showed a significant difference (p < 0.05) in favor of direct bypass.

Conclusions. The effect of STA–MCA bypass on the prevention of recurrent hemorrhage or an ischemic event in patients with hemorrhagic moyamoya disease has been statistically confirmed in this study.

KEY WORDS • intracranial hemorrhage • moyamoya disease • superficial temporal–middle cerebral artery bypass

MOYAMOYA disease is a well-known clinical entity characterized by a progressive unilateral or bilateral occlusive arterial condition, which preferentially affects the distal internal carotid artery, proximal MCA, and anterior cerebral artery, and by a spontaneously developed collateral vascular network at the base of the brain consisting of the so-called moyamoya vessels.6,15

18,2123 The clinical symptoms of moyamoya disease relate directly to this abnormal vasculature.5 Most juvenile patients present with recurrent cerebral ischemic attacks; in contrast, most adult patients present with intracranial hemorrhage.15 In patients presenting with an ischemic attack, previous reports have shown that direct or indirect revascularization surgery can improve clinical symptoms and outcome.9,10,14 However, it has not been clear what is the best treatment for prevention of recurrent intracranial hemorrhage or ischemic events in the type of moyamoya disease characterized by hemorrhage.6,7,25 In this study, we examined the effects of a direct arterial bypass between the STA and MCA in the prevention of future stroke, including rebleeding or ischemic events, in patients suffering from hemorrhagic moyamoya disease. We then compared the effects of this treatment with those of indirect bypass or conservative treatment in other patients with the same disease.

Clinical Material and Methods

Twenty-five patients with hemorrhagic moyamoya disease were treated at Nara Medical University Hospital and its affiliated hospitals between January 1983 and June 1998. Computerized tomography scans revealed the presence of ICH without IVH in nine patients, ICH with IVH in seven patients, and IVH without ICH in nine patients. In all patients moyamoya disease was diagnosed based on angiographic findings that were compatible with the diagnostic guidelines for this disease proposed by the Ministry of Health and Welfare of Japan.17 An additional patient in whom an aneurysm was revealed by angiography was excluded from this study. During the acute stage of this disease, evacuation of intracranial hemorrhage was performed in five cases and ventricular drainage was performed in five cases. Among the 25 patients, three were excluded from the study because they died as a result of the initial intracranial hemorrhage within 3 months after onset. We evaluated and analyzed the other 22 cases of
hemorrhagic moyamoya disease by reviewing the patients’ clinical charts, focusing on their treatment and clinical course after the initial hemorrhagic episode. The 22 patients ranged in age from 21 to 61 years, with a mean age of 43 years. Seven patients were men and 15 were women. Each patient’s clinical status at presentation was determined using the RDS:21 14 patients had a score of 1, five patients had a score of 2, and three patients had a score of 3.

The effectiveness of revascularization surgery was evaluated according to changes in moyamoya vessels observed on postoperative angiograms obtained 3 to 6 months after surgery. The outcome of revascularization surgery was determined to be good if the number of moyamoya vessels decreased to less than one third of those counted preoperatively and moderate if they numbered two thirds of those counted preoperatively. If the aforementioned criteria were not met, the surgical outcome was determined to be poor. The follow-up period was 0.8 to 15.1 years, with a mean of 8 years. During the follow-up period, any neurological sign or symptom in the patient age (yrs)† 48.7 ± 10.9 39.8 ± 9.3 34.6 ± 11.1

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<th>Parameter</th>
<th>Conservative</th>
<th>STA–MCA Bypass</th>
<th>EDAS</th>
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<td>patient age (yrs)†</td>
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<td>timing of surgery after hemor-</td>
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<td>48.0 ± 21.5</td>
<td>47.0 ± 11.3</td>
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<td>rhage onset (days)†</td>
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<td>follow-up period (yrs)†</td>
<td>8.7 ± 3.0</td>
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<td>6.8 ± 2.1</td>
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* There was no statistically significant difference among treatments for any parameter. Abbreviation: NA = not applicable.
† Values are expressed as the means ± standard deviation.

### Results

#### Types of Treatment

Revascularization surgery was recommended for each of the 22 patients based on a CBF study, which was performed using the single-photon emission CT procedure when the patient was resting and during the acetazolamide activation stage. The CBF study revealed a decrease in resting CBF with a disturbed response to acetazolamide in all cases. Eleven patients refused revascularization surgery; these 11 (50%) were conservatively treated. The other 11 patients underwent revascularization surgery, which was performed more than 1 month after onset of initial hemorrhage. The planned method of surgical revascularization was direct bypass such as the STA–MCA bypass. However, if during surgery a suitable recipient artery could not be found, an indirect form of surgery such as EDAS was performed instead of the STA–MCA bypass. Among the 11 surgically treated patients, six (27%) underwent STA–MCA bypass and five (23%) underwent EDAS. There were no significant differences in age, sex, initial clinical status, or length of follow-up period among patients when grouped according to treatment modality in this series (Table 1). Among patients who underwent STA–MCA bypass or EDAS, there was no significant difference in the average interval from hemorrhage onset to surgery and no incidence of surgical morbidity or mortality.

#### Occurrence of Stroke Events During the Follow-Up Period

During the follow-up period after the initial ictus or revascularization surgery, nine (41%) of the 22 patients presented with an ischemic or rebleeding event. The incidences of future stroke events after using each treatment modality were as follows: six (54%) of 11 patients treated with conservative management, none of the six patients treated with an STA–MCA bypass, and three (60%) of the five patients treated with EDAS. As is evident in Table 2, the incidence of a future stroke event in patients who underwent the STA–MCA bypass procedure was significantly lower (p < 0.05) than that in patients treated conservatively or with EDAS.

Kaplan–Meier plots of stroke-free time in patients who had undergone direct bypass were compared with those in patients who had been treated conservatively or who had undergone indirect bypass. These plots showed a significant difference (p < 0.05) in favor of direct bypass (Fig. 1). The mean (± standard error of the mean) stroke-free times were 8.5 ± 1.3 years in patients who underwent direct bypass, 6.1 ± 1.5 years in those treated conservative-
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ly, and 4 ± 1.5 years in those who underwent indirect bypass.

In the nine patients who suffered another stroke during the follow-up period, recurrent intracranial hemorrhage was experienced by four patients and an ischemic event by five patients (Table 3). The time that elapsed between the initial intracranial hemorrhage or surgical treatment and the recurrent stroke event ranged from 0.3 to 6.9 years (mean 2.4 years). After the second stroke event, four (44%) of nine patients experienced worsening of their clinical symptoms. A poor prognosis was seen in patients with recurrent intracranial hemorrhage. Of the four patients who experienced recurrent intracranial hemorrhage, two (50%) deteriorated to a persistent vegetative stage, one (25%) was severely disabled, and one (25%) had a good recovery.

Final Clinical Status

Clinical status at the end of the study was assessed using the RDS.21 Eleven patients had a score of 1, five patients a score of 2, two patients a score of 3, one patient a score of 4, and three patients a score of 5. Two (18%) of the patients treated conservatively and two (40%) of the five patients who underwent EDAS had worse RDS scores at the final follow-up examination. However, there were no patients with worse RDS scores among patients who underwent STA–MCA bypass.

Angiographic Findings

The effects of revascularization by performing an STA–MCA bypass were good in no patients, moderate in four patients, and poor in two patients. On the other hand, no patient who underwent EDAS had either good or moderate revascularization effects; in all five of these patients a poor effect was demonstrated in postoperative angiography studies. There was a significant difference in the decrease of moyamoya vessels between the patients treated with STA–MCA bypass and those treated with EDAS (p < 0.05).

Discussion

Patients with moyamoya disease can present with cere-

bral ischemia or intracranial hemorrhage. Cerebral ischemic attacks are generally observed in pediatric patients, whereas intracranial hemorrhages are more common in adults. The incidence of hemorrhage is reported to exceed 60% in adults, whereas it is only 10% in children.6 The difference in the incidence of ischemic episodes between children and adults may reflect the stability of systemic hemodynamics in adults rather than that of cerebral hemodynamics.13 The reason why intracranial hemorrhage frequently occurs in adult patients is unclear. It is thought to result from the existence of several vascular lesions and the severity of these lesions, which are closely related to the hemodynamic stress of basal moyamoya vessels and the age of the patients.20 Morimoto, et al.,13 speculated that moyamoya vessels may be more inflexible in adults than in children.

Regardless of whether patients initially experience intracranial hemorrhage, a secondary cerebral ischemic attack or recurrent hemorrhage may occur during the follow-up period. Therefore, patients with moyamoya disease should be treated with the aim of preventing future hemorrhagic or ischemic attacks. There are a number of surgical methods of revascularization used in the treatment of moyamoya disease. These include direct bypass surgery, such as STA–MCA bypass, as well as indirect bypass procedures, such as EDAS, encephalo-duromyo-arteriosynangiosis, encephalomyosynangiosis, encephalomyoarteriosynangiosis, placement of cranial burr holes over the affected region, and placement of an omental graft.2 There have also been many reports on technical aspects, indications, pitfalls, and effects of direct or indirect bypass for the prevention of ischemic events, especially in childhood-onset moyamoya disease. Direct bypass can be an effective procedure to revascularize the ischemic brain. However, it is difficult to find both good donor and recipient arteries with sufficient calibers in some patients with moyamoya disease.24 In the present series, the STA–MCA bypass was not performed in five patients (45%) because of the lack of an appropriate recipient artery. On the other hand, an indirect bypass is easier and safer to perform than an STA–MCA bypass, and neovascularization from extracranial arterial and soft-tissue systems to the ischemic brain can still be expected to develop.25 In this series, there was no incidence of surgical mortality or morbidity in any
surgical procedure. Performing direct or indirect bypass procedures in adult patients with moyamoya disease is still controversial, especially when used to prevent recurrent intracranial hemorrhage. It has been reported that indirect bypass surgery for hemorrhagic moyamoya disease results in successful revascularization on angiographic studies and that a reduction in the number of moyamoya vessels does not necessarily eliminate the risk of further intracranial hemorrhage.\(^2\)\(^,\)\(^6\) The STA–MCA bypass is much more effective than indirect revascularization for treating moyamoya disease in adults.\(^2\) However, the effects of direct bypass surgery in these cases demonstrate no statistical significance in the prevention of recurrent hemorrhage.\(^3\)\(^,\)\(^8\)\(^,\)\(^9\)^\(^,\)\(^10\)\(^,\)\(^20\)\(^,\)\(^27\)\(^,\)\(^28\) Previously, we reported on a treatment regimen for aneurysms associated with moyamoya disease and a treatment strategy for hemorrhagic moyamoya disease in the acute stage.\(^1\)\(^,\)\(^10\)\(^,\)\(^12\) In the present report, we have clarified the best treatment for hemorrhagic moyamoya disease for the prevention of future stroke events.

In this study, any patient in whom the presence of an aneurysm was confirmed by angiography was excluded from the study group. Therefore, the intracranial hemorrhages observed in the patients were caused by a rupture in the network of moyamoya vessels, which occurred as a result of hemodynamic stress, and that network had developed as compensation for low local CBF.\(^1\)\(^,\)\(^19\)\(^,\)\(^27\)\(^,\)\(^28\) It is well known that outcome in patients with rebleeding is very poor. In this series, patients who experienced recurrent intracranial hemorrhage also had poor outcomes. Therefore, prevention of rebleeding is one major goal in the treatment of hemorrhagic moyamoya disease.\(^2\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^20\) Surgical revascularization for hemorrhagic moyamoya disease decreases hemodynamic stress, thereby reducing the number of moyamoya vessels and helping to prevent recurrent intracranial hemorrhage.\(^1\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^20\) Conservative management, however, does not produce any improvement in hemodynamic compromise in moyamoya vessels. In our series, among patients receiving conservative treatment, two (18%) experienced a recurrent intracranial hemorrhage and four (36%) experienced an ischemic event during the follow-up period. In contrast, among patients who underwent STA–MCA bypass surgery, none had any recurrent intracranial hemorrhage or an ischemic event. During the follow-up period, there were fewer ischemic or hemorrhagic events in patients who underwent STA–MCA bypass than in those who were conservatively treated, and this difference was statistically significant. Moreover, the stroke-free time was also significantly longer in patients treated with STA–MCA bypass than in those treated conservatively. We therefore recommend direct bypass for hemorrhagic moyamoya disease for the prevention of future stroke events.

In this series STA–MCA bypass was performed in six patients and EDAS was performed in five patients. It is well known that, in adult-onset moyamoya disease, direct revascularization accomplished by STA–MCA bypass is much more effective than indirect revascularization. This is because STA–MCA bypass is superior to indirect bypass surgery in establishing rapid improvement in CBF as it travels from high-flow to hemodynamically compromised territories.\(^2\)\(^,\)\(^28\) In this series, the decrease in the number of moyamoya vessels was confirmed on postoperative angiography in patients who had undergone either direct or indirect bypass surgery. The degree of decrease in the number of moyamoya vessels was significantly greater in patients treated with direct bypass surgery than in those treated with indirect revascularization surgery. Recurrent intracranial hemorrhage and ischemic events occurred significantly less frequently in patients who underwent STA–MCA bypass than in those who underwent EDAS. Therefore, we recommend direct bypass over indirect bypass for patients presenting with intracranial hemorrhage.

This study focused on a very small series and was not a prospective randomized study. There may have been a potential bias in the patient selection and demographics in this study. Fortunately, there was no statistically significant difference in the demographic data among the three treatment groups. After the acute stage, revascularization surgery was recommended to each patient. However, at the time we recommended revascularization surgery less strongly because of the lack of scientific data on its usefulness in hemorrhagic moyamoya disease. We performed simple STA–MCA bypass or EDAS. Indirect bypass was performed only as a salvage surgical procedure because there was no proper recipient artery for STA–MCA bypass. Because of the absence of adequate recipient arteries during surgery, a more severe hemodynamic compromise might have been seen in patients who underwent EDAS than in patients who underwent STA–MCA bypass. This may be a source of potential bias in this study.

Matsushima and colleagues\(^3\) reported that STA–MCA bypass with encephalomyosynangiosis was superior to EDAS both in the development of collateral circulation and in postoperative clinical improvement in pediatric patients presenting with ischemic events. Therefore, some indirect bypass procedures are useful if combined with direct bypass. In the future, it will prove useful to examine the effects of direct bypass and/or indirect bypass procedures and to compare the results with those achieved with conservative management for the prevention of future stroke in patients with hemorrhagic moyamoya disease.

**Conclusions**

The usefulness of STA–MCA bypass in patients with moyamoya disease presenting with intracranial hemorrhage for the prevention of the recurrent hemorrhage or ischemic events was statistically confirmed in this study. The STA–MCA bypass is recommended over conservative management or indirect bypass surgery for the treatment of hemorrhagic moyamoya disease to prevent future stroke events.

**References**


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