

Long-term outcome of superficial temporal artery–middle cerebral artery bypass for patients with moyamoya disease in the US

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Object. The authors report the long-term results of a series of direct superficial temporal artery–middle cerebral artery (STA–MCA) bypass procedures in patients with moyamoya disease from the western US.

Methods. All patients with moyamoya disease treated at the University of Washington from 1990 through 2004 (39 patients) were included in this study. Patients underwent pre- and postoperative evaluation of cerebral perfusion dynamics. Surgical revascularization procedures were performed in all patients with impaired cerebral blood flow (CBF) findings.

Results. The mean age of patients at diagnosis was 34 years (range 10–55 years). All 39 patients had impaired CBF and/or vasomotor reserve and underwent revascularization procedures: 26 patients underwent bilateral operations, 13 unilateral (65 total procedures). An STA–MCA bypass was technically possible in 56 procedures (86.2%); saphenous vein interposition grafts were required in 3 procedures (4.6%); encephaloduroarteriosynangiosis was performed in 6 procedures (9.2%). Three patients died due to postoperative complications, yielding a procedure-related mortality rate of 4.61%, and 8 experienced non-life threatening complications (for a procedure-related rate of 12.3%). Long-term follow-up appeared to indicate a reduction in further ischemic events in surviving patients compared with the natural history. Cerebral perfusion dynamics improved postoperatively in all 36 surviving patients.

Conclusions. Moyamoya disease may differ in the US and Asia, and STA–MCA bypass procedures may prevent future ischemic events in patients with this condition. (DOI: 10.3171/FOC/2008/24/2/E15)

KEY WORDS • bypass surgery • cerebral blood flow • cerebral hemorrhage • ischemic stroke • moyamoya disease

MOYAMOYA disease is a rare cerebrovascular condition characterized by progressive, idiopathic occlusion of the bilateral supraclinoid ICAs, proximal MCAs, and ACAs. Since its first description by Takeuchi and Shimizu in 1957²⁴ and subsequent angiographic characterization and naming by Suzuki and Takaku in 1969,²² several thousand cases have been documented worldwide.¹

Depending on the country of origin, patients with moyamoya disease appear to have differences in age distribution and clinical features. In Japan, where the vast majority of cases have been documented, a bimodal age distribution exists, with the first peak in early childhood and a second

peak in the fourth decade of life.⁵ Ischemic symptoms are more common in children, while hemorrhagic events are more characteristic in adults. Similar findings have been reported in Europe.²⁸ In contrast, studies from the US suggest that moyamoya disease differs in its clinical expression in American populations.^{1,2}

Nonetheless, surgical revascularization is considered beneficial in moyamoya patients. This is true in the pediatric population, regardless of the country of origin.^{13,14,20,23} There is less experience with adult patients, particularly in North America, and the majority of published results relate to indirect revascularization.^{3,4,6,7,9–12,15–17}

In an effort to further define the characteristics of moyamoya disease in the US and the role of revascularization procedures, we reviewed our long-term experience in our cohort of patients.

Clinical Materials and Methods

Data collection and chart reviews were performed with the approval of the local human participants research committee and conformed to all guidelines set by this review board.

Abbreviations used in this paper: ACA = anterior cerebral artery; CBF = cerebral blood flow; CT = computed tomography; EC–IC = extracranial–intracranial; EDAS = encephaloduroarteriosynangiosis; = internal carotid; ICA = internal carotid artery; MCA = middle cerebral artery; SPECT = single-photon emission computed tomography; STA = superficial temporal artery; SVIG = saphenous vein interposition graft; TCD = transcranial Doppler ultrasonography; TIA = transient ischemic attack.

All patients treated for moyamoya disease at our institution from 1990 through 2004 were included in this study. Patients were referred to our facility from a 5-state region that included Alaska, Idaho, Montana, Washington, and Wyoming. All patients had angiographically proven disease, and those with “secondary” moyamoya disease due to other etiologies were excluded. Patients had been followed up since their initial referral to our system, and all data was collected in our departmental files. Clinical features and demographic information were analyzed from these records.

Cerebral blood flow dynamics and vasomotor reactivity were evaluated using a combination of Xe-CT with acetazolamide challenge, SPECT with acetazolamide challenge, and TCD with CO₂ challenge. The details of these specific procedures have been described elsewhere,^{8,18,26} and their use for evaluating cerebral perfusion dynamics in moyamoya disease is well established. For Xe-CT, SPECT, and TCD studies, the summary findings for each report were utilized; in this way, numerical values for CBF and velocity were not recorded, but general findings such as, “normal,” “impaired,” and “exhausted” were. This process simplified data collection and more closely followed clinical practice in terms of decision making.

All patients with impaired CBF and/or abnormal vasomotor reactivity were offered surgical revascularization. Two general types of operations were presented to patients: a direct EC-IC bypass, consisting of STA to MCA anastomosis, when possible; or an indirect EC-IC bypass, using STA to MCA territory EDAS, if the vessels were inadequate. If a direct bypass was performed, the STA was directly connected to an MCA branch, thereby augmenting CBF. Alternatively, if an EDAS was used, the STA and a pedicle of temporalis muscle and dura mater were placed on the surface of the brain, with the hope that arterial collaterals would eventually develop from the STA to the MCA. All surgeries were performed by the senior author. The technical aspects of these procedures have been clearly outlined in the literature.²¹

Patients were followed up long term after surgery, and additional CBF studies were obtained, as mentioned above.

Results

Clinical Characteristics

Thirty-nine patients with moyamoya disease were identified. There were 30 female and 9 male patients, with a mean age at clinical presentation and diagnosis of 34 years (range 10–55 years). Seven patients were < 21 years of age. Twenty-seven patients were Caucasian and 12 were of Asian heritage. Ischemic symptoms were most common (33 patients), whereas hemorrhagic presentations were infrequent (5 patients). One patient was asymptomatic, having been diagnosed with moyamoya disease as a result of a screening magnetic resonance angiogram due to a family history of the condition.

Preoperative Cerebral Perfusion and Hemodynamics

Table 1 lists the preoperative CBF and vasomotor reactivity results. Thirty-three patients underwent Xe-CT or SPECT scanning; 6 did not. Patients who did not undergo

TABLE 1
*Preoperative cerebral perfusion/blood flow and vasomotor reactivity results**

Variable	Xe-CT w/ AZ Challenge	SPECT w/ AZ Challenge	TCD	TCD w/ CO ₂ Reactivity
no. of patients evaluated	3	30	8	29
normal baseline cerebral perfusion/blood flow	0	1	0	0
abnormal cerebral perfusion/ blood flow	3	29	8	29
impaired vasomotor reserve	2	21	NA	29

* AZ = acetazolamide; NA = not applicable.

cerebral perfusion scanning were claustrophobic, refused the examination, or could not tolerate the procedure. Nearly all patients demonstrated impaired cerebral perfusion at baseline (32 patients), while a majority (23 patients) exhibited impaired vasomotor reserve on acetazolamide challenge. One patient who was asymptomatic had normal results of perfusion imaging at baseline and on acetazolamide challenge. Thirty-seven patients underwent preoperative TCD evaluations: 29 underwent TCD testing with CO₂ reactivity challenge, while 8 underwent TCD testing without CO₂ reactivity challenge. In the 8 cases in which CO₂ reactivity was not performed, technical difficulties or the patient’s inability to tolerate the test precluded its completion. The 6 patients who did not undergo preoperative perfusion imaging studies completed TCD testing with CO₂ reactivity evaluations. In all 37 patients who underwent preoperative TCD evaluations, the results demonstrated abnormal CBF; CO₂ reactivity testing revealed impaired vasomotor reserve in all 29 patients studied.

Procedures Performed, Complications, and Bypass Patency Rates

Based on their preoperative cerebral angiograms (images and data not shown) and cerebral perfusion studies, all 39 patients underwent surgical revascularization procedures. Of these, 26 patients required bilateral bypass procedures. As shown in Table 2, direct EC-IC bypass was performed in 36 patients, while 3 patients underwent an indirect EC-IC bypass (EDAS). Sixty-five cerebral hemispheres (out of a possible 78, 2 cerebral hemispheres per patient) were operated upon, and direct bypasses were performed in 59 cases. The majority of direct bypasses consisted of an STA-MCA anastomosis (56 cases); an SVIG was used to directly connect the STA to the MCA in the remainder (3 cases). A total of 6 indirect bypasses (EDAS) were created due to the technical or anatomical inability to create a direct EC-IC bypass (because of occluded STA, atretic STA, size mismatch, previous STA biopsy, among other reasons) and contraindications for saphenous vein harvesting.

Non-life-threatening postoperative complications occurred in 8 (12.3%) of 65 procedures, all direct EC-IC bypasses (7 of the 8 were in STA-MCA cases, 1 in an SVIG case). These complications were relatively minor, consisting of wound infections (3 cases) and silent infarcts (5 cases, detected on postoperative diffusion weighted magnetic resonance imaging). Three deaths occurred in the immediate postoperative period, 1 related to an acute myocardial infarction, and 2 secondary to postoperative intracerebral

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TABLE 2
Procedures performed, associated complications, and long-term patency

Variable	Direct STA–MCA Bypass	Direct STA–MCA Bypass Using SVIG	Indirect STA–MCA Bypass (EDAS)
no. of patients	33	3	3
no. of procedures performed	56	3	6
complications	7	1	0
deaths	3	0	0
graft occlusions	2	1	0

hemorrhages remote from the site of the operation; all 3 patients presented with ischemic symptoms preoperatively and underwent direct STA–MCA bypass procedures.

Intermediate-term follow-up with cerebral angiography (1–26 months postoperatively, mean 5.4 months) was performed in 32 patients. Of the 65 bypasses performed, 3 eventually occluded: 2 occlusions occurred in the direct STA–MCA bypass group (2 [3.6%] of 56 bypasses) and 1 occurred in the saphenous vein group (1 [33.3%] of 3 bypasses).

Postoperative Outcome and Cerebral Perfusion and Hemodynamics

Duration of post-bypass follow-up ranged from 5 to 100 months (mean 42.9 months), corresponding to 139.5 patient-years. Of the 5 patients who presented with hemorrhages, only 1 (20%) suffered a repeated hemorrhage, and it occurred 2 months following his second bypass operation. For patients with ischemic symptoms, ischemic events were markedly reduced, with only 6 events (all TIAs) in 6 different patients (6 [19.4%] of 31) during 139.5 patient-years of follow-up, which may represent a reduction compared with the natural history. All patients either returned to their preoperative level of function or improved following surgery. Cerebral blood flow imaging was performed in 15 patients 1–12 months (mean 2.93 months) after unilateral bypass (Table 3). In the majority of cases (12 [80.0%] of 15), CBF improved compared with preoperative studies. Twelve patients underwent cerebral perfusion imaging 1–51 months (mean 14.75 months) after their second operation; a direct EC–IC bypass was performed bilaterally in each of these 12 patients. Compared with their preoperative studies, cerebral perfusion and vasomotor reserve were markedly improved in all 12 (100%), and in 5 cases (41.7%) complete normalization of cerebral perfusion and vasomotor reactivity was noted. Similar findings were noted in 15 patients who underwent follow-up TCD after surgery (Table 3). One patient underwent TCD 8 months after a unilateral bypass; CBF was found to be improved. Follow-up TCD examinations in 6 patients (range 1–12 months after surgery, mean 8.16 months) with bilateral bypasses revealed improved blood flow in 5 (83.3%) and deterioration in 1 (16.7%). It is important to note that deterioration in blood flow was revealed in the patient who had undergone an EDAS procedure on the ipsilateral side. In 8 patients TCD testing with CO₂ reactivity challenge was performed 1–56 months (mean 22.25 months) after bilateral

TABLE 3
Postoperative cerebral perfusion/blood flow and vasomotor reactivity results

Variable	SPECT w/ AZ Challenge	TCD	CO ₂ Reactivity
patients reevaluated following unilateral bypass	15	1	0
improvement in cerebral perfusion/blood flow	12	1	NA
deterioration in cerebral perfusion/blood flow	0	0	NA
no change in cerebral perfusion/blood flow	3	0	NA
patients reevaluated following bilateral bypass	12	6	8
improvement in cerebral perfusion/blood flow	12	5	8
deterioration in cerebral perfusion/blood flow	0	1	0
no change in cerebral perfusion/blood flow	0	0	0

bypasses; all patients (100%) demonstrated improved CBF and vasomotor reserve.

Discussion

The clinical characteristics of our Pacific Northwest cohort differ significantly compared with moyamoya patients from Asia or Europe. The majority of patients were middle-aged Caucasian women who suffered TIAs. Ischemic events were more common than hemorrhagic events, both in adults and children, and no bimodal distribution was noted. Interestingly, while referral pattern biases and regional population differences may exist in the US, our findings are nearly identical to those reported from a Texas cohort in 1998.¹

Despite the clinical differences between US, European, and Asian patients with moyamoya disease, it appears that the benefits of revascularization procedures are similar. The progressive obliteration of the intracranial arterial supply in moyamoya disease decreases cerebral perfusion, producing ischemic episodes and exhausting vasomotor reserve. As abnormal collateral vessels form to provide additional blood supply to the brain, cerebral autoregulation and perfusion dynamics are further altered. Quantitative analyses of CBF and hemodynamics in these patients following revascularization operations have demonstrated marked improvements in each area evaluated. Following direct STA–MCA bypass in 6 children, Yonekawa et al.²⁷ noted that regional CBF improved in both the surgically treated and contralateral hemispheres. Okada et al.¹⁷ elegantly demonstrated similar findings for regional CBF and normalization of cortical perfusion pressure in adult patients following direct STA–MCA bypasses. Our results, while in a population with different demographics, echo these earlier findings on a more general scale. In our cohort, cerebral perfusion and vasomotor reactivity improved in all patients who underwent postoperative blood flow and TCD studies. Of particular interest, 5 patients who had suffered only TIAs experienced a complete normalization of cerebral perfusion and vasomotor reactivity following their bypass procedures. This effect

appeared durable in the long term, as these patients have been asymptomatic throughout the follow-up period.

In contrast to the results reported in the Asian case series in which there was a complete resolution of ischemic symptoms following bypass operations, infrequent ischemic episodes occurred in our patients. These events occurred in 6 patients who suffered TIAs on a weekly basis prior to their bypass. One patient suffered a TIA on the 1st postoperative day, and has been event free for the following 48 months. Another patient experienced a TIA 1 week postoperatively, and has been event free for the following 7 years. The other 4 patients suffered TIAs 12–48 months postoperatively. All 6 patients underwent TCD testing with CO₂ reactivity challenge as part of their postoperative TIA workup; 5 of the 6 patients had improved blood flow and vasomotor reactivity. The other patient presented with a single TIA 12 months following her second operation and was found to have an occluded saphenous vein graft (by TCD) on the same side as her ischemic symptoms (an EDAS procedure had been performed on the other side). She declined further workup and has been asymptomatic for the subsequent 6 years. Thus, when the entire study group is considered, functional improvement in CBF was universal.

The mechanism through which a reduction in hemorrhage rate occurs following revascularization procedures is difficult to explain. Other authors have demonstrated a reduction of abnormal moyamoya vessels following surgery and suggest that the abnormal collaterals are responsible for hemorrhage. This is problematic, however. Published series of revascularization procedures have not demonstrated a significant correlation between reduction in moyamoya vessels and prevention of hemorrhagic events. In fact, reduction in moyamoya vessels is observed in only 25–65% of patients.²¹ Moreover, the ability of surgery to prevent or reduce the frequency of hemorrhagic events has been disappointing. Okada et al.¹⁷ reported that 20% of patients who presented with hemorrhagic events suffered additional hemorrhagic events following direct STA–MCA bypass. Yonekawa et al.²⁹ reported that the rate of rebleeding following surgery was not different from what was seen in the natural history of the disease. In our 5 patients with the hemorrhagic variety of moyamoya, 1 experienced an additional hemorrhagic event, despite successful STA–MCA bypass. A follow-up cerebral angiogram performed at the time of the patient's new hemorrhage, 2 months after his second STA–MCA bypass, revealed a near-complete resolution of moyamoya vessels. This finding suggests that the presence of these abnormal collateral vessels, or the lack thereof, is unrelated to the predisposition to hemorrhage. Alternatively, the risk of a perioperative hemorrhagic event may be related to the lack of cerebral autoregulation in these patients, analogous to breakthrough bleeding or hyperperfusion²⁵ following carotid endarterectomy.

The risks of surgical intervention in these relatively high-risk patients must also be considered. Perioperative ischemic events are more common in moyamoya disease than in other cerebrovascular occlusive diseases.¹⁹ Attention must be paid to intraoperative fluid dynamics, blood loss, anesthetic cerebral protection, and blood pressure control. Similarly, fragility of abnormal moyamoya vessels may predispose them to hemorrhage; hypertensive spikes must be avoided, while ensuring that adequate intravascu-

lar pressure exists to maximize graft patency and cerebral perfusion. Graft occlusions may occur if there is prolonged hypotension, relative intravascular hypovolemia, or increased blood viscosity or if there are technical difficulties in creating an anastomosis between the graft and recipient vessel. The graft occlusions that occurred in our patients were probably the result of relative intraoperative hypotension in the STA–MCA bypasses (2 cases) and thrombogenicity of the saphenous vein graft (1 case). As mentioned previously, increased blood flow provided by the bypass may lead to breakthrough bleeding. This particular issue may have contributed to 2 of the 3 deaths in our study group. Both patients suffered massive intracranial hemorrhages immediately postoperatively; there was no evidence of aneurysms or arteriovenous malformations on their preoperative cerebral angiograms. Additionally, their hemorrhages occurred at sites remote from the craniotomy, in unexposed brain. Last, systemic comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease may lead to complications. This was evident in one of our patients who underwent extensive preoperative cardiovascular testing in order to prepare the patient for surgery. Despite medical clearance from her cardiologist, she suffered a major myocardial infarct 3 days postoperatively and died several weeks later. Other complications, such as wound infections or breakdown, can be attributed to the fragile skin flap that results from harvesting the STA.

Surgical revascularization for the treatment of moyamoya disease may provide long-term reduction in ischemic events compared with the natural history of the disease,¹ although this was an observational study. Regardless of the differences that exist between the demographic characteristics of moyamoya patients in the Western and Eastern hemispheres, surgical revascularization can be expected to result in improvement in cerebral perfusion and vasomotor reactivity, correlating to a reduction in ischemic events. The number of hemorrhagic cases in our cohort was probably too small to make a definite statement regarding reduction of hemorrhagic risk. Further investigations are required to determine the etiology of hemorrhagic events in moyamoya disease, and a larger population with the hemorrhagic variety of moyamoya disease must be evaluated to clarify the mechanisms through which surgical revascularization alters the frequency of these events.

Acknowledgment

We thank Marilyn F. McGlashan for her assistance in data collection.

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Manuscript submitted November 10, 2007.

Accepted December 14, 2007.

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