Direct and Combined Revascularization in Pediatric Moyamoya Disease

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OBJECTIVE: **Surgical revascularization of moyamoya disease can improve neurological outcomes, compared with the natural history of the disease or the results of medical treatment. Controversy exists regarding whether direct or indirect revascularization yields better outcomes. This study involves a single-center experience with direct anastomosis and is the first North American series using direct revascularization for pediatric patients with moyamoya disease.**

METHODS: **Twelve patients (age range, 5–17 yr; mean age, 10.2 yr) underwent direct revascularization of 21 hemispheres. Two patients had experienced failure of previous indirect revascularization procedures, with continued clinical deterioration. Superficial temporal artery-middle cerebral artery anastomosis was performed in 19 hemispheres (with concurrent encephaloduroarteriosynangiosis in 6). Middle meningeal artery-middle cerebral artery anastomosis and omental transposition were each performed in one hemisphere. Follow-up periods ranged from 12 to 65 months (mean, 35 mo), and monitoring included neurological examinations, angiography, magnetic resonance imaging, and cerebral blood flow studies.**

RESULTS: **The neurological conditions of all patients were stable or improved after surgery. None of the patients developed new strokes, and no new ischemic lesions were seen in magnetic resonance imaging scans. All grafts evaluated by follow-up angiography were patent. Postoperative cerebral blood flow studies showed significantly improved blood flow (54.4 versus 42.5 ml/100 g/min; $P = 0.017$, n = 4) and hemodynamic reserve (70.3 versus 43.9 ml/100 g/min; $P = 0.009$, n = 4), compared with preoperative studies.**

CONCLUSION: **Surgical revascularization by direct anastomosis in pediatric patients is technically feasible, is well tolerated, and can improve the progressive natural history, the angiographic appearance, and the cerebral blood flow abnormalities associated with the disease. Direct revascularization has the advantage of providing immediate and high-flow revascularization and is particularly useful for patients who have experienced failure of previous indirect revascularization procedures.** (Neurosurgery 45:50–60, 1999)

Key words: Cerebral blood flow, Extracranial-intracranial arterial bypass, Moyamoya disease, Revascularization

Moyamoya disease is a rare cerebrovascular disorder characterized by progressive occlusion of the intracranial carotid arteries. The disease is far more common in those of Japanese ancestry than in other ethnic groups, for unknown reasons (11). Presentation varies with age; children present with ischemic strokes, transient ischemic attacks (TIAs), and seizures resulting from hemodynamically mediated ischemia. Adults more frequently present with hemorrhage, probably resulting from ischemia-induced proliferation of perforating vessels at the base of the brain (28). In most cases, the disease is progressive and does not respond to medical therapy with vasodilators or antithrombotic agents (13).

Several surgical options have been used in the treatment of moyamoya disease. The earliest surgical attempts included stellate ganglion ablation and cervical carotid sympathectomy (30), which have not proven useful. Currently, all surgical therapies aim to reverse the ongoing ischemia and resultant abnormal angiogenesis by providing an alternative source of blood flow to the hemispheres. Direct revascularization involving extracranial-intracranial anastomoses provides immediate blood flow but is technically difficult, especially in children. Several alternative indirect methods that are technically simpler have been developed. These methods involve applying either vascularized muscle (encephalomyosynangiosis

[EMS]) or the intact superficial temporal artery (STA) to the surface of the brain, with various modifications (encephaloduroarteriosynangiosis [EDAS] or pial synangiosis). Ingrowth of vessels from the graft depends on the elaboration of angiogenic factors produced by ischemic brain tissue (15, 21). There has been much debate regarding the relative merits of these procedures. This article presents our results with direct anastomosis in 12 pediatric patients (21 hemispheres) with moyamoya disease.

PATIENTS AND METHODS

Between August 1992 and April 1998, 16 pediatric patients with moyamoya disease were treated at Lucille Packard Children's Hospital and Stanford University Medical Center. This report focuses on 12 patients who underwent direct revascularization, which has become our procedure of choice. The other four children were treated with EDAS either before we had experience with direct anastomosis in pediatric patients or because of very young age (<2 yr) and extremely small (<1 mm in diameter) donor or recipient arteries.

The patients ranged in age from 5 to 17 years (mean, 10.2 yr). There were five female and seven male patients. Two children were of Japanese ancestry and two of non-Japanese Asian ancestry. The family of one patient was of Indian origin, and the remainder of the patients were of European origin. Three patients presented with reversible neurological deficits without evidence of stroke in magnetic resonance imaging (MRI) scans. Five patients presented with completed strokes, using clinical and radiographic criteria. Three patients had both completed strokes and ongoing transient ischemia. One child presented with seizures in addition to a cerebrovascular accident. One patient presented with unilateral chorea, TIAs, and headaches. There were no cerebral hemorrhages at presentation. Ten patients were receiving antiplatelet medication or calcium channel blockers and one was undergoing anticoagulation therapy with warfarin at the time of referral for surgical treatment. Two patients had been previously surgically treated for moyamoya disease, one with burr holes and one with EDAS. Associated conditions included subaortic stenosis in one patient and Type I glycogen storage disease in one patient. One patient had Down syndrome.

Studies

Preoperative evaluations included five-vessel cerebral angiography (bilateral internal carotid artery, bilateral external carotid artery, and vertebrobasilar artery injections) for all patients. Postoperative angiograms were available for 11 patients. MRI was performed preoperatively for all patients and postoperatively for nine patients. The most recent postoperative scans (obtained 1–63 mo after surgery; mean, 21 mo) were reviewed. Cerebral blood flow (CBF) studies were performed preoperatively for eight patients and postoperatively for eight patients. Pre- and postoperative evaluations also included neurological examinations.

All angiograms were independently reviewed by a neuroradiologist with a special interest in cerebrovascular pathology. Angiograms were evaluated for the patency of the carotid arteries, the presence of moyamoya vessels, and blood flow through both native and surgical collateral vessels. Flow through the surgical anastomoses was graded using a previously described scale (18). This classification scheme grades the degree of filling of the middle cerebral artery (MCA) territory by the graft. Grades are assigned as A when the area supplied covers more than two-thirds of the MCA territory, B when one-third to two-thirds of the MCA distribution is supplied, and C when only one cortical branch is supplied or there is no collateral supply.

Xenon computed tomography (CT) CBF studies were performed before and after acetazolamide challenge, to assess reserve, using a previously described method for stable xenon CBF determinations (8). Acetazolamide (Diamox; Wyeth-Ayerst, Philadelphia, PA) was administered intravenously 20 minutes before the postchallenge CBF study was performed (23). Regions of interest were marked along the cortical margin of the CBF maps and divided into anterior cerebral artery (ACA), MCA, and posterior cerebral artery (PCA) territories for quantitative evaluation (*Fig. 1*). Absolute CBF values (milliliters per 100 g per minute), as well as ratios of postacetazolamide to preacetazolamide CBF values, were calculated. Pre- and postoperative values were compared using Student's paired *t* test.

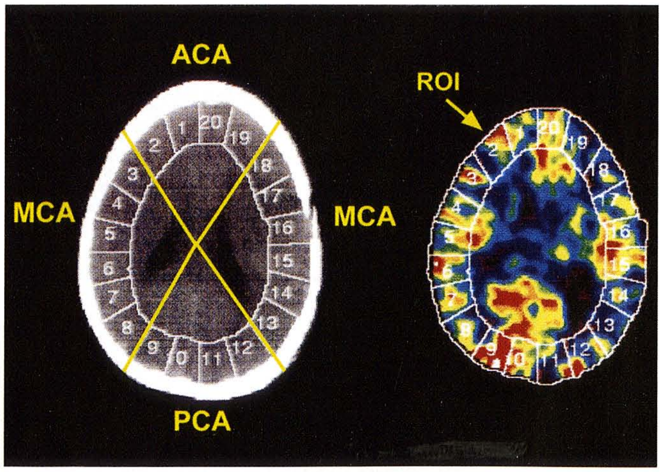

FIGURE 1. Xenon CT at the level of the centrum semiovale, with regions of interest (*ROI*) marked along the cortical margin. Territories have been divided into ACA, MCA, and PCA areas for calculation purposes. Mean blood flow may then be calculated for each territory.

Surgical technique

Direct revascularization procedures were performed on 21 hemispheres in 12 patients. Six hemispheres underwent concomitant EDAS using a second branch of the STA. One patient underwent middle meningeal artery-MCA anastomosis plus EDAS because the donor STA was of poor quality. Omental transposition was used on one side in a patient with a poor donor artery and is included in the analysis.

The technique used for the combined direct and indirect procedure briefly outlined here has been described more fully (9, 10, 29, 32, 34). Throughout the procedure, careful anesthetic management of hemodynamic and respiratory parameters is rendered. Normocapnia is maintained and blood pressure is supported in the normal to high range for each patient. The patient is cooled to 33°C and given a bolus dose of thiopental for neuroprotection during cross-clamping.

The patient is positioned with the head turned 90 degrees away from the surgical side. The frontal and parietal branches of the STA are located using a hand-held Doppler probe. The initial skin incision is made over the course of the donor artery. The vessels are carefully dissected free of connective tissue. Care is taken to avoid excess manipulation, and papaverine is liberally applied to minimize spasm. The scalp incision is then extended into a modified horseshoe flap, and the temporalis muscle is incised and reflected with the scalp. A small craniotomy flap is made over the sylvian fissure, and the dura is opened in a cruciate fashion. A suitable recipient M3 or M4 MCA branch, preferably measuring ≥1 mm in diameter and free of microperforators, is identified. A small, straight, temporary, Sugita aneurysm clip is placed proximally on the parietal or frontal STA, and the distal vessel is ligated and divided, leaving sufficient length to reach the recipient vessel. The lumen is prepared for anastomosis by dissection of the soft-tissue cuff. The selected MCA branch is clamped proximally and distally with temporary mini-Sugita aneurysm clips or microvascular clips (Mizuho, Inc., Beverly, MA). End-to-side anastomosis is performed using interrupted 10-0 nylon sutures (*Fig.* 2). Clips are removed from the MCA branch, and the patency and hemostasis of the anastomosis are checked. The clip is then removed from the donor STA, and flow is assessed with a micro-Doppler probe.

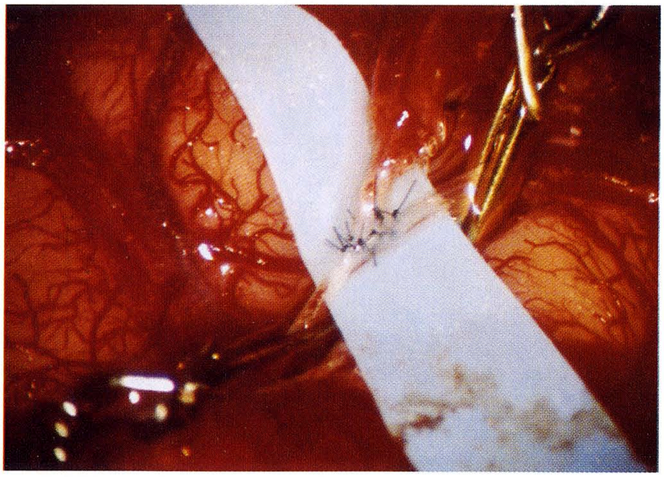

FIGURE 2. Intraoperative photograph of a STA-MCA end-to-side anastomosis.

When a suitable second STA branch is found, this is dissected free of its investing tissue, laid on the pia, and sutured to the dura. The distal end is kept intact. The dura is then carefully closed without kinking of the graft. The bone flap is replaced and secured. If necessary, a small area of bone is removed to allow free passage of the donor vessels. The temporalis muscle and scalp are reapproximated. Patients are generally extubated in the operating room and taken to the pediatric intensive care unit for postoperative care. Blood pressure and volume status are carefully controlled.

RESULTS

Clinical outcomes

Twelve patients were evaluated and treated (*Table 1*). All experienced stabilization or improvement of their symptoms during a follow-up period of 12 to 65 months (mean, 35 mo). One patient developed symptoms from new disease in the previously unaffected contralateral hemisphere, requiring surgical intervention. No new strokes were detected clinically or by MRI. Of the seven patients who presented with TIAs, five experienced complete resolution and two experienced significant reduction in the frequency of TIAs. The patient who presented with chorea experienced complete resolution of symptoms. Perioperatively, several patients exhibited transient neurological symptoms (headache, visual changes, and subjective sensory changes), with a paucity of clinical signs. These patients were treated with intravenous volume expansion, and all symptoms resolved within a few days. Reduction of TIA frequency was noted at the time of discharge from the hospital or by the first postoperative examination. Two patients experienced later recurrence of TIAs after discontinuation of aspirin administration, which resolved completely after resumption of drug administration. Improvement has been sustained, with no late recurrence of symptoms.

Angiographic findings

Preoperative angiograms confirmed a moyamoya pattern in all patients. Three cases showed only unilateral involvement. No antegrade filling of the MCA territory was seen in 16 hemispheres. Minimal filling was demonstrated in five hemispheres, and three sides showed normal antegrade filling (in patients with only unilateral involvement). Native collateral filling via the external carotid circulation was also evaluated in 11 patients. There was a paucity of collateral vessels in 14 hemispheres, 5 hemispheres were judged to have moderate to good collateral vessels, and the three uninvolved hemispheres did not show significant collateral formation. The presence and number of moyamoya vessels were assessed. These were symmetrical in all cases with bilateral disease. There were no or few moyamoya vessels in two patients, a moderate number in five patients, and many in four patients (*Fig.* 3).

TABLE 1. Clinical Presentation, Procedures, and Outcomes[a]

Patient No.	Sex/Age (yr)	Presentation	Procedure	Clinical Outcome	Follow-up Period (mo)
1	F/13	L CVA and TIAs	B STA-MCA	Resolution of TIAs, no further events	65
2	F/7	TIAs	B STA-MCA	Significantly reduced TIAs	65
3	M/5	TIAs	R STA-MCA, L STA-MCA + EDAS	Resolution of TIAs	57
4	F/17	R CVA and TIAs	R STA-MCA, L MMA-MCA + EDAS	Stabilized, no further events	48
5	M/11	CVA, seizures, cognitive decline	B STA-MCA	Stabilized, no further events, seizure disorder	46
6	M/9	L CVA, daily TIAs	R STA-MCA + EMS, L omental graft	Resolution of TIAs, no further events	42
7	M/6	R CVA (unilateral disease)	R STA-MCA (previous burr holes)	No further events	16
8	M/8	L CVA	B STA-MCA + EDAS	No further events, improvement in neurological deficit	20
9	M/7	L CVA, seizures, aphasia (unilateral disease)	L STA-MCA (previous EDAS)	Reduced ipsilateral events, contralateral TIAs, contralateral side surgically treated	17
10	M/9	L TIAs, headaches, syncope	R STA-MCA + EDAS, L STA-MCA	Resolution of TIAs, no further events	15
11	F/8	TIAs, R hemichorea, headaches	B STA-MCA + EDAS	Resolution of TIAs and hemichorea, no further events	15
12	F/17	R CVA $\times$ 3 (unilateral disease)	R STA-MCA	No further events	12

[a] CVA, completed stroke (by clinical or radiographic criteria); TIA, transient ischemic attack; EMS, encephalomyosynangiosis; L, left; R, right; B, bilateral; STA-MCA, superficial temporal artery-middle cerebral artery anastomosis; EDAS, encephaloduroarteriosynangiosis; MMA-MCA, middle meningeal artery-middle cerebral artery anastomosis.

Postoperative angiograms were available for independent review for 18 symptomatic hemispheres in 10 patients (*Fig. 3*). The time interval between surgery and angiography ranged from 2 to 29 months (mean, 9 mo). Eleven hemispheres were graded A according to the scale proposed by Matsushima et al. (18), with more than two-thirds of the MCA territory filling. Four hemispheres were Grade B, and two were Grade C. A grade could not be assigned to one hemisphere because no external carotid artery injection was performed. Previous infarction in a given hemisphere, detected as encephalomalacia in preoperative MRI scans, was correlated with development of poorer collateral filling of that area but not of adjacent uninfarcted areas. When the grading scale was applied to these cases, the filling of the residual uninfarcted area was graded. Postoperative angiograms were also evaluated for changes in the number of moyamoya vessels. These vessels increased in number in four hemispheres, were unchanged in number in eight hemispheres, and decreased in eight hemispheres. Increases in the number of moyamoya vessels were seen in patients with relatively worse filling through surgical collateral vessels (Patients 1 and 5), and decreases in the number of vessels were usually seen with the most extensive surgical collateral filling (Patients 3, 6, 8, 10, and 11) (*Table 2*).

CBF study findings

The mean interval between surgery and follow-up CBF studies was 7.6 months (range, 3–18 mo). Preoperative CBF values ranged from 18 to 102 ml/100 g/min, with all but two patients having areas of flow of less than 35 ml/100 g/min. Mean preoperative CBF was 44.0, 45.9, and 51.9 ml/100 g/min in the ACA, MCA, and PCA distributions, respectively. All patients had areas that failed to augment blood flow after acetazolamide administration. Of 66 regions evaluated, 35 showed abnormal augmentation in response to acetazolamide challenge and 31 regions showed augmentation. Abnormal baseline blood flow and augmentation were seen in all vascular distributions. Of 76 regions evaluated postoperatively, eight still showed decreases in or no augmentation of flow and 68 demonstrated augmentation (χ^2, $P < 0.001$, compared with preoperative values) (*Fig. 4*). Three patients underwent additional follow-up studies 10 to 29 months after surgery; two showed further improvement and one exhibited stable results.

Four patients underwent complete CBF studies before and after acetazolamide challenge both pre- and postoperatively, allowing direct comparison of eight hemispheres. Baseline blood flows were significantly improved for MCA (58.1 versus 40.5 ml/100 g/min; $P = 0.018$) and PCA (54.4 versus 42.2 ml/100 g/min; $P = 0.044$) territories and for the hemisphere as a whole (54.4 versus 42.5 ml/100 g/min; $P = 0.017$). Significant improvement was also seen in response to acetazolamide challenge in the MCA (72.8 versus 38.2 ml/100 g/min; $P < 0.001$) and PCA (70.8 versus 41.3 ml/100 g/min; $P < 0.001$) regions, as well as in the hemisphere as a whole (70.3 versus 43.9 ml/100 g/min; $P = 0.009$). Both baseline and

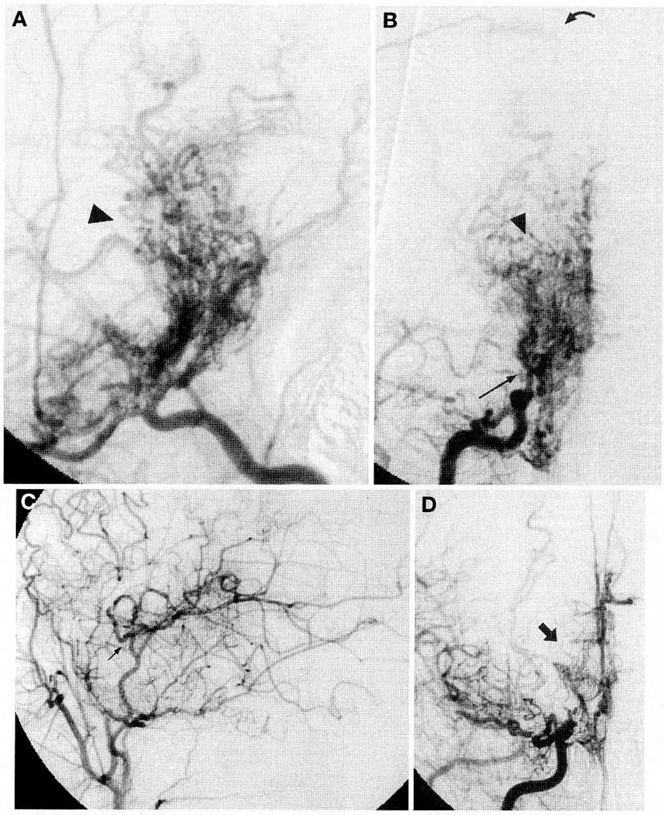

FIGURE 3. ***A* and *B*, preoperative lateral (*A*) and anteroposterior (*B*) views of common carotid artery injections for Patient 10, demonstrating occlusion of the MCA (*arrow*), profusion of moyamoya collateral vessels (*arrowheads*), and little filling through a spontaneous extracranial-intracranial anastomosis (*curved arrow*). *C* (lateral) and *D* (anteroposterior), follow-up results for the same patient, obtained 2 months after surgery, demonstrating excellent filling of the MCA territory through the STA-MCA anastomosis (*arrow*), with a contribution from scalp and meningeal arteries. Moyamoya vessels have diminished (*thick arrow*).**

postchallenge blood flows improved in the ACA distribution, but this was not statistically significant (*Table 3*). The ratios of postacetazolamide to preacetazolamide flows were improved in all vascular distributions, but this was not statistically significant (*Table 4*). There was a trend for improvement of the MCA distribution ratio (1.27 versus 0.96; $P = 0.07$).

DISCUSSION

Moyamoya disease causes progressive neurological deterioration in affected patients. The morbidity rate for untreated moyamoya disease has been reported to be more than 70% (22, 36). Revascularization by both direct and indirect methods can improve neurological outcomes (6). However, much debate has centered on which method is preferable. Proponents of indirect revascularization emphasize its noninvasiveness, safety, and technical ease, particularly for young children. Surgeons who perform direct anastomoses think that these procedures are more efficacious and are equally safe. Also, previous EDAS or EMS may render the STA no longer suitable as a donor artery in patients who experience failure of such procedures. The technical difficulty of direct anastomosis in children, because of the smaller size of both recipient and donor arteries, has been emphasized. In our experience, vessels smaller than 1 mm are not good candidates for anastomosis and have a lower patency rate (32). We have, however, successfully created anastomoses in children as young as 5 years of age. To our knowledge, this is the only North American series describing direct revascularization in pediatric patients.

Clinical outcomes

There have been no controlled prospective studies comparing direct and indirect revascularization procedures. Matsushima et al. (18) retrospectively reviewed results for 40 children who underwent either EDAS or STA-MCA anastomosis with EMS. They reported that the direct procedures resulted in better angiographic collateral filling and improved clinical outcomes. There are multiple reports of successful direct revascularization in pediatric patients (3, 9, 10, 19), primarily from the large Japanese series of Karasawa and co-workers. The advantage is immediate high-flow revascularization.

There are multiple reports of successful revascularization using a variety of indirect procedures (1, 17, 24). However, there are a significant number of patients who experience failure of these procedures. Touho et al. (31) reported 31 patients who had experienced failure of previous indirect revascularization with EMS or EDAS and were subsequently treated using direct STA-MCA bypass. Clinical improvement was seen for all patients except one, who had already experienced a completed infarction. Cahan (4) also reported that the conditions of some patients were refractory to EDAS. We have observed no treatment failures using direct anastomosis, albeit in a small group of patients.

Perhaps most importantly, children often present with acute exacerbations and crescendo TIAs, as the balance between blood flow and demand becomes altered at some point in the disease. Indirect methods do not immediately provide increased blood flow but instead depend on the ingrowth of vessels, which can take months. Matsushima and Inaba (16) reported that angiographically visible revascularization after EDAS was present by 6 months. Strokes that occur during this time period can be devastating. Our results with direct revascularization have shown that patients often experience rapid resolution (usually before hospital discharge) of preoperative TIAs. In the present series, good revascularization was radiographically confirmed as early as 6 weeks to 3 months after surgery. However, there are no good serial radiographic data evaluating the time course of revascularization after either direct or indirect procedures.

Indirect methods are thought to be safer than direct anastomosis because no temporary occlusion of the MCA branch, which might lead to perioperative stroke, is required (1). However, Iwama et al. (7), in their retrospective analysis of perioperative complications, found that the rates of stroke

TABLE 2. Angiographic Results[a]

Patient No.	Preoperative			Postoperative	
	Antegrade MCA Filling	Collateral MCA Filling	Moyamoya Vessels[b]	MCA Filling via Graft[c]	Moyamoya Vessels
1	R little	R little	++	R B	R increased
	L little	L little		L B	L increased
2	R none	R moderate	++	R A	R no change
	L none	L moderate		L B	L no change
3	R none	R little	+++	R A	R decreased
	L none	L little		L A	L decreased
4	R none				
	L little				
5	R none	R little	+	R C	R increased
	L none	L little		L C	L increased
6	R none	R little	+++	R A	R decreased
	L none	L little		L A	L decreased
7	R little	R little	++		
	L normal	L NA			
8	R none	R good	++	R B	R decreased
	L none	L little		L A	L decreased
9	R normal	R NA	++	R normal	R NA
	L none	L little		L not assessable	L decreased
10	R none	R little	+++	R A	R decreased
	L none	L little		L A	L no change
11	R none	R good	+++	R A	R no change
	L little	L good		L A	L decreased
12	R none	R little	None	R A	R no change
	L normal	L NA		L NA	L no change

[a] MCA, middle cerebral artery; L, left; R, right; NA, not applicable.
[b] Moyamoya vessels: +, few; ++, moderate, +++, many.
[c] Filling via graft: A, more than two-thirds of the MCA territory fills via the graft (according to the scale of Matsushima et al. [18]); B, between one-third and two-thirds of the MCA territory fills; C, one cortical MCA branch or less fills.

were almost identical for patients undergoing STA-MCA anastomosis (8.4%) or EMS (8.3%). Because impaired cerebral vascular reserve makes patients vulnerable to the hemodynamic stresses of surgery regardless of the surgical technique, several groups have emphasized the importance of close hemodynamic monitoring and aggressive intraoperative management of blood pressure and partial pressure of CO_2, to avoid strokes (7, 27). A number of perioperative events may be unavoidable, and the best strategy may be to perform bilateral procedures in a single session to minimize complications, although published data are lacking. We have used staged procedures with careful anesthetic management and neuroprotection and to date have observed no perioperative strokes.

When the STA anatomic features are favorable, a combination of direct anastomosis and EDAS from a second STA branch may be the preferred revascularization method. The direct anastomosis provides an immediate and high-flow blood supply, which may help stabilize the clinical conditions of patients who have been experiencing frequent ischemia resulting from insufficient blood supply. The EDAS may allow vessel ingrowth over a larger area of cortex, eventually revascularizing a larger area than would the direct anastomosis alone. In addition, the EDAS provides an alternative route for collateralization, if the primary anastomosis fails. A recent report described the combined direct/indirect procedure and demonstrated better revascularization than with indirect procedures alone (12).

The present series includes 12 sequential pediatric patients who underwent revascularization via direct anastomosis, some of whom underwent concurrent EDAS. All patients tolerated the procedure well, and there were no perioperative strokes. We did note some transient perioperative neurological symptoms, suggesting that these patients undergo transient disturbances in blood flow that may be attributable to impaired autoregulation. This finding is consistent with the reports of perioperative stroke (some occurring up to 10 days postoperatively) among patients undergoing any mode of revascularization. These events have been more frequent among patients undergoing indirect procedures, perhaps because the patients have not yet established new collateral vessels and lack the reserve necessary in times of stress (25). Crying (which can induce hypocapnia and relative vasoconstriction) and dehydration (which can lead to hypoperfusion) have both been associated with perioperative ischemic events (26). Given these findings, maintenance of normovolemia or mild hypervolemia and special attention to pain control are of

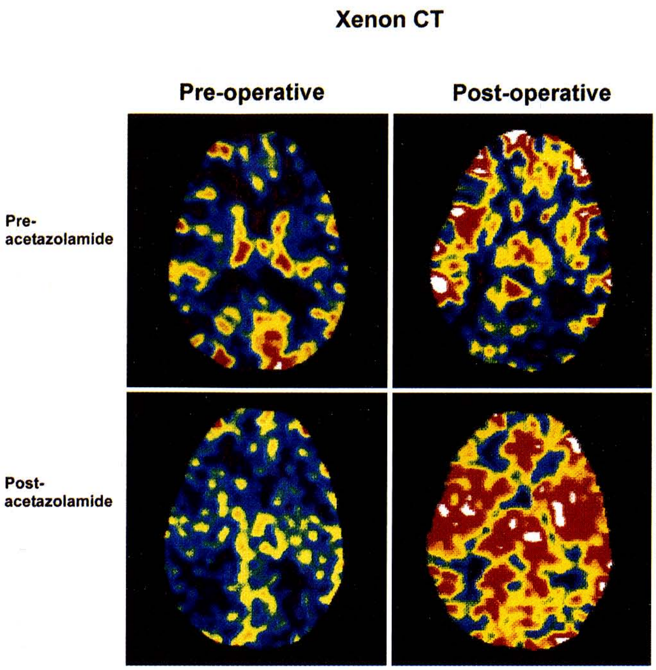

FIGURE 4. Pre- and postoperative xenon CT, with and without acetazolamide challenge, for Patient 3, demonstrating preoperative low blood flow and a paradoxical decrease in flow after acetazolamide administration. Increased baseline blood flow and reserve are seen after surgery.

particular importance. Direct revascularization, with its immediate augmentation of blood flow, may be partially protective against such events.

Three patients in this series presented with unilateral disease. This relatively high percentage may be more common in areas outside Japan, where moyamoya syndrome, rather than classic moyamoya disease, constitutes some of the cases. One of these patients later developed contralateral disease, emphasizing the importance of continued follow-up monitoring for all of these patients.

Radiographic outcomes

Radiographic studies confirmed moyamoya disease and provided evidence of successful revascularization. Preoperative angiography demonstrated the classic appearance of moyamoya disease, with pruning of the intracranial branches

TABLE 4. Ratio of Postacetazolamide to Preacetazolamide Blood Flows[a]

	ACA	MCA	PCA
Preoperative ratio	1.18 ± 0.24	0.96 ± 0.19	1.03 ± 0.29
Postoperative ratio	1.34 ± 0.21	1.27 ± 0.25	1.31 ± 0.23
P	0.19	0.07	0.16

[a] ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery. Values are mean ± standard deviation (n = 8 hemispheres).

of the internal carotid artery and fine basal ganglion anastomotic vessels. Neither the degree of stenosis nor the quantity of moyamoya vessels was correlated with the clinical severity of the disease at presentation. Collateral filling was generally poor, and the presence of relatively good collateral vessels did not seem to confer protection to that hemisphere. In general, there was excellent filling via surgically created collateral vessels. The use of a grading scale, such as the one applied here, may be helpful for quantification of the degree of collateralization. However, this technique may not fully describe the success of revascularization. For instance, where there is a large area of encephalomalacia, there may be poor or no surgical collateral vessels; nevertheless, the remaining uninfarcted territory may be well revascularized (*Fig. 5*). Patients with increases in moyamoya vessels exhibited relatively worse collateral filling, whereas patients with marked decreases in moyamoya vessels were those with the best surgical collateral vessels. This may be viewed as evidence of decreased ischemia-induced angioproliferative factors, indicating successful revascularization. Hemispheres treated with combined revascularization were more likely to exhibit decreases in moyamoya vessels, although, in this heterogeneous group, the numbers of cases are insufficient to allow any definite conclusions to be drawn from these data.

CBF studies may provide the best method for evaluating moyamoya disease after the diagnosis has been confirmed angiographically. Universally diminished baseline blood flows were seen in the patients in this series. All vascular distributions seemed to be affected. Most striking was the impaired response to acetazolamide-induced vasodilation. Although the prognostic significance of this pattern of CBF changes is uncertain, a study by Yonas et al. (35) found that patients with other cerebrovascular diseases with such findings might face an increased risk of stroke. CBF studies using

TABLE 3. Cerebral Blood Flow[a]

	Cerebral Blood Flow (ml/100 g/min)					
	Baseline			Postchallenge		
	Preoperative	Postoperative	*P*	Preoperative	Postoperative	*P*
Hemisphere	42.5 ± 7.0	54.4 ± 8.8	0.017	43.9 ± 10.7	70.3 ± 14.1	0.009
ACA	44.9 ± 18.1	50.7 ± 13.2	0.45	52.2 ± 22.8	67.3 ± 19.4	0.2
MCA	40.5 ± 11.2	58.1 ± 10.2	0.02	38.2 ± 10.4	72.8 ± 13.1	<0.001
PCA	42.2 ± 12.7	54.4 ± 8.3	0.04	41.3 ± 10.4	70.8 ± 14.9	<0.001

[a] ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery. Values are mean ± standard deviation (n = 8 hemispheres).

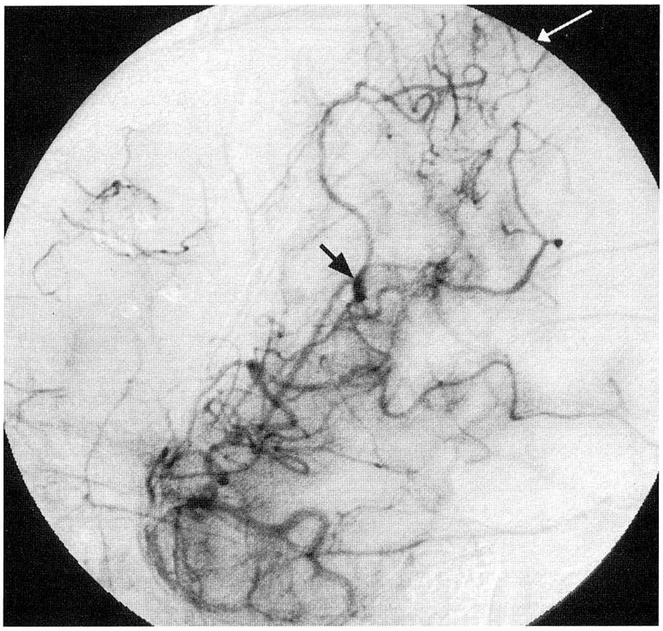

FIGURE 5. Postoperative lateral view of external carotid artery injection for Patient 12, demonstrating no filling of the area of a previous stroke, which affected most of the MCA territory. However, filling of adjacent normal areas through the graft (*black arrow*) is excellent (*white arrow*).

positron emission tomography have shown that elevated oxygen extraction fractions and elevated cerebral blood volumes are correlated with "misery perfusion," which is the most reliable indicator of hemodynamic stress (2, 5). There have been several studies demonstrating that failure to augment flow or paradoxical decreased flow in response to acetazolamide challenge, as detected using xenon CT, is well correlated with hemodynamic compromise (14, 20).

Xenon CT is an excellent method for monitoring CBF peri- and postoperatively, because it is quantitative, noninvasive, and readily repeatable. Data from different studies can be readily compared, because absolute measures of blood flow are provided. This technique may therefore be particularly useful for evaluation of the time course for the development of surgical collateral vessels. In addition, xenon CT may help to address the issue of which revascularization procedures are most beneficial in the treatment of this disease. There are few studies comparing pre- and postoperative CBF in pediatric patients. Nariai et al. (21) pre- and postoperatively studied 10 of 11 pediatric patients undergoing indirect revascularization, with xenon CT or positron emission tomography. The authors found that the degree of preoperative hemodynamic compromise was correlated with the extent of revascularization and that postoperative CBF and reserve were increased (21). The other study comparing pre- and postoperative findings produced different results; four children who underwent unspecified revascularization procedures exhibited increased CBF but unchanged cerebrovascular reserve (33). In our series, postoperative studies were notable for improved baseline blood flow and increased reserve. These results tended to be stable or improved with time among the patients who underwent serial studies.

CONCLUSION

Surgical revascularization by direct anastomosis in pediatric patients is technically feasible, is well tolerated, and can alter the progressive natural history, the angiographic appearance, and the CBF results of the disease. Direct revascularization has the advantages of providing immediate and high-flow revascularization and is particularly useful for patients who have experienced failure of previous indirect revascularization. Radiographic data confirming successful revascularization include evidence of graft patency, filling of a large portion of the MCA territory, and quantitative CBF studies showing improved blood flow and reactivity.

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REFERENCES

1. Adelson PD, Scott RM: Pial synangiosis for moyamoya syndrome in children. **Pediatr Neurosurg** 23:26–33, 1995.
2. Baron J, Bousser M, Comar D, Soussaline F, Castaigne P: Noninvasive tomographic study of cerebral blood flow and oxygen metabolism in vivo. **Eur Neurol** 20:237–284, 1981.
3. Bowen M, Marks MP, Steinberg GK: Neuropsychological recovery from childhood moyamoya disease. **Brain Dev** 20:119–123, 1997.
4. Cahan LD: Failure of encephalo-duro-arterio-synangiosis procedure in moyamoya disease. **Pediatr Neurosci** 12:58–62, 1985.
5. Gibbs JM, Wise RJS, Leenders KL, Jones T: Evaluation of cerebral perfusion reserve in patients with carotid-artery occlusion. **Lancet** 1:310–314, 1984.
6. Imaizumi T, Hayashi K, Saito K, Osawa M, Fukuyama Y: Long-term outcome of pediatric moyamoya disease monitored to adulthood. **Pediatr Neurol** 18:321–325, 1998.
7. Iwama T, Hashimoto N, Yonekawa Y: The relevance of hemodynamic factors to perioperative ischemic complications in childhood moyamoya disease. **Neurosurgery** 38:1120–1126, 1996.
8. Johnson DW, Stringer WA, Marks MP, Yonas H, Good WF, Gur D: Stable xenon CT cerebral blood flow imaging: Rationale for and role in clinical decision making. **AJNR Am J Neuroradiol** 12:201–213, 1991.
9. Karasawa J, Kikuchi H, Furuse S, Kawamura J, Sakaki T: Treatment of moyamoya disease with STA-MCA anastomosis. **J Neurosurg** 49:679–688, 1978.
10. Karasawa J, Touho H, Ohnishi H, Miyamoto S, Kikuchi H: Long-term follow-up study after extracranial-intracranial bypass surgery for anterior circulation ischemia in childhood moyamoya disease. **J Neurosurg** 77:84–89, 1992.
11. Kijihara T, Ariga N, Yamamura A, Makino H, Maki Y: Familial occurrence of moyamoya disease: Report of three Japanese families. **J Neurol Neurosurg Psychiatry** 42:208–214, 1979.
12. Kim DS, Kye DK, Cho KS, Song JU, Kang JK: Combined direct and indirect reconstructive vascular surgery on the fronto-parieto-occipital region in moyamoya disease. **Clin Neurol Neurosurg** 99[Suppl 2]:S137–S141, 1997.

13. Kurokawa T, Tomita S, Ueda K, Narazaki O, Hanai T, Hasuo K, Matsushima T, Kitamura K: Prognosis of occlusive disease of the circle of Willis (moyamoya disease) in children. **Pediatr Neurol** 1:274–277, 1985.
14. Luroda S, Houkin K, Kamiyama H, Abe H, Mitsumori K: Regional cerebral hemodynamics in childhood moyamoya disease. **Childs Nerv Syst** 11:584–590, 1995.
15. Malek AM, Connors S, Robertson RL, Folkman J, Scott RM: Elevation of cerebrospinal fluid levels of basic fibroblast growth factor in moyamoya and central nervous system disorders. **Pediatr Neurosurg** 27:182–189, 1997.
16. Matsushima Y, Inaba Y: Moyamoya disease in children and its surgical treatment: Introduction of a new surgical procedure and its follow-up angiograms. **Childs Brain** 11:155–170, 1984.
17. Matsushima Y, Fujiwara S, Nagata S, Fujii K, Fukui K, Kitamura K, Hasuo K: Surgical treatment for paediatric patients with moyamoya disease by indirect revascularization procedures (EDAS, EMS, EMAS). **Acta Neurochir (Wien)** 98:135–140, 1989.
18. Matsushima T, Inoue T, Suzuki SO, Fujii K, Fukui M, Hasuo K: Surgical treatment of moyamoya disease in pediatric patients: Comparison between the results of indirect and direct revascularization procedures. **Neurosurgery** 31:401–405, 1992.
19. Miyamoto S, Kikuchi H, Karasawa J, Nagata I, Yamazoe N, Akiyama Y: Pitfalls in the surgical treatment of moyamoya disease: Operative techniques for refractory cases. **J Neurosurg** 68: 537–543, 1988.
20. Nariai T, Suzuki R, Hirakawa K, Maehara T, Ishii K, Senda M: Vascular reserve in chronic cerebral ischemia measured by the acetazolamide challenge test: Comparison with positron emission tomography. **AJNR Am J Neuroradiol** 16:563–570, 1995.
21. Nariai T, Suzuki R, Matsushima Y, Ichimura K, Hirakawa K, Ishii K, Senda M: Surgically induced angiogenesis to compensate for hemodynamic cerebral ischemia. **Stroke** 25:1014–1021, 1994.
22. Olds MV, Griebel RW, Hoffman HJ, Craven M, Chuang S, Schutz H: The surgical treatment of childhood moyamoya disease. **J Neurosurg** 66:675–680, 1987.
23. Rogg J, Rutigliano M, Yonas H, Johnson DW, Pentheny S, Latchaw RE: The acetazolamide challenge: Imaging techniques designed to evaluate cerebral blood flow reserve. **AJR Am J Roentgenol** 153:605–612, 1989.
24. Ross IB, Shevell MI, Montes JL, Rosenblatt B, Watters GV, Farmer JP, O'Gorman AM: Encephaloduroarteriosynangiosis (EDAS) for the treatment of childhood moyamoya disease. **Pediatr Neurol** 10:199–204, 1994.
25. Sakamoto T, Kawaguchi M, Kurehara K, Kitaguchi K, Furuya H, Karasawa J: Risk factors for neurologic deterioration after revascularization surgery in patients with moyamoya disease. **Anesth Analg** 85:1060–1065, 1997.
26. Sakamoto T, Kawaguchi M, Kurehara K, Kitaguchi K, Furuya H, Karasawa J: Post-operative neurologic deterioration following the revascularization surgery in children with moyamoya disease. **Neurosurg Anesth** 10:37–41, 1998.
27. Soriano SG, Sethna NF, Scott RM: Anesthetic management of children with moyamoya syndrome. **Anesth Analg** 77:1066–1070, 1993.
28. Suzuki J, Kodama N: Moyamoya disease: A review. **Stroke** 14: 104–109, 1983.
29. Suzuki Y, Negoro M, Shibuya M, Yoshida J, Negoro T, Watanabe K: Surgical treatment for pediatric moyamoya disease: Use of the superficial temporal artery for both areas supplied by the anterior and middle cerebral arteries. **Neurosurgery** 40:324–330, 1997.
30. Suzuki J, Takaku A, Kodama N, Sato S: An attempt to treat cerebrovascular 'moyamoya' disease in children. **Childs Brain** 1:193–206, 1975.
31. Touho H, Karasawa J, Ohnishi H, Yamada K, Shibamota K: Surgical reconstruction of failed indirect anastomosis in childhood moyamoya disease. **Neurosurgery** 32:935–940, 1993.
32. Wang MY, Steinberg GK: Rapid and near-complete resolution of moyamoya vessels in a patient with moyamoya disease treated with superficial temporal artery-middle cerebral artery bypass. **Pediatr Neurosurg** 24:145–150, 1996.
33. Yamashita T, Kashiwagi S, Nakashima K, Ishihara H, Kitahara T, Nakano S, Ito H: Modulation of cerebral hemodynamics by surgical revascularization in patients with moyamoya disease. **Acta Neurol Scand** 166[Suppl]:82–84, 1996.
34. Yasargil MG: Experimental small vessel surgery in the dog including patching and grafting of cerebral vessels and formation of functional and extra-intracranial shunts, in Donaghy RMP, Yasargil MG (eds): *Microvascular Surgery*. Stuttgart, George-Thieme, 1967, pp 87–126.
35. Yonas H, Smith HA, Durham SR, Pentheny SL, Johnson DW: Increased stroke risk predicted by compromised cerebral blood flow reactivity. **J Neurosurg** 79:483–489, 1993.
36. Yonekawa Y, Kawano T: Follow-up study of 632 cases in spontaneous occlusion of the circle of Willis registered from 1983 to 1991, in Yonekawa (ed): *The Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan: Annual Report 1991*. Osaka, Japan, National Cardiovascular Center, 1992, pp 41–47.

COMMENTS

Golby et al. summarize their experience in treating pediatric patients with moyamoya disease. Twelve patients (21 hemispheres) underwent direct revascularization, and six patients underwent concurrent indirect revascularization in the form of encephaloduroarteriosynangiosis or encephalomyosynangiosis. The clinical outcomes for these patients were impressive; with a mean follow-up period of 35 months, the conditions of all patients were stable or improved after surgery. The authors recommend direct anastomosis for treatment of pediatric patients with moyamoya disease. In our practice, for pediatric patients (more than 5 yr of age) with moyamoya disease, especially those with rapidly progressive disease, we usually perform combined direct and indirect revascularization, using all available branches of the external carotid artery to revascularize the ischemic brain tissue. The direct superficial temporal artery (STA)-middle cerebral artery (MCA) anastomosis establishes immediate flow to the ischemic territories, whereas the indirect procedures, although not immediately effective, permit neovascularization to develop over a larger area of the brain than observed with direct anastomosis.

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This article raises a number of important issues regarding the appropriate treatment for children with moyamoya disease. The authors present a detailed review of appropriate intraoperative, anesthetic, and hemodynamic care for these patients. Postoperative care is also detailed, and all of the considerations included can help to improve our understanding of the appropriate care for these children in the perioperative period.

In the past there has been the presumption that direct procedures cannot be performed in children. This was based not on the efficacy of the procedure in children but on the efficacy for all cases of moyamoya disease, in children or in adults. Indirect procedures were performed by the authors for very young children (those under 2 yr of age). Direct procedures in children of more than 5 years of age involved vessels that were more than 1 mm in diameter. Given the mass of the brains of children of at least 4 years of age, vessel caliber, compared with that of adults (for consideration of technical feasibility), is not necessarily a pediatric issue but is related to actual vessel diameter.

A weakness of the current study is the difficulty of a single institution accruing a large series of children with moyamoya disease in North America, compared with the much larger Asian series. Despite this, I agree that it is important to document our experiences in the literature, considering the heterogeneity of our patient population. The authors have documented the safety and efficacy of this technique, with results comparable to those of other larger series, based on the Matsushima rating scale.

Important questions remain regarding this series. An important consideration is the potential efficacy of cerebral blood flow (CBF) measurements in these children. Questions remain regarding the reliability of these studies in the presence of diffuse infarction and the relationship between postacetazolamide studies and actual-flow CBF studies. These studies cannot establish whether vasoregulatory systems actually remain intact. Finally, CBF studies do not establish which patients are optimal candidates for revascularization procedures (direct or indirect) and, furthermore, cannot answer the question of which patients are at greatest risk for potential stroke or require immediate surgery.

An important consideration in the treatment of moyamoya disease is that the outcomes for direct and indirect revascularization techniques are similar. The important difference is that the direct procedures are of immediate benefit, whereas indirect approach benefits are delayed. The angiograms in the current series document collateralization of scalp vessels and branches of the middle meningeal artery to the cerebrum, as is commonly noted after indirect procedures. Postoperative angiograms in the current study suggest that optimal results were obtained with combined procedures.

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This report is an excellent contribution to the literature on the surgical treatment of moyamoya syndrome in children. The article demonstrates that STA-MCA anastomosis can be used for certain children with moyamoya syndrome, to augment cerebral circulation, and it discusses the advantages and disadvantages of vessel anastomosis techniques in the pediatric population.

Performing these anastomoses in children is an accomplishment. Most STAs in children are far less than 1 mm in diameter; most of our patients have vessels with external diameters of less than 0.5 mm (as determined by actual operating room measurements). The actual measurements for the donor vessels used by the authors would therefore have been of great interest. To accomplish successful anastomoses using vessels of such small diameters requires great surgical skill; the authors even report the use of the middle meningeal artery for one of their anastomoses, which I had always thought was impossible. In addition, I have always been concerned that theflow through such small-diameter anastomoses would be inconsequential and that the multiple proximal stenoses present in most children with moyamoya syndrome would tend to minimize the vascular territory irrigated by the bypass. The authors have shown, at least for Patient 10, with good postoperative angiographic results, that extensive irrigation of the MCA territory through the anastomosis is possible in certain patients. However, considerable collateralization to the brain via the middle meningeal artery and other assorted scalp arteries in the vicinity of the craniotomy can be seen in the postoperative angiograms; this is a common finding after most revascularization procedures in this population.

This article makes a number of noteworthy points regarding the disease process itself. Virtually all patients with unilateral disease at presentation experience progression to bilateral disease; the authors noted this finding for one of their three patients with initially unilateral disease and, if only a single side is treated, patients require careful continual observation. One of their patients exhibited choreiform movements as part of the clinical presentation (we have observed this in several patients and presume that it must be related to basal ganglion ischemia or perhaps a mass effect from the hypertrophied moyamoya collateral vessels), and this symptom does respond quite well to revascularization. Postoperative aspirin therapy is extremely important in the treatment of these children, as demonstrated in this report for two patients whose transient ischemic attacks resumed when aspirin therapy was discontinued after surgery and resolved again when therapy was restarted. The Matsushima scale, which the authors used to evaluate their postoperative angiograms, was also used by our group to evaluate the postoperative collateral system seen after pial synangiosis, and our report (1) documents filling of the MCA territory after pial synangiosis (84% good to excellent on the Matsushima scale), similar to the results of the authors with direct bypass procedures.

The CBF data are quite interesting but, as the authors point out, may be difficult to interpret, particularly when there are relatively large areas of infarction or when there are changes in flow patterns after acetazolamide administration. Do changes in blood flow patterns with acetazolamide administration indicate that constriction of maximally dilated vessels has occurred, that the circulation of the patient is unstable, and that the patient is therefore a good candidate for revascularization? If there are no changes with acetazolamide and the patient is experiencing transient ischemic attacks, does that indicate that all vessels have lost their vasoreactivity or that the circulation is stable and all vessels are constricting equally? In other words, these tests are frequently open to variable interpretation and we have used them less frequently in the past few years, thinking that they have not been helpful in guiding surgical decisions.

The authors emphasize the surgical risks related to anesthesia alone for these patients; this is an excellent point, because a number of patients in our own series presented with strokes after general anesthesia for procedures unrelated to moyamoya syndrome. The authors stress the importance of careful intraoperative monitoring and hemodynamic management, a point also emphasized in a report on anesthesia from our institution (Ref. 27 in the article).

The authors correctly emphasize an important difference between the indirect and direct revascularization techniques. STA-MCA anastomosis may be preferred if it can establish immediate high flow to ischemic territories; the indirect procedures, such as pial synangiosis, may permit vessel ingrowth over a larger area than an anastomosis alone but are not immediately effective. I have always thought that an important factor for successful operations in these children is wide opening of the arachnoid membrane, which removes a barrier to the ingrowth of new collateral vessels and which is common to both procedures. We think that growth factors in the cerebrospinal fluid of these children almost certainly play a role in the success of such surgery for these patients (Ref. 15 in the article).

As a technical point, to avoid constriction of the donor artery, I have never closed the dura in patients undergoing STA-MCA anastomosis or in children undergoing pial synangioses, and we have not observed a significant cerebrospinal fluid leak in more than 185 surgical procedures. I do not think there is any need to even partially close the dura at the completion of these operations.

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1. Robertson RL, Burrows PE, Barnes PD, Robson DC, Poussaint TY, Scott RM: Angiographic changes following pial synangiosis in moyamoya syndrome. **AJNR Am J Neuroradiol** 18:837–845, 1997.

Golby et al. review their results with direct revascularization of 21 hemispheres affected by moyamoya disease in children of age 5 to 17 years. They report good neurological results, improvements in CBF (as determined by xenon computed tomography), and improvements in hemodynamic reserve.

The low incidence of perioperative morbidity in this series and in other series of direct revascularization procedures suggests that these procedures may be superior to indirect procedures such as encephaloduroarteriosynangiosis. However, some patients do not have donor or recipient vessels that are suitable for this type of direct procedure. For these patients, encephaloduroarteriosynangiosis is a suitable alternative procedure. The very good hemodynamic responses reported in this article provide new information suggesting that STA-MCA anastomosis is a safe and effective management approach for patients with pediatric moyamoya disease.

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