Direct Bypass Techniques for the Treatment of Pediatric Moyamoya Disease

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KEYWORDS

• Moyamoya disease • Pediatric • Direct bypass

INDICATIONS

Moyamoya disease (MMD) has been recognized as a devastating condition in adults and in pediatric patients. Large pediatric epidemiologic studies have shown that MMD is a significant contributor to childhood stroke. Independent studies in the American, Asian, and European literature found a pediatric stroke incidence between 2.1 and 13/100,000/y,[1–3] with MMD accounting for 6% of the ischemic strokes.[1,3] With an untreated morbidity estimated to be greater than 70%,[4] and with a 5-year risk of recurrent ipsilateral stroke of 65% in medically treated symptomatic hemispheres,[5] surgical intervention has become the standard of treatment of patients with MMD.[6–8] In children, the most common presentation is cerebral ischemia. In a study by Scott and colleagues of 143 pediatric patients diagnosed with MMD in North America, nearly all patients presented with either symptoms of stroke or transient ischemic attack (TIA).[9] Similarly, in large populations of Asian patients, approximately 40% of those less than 10 years of age presented with a TIA and nearly 30% presented with cerebral infarction,[10] although some presented with headaches and seizures. Similar findings were made in European studies.[4,11] In our series including 272 adult and 96 pediatric patients with MMD, we found stroke and TIA to be the most common presenting symptoms in the pediatric patients followed by headache, seizures, and rarely intracerebral hemorrhage (**Fig. 1**).[12]

The diagnostic guidelines for identifying patients with MMD differ in centers around the world. The Research Committee on MMD of the Ministry of Health and Welfare of Japan has identified 4 criteria necessary for the diagnosis of MMD: (1) stenosis or occlusion of the terminal portion of the internal carotid artery (ICA); (2) a coexisting abnormal vascular network in the base of the brain or basal ganglia; (3) bilaterality; and (4) no other identifiable cause.[13,14] These guidelines have been modified case by case at various institutions around the United States. Although classically bilateral, unilateral MMD can occur. Patients with the characteristic moyamoya vasculopathy who also have well-recognized associated conditions are categorized as having moyamoya syndrome, whereas patients with no known associated risk factors have MMD. In our series 21% of the children had unilateral disease. We have previously reported that 71% of patients with equivocal or mild stenotic changes in the initially unaffected side eventually progressed to bilateral MMD at a mean follow-up time of 12.7 months.[15]

In light of the findings describing a natural history with a devastating disease course,

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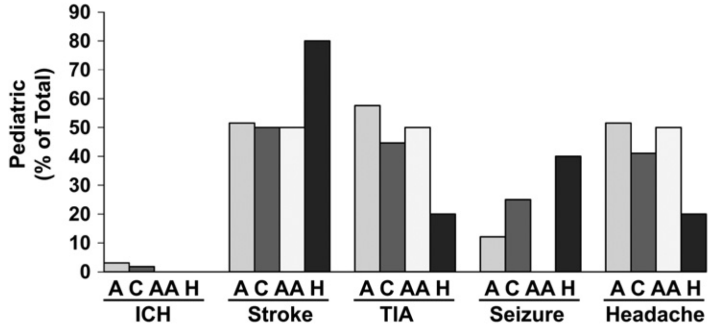

Fig. 1. Presenting symptoms in 96 pediatric patients consisting of intracerebral hemorrhage (ICH), stroke, TIA, seizures and headaches. Comparison between Asian (A), White (C), African American (AA), and Hispanic (H) patients did not reveal any statistically significant differences. Note that the high incidence of stroke in Hispanic pediatric patients is based on a small n. (*Data from* Guzman R, Lee M, Achrol A, et al. Clinical outcome after 450 revascularization procedures for moyamoya disease. J Neurosurg 2009;11(5):927–35.)

a poor response to medical therapy, and a good response to surgery, we strongly advocate surgical treatment of symptomatic pediatric patients with MMD. There is ongoing debate about the treatment of asymptomatic or incidentally discovered MMD. Because there are only limited data on the natural history of MMD in children, decision-making is complex. However, substantial evidence suggests inevitable disease progression and therefore close follow-up would be recommended. In our experience, careful history taking and physical examination often uncover signs and symptoms suggestive of cerebral hypoperfusion, such as recurrent TIAs. To avoid devastating strokes, early treatment is advocated.

PATIENT SELECTION

All patients undergo a detailed clinical assessment as part of the evaluation as a potential surgical candidate. In particular subgroups of patients with syndromes known to be associated with moyamoya, such as neurofibromatosis, Down syndrome, and primordial dwarfism, identifying comorbidities is essential. At our institution, we found a higher risk of postsurgical morbidities in patients with moyamoya syndrome compared with the rest of our cohort (odds ratio 4.16, $P = .09$[12]). Diagnosis of MMD is made based on angiography according to published guidelines.[13] All patients are evaluated with magnetic resonance (MR) imaging including diffusion-weighted imaging (DWI) and fluid attenuated inversed recovery imaging to assess the overall stroke burden. Acute strokes, as identified by diffusion-weighted MR imaging, have to be recognized, because they may put patients at a greater risk for perioperative strokes. The preoperative 6-vessel (including both external carotid arteries [ECAs], both ICAs, and 1 or both vertebral arteries) catheter angiography is important to determine the severity of the disease[16] and to evaluate the presence of the superficial temporal artery (STA) (**Fig. 2**). All patients undergo a cerebral blood flow analysis using MR imaging and single-photon emission computed tomography (SPECT) studies with and without acetazolamide (Diamox) challenge.

Surgical interventions for MMD have been divided into direct and indirect bypass techniques. The principal difference between the 2 strategies lies in the method of cerebral reperfusion. Whereas direct methods are believed to provide immediate flow increase in the affected areas of the brain, indirect methods aim to stimulate the development of a new vascular network over time. The arteriopathy of moyamoya affects the ICA and spares the ECA. Surgical treatment of moyamoya typically uses the ECA as a source of new blood flow to the ischemic hemisphere. Two general methods of revascularization are used: direct and indirect. In direct revascularization, a branch of the ECA (usually the STA) is directly anastomosed to a cortical artery. Indirect techniques involve the placement of vascularized tissue supplied by the ECA such as dura, temporalis muscle, or the STA itself in direct contact with the brain, leading to an ingrowth of new blood vessels to the underlying cortex. The direct bypass techniques that have been proposed include STA to middle cerebral artery (MCA), occipital artery to MCA, and middle meningeal artery[17] to MCA anastomoses. The indirect techniques include encephalomyosynangiosis (EMS), encephaloduroarteriosynangiosis (EDAS),[9,18,19]

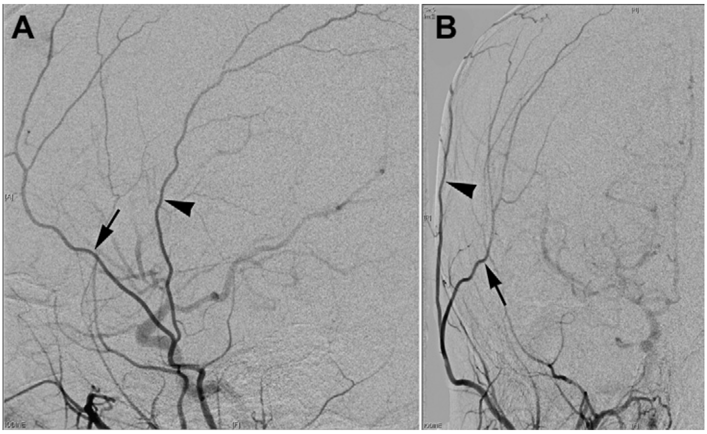

Fig. 2. Angiogram with injection of the ECA on the right side in the lateral (*A*) and anteroposterior view (*B*). Example of the STA splitting into a frontal (*arrow*) and parietal (*arrowhead*) branch.

encephaloduroarteriomyosynangiosis (EDAMS), encephalomyoarteriosynangiosis, multiple cranial bur holes,[4] and omental transposition.

There has not been a controlled randomized trial comparing direct and indirect revascularization techniques. Therefore, there are currently no data to support either direct or indirect revascularization techniques in the pediatric population with MMD.[20] Some investigators advocate that indirect techniques do not result in an immediate revascularization and may carry an increased risk for postoperative stroke.[18,21] Thus, it has been suggested to combine direct and indirect techniques to take advantage of immediate revascularization with the security of more diffuse neovascularization.

We advocate the use of direct bypass techniques when possible. In our pediatric series of 96 patients 67% received a direct bypass. The strongest predictor of the feasibility of a direct bypass was the age at surgery.[12] The mean age of pediatric patients undergoing indirect surgery was 6.5 years, whereas it was 11.2 years in children undergoing direct surgery ($P<.05$) (**Fig. 3**). The youngest child to receive a direct bypass was 4.3 years old.[12] The presence of the STA has to be confirmed on cerebral angiogram. However, we found that a small STA on angiogram does not necessarily preclude a direct bypass approach. Generally we consider a direct bypass possible if the STA and the MCA are 0.6 mm or greater.

At our institution, it is our practice to operate on the most symptomatic side first. If both hemispheres are symptomatic, we revascularize the right side first. In bilateral MMD, the second side is usually revascularized 1 week after the first surgery if tolerated by the patient.

OVERVIEW OF TECHNIQUE

All surgeries are performed under mild hypothermia with a target core temperature of 33°C. Cooling is achieved either with surface cooling using a cooling blanket or through placement of an intravenous catheter (Innercool Therapies, San Diego, CA, USA) into the inferior vena cava as described earlier.[17] The Innercool method is applicable only in older children and adults. Patients are monitored intraoperatively with somatosensory evoked potentials and electroencephalography (EEG). The patients are positioned supine with a shoulder role on the side ipsilateral to the surgery and fixed in a Mayfield 3-pin head

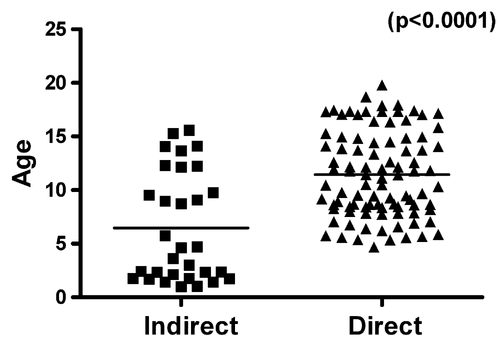

Fig. 3. Mean age at surgery of 96 patients undergoing either indirect or direct revascularization surgery. Patients undergoing an indirect bypass were significantly younger than patients undergoing a direct bypass ($P<.0001$).

clamp. Starting in front of the tragus within the hairline the STA is mapped for 7 to 8 cm. The size of the frontal and parietal branch of the STA is determined on the ECA angiography and the decision is made whether the frontal or parietal branch is to be used based on artery diameter. The STA is prepared under the surgical microscope, leaving an approximately 8-mm tissue cuff around the vessel (**Figs. 4–6**). A 4 × 4-cm craniotomy is performed over the sylvian fissure and the size of the M4 branches of the MCA evaluated at high magnification. The largest M4

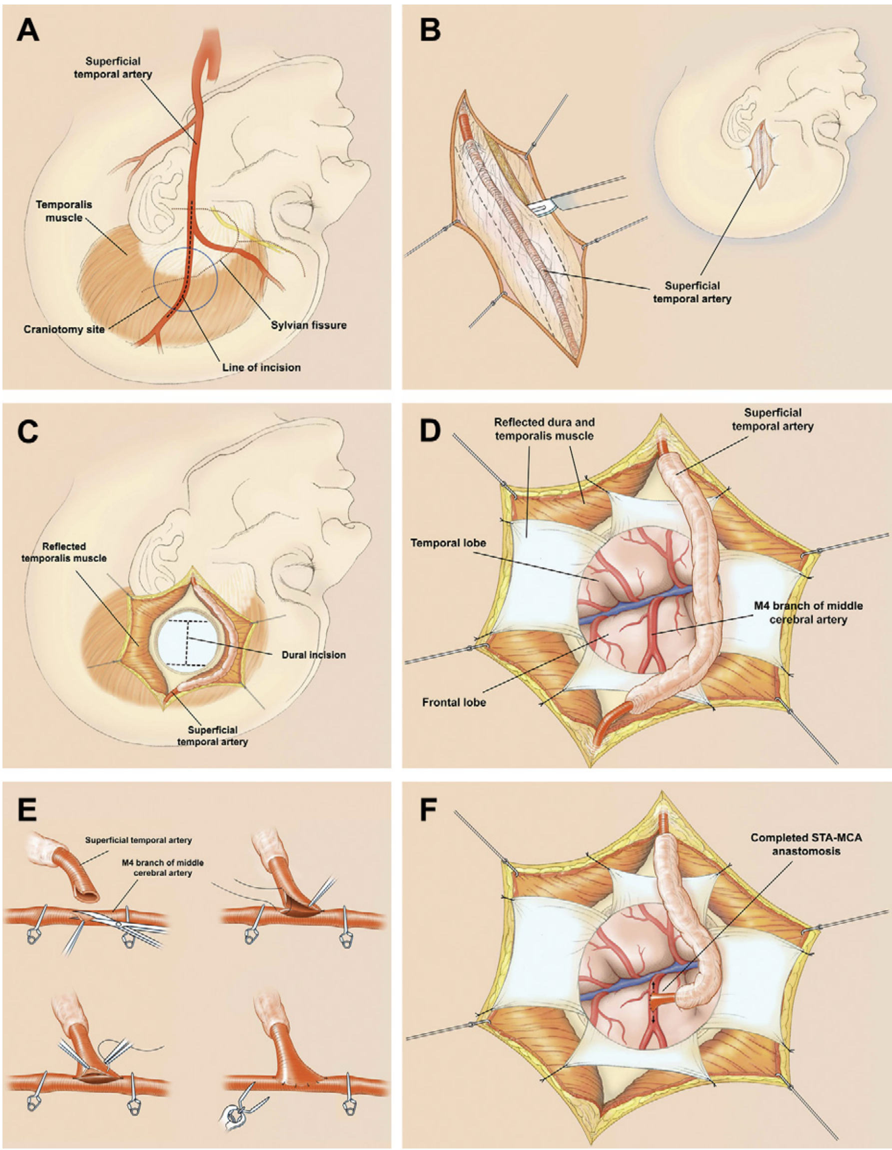

Fig. 4. Each step of the direct bypass surgery. Starting in front of the tragus within the hairline the STA is mapped for 7 to 8 cm (*A*). The STA is prepared under the surgical microscope, leaving an approximately 8-mm tissue cuff around the vessel (*B*). A 4- × 4-cm craniotomy is performed over the sylvian fissure (*C*) and the size of the M4 branches of the MCA evaluated at high magnification (*D*). The largest M4 branch is chosen as recipient. The STA is fishmouthed and the wall of the MCA cut using microscissors, removing a tiny elliptical piece of the superior wall (*E*). Under high magnification a bypass between the STA and MCA is performed using 10.0 interrupted sutures (*E*). After completing the direct anastamosis, the STA with its cuff of soft tissue is laid on the cortical surface to induce an additional indirect revascularization (*F*).

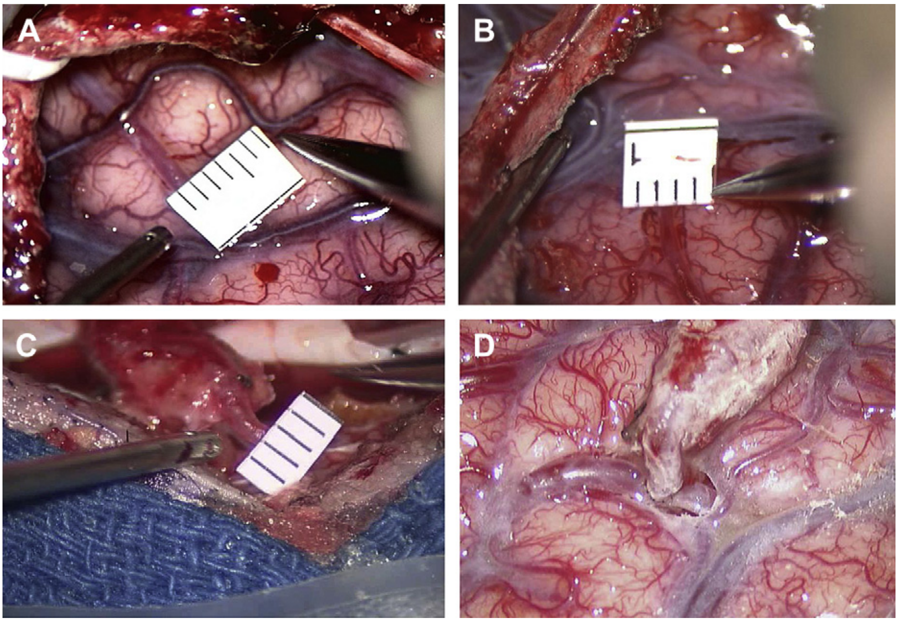

Fig. 5. Intraoperative view of a 1-mm (*A*) and 0.6-mm (*B*) M4 branch of the MCA on the cortical surface. Example of a 1-mm STA at its distal end, prepared for anastomosis (*C*). Completed STA-MCA bypass (*D*).

branch is chosen as recipient. In patients in whom either the STA or the MCA were considered too small (<0.6 mm) or too fragile for a direct bypass, indirect revascularization procedures, such as EDAS, are performed.

The flow within the STA and the MCA are measured with microflow Doppler (Transonic Systems Inc, Ithaca, NY, USA). The STA is fish-mouthed and the wall of the MCA cut using micro-scissors, removing a tiny elliptical piece of the superior wall. Before and during clamping the patient is given thiopental to achieve burst suppression on the EEG. Under high magnification a bypass between the STA and MCA is performed using 10.0 interrupted sutures (see **Figs. 4** and **5**). After completing the direct anastamosis, the STA with its cuff of soft tissue is laid on the cortical surface to induce an additional indirect revascularization (see **Figs. 4** and **5**). Again the flow Doppler is used to measure flow velocities in the proximal and distal MCA as well as the STA.

After surgery patients are kept in the intensive care unit overnight with a tight blood pressure control, usually a mean arterial pressure between 70 and 80 mm Hg for children or 10 mm Hg above their baseline. Aspirin (81 mg) is started the day after surgery. MR imaging including DWI is performed the day after the second surgery to exclude new strokes. Patients are usually discharged 3 to 4 days after surgery.

OUTCOME

The independent use of a direct STA-MCA bypass in pediatric patients with MMD has rarely been reported in the literature. Results of studies performing direct STA-MCA bypasses in children are shown in **Table 1**. Previously, we described the outcomes of direct STA-MCA bypass and STA-MCA + EDAS in a pediatric population.[18] In a group of 12 patients, 21 hemispheres were treated with direct bypass techniques. Concomitant EDAS was applied in 6 hemispheres by using a second branch of the STA, 1 patient underwent MMA-MCA anastomosis plus EDAS, and 1 patient underwent omental transposition. Outcomes in this population included a global reduction in preoperative symptoms and no perioperative strokes. Some patients experienced transient perioperative neurologic symptoms that the investigators attributed to possible impaired autoregulation of the cerebral vasculature. Cerebral blood flow analysis in many of these patients revealed increased flow in 68 of the 76 regions as identified by SPECT. Sakamoto and associates[27] altered the direct bypass technique by including a double STA-MCA anastomoses and EMS. Specifically, the frontal and parietal branches of the STA were harvested as donor vessels for the recipient MCA. The study included 20 pediatric hemispheres, and the combined

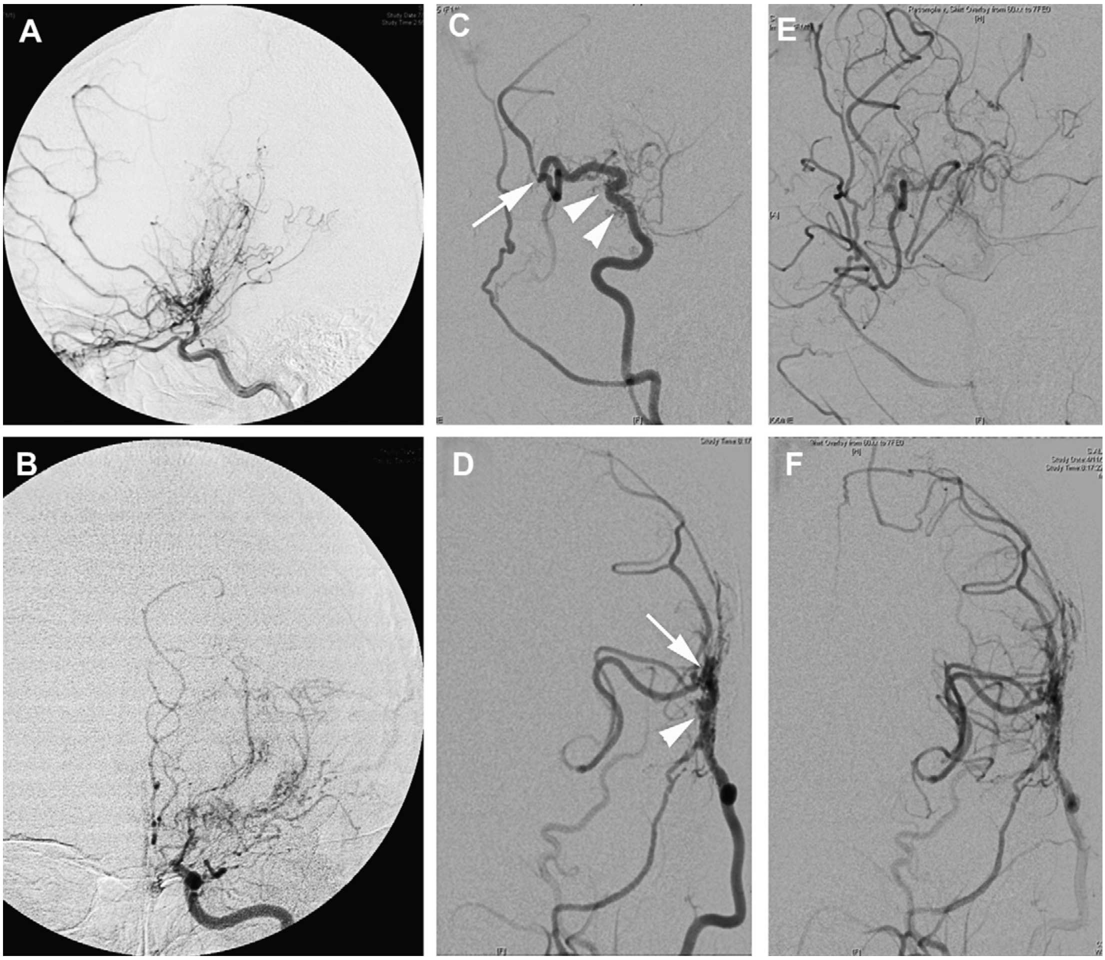

Fig. 6. Angiogram of a patient with severe MMD and completed STA-MCA bypass. The lateral (*A*) and anteroposterior (*B*) ICA injections show occlusion of the supraclinoid segment of the carotid artery with development of moyamoya vessels. Injection of the ECA after bypass surgery shows a robust STA in the lateral (*C*) and anteroposterior (*D*) view with some indirect revascularization (*arrowhead*) proximal to the anastomosis (*arrow*). In the later angiographic phase a robust arterial filling from the graft is noted (*E, F*).

procedure was undertaken in 19. Results from the study showed that of the 38 completed anastomoses, 37 maintained patency on angiography at the 1- to 2-month follow-up. Clinical outcome mirrored radiographically proven success; none of the 10 patients showed any significant ischemic episodes, disease progression, or the development of mental retardation at a mean follow-up of 4 years (range 1–10 years).

In our overall adult and pediatric series we found an excellent long-term patency of the direct bypasses of 98% at a mean angiographic follow-up of 1.5 years.[12] The overall surgical morbidity among pediatric patients was 1.8% per procedure or 3.1% per patient.[12] One patient with mitochondrial encephalopathy with lactic acidosis and strokelike episodes died 10 days after the bypass procedure as a result of multiple strokes, leading to a 1% mortality.[32] There was no statistically significant difference in postoperative morbidity or mortality between children undergoing direct versus indirect revascularization. In the long-term outcome analysis with a mean follow-up time of 4.8 years (median 3 years) no patients suffered a new clinical stroke or hemorrhage among the pediatric population. The combined overall adult and pediatric 5-year risk of recurrent stroke or hemorrhage after bypass surgery was 5.5% in our series.[12]

Table 1
Results of studies on direct STA-MCA bypasses in children

Authors	Year	Country	Intervention	Number of Children (Hemispheres)	Outcome
Matsushima et al[22]	1992	Japan	STA-MCA+EMS or EDAS	16 (20)	Complete resolution of symptoms in 3 of 13 (23%) with EDAS and in 7/7 100% with STA-MCA+EMS (*P*<.01)
Mizoi et al[23]	1996	Japan	STA-MCA+EMS, (+EDAS)	23	Moderate to poor filling with direct bypass compared with good to moderate with indirect method
Suzuki et al[24]	1997	Japan	STA-MCA+EDAS or EMS or BH	36	Frequency of TIAs reduced/resolved within 1 year in 25 of 31 (81%) patients
Ishikawa et al[25]	1997	Japan	STA-MCA+EDAMS or EDAMS	34 (64)	Incidence of postoperative ischemia significantly reduced in the combined group (10%) versus indirect group (56%; *P*<.01)
Iwama et al[26]	1997	Japan	STA-ACA and/or STA-MCA	5	TIAs resolved in 4 patients and reduced in 1 patient
Sakamoto et al[27]	1997	Japan	Bilateral, double STA-MCA+ EMS	10 (19)	All patients were free of significant ischemic episodes, disease progression, and MR
Miyamoto et al[28]	1998	Japan	STA-MCA and/or EMS	113	Resolution of stroke in 110 (97.3%) of 113 patients. Independent lifestyle achieved in 100/113 (88.5%) patients
Golby et al[18]	1999	United States	STA-MCA or STA-MCA+ EDAS or MMA-MCA+EDAS	12 (21)	No perioperative strokes, global reduction of preoperative symptoms, and improved cerebral blood flow
Houkin et al[29]	2000	Japan	STA-MCA or EDAMS	34	Patency of direct bypass verified in 15 sides (53%) versus indirect procedure yielded neovascularization in > 90%
Khan et al[11]	2003	Switzerland	STA-MCA and STA-ACA	19 (35)	No perioperative strokes, stabilization of disease in all patients, and cognitive improvement in 6 of 19 patients
Kim et al[30]	2007	Korea	STA-MCA+EDAMS or EDAS or EDAMS	7 (12)	EDAMS/STA-MCA-EDAMS radiographically superior, all indirect techniques had same clinical outcome
Czabanka et al[31]	2009	Germany	STA-MCA and EMS	10 (20)	Improvement of disease in 14 and stable disease in 6 hemispheres. Moderate to good filling in all EMS at last angiography
Guzman et al[12]	2009	United States	STA-MCA+EDAS or EDAS	96 (168)	No difference in morbidity between 113 direct bypass and 55 indirect revascularization surgeries. Excellent long-term outcome

SUMMARY

Moyamoya is an increasingly recognized cause of stroke in children and adults. Identification of the disease early in its course with prompt institution of therapy is critical to providing the best outcome for patients. Revascularization surgery seems to be effective in preventing stroke in moyamoya, with direct techniques providing durable protection when performed at experienced centers.

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