Moyamoya disease is a progressive, occlusive disease of the distal ICAs associated with secondary stenosis of the circle of Willis. The associated tuft of collateral vessels that forms at the base of the skull gives the angiographic appearance of a hazy “puff of smoke,” or “moyamoya” in Japanese. First described in 1957 by Takeuchi and Shimizu, the disease was initially thought to be endemic only to Japan and Asia. The disease, however, is also present in Europe and the Western hemisphere, although at a much lower prevalence. The classic presenting symptoms are intracerebral hemorrhage in adults and ischemic strokes in children. The exact cause of MMD has yet to be elucidated, and the natural history of the disease is often debilitating. Furthermore, the chronic vasculopathy tends to be unresponsive to standard medical therapy. Direct and indirect bypass techniques have been devised with the goals of promoting neoangiogenesis, inducing collateral vessel formation, and restoring perfusion to oxygen-deprived areas of the brain (Table 1). The direct techniques can immediately augment the blood supply as well as promote neoangiogenesis. Results from surgical intervention have been mixed. Overall, however, the response to surgical treatment appears to be favorable, particularly in decreasing recurrent ischemic events. This article reviews the major surgical options available for the treatment of MMD.

Surgical Options

Superficial Temporal Artery-to-Middle Cerebral Artery Bypass

In 1967, soon after the advent of microsurgical tools, Yaşargil and Donaghy performed the first direct extracranial-to-intracranial revascularization for the treatment of cerebral ischemia. In 1973, Kikuchi and Karasawa performed...
used STA-MCA bypass specifically for the treatment of MMD. After the frontal or parietal branch of the STA is identified and dissected, a frontotemporal craniotomy is performed over the sylvian fissure, and the dura mater is incised to identify the MCA or another recipient branch (Fig. 1). The donor artery is cut obliquely, and the 2 vessels are anastomosed. The arterial intima is included in each stitch. Closure of the dura, bone flap, and scalp must be loose enough to avoid undue pressure on the new graft.

Overall, the rate of patency for this procedure is considered excellent. In one study, it was as high as 91% at long-term follow-up.\(^2\) When the diameter of the STA is too small for direct anastomosis, the occipital artery can be considered as a donor artery, or an indirect revascularization procedure can be considered.\(^3\)

Superficial temporal artery-to-MCA bypasses have been associated with good clinical outcomes, particularly in diminishing the incidence of recurrent ischemic events.\(^2\) Marcinkevicius et al.\(^2\) reported on 14 patients with MMD treated at a single institution. They performed a direct STA-MCA anastomosis in 6 patients who presented with cerebral ischemia. Over a mean follow-up of 36 months, neither recurrent ischemia nor new hemorrhages were observed. The bypass graft was deemed patent in all patients by transcranial Doppler ultrasonography, and SPECT showed notable improvement in cerebral perfusion. In a study of 39 patients with MMD who were treated surgically over 14 years, Mesiwala et al.\(^2\) demonstrated significantly improved hemispheric perfusion after about 43 months. Most patients underwent direct bypass.

Direct revascularization has been associated, however, with significant complications, including the risk of intra- or perioperative ischemic injury due to temporary arterial occlusion, anesthesia, and blood pressure fluctuations as well as seizures. Immediately after surgery, this technique increases CBF, which can cause symptomatic hyperperfusion in some adults.\(^5\) This sudden increase in CBF could contribute to the transient neurological deterioration found in 17–27.5% of patients after the procedure.\(^5\) Finally, several studies indicate that surgical revascularization may accelerate progressive stenotic changes of the ICA in the presence of MMD.\(^1\)

In their treatment of MMD, Mesiwala et al.\(^2\) reported postoperative complication and mortality rates of 12.3 and 4.6%, respectively. Notably, 86% of the procedures in

### TABLE 1: Case series involving surgical options for treatment of moyamoya disease

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>No. of Patients</th>
<th>Principal Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesiwala et al., 2008</td>
<td>39</td>
<td>STA-MCA bypass in 86% of ops</td>
</tr>
<tr>
<td>Tripathi et al., 2007</td>
<td>8</td>
<td>EDAS</td>
</tr>
<tr>
<td>Kim et al., 2007</td>
<td>17</td>
<td>EDAMS or EDAS</td>
</tr>
<tr>
<td>Sainte-Rose et al., 2006</td>
<td>14</td>
<td>multiple cranial bur holes in pediatric cases</td>
</tr>
<tr>
<td>Marcinkevicius et al., 2006</td>
<td>14</td>
<td>STA-MCA bypass</td>
</tr>
<tr>
<td>Scott et al., 2004</td>
<td>143</td>
<td>EDAS w/ modified pial synangiosis technique</td>
</tr>
<tr>
<td>Gerber &amp; Spetzler, 2002</td>
<td>1</td>
<td>multiple cranial bur holes after failed bilat EDAS</td>
</tr>
<tr>
<td>Isono et al., 2002</td>
<td>11</td>
<td>EDAS or EMS in pediatric cases</td>
</tr>
<tr>
<td>Irikura et al., 2000</td>
<td>13</td>
<td>EMS w/ temporalis muscle grafts</td>
</tr>
<tr>
<td>Yoshioka &amp; Tomimura, 1998</td>
<td>3</td>
<td>EMS w/ latissimus dorsi or serratus anterior muscle grafts</td>
</tr>
<tr>
<td>Houkin et al., 1996</td>
<td>47</td>
<td>EDAMS or STA-MCA bypass</td>
</tr>
<tr>
<td>Kawaguchi et al., 1996</td>
<td>10</td>
<td>multiple cranial bur holes</td>
</tr>
<tr>
<td>Touho et al., 1996</td>
<td>5</td>
<td>omental graft in pediatric cases after failed direct &amp; indirect procedures</td>
</tr>
<tr>
<td>Kinugasa et al., 1993</td>
<td>17</td>
<td>EDAMS</td>
</tr>
<tr>
<td>Karasawa et al., 1993</td>
<td>30</td>
<td>omental graft to areas of the anterior &amp; posterior cerebral arteries</td>
</tr>
<tr>
<td>Havlik et al., 1992</td>
<td>1</td>
<td>omental graft in patient w/ failed STA-MCA bypass</td>
</tr>
<tr>
<td>Endo et al., 1989</td>
<td>6</td>
<td>multiple cranial bur holes in pediatric cases</td>
</tr>
<tr>
<td>Fujita et al., 1986</td>
<td>10</td>
<td>EDAS &amp;/or EMS</td>
</tr>
<tr>
<td>Andrews et al., 1985</td>
<td>63</td>
<td>STA-to-MCA bypass for patients w/ MCA occlusion</td>
</tr>
<tr>
<td>Takeuchi et al., 1983</td>
<td>10</td>
<td>EMS w/ temporalis muscle grafts</td>
</tr>
</tbody>
</table>

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**Fig. 1.** Illustration of direct STA-MCA bypass. Used with permission from Barrow Neurological Institute.
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their case series were direct revascularizations. In a series of 63 cases involving patients treated for MCA occlusion with an STA-MCA anastomosis alone, the overall surgical morbidity rate was 9.2%. The indirect EMS technique also has disadvantages. First, it requires a larger craniotomy and dural opening than an STA-MCA bypass. Postoperative complications have included seizures and significant mass effect. Touho reported a 14-year-old girl admitted with transient paralysis of the left side of her face and upper extremity 6 years after undergoing EMS surgery. Magnetic resonance imaging and CT showed that the cerebrum was compressed under a hypertrophied and ossified temporalis muscle graft, causing symptomatic ischemia and necessitating graft removal.

**Encephalomyosynangiosis**

Several factors led to the development of indirect revascularization techniques for the treatment of MMD. These factors included the technical difficulty associated with a direct STA-MCA bypass as well as the accessibility and small size of the STA (especially in children). These indirect procedures tend to be less invasive, take less operative time, and do not necessarily restrict the surgeon to the distribution of the MCA alone. Moreover, they do not require the temporary clamping of large arteries and can be used when no acceptable donor or recipient artery is available.

Encephalomyosynangiosis involves placing a section of temporalis muscle directly over the underlying cerebral cortex after the arachnoid layer has been removed. The dural flap is then closed and sutured back in place over the muscle (Fig. 2). Over time, collateral vessels form between the blood-rich muscle and ischemic neural tissue. Care must be taken to ensure that the inflow vessels of the transplant are maintained. This technique is associated with a lower risk for severe complications than direct anastomosis, but it does not immediately increase blood flow to ischemic areas of the brain. The process of angiogenesis may take several weeks or months before revascularization from the deep temporal artery is sufficient.

Takeuchi et al. treated 10 pediatric patients with signs of cerebral ischemia without intracranial hemorrhage with temporal muscle grafts. Transient ischemic attacks were halted completely in 4 of 7 patients and decreased significantly in the remaining 3. Along with promoting angiogenesis, the procedure can also significantly affect the preexisting abnormal vessels of patients with MMD. Encephalomyosynangiosis performed on 13 patients (24 sides) provided significant revascularization (more than a third of the MCA distribution) in 75% of the cases. In most of this subset of successfully treated patients, the number of pathological basal collateral vessels and medullary arteries decreased. In adults with MMD, the medullary arteries are thought to be a source of intraventricular hemorrhage.43

In 1980 encephaloduroarteriosynangiosis (EDAS) was introduced as a surgical option for the treatment of MMD. About the same time Špetzl et al. found that simply placing the STA near the cerebrum was sufficient to promote angiogenesis and to reduce recurrent ischemic attacks. This procedure was based on the premise that the vascular dura supplied by the middle meningeal artery could readily form collateral vessels with the cerebral cortex and scalp and that it was more inclined to do so in MMD.

The EDAS procedure entails suturing a galeal cuff with the intact STA onto the cortical surface once the dura has been removed. The integrity of the STA is maintained; the vessel is not harvested as in the direct bypass technique. In some variations of EDAS, a portion of dura is simply inverted or split into both its layers to encourage neovascularization.

Matsushima et al. first used EDAS to treat a 9-year-old boy with hemiparesis, seizures, and “immature behavior.” A 6-month follow-up angiogram showed good revascularization with clinical improvement and no complications. Tripathi et al. also demonstrated good outcomes with EDAS. During a 2-year follow-up period, no stroke or transient ischemic attack was observed in 8 children with symptomatic MMD selected for EDAS. Using the Weschler Adult Intelligence Scale to test a separate group of EDAS-treated patients, Matsushima et al. found that patients had a normal mean intelligence quotient 9.5 years after the operation. Given that MMD patients routinely lose cognitive function over time, this finding was significant.

Isono et al. investigated the long-term outcome in 11 cases involving children treated with EDAS, EMS, or both procedures concurrently. Although the sample was small, significantly better revascularization was associ-
ated with EDAS (92% of patients showed improvement) than with EMS (50% of patients improved). Fujita et al. performed a similar comparison in 10 patients. Both EMS and EDAS were used in 7 patients who underwent one operation on each side (that is, EMS on one side and EDAS on the other). The remaining 3 patients underwent bilateral EDAS. Revascularization from the external carotid artery was better in areas involved in EDAS than with EMS.

Smith and Scott introduced a slight technical modification termed pial synangiosis. In this procedure, the dural flaps are created and the arachnoid is removed in the region of the dural opening. The authors believed that this layer served as a barrier to the ingrowth of vessels and that once cleared away, the adventitia of the donor vessel could be sutured directly to the pia. Although the dura was left unsealed, only one cerebrospinal fluid (CSF) leak was reported in more than 200 pediatric patients. Of 143 pediatric MMD patients who underwent this modified procedure in another study, only 3.2% had strokes after 1 year compared with 67% preoperatively.

A combination of EMS and EDAS known as encephalomyoarteriosynangiosis (EMAS) has been proposed. Rather than using a piece of muscle alone, a superficial branch of the STA is placed along with the muscle graft. The efficacy of this procedure is not yet well established. In a study of 12 pediatric patients, those treated with frontal EMAS in combination with EMS and EDAS fared better than those treated with EDAS alone.

The EDAS data from a number of studies have been encouraging, but the procedure still has disadvantages. As with all indirect revascularization procedures, months can be required for development of adequate collateral circulation and symptom relief. Furthermore, if results are unsatisfactory, the use of the STA graft in EDAS can preclude a direct STA-MCA bypass from being performed ipsilaterally in the future.

Encephaloduroarteriomyosynangiosis

In 1984 the encephaloduroarteriomyosynangiosis (EDAMS) procedure was proposed to combine aspects of all the indirect revascularization procedures. It involves the placement of temporalis muscle, a segment of the STA, and a section of galeal flap directly over the ischemic cerebrum. Unlike other procedures, in EDAMS the middle meningeal artery is also used to promote angiogenesis. While still attached to a fascial cuff, branches of the STA are identified and removed. A portion of the temporalis muscle is then excised, and a craniotomy is performed. Several leaflike cuts are made in the dura, and the dural flaps are then folded inward to contact the cortical surface of the brain. Next, the STA, galea, and temporalis muscle are sutured together and attached to the free dural edges.

In a slightly modified version of EDAMS developed by Ozgur, a large dural window is created, and the resulting dural flap is excised completely. Small incisions are made in the cerebral cortex with a small scalpel, while vascular structures are avoided. The STA and muscle grafts are then reattached. Ozgur and colleagues reported encouraging results from 10 years of experience with this adapted procedure.

Kim et al. compared angiographic and clinical differences in 12 pediatric patients with MMD who underwent EDAS and 5 who underwent EDAMS. The most extensive collateral formation was observed in the patients undergoing EDAMS. Even when compared with a combined operation of EDAMS plus an STA-MCA bypass, EDAMS alone provided sufficient CBF. This angiographic finding, however, failed to correlate with clinical outcomes.

Kinugasa and colleagues treated 17 patients (28 sides) with confirmed MMD with EDAMS. Based on their postoperative neurological status, 13 patients had good or excellent surgical outcomes. Three patients had fair or poor outcomes—either their status was unchanged or their presenting symptoms worsened. The authors then reviewed cases involving patients treated with EDAS at their institution before 1984. The more recent EDAMS procedure was associated with a higher ratio of extensive collateral vessels and better clinical gains than earlier treatments.

Compared to direct microanastomosis, EDAMS may be better suited for pediatric patients with MMD. Houkin et al. studied patients with MMD treated with STA-MCA bypass or EDAMS after an intracerebral hemorrhage. In adults, direct revascularization was significantly more effective than indirect revascularization (100% of patients treated with a direct bypass had a good outcome compared with 38% treated with EDAMS). In the subset of children studied, however, the results were the opposite. Only 68% of patients had a good outcome after an STA-MCA bypass compared with 100% of patients treated with EDAMS. The authors attributed this finding that indirect revascularization is less effective in adults to the less severe cerebral ischemia found in adults (with severe ischemia being key for new vessel formation) and to the relative abundance of fibroblast growth factor in pediatric CSF. (Fibroblast growth factor is a cytokine that is considered important in inducing neovascularization in moyamoya disease.) Both factors could contribute to the heightened neoangiogenesis in pediatric patients after indirect revascularization.

Omental Transplant

Based on promising studies in canine models, Goldsmith et al. first proposed the technique of omental transposition for the treatment of cerebral ischemia in 1973. Grafts of the fatty layer that sits atop the peritoneal organs were known to reduce edema and fibrosis in the central nervous system. Based on this information, Karasawa et al. performed one of the first omental transplants in 1978 in a quadriparetic and blind 56-year-old woman with stenosis of the distal ICA and proximal anterior cerebral and middle cerebral arteries. The procedure consisted of omental transplantation over the cortex with end-to-end anastomosis of the STA and vein to the respective gastroepiploic vessels. Although her blindness persisted, the patient was ambulatory with assistance and free of ischemic events over the next 2 years.

The highly vascular omentum can be tunneled subcu-
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![Image: Illustration of bur hole technique: the dura within the bur hole is carefully incised and cauterized.]

Touho et al.45 performed an omental transplant in 5 pediatric patients with MMD who had already been treated unsuccessfully with EMS, EDAS, or an STA-MCA bypass. After their failed operations, many of the children still showed signs of progressive mental retardation, urinary incontinence, and paraparesis. By using the STA branch from the prior EDAS, the authors successfully attached an omental graft to the ischemic brain. After several months all 5 patients experienced almost complete resolution of their neurological deficits. Havlik et al.31 reported another case of successful omental pedicle graft after a prior direct STA-MCA anastomosis failed to alleviate the patient’s symptoms. At a 2.5-year follow-up examination, the patient’s condition had improved dramatically.

Karasawa et al.30 studied 30 pediatric patients with MMD for 4 years. All received an omental graft to the distribution of either the posterior cerebral or anterior cerebral artery. Postoperatively, all 19 patients undergoing the anterior treatment and 12 of 13 patients undergoing the posterior treatment demonstrated neurological improvement. The number of newly formed collateral vessels and patients’ rates of recovery were directly correlated.

Cranial Bur Holes

Although both direct and indirect revascularization methods improve clinical symptoms in patients with MMD, these techniques do not promote adequate revascularization of the territories of the anterior or posterior cerebral arteries. In 1984 Endo et al.2 advanced the notion that bur holes alone promote neovascularization. This concept was based on the serendipitous finding 2 years earlier of neovascularization in the region of frontal bur holes placed for ventriculostomies for the treatment of intraventricular hemorrhage. The patient treated by Endo et al. was a 10-year-old boy who underwent bilateral EMS in addition to having frontal bur holes placed. Care was taken to open the dura and to strip the arachnoid to allow newly formed vessels to reach the brain (Fig. 3). Follow-up angiography demonstrated neovascularization at both the EMS and bur hole sites. After this success, a similar surgery was scheduled for a 12-year-old girl, who also had a good outcome. Further investigation by the authors revealed that occipital bur holes could be used to revascularize the posterior cerebrum.

Sainte-Rose et al.32 placed multiple bur holes in 14 children with MMD. Depending on the extent of the disease, 10–24 bur holes were made in each hemisphere. Postoperative perfusion MR imaging showed that cortical perfusion was restored as soon as 3 months later. The finding was confirmed by angiographic studies performed 8 and 12 months thereafter. None of the patients had further ischemic attacks. Of the 18 procedures, 5 were complicated by pseudomeningoceles that resolved with tapping and compressive head dressings. A lumbar drain was needed in only 1 of those cases.

Kawaguchi et al.21 reinforced the efficacy of this relatively simple technique, showing that neovascularization as seen on angiograms 6 months postoperatively was associated with 41 of 43 bur holes. The presenting symptoms such as transient ischemic attacks improved markedly in all 10 patients studied. Moreover, patients exhibited an increased sensitivity to acetazolamide during a postoperative SPECT study.

Gerber and Spetzler7 reported the case of a 12-year-old girl initially evaluated for bitemporal headache, upper extremity numbness, and difficulty speaking. After MMD was confirmed by cerebral angiography, the patient underwent successful bilateral EDAS and was clinically stable for 2 years. Her symptoms, however, returned, and tests revealed poor perfusion to her right hemisphere. One year after the placement of 6 bur holes on each side of the cranium, angiogenesis was observed at each surgical site. Patients can undergo this procedure under local anesthesia. Therefore, the placement of multiple bur holes is associated with a relatively low risk of perioperative complications and is less complex than its more invasive surgical counterparts. In some cases, multiple bur holes may be placed as an adjunct to other treatments for MMD.
Conclusions

The most appropriate revascularization procedure for patients with MMD is not yet well defined. Nonetheless, ample evidence suggests that surgical intervention improves the outcomes of patients with symptomatic MMD.

Each procedure has clear advantages and disadvantages. Direct revascularization may lead to immediate improvement of symptoms. In particular, direct bypass decreases the short-term rate of recurrent ischemic events. Bypass, however, is technically demanding and can be associated with devastating hemorrhages. Nevertheless, direct bypasses remain the procedure of choice for patients with uni- or bilateral symptomatic MMD.

The pediatric population is typically treated with indirect revascularization for 2 reasons: 1) The likelihood of angiogenesis is higher in children than in adults. 2) A direct bypass is technically challenging. In addition, performing an anastomosis with very small vessels carries a greater risk of thrombosis of the donor graft or recipient artery. However, collateral formation and angiogenesis take longer to develop after indirect revascularization compared with direct revascularization. Furthermore, indirect revascularization may preclude the option of subsequent direct bypass if the STA is used or compromised.

Direct and indirect revascularization will continue to play a major role in the treatment of MMD. The choice of procedure appears to depend on the surgeon’s comfort level and skill as well as on the nature of the patient’s symptoms (unilateral vs bilateral) and age. Randomized prospective clinical trials comparing the various procedures may better define the most appropriate indications and use of these procedures.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

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