Considerable debate exists regarding the relative merits and shortcomings of the two common approaches used for revascularization in moyamoya disease: direct revascularization, involving an anastomosis of a branch of the superficial temporal artery (STA) to the brain; and indirect revascularization, placing vascularized tissue in contact with the brain to foster growth of new collaterals. Some centers advocate combinations of both approaches. A recent review of the literature concerning optimal treatment concludes that there is evidence that both direct and indirect revascularization are of benefit, but determining the most effective treatment awaits further studies. In the absence of randomized trials, the choice of treatment is often dependent on the preference and training of the cerebrovascular neurosurgeon, with most US hospitals using direct approaches for adults.

In this paper we present data from our center on pial synangiosis (an indirect revascularization procedure) in adult patients with moyamoya disease, supporting this approach as an efficacious and safe treatment for this population.

**Methods**

**Patient Selection**

A consecutive surgical series of patients with moyamoya disease who underwent pial synangiosis surgery at a single institution was reviewed. The mean age at surgery was 28.3 years, and 30 patients were female. Twenty-eight patients (77.8%) presented with transient ischemic attacks (TIAs), 24 (66.7%) with stroke, and 3 (8.3%) with hemorrhage. Preoperative Suzuki stage was III or higher in 50 hemispheres (75.8%) and 3 patients had undergone prior treatments to the affected hemisphere before pial synangiosis surgery. Clinical follow-up was available for an average of 5.8 years (range 0.6–14.1 years), with 26 patients (72.2%) followed for longer than 2 years. Postoperative angiography was available for 24 patients and 46 revascularized hemispheres, and 39 (84.8%) of the 46 hemispheres demonstrated good collateral formation (Matsushima Grade A or B). Postoperative complications included 3 strokes, 5 TIAs, and 2 seizures, and there was no hemorrhage during the follow-up period. One patient required additional revascularization surgery 8 months after pial synangiosis.

**Conclusions.** Pial synangiosis is a safe and durable method of cerebral revascularization in adult patients with moyamoya and can be considered as a potential treatment option for moyamoya disease in adults.
Pial synangiosis in adult moyamoya disease

moya arteriopathy who underwent pial synangiosis between 1985 and 2010 was reviewed to identify all patients 18 years of age or older at the time of surgery. All patients within this time period were included. In accordance with a protocol approved by the institutional review board, medical records of these patients were retrospectively reviewed to determine demographic and clinical information such as age at presentation, sex, medical comorbidities, symptoms, and results of radiographic studies (including CT, MRI/MR angiography, and conventional angiography) interpreted by fellowship-trained Board-certified pediatric neuroradiologists and attending neurosurgeons. The neurological examination was documented preoperatively (using modified Rankin Scale [mRS] scores) and Suzuki stage on preoperative digital subtraction angiography (DSA). Treatment course and outcome variables included perioperative and late complications, length of follow-up, and long-term clinical and radiographic results, all recorded and maintained by the attending neurosurgeons and nurse practitioners as per the protocol approved by the institutional review board.

Surgical Treatment

The technique of pial synangiosis has been described previously.18 Briefly, the parietal branch of the STA is mapped with Doppler ultrasonography, and an STA graft of 9–10 cm is isolated and dissected free, maintaining continuity of blood flow in the donor artery. A large craniotomy is performed and the dura mater is opened into multiple flaps. The arachnoid membrane is dissected widely to expose the pial surface, and the STA graft is affixed to the pia with 10-0 monofilament nylon sutures. Patients routinely are administered aspirin throughout the perioperative period.

Adult patients who present with bilateral disease and require treatments to both hemispheres are usually managed with staged operations, with an interval of 1–6 weeks between the two surgeries. As recently as 2006, our practice has been to perform both sides in bilateral cases under a single anesthesia procedure, assuming no intraoperative complications or other technical considerations arise.

Statistical Analysis

The differences in demographic and clinical characteristics were examined using chi-square and 2-tailed t-tests for binary and continuous variables, respectively. The association between postoperative outcome and age, sex, severity of arteriopathy, and syndromic conditions (neurofibromatosis Type 1, Down syndrome, sickle cell anemia, and previous radiation treatment) was evaluated.

Results

Patient Population

Of all moyamoya patients who were treated between 1985 and 2010, 36 patients were over 18 years of age at the time of pial synangiosis. Demographic and clinical information of the patients in the study are summarized in Table 1. The mean age was 27.5 ± 6.8 years (range 18.1–50.9 years); 30 patients were female, and 6 patients were Asian. Seven patients in the cohort had syndromic conditions, including neurofibromatosis Type 1 (n = 2), Down syndrome (n = 4), and sickle cell anemia (n = 1). Three patients had a history of craniopharyngioma and had prior cranial radiation treatment. Four patients had unilateral moyamoya disease and underwent revascularization of the affected hemisphere only, and 32 had bilateral moyamoya. Of these, 1 patient who was operated on at the age of 14 for left-sided moyamoya disease developed right-sided moyamoya in adulthood, and underwent right pial synangiosis at 23 years of age. Another patient underwent previous bilateral pial synangiosis at age 15 and had frontal failure presenting as drop attacks (transient episodes of acute loss of body tone), and thus underwent pial synangiosis in the right anterior cerebral artery territory at age 22 using a frontal STA supply. As a result, a total of 66 hemispheres were included in the analyses.

The unilateral cases bear specific mention. As noted, 4 patients had only unilateral disease. However, of the 32 other patients with bilateral disease, it is important to recognize that 5 of them initially presented with unilateral moyamoya, then progressed to develop bilateral disease (with subsequent treatment) during the period of the
study. Consequently, 9 patients initially presented with unilateral moyamoya, but 5 (55.6%) of these 9 progressed to develop bilateral moyamoya.

Three patients received treatments to the affected hemisphere prior to the pial synangiosis surgery. One patient who underwent left encephaloduroarteriosynangiosis (EDAS) at another institution continued to experience episodes of transient ischemic attacks (TIAs), and was treated with bilateral pial synangiosis at 51 years of age. Another patient had undergone unsuccessful angioplasty of the right middle cerebral artery (MCA) prior to right pial synangiosis. The third patient had undergone bilateral pial synangiosis and continued drop attacks.

Clinical and Radiographic Characteristics

Transient ischemic attack was the most frequent presenting symptom in the study cohort (28/36, 77.8%). Twenty-four patients (66.7%) experienced clinical strokes prior to surgical treatment, and 3 (8.3%) presented with hemorrhage. Preoperative vascular risk factors included diabetes (n = 2), hypertension (n = 4), and smoking (n = 6).

Magnetic resonance imaging and DSA were routinely obtained during preoperative workup, and these results are summarized in Table 2. Fifty affected hemispheres (50/66, 75.8%) exhibited evidence of slow cortical blood flow (the ivy sign) on MRI FLAIR sequences, and 42 (63.6%) demonstrated the presence of stroke. Digital subtraction angiography prior to surgery was available to review in 30 patients (86%) and 54 hemispheres (84%). Severity of moyamoya disease was quantified with Suzuki stage (I–VI, with Stage VI the most severe). The majority of the affected hemispheres (36/66, 54.5%) had Suzuki Stage III–IV, and the average Suzuki stage of the study cohort was 3.6.

Surgical Management and Perioperative Complications

Pial synangiosis was successfully performed in all patients in the study cohort. The average length of the STA graft was 8.9 ± 1.4 cm. One patient underwent STA-MCA bypass for the left hemisphere and pial synangiosis for the right, and another underwent encephalomyosynangiosis for the left hemisphere because the STA had been sacrificed in a previous jaw surgery. Of the 32 patients who underwent surgery for bilateral moyamoya disease as adults, 8 patients had both procedures under a single anesthesia procedure, 18 had planned staged operations with an interval of 1–6 weeks between surgeries, and 3 had a delayed second operation due to disease progression (between 36 and 172 weeks after the first surgery).

Postoperative TIAs and seizures occurred in 5 and 2 patients, respectively (Table 3). Three patients suffered a stroke in the ipsilateral hemisphere within 48 hours after surgery, one of whom underwent encephalomyosynangiosis surgery instead of pial synangiosis. There was no contralateral stroke, intracranial hemorrhage, or death in the perioperative period.

Follow-Up and Postoperative Angiographic Results

Follow-up information was available for all 36 patients, and the mean follow-up period was 5.8 years (range 0.6–14.1 years), with 26 patients followed for more than 2 years. There was no stroke or hemorrhage during the follow-up period. One patient died of lung cancer 5 years after undergoing right pial synangiosis. Two patients continued to experience TIAs after surgery but did not experience new strokes, according to follow-up MRI. One of these patients spontaneously improved 6 months after surgery, and the other had poor collateral

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suzuki stage</td>
<td></td>
</tr>
<tr>
<td>I–II</td>
<td>6 (9.1)</td>
</tr>
<tr>
<td>III–IV</td>
<td>36 (54.5)</td>
</tr>
<tr>
<td>V–VI</td>
<td>14 (21.2)</td>
</tr>
<tr>
<td>not applicable</td>
<td>10 (15.2)</td>
</tr>
<tr>
<td>slow cortical blood flow (ivy sign)</td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>50 (75.8)</td>
</tr>
<tr>
<td>absent</td>
<td>16 (24.2)</td>
</tr>
<tr>
<td>evidence of stroke</td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>42 (63.6)</td>
</tr>
<tr>
<td>absent</td>
<td>24 (36.4)</td>
</tr>
</tbody>
</table>

TABLE 3: Postoperative and long-term outcome after pial synangiosis

| Variable | Value (%)
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>postop complications</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>5</td>
</tr>
<tr>
<td>infarction</td>
<td>3</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>0</td>
</tr>
<tr>
<td>seizure</td>
<td>2</td>
</tr>
<tr>
<td>wound infection</td>
<td>1</td>
</tr>
<tr>
<td>death</td>
<td>0</td>
</tr>
<tr>
<td>follow-up events</td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>2</td>
</tr>
<tr>
<td>infarction</td>
<td>0</td>
</tr>
<tr>
<td>hemorrhage</td>
<td>0</td>
</tr>
<tr>
<td>seizure</td>
<td>2</td>
</tr>
<tr>
<td>reoperation</td>
<td>1</td>
</tr>
</tbody>
</table>
| death | 1*

* Patient died of lung cancer 5 years after undergoing right pial synangiosis.
† Values represent the number of patients (%).
‡ Values represent the number of hemispheres (%).
formation on the right hemisphere on postoperative DSA and underwent STA-MCA bypass 8 months after pial synangiosis (Table 3). Functional results were assessed by mRS scores assigned to 32 patients (88.9%) agreeing to be assessed using the mRS during the last follow-up appointment, and 29 (90.6%) of these 32 patients had favorable outcomes (mRS Score 0–2), whereas 3 (9.4%) had unfavorable outcomes.

Postoperative DSA was obtained 10–12 months after the surgery and was available for 24 patients with 46 treated hemispheres (69.7%). The degree of cerebral revascularization was evaluated with the Matsushima scale[18] (Table 3), and good collateralization (Matsushima Grade A or B) was found in 39 hemispheres (84.8%).

Discussion

Moyamoya disease is a progressive arteriopathy characterized by stenosis and occlusion of the intracranial internal carotid artery.[15,19] It is a rare entity and is most commonly found in Japan, but has been increasingly recognized in the US and western countries. A hallmark of moyamoya disease in children is its relentless progression, and if left untreated, more than two-thirds of patients may develop new symptoms within a 5-year period.[17,20,21] Moyamoya in adults is believed to be a less aggressive process than in the pediatric population;[22] nevertheless, natural history studies have indicated that more than 20% of adult patients experience symptomatic progression,[16] and medical therapy does not halt disease progression. Moreover, the cognitive effect of moyamoya disease in adult patients has only recently been studied,[2,5,6,27] and it was reported that hypoperfusion in the affected hemispheres correlated with significant impairment in memory and learning, which could improve after surgical revascularization.[28] The cumulative evidence suggested that moyamoya disease in symptomatic adult patients warranted similar aggressive intervention as in children to prevent further deleterious consequences.

Historically, direct bypass procedures (STA-MCA bypass) have been successfully used to treat moyamoya disease in adult patients and it has the advantage of providing immediate augmentation of blood flow to the ischemic brain after surgery.[2,24] Guzman et al.[10] reviewed a large single-institution series of 233 adult patients with moyamoya (389 treated hemispheres) who underwent STA-MCA bypass and demonstrated that more than 90% of patients experienced improved or the same quality of life after surgery (Table 4). Eight adult patients suffered ischemic strokes and 8 suffered a hemorrhage during the postoperative period (within 30 days of surgery) and long-term follow-up (mean 4.9 years), which translated into an approximately 3%-4% risk for each complication. On the other hand, indirect revascularization techniques such as EDAS have recently been reported as an alternative treatment for adult patients with moyamoya, especially when direct bypass is not technically feasible.[14] Starke et al.[25] analyzed 43 North American patients (67 affected hemispheres) who underwent EDAS and showed that 88% of patients had preserved or improved functional status after surgery, as measured by mRS score. The authors also reported a higher risk of ischemic complications in the cohort than postoperative hemorrhage: 8 patients developed ischemic strokes (18.6%), but there was only 1 hemorrhagic event (2.3%). Most recently, Bao et al.[1] reported on a cohort of 470 Chinese adult patients with moyamoya treated with EDAS, and found similar patterns of postoperative complications. The rate of postoperative ischemic events or hemorrhage was 5.9%. When calculating with the number of hemispheres treated, the overall stroke risk was approximately 10% per hemisphere in the first 2 years, and the 5-year Kaplan-Meier risk of stroke was 13% after surgery for all patients treated using surgical revascularization. Duan et al., in a series of 802 adult Chinese patients with moyamoya treated at a single institution, reported a 12.7% risk of stroke in patients with surgical revascularization.[3] A summary of previously reported surgical series on adult patients with moyamoya disease is presented in Table 4.

In our study, 36 adult patients underwent 66 pial synangiosis operations. There were 3 immediate postoperative strokes and no delayed ischemic or hemorrhagic events, and 90.6% (29/32) of evaluated patients had a favorable outcome after a mean follow-up period of 5.8 years. The overall stroke rate was 8.3% (4.5% per treated hemisphere). These data compare favorably with other reported series of indirect bypass procedures for adult patients with moyamoya disease,[1-3,25,27,28] and suggest that pial synangiosis is safe, effective, and durable for cerebral ischemic protection. The complication profile in this

**TABLE 4: Summary of literature search on the outcome of adult patients with moyamoya disease**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients/ Hemispheres</th>
<th>Mean Age (yrs)</th>
<th>Treatment</th>
<th>Follow-Up (yrs)</th>
<th>Stroke†</th>
<th>Hemorrhage‡</th>
<th>Favorable Outcome§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guzman et al., 2009</td>
<td>233/389</td>
<td>39.5</td>
<td>STA-MCA</td>
<td>4.9</td>
<td>8 (3.4%)</td>
<td>8 (3.4%)</td>
<td>94.8%</td>
</tr>
<tr>
<td>Bao et al., 2012</td>
<td>470/752</td>
<td>36.8</td>
<td>EDAS</td>
<td>2.2</td>
<td>77 (16.4%)</td>
<td>20 (4.3%)</td>
<td>343 (73.2%)</td>
</tr>
<tr>
<td>Czabanka et al., 2009</td>
<td>10/19</td>
<td>38.4</td>
<td>STA-MCA &amp; EMS</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>10 (100%)</td>
</tr>
<tr>
<td>Starke et al., 2009</td>
<td>43/67</td>
<td>40.0</td>
<td>EDAS</td>
<td>3.4</td>
<td>8 (18.6%)</td>
<td>1 (2.3%)</td>
<td>38 (88.4%)</td>
</tr>
<tr>
<td>Lin et al., 2011</td>
<td>36/66</td>
<td>28.3</td>
<td>pial synangiosis</td>
<td>5.8</td>
<td>3 (8.3%)</td>
<td>0 (0%)</td>
<td>29 (90.6%)</td>
</tr>
</tbody>
</table>

* EMS = encephalomyosynangiosis.
† Indicates overall risk of new strokes during the entire follow-up period, including the postoperative period.
‡ Indicates overall risk of hemorrhage during the entire follow-up period, including the postoperative period.
§ Measured as preserved or improved functional status, or mRS score < 2.
study was consistent with other reports in the literature and indicated that, compared with direct bypass, those treated with indirect bypass might have a higher risk of postoperative stroke and a lower risk of hemorrhage. Revascularization usually does not occur for several weeks using indirect techniques, which could account for the higher rate of postoperative ischemia; nevertheless, gradual augmentation of cerebral blood flow might reduce the risk of hyperperfusion and perioperative hemorrhage. While the relative merits and shortcomings of the two approaches will continue to be debated, pial synangiosis can be appealing in an adult population, especially for those with diminutive donor or recipient graft vessels.

Of the 36 patients in our series, 32 were discovered to have significant moyamoya in both hemispheres at presentation and were treated bilaterally. The remaining 4 patients were treated unilaterally at the beginning, but 5 (55.6%) developed progression of disease during the follow-up period and required additional surgery. This observation confirmed the evidence reported in the literature that moyamoya progression can be relentless even in adults, and close follow-up is needed to detect early signs of radiographic progression before symptoms occur.17

Conclusions

Although the optimal treatment for moyamoya disease in the adult population remains unclear, our patient series demonstrated that collateral formation following pial synangiosis is sufficient to prevent new infarcts and can provide adequate intracranial perfusion through an extended follow-up period. The complication rate in the perioperative period and beyond was relatively low and the procedure was well tolerated. These data collectively suggest that indirect revascularization via pial synangiosis is an additional safe and durable option for the treatment of moyamoya disease in adults.

Disclosure

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

Author contributions to the study and manuscript preparation include the following. Conception and design: Smith, Lin, Aronson, Scott. Acquisition of data: Smith, Lin, Aronson. Analysis and interpretation of data: Smith, Lin, Aronson. Drafting the article: Lin, Aronson, Scott. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Smith. Administrative/technical/material support: Smith. Study supervision: Smith, Scott.

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