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Clinical outcomes after revascularization for pediatric moyamoya disease and syndrome: a single-center series

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Abstract

Moyamoya is a progressive cerebrovascular arteriopathy that affects children of any age. The goal of this study was to determine imaging and clinical outcomes as well as complication rates in a pediatric cohort undergoing either a combined direct/indirect or indirect-only revascularization approach. Patients with moyamoya disease or syndrome ≤18 years of age at the time of initial surgery were identified, and clinical data were collected retrospectively. Over a 12-year period, 26 patients underwent revascularization procedures on 49 hemispheres with a median follow-up of 2.6 years from surgery. Median age at surgery was 7.3 years (range 1.4 – 18.0 years). Thirty-three hemispheres (67.3%) underwent combined revascularization with a direct bypass and encephalomyosynangiosis, and sixteen hemispheres (32.7%) underwent indirect-only revascularization The rate of 30-day perioperative complication was 10.2%, and the rate of postoperative clinical stroke by end of follow-up was 10.2% by hemisphere. There was a 5.7% rate of intraoperative bypass failure requiring conversion to an indirect revascularization approach. On follow-up imaging, 96.9% of direct bypasses remained patent. On multivariate analysis, higher preoperative Pediatric Stroke Outcome Measure (PSOM) scores were associated with lower rates of good clinical outcome on follow-up (unit OR 0.03; p=.03). Patients with age <5.4 years had lower rates of good clinical outcome on follow-up. In this North American cohort, both combined

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direct/indirect and indirect only revascularization techniques were feasible. However, younger children < 5.4 years of age have worse outcomes than older children, similar to east Asian cohorts.

Keywords

moyamoya disease; direct and indirect revascularization technique; STA-MCA bypass; vascular disorders

Introduction

Moyamoya disease is a progressive cerebrovascular arteriopathy that affects both children and adults [1], resulting in narrowing and eventual occlusion of the internal carotid arteries and their branches. As collateral blood supply develops, new vessels with a small caliber form a cloudy, smoke-like appearance on catheter angiography leading to its name, “moyamoya” [2]. Secondary moyamoya (i.e. moyamoya syndrome) is found in association with other conditions such as neurofibromatosis, sickle cell disease, post-irradiation, and trisomy 21 [3,4]. The presenting symptoms include stroke, transient ischemic attack (TIA), and hemorrhage [4,5]. Surgical intervention is the primary definitive treatment with decreased stroke incidence when compared to patients only receiving medical therapy [4]. Some patients are capable of independent daily activity following treatment, but many will have intellectual impairment, focal neurologic deficits, and headaches [6]. Younger children are thought to be at higher risk of procedural complications and poorer long-term outcomes [7], despite some reports of better revascularization rates [8].

Various direct and indirect surgical revascularization procedures have been used to treat moyamoya in children. Indirect revascularization includes procedures that facilitate the development of new vascular pathways through the dura to create leptomeningeal collaterals. These techniques include burr holes to create openings for collateral formation, or apposition of various structures, such as the dura, superficial temporal artery (STA), muscle, or a combination, to the surface of the brain [9–12]. Direct revascularization, typically with an STA to middle cerebral artery (MCA) bypass, is used less commonly in children due to the small caliber of vessels and need for temporary occlusion of an MCA branch required for anastomosis. However, this technique provides immediate improvement in cerebral hemodynamics compared to indirect procedures, and prior reports demonstrate good perioperative outcomes [11,13,14]. Others have combined both direct and indirect techniques [8,15,16]. In one of the larger cohorts of pediatric patients undergoing a combined direct/indirect approach, Uchino et al. observed adequate development of direct or indirect bypasses on follow-up (defined as either increased or stable STA diameter) in 87% and 95% of the pediatric cohort, respectively, with 56% of hemispheres showing dual direct/indirect revascularization development and no cases of dual insufficiency [8]. Thus, including the addition of an indirect bypass step to a direct extracranial-intracranial bypass may decrease the risk of future regional vascular insufficiency.

In this study, we aimed to describe clinical and imaging outcomes in a series of 26 children who underwent revascularization of 49 hemispheres. We hypothesized that age may be an important determinant of successful revascularization and neurologic outcomes. Thus, we examined various cut-points of age at diagnosis for predicting post-operative stroke or good clinical outcomes, and compared these between young and older children.

Methods

Patient Selection, Cohort Characteristics, and Imaging Findings

This study was approved by the University of California San Francisco (UCSF) institutional review board. Consecutive patients were identified from a UCSF prospective registry of revascularization procedures performed between 2006 to 2018. Inclusion criteria were: 1) a diagnosis of moyamoya disease or syndrome as confirmed by imaging and clinical review, and 2)age ≤ 18 at time of initial surgery. Data were collected retrospectively from the UCSF electronic medical record, including demographics, stroke-related risk factors, clinical presentation, neuroimaging features, treatment, pre-and post-operative stroke events, Pediatrics Stroke Outcomes Measure (PSOM) at diagnosis and date of last follow-up.

A transient ischemic attack (TIA) was defined as neurological dysfunction with symptoms lasting less than 24 hours. Ischemic stroke was defined as acute onset of focal neurologic deficit and neuroimaging findings consistent with ischemic stroke. Preoperative Suzuki staging, bypass patency, and radiographic outcomes at last follow-up (reported stable versus worse) were assessed by two neurointerventional radiologists (D.M., S.H.) who were blinded to other clinical variables and outcomes; consensus scores and outcomes were reported. Findings were generated based on available magnetic resonance angiography imaging or catheter angiography images.

Surgical Techniques

The surgical approach of preference from this institutional series was a combined direct bypass with indirect revascularization if there was an available STA donor vessel and large enough cortical recipient branch (≥ 1 mm in diameter). Selection of surgical approach also took into consideration severity and frequency of clinical symptoms with a direct bypass favored for patients with acutely progressive disease. For combined direct and indirect bypass, the following technique was used: after harvesting both the frontal and parietal STA branches when available, the more prominent branch was chosen for direct anastomosis. A small craniotomy overlying the MCA territory was performed. The STA lumen was widened using a ‘fish-mouth’ technique and sutured with continuous 10–0 sutures to a cortical middle cerebral artery branch in an end-to-side technique. Bypass patency was confirmed intraoperatively with indocyanine green videoangiography. All patients were started on a daily aspirin after the bypass procedure. After completing the direct bypass, encephalomyosynangiosis (EMS) was performed. The arachnoid mater was widely opened, and the temporalis muscle was split in half in its sagittal plan with the inner portion used as an indirect on-lay graft on the cortex. After replacing the bone flap, the outer portion of muscle was reapproximated with the muscle cuff at the superior temporal line. For one patient with moyamoya syndrome secondary to an *ACTA2* mutation, a frontal craniotomy was performed with end-to-side anastomosis of the frontal STA branch to the anterior cerebral artery (ACA). In a separate case, an additional occipital artery was harvested and anastomosis was performed to an available MCA branch in addition to a separate STA-MCA bypass.

For indirect-only bypass, the following techniques were used. After harvesting the STA branches, a small craniotomy was performed overlying the MCA territory. After opening the dura, the STA was secured with 9–0 suture to the pial surface of the brain and, in addition, the inner leaflet of the split temporalis muscle was placed over the exposed brain surface. In some cases (depending on surgeon preference and anatomic limitations), the temporalis muscle was not split and secured to the surface of the brain.

Outcome Measures

Outcomes were measured using the PSOM scored retrospectively from the neurologic examination documented preoperatively and at the last follow-up. This scoring system has been validated previously in the pediatric population [17]. Five subscales (right sensorimotor, left sensorimotor, language production, language comprehension, and cognitive/behavioral) are each scored as 0 for no deficit, 0.5 if minor exam abnormality detectable with no impact on function, 1 if deficit impairs function, and 2 if at least one function is missing. The sum of the five subscales comprise the Total PSOM score. Higher values reflect greater disability. A “good clinical outcome” was defined as a score of ≤0.5 in all 5 subscales on the PSOM. A “worse” radiographic finding on follow-up was defined as evidence of new infarcts or worsening encephalomalacia whereas “stable” imaging lacked these progressive features. Bypass patency on follow-up was assessed by available MRA, digital subtraction angiography, or CTA depending on the available study. For measurement of STA diameter, vessel diameter was measured at the level of the floor of the middle fossa to allow for consistency in measurement on both preoperative vessel imaging as well as on imaging at the time of last imaging follow-up.

Statistical Analysis

Statistical analysis was performed using JMP Pro 13 (SAS Institute, Cary, NC). Descriptive statistics were used to define the patient cohort including patient demographics, moyamoya etiology, preoperative Suzuki stage, treatment details, and clinical and imaging outcomes. A $\chi 2$ test was performed for statistical comparison for other categorical variables. A Fisher t-test was performed to compare preoperative and follow-up STA diameter and age for subgroup analysis. Univariate and multivariate generalized logistic regression analyses were performed to assess for factors predictive of 30-day postoperative complications, postoperative stroke, and good clinical outcome. All predictor variables from the univariate analysis with a P-value ≤ .2 were then included in the multivariate logistic regression. A stepwise regression model was used to confirm the findings of the generalized logistic regression model. Of note, no variables met significance criteria for the univariate analysis for 30-day postoperative complications, precluding a multivariate analysis. Receiver operating characteristics (ROC) curves of age versus good clinical outcome were generated to determine optimal cut-offs (based on Sensitivity – (1-Specificity)) for age at surgery for predicting good clinical outcome. A cut-off of 5.4 years of age was identified, and the binary variable produced was then used to examine differences by age. The level of significance was 0.05 for all analyses.

Results

Patient Characteristics and Clinical Presentation

Demographic details of the cohort are presented in Table 1. This pediatric cohort consisted of 26 patients (38.5% male) with a median age of 6.9 years at diagnosis (range 1.1 – 17.3 years). The median age at the time of surgery was 7.3 years (range 1.4 – 18.0 years). The youngest patient to receive a direct bypass was 16.8 months old. Fifteen patients had idiopathic moyamoya disease without obvious risk factors. Eleven patients (42.3% of the cohort) had secondary moyamoya syndrome with the most common risk factors being neurofibromatosis and ACTA2 mutation. The most common ethnicity/race in the cohort was white/Caucasian (65.4%). The most common presenting symptoms were stroke or TIA with 76.9% of patients presenting with either. There were no observed cases of hemorrhage at presentation in the cohort. All patients in the cohort had bilateral disease except for 1 patient with NF1 who had unilateral disease only, totaling 51 affected hemispheres in the cohort.

Treatment Characteristics

Treatment details are presented in Table 2. In total, 46 procedures were performed at our institution involving 49 hemispheres (two additional hemispheres had been treated at outside institutions). Thirty-three cases involved a combined direct and indirect revascularization approach with 93.9% involving a superficial temporal artery to middle cerebral artery (STA-to-MCA) bypass as well as secondary encephalomyosynangiosis (EMS). For three procedures, bilateral combined direct and indirect revascularization was performed during a single operation. Additionally, there were 16 indirect-only revascularization procedures performed [either encephaloduroarteriomyosynangiosis (EDAMS) or encephaloduroarteriosynangiosis (EDAS)]. During seven of these procedures, there was an intent to perform a direct bypass. In five cases, there was no appropriate accepting vessel identified intraoperatively, and in two cases, there was intraoperative failure of the bypass requiring conversion to an indirect revascularization approach (failure rate of 5.7% of total bypasses attempted). Patient factors associated with surgical approach are depicted in Table 3. Indirect-only approaches were used more frequently for patients with secondary moyamoya syndrome but otherwise surgical approach was not significantly associated with sex, age, hemisphere side, pre-operative Suzuki grade, and pre-operative PSOM score.

Perioperative Morbidity

Perioperative clinical outcomes are listed in Table 1. There were no patients who suffered a 30-day postoperative complication using an indirect revascularization approach compared to 5 patients who underwent a combined revascularization approach. There were 2 patients who had wound infections requiring surgical revision. Three patients developed an ipsilateral ischemic stroke within 30 days of surgery (6.1% risk of stroke by hemisphere). A 6-year old girl developed a right hemiparesis and aphasia on postoperative day three with evidence of an acute left-sided cerebral infarction in the anterior and middle cerebral artery territories ipsilateral to the bypass on MR imaging. Additional small punctate acute infarcts were also seen in the left putamen and right caudate head. There had been no recent hemodynamic changes noted. The stroke was thought to be secondary to artery-to-artery emboli from the ipsilateral arteriopathy. Imaging studies demonstrated that the vascular bypass was patent. The second patient was a 23-month old girl who developed acute left hemiparesis on postoperative day one with MRI demonstrating bilateral watershed territory infarcts despite maintenance of goal mean arterial pressure targets. Imaging studies demonstrated that the vascular bypass was patent. The third patient was a 13-year old boy with Schimke immuno-osseous dysplasia who developed numerous medical complications postoperatively including hemoptysis secondary to rupture of previously undiagnosed esophageal varices, resulting in hypotension and an associated right middle cerebral artery territory infarct on postoperative day 15. He subsequently had recurrent variceal bleeding requiring transjugular intrahepatic portosystemic shunt. He then developed pulmonary hypertension due to multiple medical comorbidities and died due to hypoxia and cardiac arrest 1.5 months after surgery. No other patients had a new deficit in their neurological exam or mortality within 30-days after a surgical procedure.

Clinical and Imaging Outcomes

Clinical and imaging outcomes are listed in Table 1. Median follow-up was 3.6 years after moyamoya diagnosis and 2.6 years after initial surgery. In the period between 30 days post-operative and last follow-up, there were 2 cases of hemorrhagic stroke ipsilateral to prior sites of surgery for a total of 5 strokes postoperatively by end of follow-up. These two intraparenchymal hemorrhages occurred 6.9 and 8.3 years after the initial surgery at 10.2 and 17.5 years of age, respectively. The overall ischemic or hemorrhagic stroke rate for the cohort was 0.05 strokes per person-years. There were 2 deaths in the cohort. The first was the 13-year old boy with Schimke Immuno-osseous dysplasia described above. The second was a boy who had a unilateral hemorrhagic stroke leading to death 8 years after unilateral indirect bypass.

The PSOM was used to compare preoperative and last follow-up functional status. Preoperative and last follow-up PSOM scores for surviving patients are depicted in Figure 1. Median preoperative and follow-up PSOM scores were 0.5 (IQR 0–1) and 0 (IQR 0–1), respectively. Good clinical outcome (defined as a score of ≤0.5 in all 5 categories on the PSOM) was seen in 79.2% of patients at last follow-up. Overall, 42.3% of patients experienced an improvement in the PSOM and another 34.6% of patient had stable scores by end of follow-up.

By the end of follow-up in surviving patients, 84.1% had evidence of stable arteriopathy and 15.9% had progressive disease when comparing preoperative and last follow-up imaging. By end of follow-up, 96.9% of direct bypasses were patent. In patients receiving a direct bypass, superficial temporal artery (STA) diameter based on last available imaging was measured and compared to preoperative diameter and was found to increase (post-operative STA diameter vs pre-operative STA diameter: 2.0±0.07 mm vs 1.6±0.07 mm, respectively; p=0.0002) (Figure 2).

Clinical Factors Associated with Outcomes

Univariate and multivariate logistic regression analyses were performed to determine patient and treatment factors associated with postoperative complications, postoperative stroke by end of follow-up, and good clinical outcome (Tables 4). There were no significant predictors of 30-day postoperative complications on logistic regression analysis precluding a multivariate analysis, although a combined approach was associated with a higher rate of postoperative complications on $\chi 2$ testing (p<.05). On multivariate analyses, there was a trend towards the association of secondary moyamoya syndrome (OR 15.9, 95% CI 0.96–265.7, p=.054) and a higher preoperative total PSOM score (unit OR 2.2, 95% CI 0.9–5.2, p=.08) with postoperative stroke. On multivariate analysis, preoperative total PSOM score (unit OR 0.03, 95%CI 0.002–0.7, p=.03) was associated with good clinical outcome. A stepwise regression model yielded similar results to those obtained using a generalized logistic regression model. Despite the higher complication rate seen in patients undergoing a combined surgical approach, there was no difference in the rate of good clinical outcome or postoperative strokes between this group and indirect only procedures at last follow-up.

Age Differences Associated with Outcomes

We next examined whether an age cutoff was predictive of good clinical outcomes. Using the ROC curve of age at surgery versus good clinical outcomes, an age of 5.4 was identified as the optimal split point (<5.4 years, n = 16; ≥5.4 years, n= 33) (AUC = 0.68). Table 5 depicts differences between these two age groups. Patients with age <5.4 had lower rates of good clinical outcome on follow-up (p=0.01) which may have been due to higher preoperative PSOM scores.

Discussion

Overall, clinical and radiographic outcomes were both favorable in our cohort. The majority of patients had improvement or stable clinical outcomes based on PSOM scores postoperatively. The overall stroke rate of the cohort was similar to that reported in the literature (about 7–11% by end of follow-up) [3,9,10] and given the reassuring clinical outcomes scores, this suggests that most patients are able to make good functional recovery long-term. The 30-day perioperative mortality rate and stroke rate was 0% and 6.1%, respectively. A 2004 systematic review and meta-analysis including data on over 1,400 patients reported a 4.4% rate of stroke as a complication of the revascularization surgery itself [18]. Our comparable stroke rate as a complication of the revascularization may reflect both careful surgical technique and anesthesia care. Institutional guidelines for avoidance of hypotension, hypovolemia, hyperthermia and hypocarbia, which are factors thought to precipitate intra- and perioperative ischemic events [19,20], may help to minimize procedural strokes risk before, during, and after procedures under anesthesia.

Younger children are thought to be at higher risk of procedural complications and worse outcomes on follow-up. In this cohort of patients, an age cut-off of < 5.4 years of age was found to be a critical threshold for predicting worse outcomes. Prior data from East Asian cohorts also suggest that outcomes appear to be worse in younger pediatric patients. Kim et al. has previously identified younger patients to have higher risk of worse outcome and reported a 39% risk of stroke in patients < 3 years old compared with 6% for patients 3–6 years old, and 0.6% for patients > 6 years old [7]. In a cohort of 37 children, Muraoka et al. also found that postoperative stroke within 7 days as seen on MRI was more frequent in younger patients. The mean age of patients with postoperative cerebral infarction was 4.2

years versus 7.0 years for patients without infarction [21]. Our results could support the possibility that younger children have poorer outcomes after revascularization surgery than older children. However, preoperative PSOM scores were higher in the younger patients in our cohort (similar to other studies[7]) and the rate of preoperative stroke was also higher, suggesting a more aggressive disease phenotype in children who present at younger ages compared to older children. These results provide insight into the expected risk profile in the younger population and may be important when counseling families preoperatively. Neurosurgeons must be particularly careful in the younger age group regardless of the surgical approach, and a multidisciplinary team at our institution has develop strict guidelines around blood pressure control, the use of preoperative intravenous fluids, aspirin use, and postoperative activity precautions for such high-risk patients.

Moyamoya disease is characterized by poor clinical outcomes if left untreated, and surgical revascularization is indicated for most patients [22]. Direct revascularization provides immediate blood flow augmentation and protects the hemisphere at risk from further strokes, which may be especially beneficial in patients with recent and frequent stroke symptoms. The combined approach with temporalis muscle on-lay allows for the opportunity for further collaterals to form overtime. Direct revascularization can be challenging in the pediatric patients, and there is a general concern that the small arterial diameters in children may hinder this technique. Yet, failure of the bypass attempt with intra-operative conversion to an indirect approach only occurred in two instances. Persistence of bypass patency was demonstrated on last follow-up imaging in all but one patient in our series, and overall, STA diameter significantly increased on follow-up (a surrogate marker for increased flow through the bypass). Our group has previously reported favorable outcomes in patients less than 3 years of age who had undergone direct bypass in combination with EMS, suggesting this approach may be feasible for even young pediatric patients with an aggressive clinical phenotype [14]. Indirect-only revascularization techniques (e.g. EDAS, EDAMS) may take weeks to months for augmentation to occur, but the delayed effect may not be as much of a concern for patients with incidental disease or less severe presenting symptoms (no TIA or stroke). Furthermore, this approach avoids complications related to direct bypass. As seen in this cohort, there were no complications noted in the indirect revascularization approach compared to the 5 patients in the combined revascularization approach who suffered a postoperative complication. Our practice pattern has transitioned over time to favor less invasive indirect bypass techniques unless specific circumstances warrant a direct bypass approach.

There are several limitations to this study. First, this was a retrospective analysis of treatment and outcome data in a heterogeneous disease cohort including both idiopathic and secondary moyamoya disease. The cohort does not include a group of pediatric patients managed conservatively for comparison. Selection bias potentially played a role in which patients received combined direct-indirect versus indirect bypasses based on severity of presenting symptoms. The sample size was limited by the relative rarity of this disease in the North American population. However, there is a need for more clinical series from this region, because many prior studies have been conducted in East Asian populations. The disease phenotype between these geographic regions may differ due to rates of idiopathic moyamoya disease and moyamoya syndrome, ethnicity differences, as well as associated genetic and epigenetic factors [18,23].

Conclusions

Combined direct/indirect revascularization may be considered in a select group of pediatric patients with rapidly progressive disease. The rate of direct bypass attempt failure at the time of surgery was relatively low and long-term patency rates of direct bypasses reached > 95%. Children less than 5.4 years of age have lower rates of good clinical outcomes on long-term follow-up.

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Highlights:

- The rate of direct bypass failure in children is low (5.7%).
- A combined revascularization technique is feasible even for very young children.
- High preoperative PSOM predicts worse good clinical outcome on follow-up.
- Children < 5.4 years old with moyamoya have worse clinical outcomes.

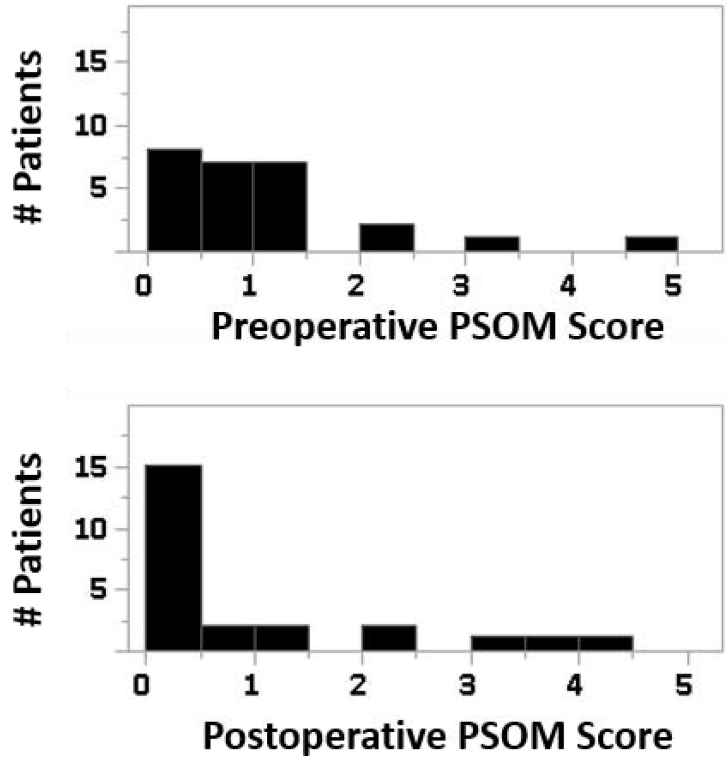

Figure 1.

Comparison of preoperative and last follow-up total PSOM scores. Median preoperative and follow-up PSOM scores were 0.5 and 0, respectively.

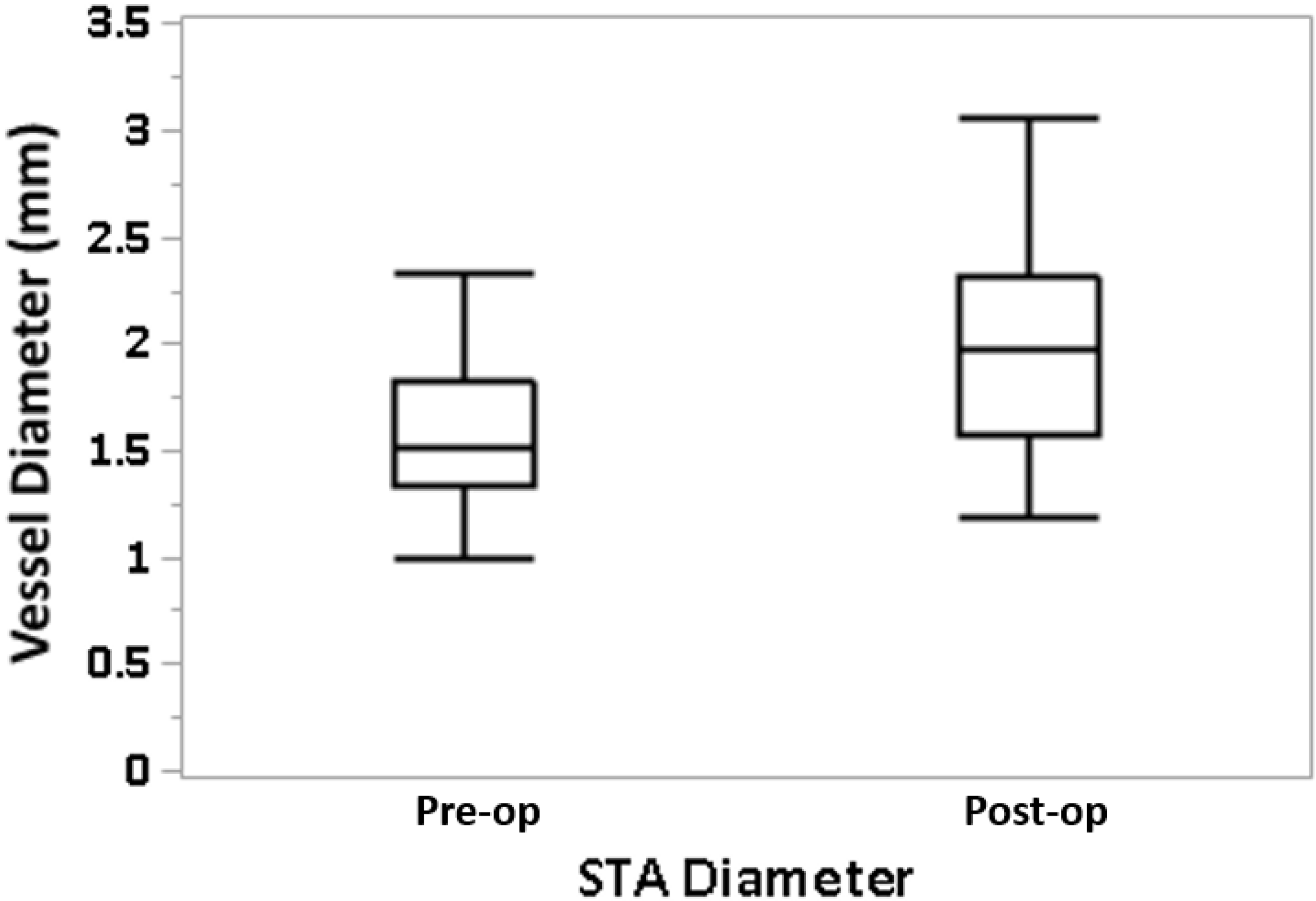

Figure 2.
Comparison of preoperative and last follow-up STA diameter. Pre-operative STA diameter vs post-operative STA diameter: 1.6±0.07 vs 2.0±0.07 mm, respectively (p=0.0002).

Table 1.

Patient Demographics and Outcomes

Number of Patients	26
Number of Hemispheres	49
Median Follow-up (yrs) [IQR]	2.6 [1.4 – 7.5]
Median Age at Diagnosis (yrs) [range]	6.9 [1.1 – 17.3]
Sex	
Male	10/26 (38.5%)
Female	16/26 (61.5%)
Ethnicity[1]	
White/Caucasian	17/26 (65.4%)
Black/African American	1/26 (3.8%)
Asian	2/26 (7.7%)
Hispanic/Latino	2/26 (7.7%)
Native Hawaiian/Pacific Islander	2/26 (7.7%)
Moyamoya Disease (Idiopathic)	15/26 (57.7%)
Moyamoya Syndrome (Secondary)	11/26 (42.3%)
NF1	4
ACTA2 Mutation	2
MOPD II	1
Schimke Immuno-osseous Dysplasia	1
Cranial Radiation	1
Trisomy 21	1
MTFMT gene deletion	1
Laterality of Disease	
Bilateral	25/26 (96.2%)
Unilateral	1/26 (3.8%)
Presenting Symptoms[2]	
Stroke/TIA	20 (76.9%)
Seizure	5 (19.2%)
Chorea	3 (11.5%)
Incidental	4 (15.4%)
Initial Suzuki Stage[3]	
II	18/49 (36.7%)
III	15/49 (30.6%)
IV	12/49 (24.5%)
V	4/49 (8.2%)

30-day Perioperative Surgical Complications	
Wound dehiscence/infection requiring revision[3]	2/49 (4.1%)
Ipsilateral stroke within 30-days[3]	3/49 (6.1%)
Perioperative Mortality[4]	0/26 (0%)
Clinical Postoperative Stroke By Follow-up[3]	
Ischemic	3/49 (6.1%)
Hemorrhagic	2/49 (4.1%)
Death[4]	2/26 (7.7%)
Direct Bypass Patency By Follow-up[5]	32/33 (96.9%)
Imaging Outcome[6]	
Stable Disease	37/44(84.1%)
Worsening Disease	7/44 (15.9%)

*1-*2 patients without documentation of ethnicity

*2-*Patients could present with more than one symptom

*3-*By hemisphere (n=49). 1 patient without adequate preoperative imaging to assess Suzuki stage.

*4–*Analysis by patient (n=26)

*5–*Analysis by hemisphere in patients who underwent direct bypass with available imaging on long-term follow-up (n=33).

*6–*Analysis by hemisphere in surviving patients only with available imaging on long-term follow-up (n=44). 1 patient with 1 affected hemisphere without available postoperative imaging.

Table 2.

Treatment Details

Number of Surgeries[1]	46
Median Age at Surgery (yrs) [range]	7.3 [1.4 – 18.0]
Number of Hemispheres	
Left	25/49 (51.0%)
Right	24/49 (49.0%)
Surgical Approach	
Combined Direct + Indirect Revascularization	33/49 (67.3%)
STA-MCA Bypass + EMS	31
STA-ACA Bypass + EMS	1
Occipital-MCA Bypass + STA-MCA Bypass + EDMS/EMS	1
Indirect Revascularization	16/49 (32.7%)
EDAS	9
EDAMS	7
Bypass Failure[2]	2/35 (5.7%)
Prior Revascularization Procedures[3]	2/26 (7.7%)

1– For 3 surgeries, bilateral combined direct and indirect revascularization was performed during the same operation. Total hemispheres operated on was 49.

2– 35 surgeries with attempted bypass with conversion of 2 to indirect-only revascularization procedures

3– By patients in cohort (n=26). Operations done at outside hospitals prior to presentation at our institution. Not included in number of surgeries.

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Table 3.

Patient Factors Associated with Surgical Approach

	Combined (N=33)	Indirect Only (N=16)	p-value
Sex (female)	14 (42.4/)	S (31.3/)	.45[1]
Age at Surgery (mean±STE)	8.5±0.9	7.6±1.2	.56[2]
Moyamoya Type			.006[1]
Primary	24 (72.7%)	5 (31.3%)	
Secondary	9 (28.3%)	11 (69.7%)	
Hemisphere Side			.92[1]
Left	17 (51.5%)	8 (50%)	
Right	16 (49.5%)	8 (50%)	
Presenting Symptom including Stroke			.62[1]
Yes	12 (36.4%)	7 (43.8%)	
No	21 (63.6%)	9 (57.2%)	
Pre-op Suzuki Grade			.22[1]
2	11 (33.3%)	7 (43.8%)	
3	9 (27.3%)	6 (37.5%)	
4	11 (33.3%)	1 (6.2%)	
5	2 (6.1%)	2 (12.5%)	
Pre-op PSOM Score (mean±STE)	0.8±0.2	0.9±0.3	.75[2]

PSOM: Pediatric Stroke Outcomes Measurement; STE: standard error.

[1-] $\chi 2$ test performed for statistical analysis

[2–] Fisher t-test performed for statistical analysis

Table 4.

Univariate and multivariate generalized logistic regression analysis of factors associated with 30-day postoperative complication, postoperative stroke, and good clinical outcome

	30-day Postop Complication[3]		**Postop Stroke**				**Good Clinical Outcome**			
	Univariate Analysis		**Univariate Analysis**		**Multivariate Analysis**		**Univariate Analysis**		**Multivariate Analysis**	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Moyamoya Type (Secondary/ Primary)	4.5 (0.8–26.1)	.09	9.3 (0.99–87.4)	.05	15.9 (0.96–265.7)	.054	0.06(0.01–0.3)	.001	0.0001 ($7.1e^{-12}$–1736.9)	.28
Pre-op PSOM Score[1]	1.4 (0.8–2.8)	.27	1.9 (0.99–3.9)	.052	2.2 (0.9–5.2)	.08	0.08 (0.01–0.4)	.003	0.03 (0.002–0.7)	.03
Presenting Symptom including Stroke (Yes/No)	1.2 (0.2–6.2)	.81	3.7 (0.6–22.8)	.15	2.0 (0.25–16.8)	.51	0.2 (0.04–0.7)	.01	0.1 (0.006–1.8)	.12
Pre-op Suzuki Grade[1]	0.8 (0.3–1.9)	.59	0.9 (0.06–12.4)	.91			0.7 (0.4–1.3)	.25		
Surgical Approach (Combined/ Indirect)[2]	37788 ($7.1e^{-76}$–$2.0e^{84}$)	.91	0.97 (0.2–5.9)	.97			0.5 (0.1–2.3)	.39		
Hemisphere Side (Left/ Right)	0.7 (0.1–3.4)	.64	0.95 (0.2–5.3)	.96			0.9 (0.2–3.1)	.81		
Sex (Male/ Female)	0.6 (0.1–3.4)	.55	1.7 (0.3–9.4)	.55			1.0 (0.3–3.7)	.98		

PSOM: Pediatric Stroke Outcomes Measurement

[1-] Units odds ratio reported

[2–] No 30-day postoperative complications noted with an indirect revascularization approach

[3–] No significant predictors of 30-day postoperative complications precluding a multivariate analysis

Table 5.

Clinical factors and outcomes based on identified age cut-off

	Age < 5.4 years	Age > 5.4 years	p-value
Female Sex	13/16 (81.3%)	17/33 (51.5%)	.04[1]
Secondary Moyamoya	6/16 (37.5%)	14/33 (42.4%)	.74[1]
Age at Diagnosis (yrs) (Mean±STE)	2.8±0.8	9.8±0.6	<.0001[2]
Age at Surgery (yrs) (Mean±STE)	3.1±0.8	10.7±0.6	<.0001[2]
Suzuki Grade			.32[1]
2	6 (37.5%)	12 (36.4%)	
3	6 (37.5%)	9 (27.3%)	
4	4 (25%)	8 (24.2%)	
5	0 (0%)	4 (12.1%)	
Presenting Symptom including Stroke	10/16 (62.5%)	9/33 (27.3%)	.02[1]
Pre-op PSOM			.03[3]
0	6 (37.5%)	10 (30.3%)	
0.5	2 (12.5%)	11 (33.3%)	
1	3 (18.8%)	10 (30.3%)	
2	2 (12.5%)	2 (6.1%)	
3	1 (6.2%)	0 (0%)	
4.5	2 (12.5%)	0 (0%)	
Surgical Approach			.88[1]
Combined	11/16 (68.8%)	22/33 (66.7%)	
Indirect	5/16 (31.2%)	11/33 (33.3%)	
Good Clinical Outcome[4]	8/16 (50%)	28/33 (84.9%)	.01[1]
Stable Imaging Outcome[5]	11/14 (78.6%)	26/30 (86.7%)	.50[1]
30-day Complications	3/16 (18.8%)	4/33 (12.1%)	.54[1]
Postoperative Stroke[4]	3/16 (18.8%)	3/33 (9.1%)	.35[1]

PSOM: Pediatric Stroke Outcomes Measurement; STE: standard error

1- $\chi 2$ test performed for statistical analysis

2- Fisher t-test performed for statistical analysis

3– Cochran Armitage Trend Test performed for statistical analysis

[4–] Includes both deceased and alive patients by end of follow-up

[5–] 5 patients without postoperative imaging available for review or were deceased at end of follow-up