Outcomes of surgical revascularization for pediatric moyamoya disease and syndrome

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Research Article

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Abstract

Purpose:

Moyamoya disease and syndrome represent rare entities characterized by progressive stenosis and/or occlusion of the intracranial blood vessels. We present our series of patients with moyamoya disease and syndrome stratified by underlying disease and analyze differences in presentation and outcome following surgical revascularization.

Methods:

This was an Institutional Review Board (IRB) approved, retrospective review of all patients surgically revascularized by the senior author (SNM) while at Children's National Hospital in Washington, DC. Demographic data, presenting symptoms and severity, surgical details, and functional and radiographic outcomes were obtained and analyzed for differences amongst the underlying cohorts of moyamoya disease and syndrome as well as by unilateral or bilateral disease and index or non-index surgeries.

Results:

Twenty-two patients were identified with the following underlying diseases: six with idiopathic moyamoya disease, six with sickle cell anemia, five with trisomy 21, and five with neurofibromatosis type 1. Thirty hemispheres were revascularized with a significantly reduced rate of stroke from 3.19 strokes/year (SD = 3.10) to 0.13 strokes/year (SD = 0.25), $p = 0.03$. When analyzed by underlying cause of moyamoya syndrome, patients with neurofibromatosis type 1 were found to be significantly less likely than the other subtypes of moyamoya syndrome to have had either a clinical stroke (0.0% vs 100.0% [sickle cell], 60.0% [trisomy 21], or 83.3% [moyamoya disease], $p < 0.01$) or radiographic stroke (0.0% vs 100.0% [sickle cell], 60.0% [trisomy 21], or 83.3% [moyamoya disease], $p < 0.01$) at time of presentation. Additionally, patients with bilateral disease demonstrated no difference in final functional outcome (mRS 0.73 (SD = 1.33) vs. 1.29 (SD = 1.60), $p = 0.63$), but second, contralateral surgeries were associated with an increased rate of temporary peri-operative ischemic events when compared to index procedures (50.0% vs 9.1%, $p = 0.03$).

Conclusion:

Surgical revascularization decreases stroke risk for pediatric patients with different forms of moyamoya disease and moyamoya syndrome. In this study, all but one patient underwent pial synangiosis for indirect revascularization.

Introduction

Pediatric arterial ischemic stroke has an annual incidence of 1.72:100,000 [1]. Though rare, these infarcts can have profound impacts on both the patients and the families responsible for caring for them.

Previous research has found that approximately 3.6–8.5% of all pediatric arterial ischemic strokes are related to moyamoya disease (MMD) or moyamoya syndrome (MMS) [1, 2].

MMD, a pathology characterized by idiopathic intracranial carotid artery stenosis, and MMS, which is radiographically identical to MMD but occurs secondary to an associated underlying condition, have classically been treated surgically through either direct or indirect revascularization. Although prior work has identified the subgroups of unilateral and bilateral disease with distinct demographic risk factors and radiological and biochemical findings [3–5], much of the published literature combines MMD and MMS secondary to any underlying disease for analysis given the rarity of the condition as a whole. This can introduce the potential for confounding of results, and potentially lead to difficulties identifying clinically meaningful subpopulations and developing individualized treatment paradigms and surgical approaches for these populations. To that end, we present our case series and analysis separating results by the underlying type of moyamoya to the growing body of literature attempting to understand and treat these disease processes.

Methods

This was an Institutional Review Board approved retrospective review of all moyamoya surgeries performed by the senior author (SNM) between 2009–2019. The electronic medical records were searched for the following data: demographic data, prior treatment history, presenting symptoms, radiographic data, neurological and functional status pre- and post-operatively, surgical details, complications, and follow-up data. Ischemic events were considered transient ischemic attacks (TIAs) if the symptoms lasted less than 24 hours and no sequelae was observed on MRI. Otherwise, all events were considered ischemic strokes. Clinical follow up data, including modified Rankin Scale score (mRS) and incidence of clinical strokes, were obtained from the last available neurosurgical, neurological, or hematological note in a patient's record. Post-operative strokes were identified through both review of these notes and interpretation of all post-operative MRIs each patient had within the hospital system. Angiographic evaluation of revascularization was determined by the Matsushima grade (defined as the percent of the ischemic area revascularized where A = > 66%, B = 33–66%, and C < 33%) on each patient's most recent angiogram.

Data were segregated for analysis in the following ways. Ischemic events were divided into those occurring peri-operatively (within 30 days of surgery) or post-operatively (after 30 days). Pre-and post-operative stroke rates were calculated by dividing the number of strokes a patient had in the time from presentation to our clinic or emergency department to surgery and the time from surgery until last follow up respectively. Each rate was then standardized over 365 days. Post-operative ischemic events were defined as ischemic events occurring in a surgically revascularized hemisphere. Additionally, the decision to preclude ischemic events prior to presentation to our team was made to bias the results towards the null rather than including events from patient-reported histories.

All demographical and outcome data were analyzed using the Statistical Package for Social Sciences (IBM Corporation, 2020). Categorical data were analyzed with a chi-square test while continuous variables were analyzed using a Kruskal-Wallis test. Comparison of pre- and post-operative stroke rates was conducted with a paired-samples sign test. Statistical significance was defined as $p < 0.05$. For the purposes of this study, perioperative refers to the follow-up period within 30 days of surgery, and postoperative refers to the follow-up period after 30 days from surgery.

Revascularization Procedure

The majority of patients were revascularized with superficial temporal artery (STA)-pial synangiosis as follows. Patients were positioned supine with their head rotated so the operative site was facing up. The STA course was mapped with a doppler and the vessel was subsequently dissected with a combination of blunt and sharp dissection under the operative microscope. Branches from the parent vessel were coagulated and cut as needed to free the artery along with a small cuff of galea. Attention was then turned back to the scalp and the temporalis was incised parallel to the STA. Self-retaining retractors were placed and a craniotomy was performed. The dura was opened in parallel with the STA and the arachnoid was opened in multiple places. Using 10 – 0 nylon suture, the galeal cuff of the STA was sewn to the pia in multiple locations to fix it to the surface of the brain. The dural leaflets were laid back onto the surface of the brain and the craniotomy burr holes were widened to allow for free passage of the STA. Finally, the bone flap was plated to the skull over the STA, the temporalis muscle was reapproximated, and the scalp was closed in layers. All patients were post-operatively managed in the pediatric ICU with close neurological monitoring, intravenous (IV) fluids, and blood pressure management. Generally, in patients with bilateral disease, the two sides were completed in a staged fashion separated by several weeks.

Results

Review of the electronic medical record identified 22 patients (40.9% male) with a mean age of 7.47 years (SD = 5.65). Of these, 16 carried a diagnosis known to predispose to MMS: six sickle-cell anemia (SCA), five trisomy-21, and five neurofibromatosis type 1 (NF1). At the time of presentation, the mean modified Rankin Scale [mRS] was 1.05 [SD = 1.59]. The majority of patients had clinical (63.6%) or radiographic (68.2%) strokes. Of note, both clinical and radiographic strokes were less frequently seen in NF1 patients ($p < 0.01$) on presentation. Children with trisomy 21 tended to present at an older age compared to other underlying causes. Additionally, 27.3% of patients were already on an antiplatelet agent at presentation to the neurosurgeon, with the remaining patients started on aspirin at the time of presentation (see Table 1).

Table 1
Demographical data for total cohort and underlying disease subgroups. Data presented as counts with percentages (%) or means with standard deviation (no labeling). * denotes p < 0.05.

Patient Population	Total Cohort	SCA	T21	NF1	MMD	p-value
N (Patients)	22	6	5	5	6	
N (Hemispheres)	30	11	5	5	9	
Gender (% Male)	9 (40.9%)	5 (83.3%)	1 (20.0%)	1 (20.0%)	2 (33.3%%)	0.09
Age at Presentation	7.5 (5.7)	5.3 (2.8)	12.7 (7.3)	5.6 (5.3)	6.9 (5.0)	0.38
Pre-Op mRS	1.05 (1.59)	1.67 (1.63)	0.60 (1.34)	0.00 (0.00)	1.67 (2.07)	0.15
Presenting Symptoms						
Stroke	14 (63.6%)	6 (100.0%)	3 (60.0%)	0 (0%)	5 (83.3%)	< 0.01*
TIA	4 (18.2%)	1 (16.7%)	0 (0%)	1 (20.0%)	2 (33.3%)	0.56
Seizure	4 (18.2%)	0 (0%)	3 (60.0%)	0 (0%)	1 (16.7%)	0.04
Radiographic Findings						
Radiographic Strokes	15 (68.2%)	6 (100.0%)	4 (80.0%)	0 (0.0%)	5 (83.3%)	< 0.01*
Ivy Sign	14 (63.6%)	4 (66.7%)	3 (60.0%)	4 (80.0%)	3 (50.0%)	0.77
Suzuki Score	3.83 (1.07)	3.50 (1.43)	4.20 (0.84)	4.00 (0.71)	3.89 (0.93)	0.64

Thirty operations were performed in the 22 patients with all but one patient (96.7%) undergoing an indirect revascularization through either a STA-to-pial synangiosis (N = 28) or a frontal pericranial-to-pial synangiosis (N = 1); one patient underwent a direct STA-to-MCA bypass. Patients requiring bilateral revascularization were more likely to have SCA than trisomy 21 or NF1 (mean number of sides 1.8 (0.8) vs. 1.0 (0.0) and 1.0 (0.0) respectively, p = 0.04). Intraoperatively, there were no ischemic complications and only 13.6% of patients had changes on electroencephalography, all of which normalized with an increase in blood pressure prior to completion of surgery. There were no intraoperative differences based on underlying etiology of MMD or MMS (see Table 2).

Table 2
Intraoperative data and peri-operative ischemic events by hemisphere for the total cohort and each underlying disease subgroups. In this study the peri-operative period refers to the first 30 days after surgery. Data presented as counts with percentages (%) or means with standard deviation (no labeling). * denotes $p < 0.05$.

	Total Cohort	SCA	T21	NF1	MMD	p-value
Intraoperative Data						
Indirect Bypass	29 (96.7%)	11 (100.0%)	4 (80.0%)	5 (100.0%)	9 (100.0%)	
EBL (mL)	117.5 (76.1)	121.8 (73.1)	102.5 (70.9)	106.0 (111.5)	125.3 (72.2)	0.74
EEG Changes	3 (10.3%)	3 (27.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.14
Intraop Complications	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	n.s.
Peri-Operative Ischemic Events						
Stroke	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (11.1%)	0.49
TIA	6 (20.0%)	2 (18.2%)	0 (0.0%)	0 (0.0%)	4 (44.4%)	0.12
Death	0	0	0	0	0	

Amongst the 30 operations, seven (23.3%) ischemic events occurred in the peri-operative period within 30 days of surgery. Six (20.0%) of these were transient ischemic attacks (TIAs) while only one (3.3%) resulted in a permanent neurological deficit (see Table 2). Additionally, non-perfusion related complications occurred in five operations: one wound infection, one case of wound breakdown, one seizure, one cerebrospinal fluid leak, and one acute hydrocephalus in a patient with a history of an endoscopic third ventriculostomy (ETV).

Additional stratification of patients by unilateral or bilateral disease as well as surgical intervention by index or second procedure was performed to better delineate differences in outcomes. There were 15 patients with unilateral disease and seven patients with bilateral disease. Demographic analysis demonstrated that the only significant difference between patients with unilateral or bilateral disease was in the rate of stroke as a presenting symptom (46.7% for unilateral disease and 100% for bilateral disease, $p = 0.02$; see Table 3). There was no difference in the incidence of peri- or post-operative ischemic events based on unilateral or bilateral disease. In the seven patients with bilateral disease requiring a contralateral revascularization, there was an increased rate of peri-operative TIAs (9.1% for index surgery and 50.0% for second surgery, $p = 0.03$) despite there being no difference in intra-operative surgical variables or rate of peri-operative strokes (see Table 4). All four TIAs were ipsilateral to the operative side and resolved without permanent symptoms.

Table 3
Demographics and peri- and post-operative ischemic events segregated by unilateral or bilateral disease. Data presented as counts with percentages (%) or means with standard deviation (no labeling). * denotes $p < 0.05$. # denotes strokes occurring within a previously revascularized hemisphere.

	Total Cohort	SCA	T21	NF1	MMD	p-value
Long term Clinical Follow Up						
Length (yrs)	3.5 (2.8)	5.2 (3.1)	3.5 (3.0)	2.9 (2.6)	2.3 (2.2)	
mRS at follow-up	0.91 (1.41)	1.33 (1.37)	0.60 (0.89)	0.00 (0.00)	1.50 (2.07)	0.18
Radiographic Follow Up						
MRI F/up Length (yrs)	3.9 (2.6)	5.1 (2.9)	4.0 (3.1)	3.7 (2.2)	2.6 (2.3)	0.44
Angio F/up Length (yrs)	1.5 (0.7)	2.0 (0.9)	1.3 (0.2)	1.0 (0.0)	1.1 (0.2)	0.03*
Matsushima A	19 (90.5%)	6 (75%)	4 (100.0%)	3 (100.0%)	6 (100.0%)	0.31
Post-Op Long term Events in Follow up Period						
Stroke#	5 (22.3%)	2 (33.3%)	1 (20.0%)	0 (0.0%)	2 (33.3%)	0.52
TIA	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	n.s.
Mortality	1 (4.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	0.43

Table 4
Intraoperative details and peri-operative (within 30 days of surgery) ischemic events by index or second surgery. Data presented as counts with percentages (%) or means with standard deviation (no labeling). * denotes $p < 0.05$.

	Index Surgery	Surgery for Second Side	p-value
Number of Hemispheres	22	8	
Intraoperative Data			
EBL (mL)	116.9 (73.6)	119.1 (87.8)	0.96
EEG Changes	1 (4.8%)	2 (25.0%)	0.18
Intraop Complications	0 (0.0%)	0 (0.0%)	n.s.
Peri-Operative Ischemic Events			
Stroke	1 (4.5%)	0 (0.0%)	1.00
TIA	2 (9.1%)	4 (50.0%)	0.03*

Patients were followed for a mean of 3.5 years clinically (SD = 2.8 years) and 3.9 years radiographically (SD = 2.6) during which time there were five post-operative strokes (22.3%) on a revascularized side, two post-operative strokes (9.1%) on a non-revascularized side, and one mortality (4.5%) with no difference between underlying disease groups for either outcome. There was also no difference in functional status based on etiology and the entire cohort's functional status remained excellent throughout the follow up period (pre-operative mRS = 1.05, SD 1.59 and post-operative mRS = 0.91, SD = 1.41 respectively, p = 0.38). Angiographic evaluation demonstrated successful revascularization of the ischemic territory with 90.5% of all patients achieving Matsushima A revascularization (see Table 5). A representative angiogram is demonstrated in Fig. 1.

Table 5

Post-operative follow-up when patients are separated by unilateral or bilateral disease. All follow-up data is presented in years. Data presented as counts with percentages (%) or means with standard deviation (no labeling). * denotes $p < 0.05$. # denotes strokes occurring within a previously revascularized hemisphere.

	Unilateral Disease	Bilateral Disease	p-value
Demographics			
N (Patients)	15 (68.2%)	7 (31.8%)	
N (Hemispheres)	15 (50%)	15 (50%)	
Gender (% Male)	4 (26.7%)	5 (71.4%)	0.07
Age	7.5 (6.2)	7.4 (4.7)	0.55
Pre-Op mRS	0.87 (1.51)	1.43 (1.81)	0.49
SCA	2 (13.3%)	4 (57.1%)	0.05
T21	5 (33.3%)	0 (0.0%)	0.14
NF1	5 (33.3%)	0 (0.0%)	0.14
MMD (idiopathic)	3 (20%)	3 (42.9%)	0.33
Presenting Stroke	7 (46.7%)	7 (100.0%)	0.02*
Radiographic Stroke	8 (53.3%)	7 (100.0%)	0.05
Ivy Sign	10 (66.7%)	4 (57.1%)	1.00
Suzuki Score	3.93 (0.88)	3.71 (1.27)	0.64
Outcomes			
Clinical F/up Length	3.0 (2.3)	4.7 (3.5)	0.30
Radiographic F/up Length	3.4 (2.2)	4.9 (3.3)	0.37
mRS	0.73 (1.33)	1.29 (1.60)	0.63
Matsushima A	81.80%	100.0%	0.16

Evaluation of the change in stroke rate was conducted for the total cohort and each underlying cause. The stroke rate decreased in the total cohort (2.45 strokes/year [SD = 3.63] pre-operatively and 0.23 strokes/year [SD = 0.77] post-operatively, $p < 0.001$) and for patients in each cohort (see Table 6). There was one patient who died in long term follow-up due to severe progressive moyamoya disease.

Table 6
Pre- and post-operative stroke rates standardized to per 365 days. Data presented as means with standard deviation. * denotes $p < 0.05$.

	Pre-Operative Stroke Rate	Post-Operative Stroke Rate	p-value
Total	2.45 (3.63)	0.23 (0.77)	< 0.001*
SCA	3.19 (3.10)	0.13 (0.25)	0.03*
T21	0.73 (0.91)	0.09 (0.19)	0.25
NF1	0.00 (0.00)	0.00 (0.00)	n.s.
MMD	5.19 (5.16)	0.63 (1.46)	0.06

Discussion

MMD/MMS remain rare entities with an annual incidence of 0.09:100,000 in the United States [6]. When these diseases are separated by the underlying etiologies however, the incidence of MMS becomes even smaller; a finding reflected in the published literature with multiple large studies on MMD but significantly fewer and smaller reports on subcategories of MMS [7–11]. Here, we have presented our case series of MMD/MMS segregated by underlying disease process. The results from this cohort demonstrate that indirect surgical revascularization is a safe and effective treatment that results in a significant reduction in stroke rate for patients with MMD or MMS from SCA, trisomy 21, or NF1. While this finding adds to the growing body of literature supporting indirect revascularization for these patients [8, 11–13], two other findings warrant further discussion.

Pediatric MMD/MMS classically presents following ischemic events with published rates of a presenting ischemic stroke ranging from 67.8–92% [7, 11, 14]. The NF1 cohort presented here, however, was significantly less likely to have suffered a clinical or radiographic stroke prior to presentation. This is similar to previously published reports of low pre-operative stroke rates in this population with clinical stroke rates between 0-43.7% and radiographic strokes rates between 6.7–56.3% [9, 10, 15]. Additionally, the cited higher rates of infarctions are seen predominantly in NF1 patients who have undergone prior cranial radiation [10]. While it is clear that earlier and incidental detection of MMS can be accomplished by the intensive intracranial screening NF1 patients receive, our population of NF1 patients demonstrated no difference in age or pre-operative Suzuki score suggesting that these patients' MMS was not necessarily detected at an earlier state, but was detected before signs of ischemic events. When this finding, which is supported by previous literature [10], is combined with the lack of ischemic complications seen in the peri- and post-operative period in both this cohort and previous reports [9, 15], it raises the possibility that the MMS variant associated with NF1 may present in a more benign manner than MMS associated with other disease processes such as SCA. Because previous work has demonstrated that NF1-associated MMS is progressive in nature [10] and that earlier surgery is

associated with improved outcomes [3, 10] surgical revascularization was still performed in our cohort without evidence of stroke, although most patients had evidence of “ivy sign” changes on MRI.

The differences between patients with unilateral MMD/MMS and those with bilateral MMD/MMS remains a clinically important distinction. While it is clear that there is a group of patients who progress from unilateral MMD/MMS to bilateral disease, determining the precise demographic [3], radiologic [4], and/or biochemical [5] factors predisposing this transition remains a subject of active research. When comparing the cohorts included here, the only difference in presentation between the groups was that patients with bilateral disease were more likely to present with a stroke than those with unilateral disease. Ultimately, this difference did not impact treatment however, as both groups were able to be safely revascularized with good functional outcomes, a finding in agreement with previous literature [3, 8, 11].

Despite the lack of difference in patient outcome, more patients did had perioperative TIA’s after second surgery than first surgery. As we elected to stage bilateral surgeries on separate days, it is unclear if performing bilateral revascularization on the same day would have led to fewer TIA’s, or if those patients would have had TIA’s regardless of the timing of the second operation. Further research into this finding could better delineate the ideal time for subsequent revascularizations.

It is important to note that, as with many retrospective reviews on MMD/MMS, the small population of included patients limits the power of statistical testing. This lack of power was accepted here rather than clustering patients with MMS together to avoid obscuring differences that may exist among different etiologies of MMS as well as to avoid confounding by underlying disease.

Conclusion

Indirect surgical revascularization can be performed safely in pediatric patients with MMD or MMS and provide significant reduction in risk of future stroke. Additionally, NF1-associated MMS may represent a more benign form of MMS than other variants. Further study through large systematic reviews and meta-analyses into these rare populations can provide a better understanding of the disease process and produce improved treatments and outcomes.

Declarations

Ethics Approval: Ethics approval was obtained from the Children’s National Medical Center Institutional Review Board without the need for patient consent due to the retrospective and anonymized nature of the data used.

Consent for Publication: No included figures require consent for publication.

Availability of Data and Materials: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests: The authors have no competing interests to disclose.

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Authors' Contributions: Jason Boulter and Suresh Magge created the plan for the project. Suresh Magge performed the surgical interventions and Jason Boulter collected the data. Jason Boulter and Nicholas Szuflita performed the analyses. Jason Boulter, Nicholas Szuflita, and Suresh Magge interpreted the data and wrote the manuscript. All authors critically evaluated and revised the manuscript.

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References

1. deVeber GA, Kirton A, Booth FA, et al. Epidemiology and Outcomes of Arterial Ischemic Stroke in Children: The Canadian Pediatric Ischemic Stroke Registry. Pediatric Neurology. 2017;69:58–70.
2. Rafay MF, Shapiro KA, Surmava A-M, et al. Spectrum of Cerebral Arteriopathies in Children with Arterial Ischemic Stroke. Neurology. 2020;94(23).
3. Smith ER, Scott RM. Progression of Disease in Unilateral Moyamoya Syndrome. Neurosurgical Focus. 2008;24(2):E17.
4. Kelly ME, Bell-Stephens TE, Marks MP, Do HM, Steinberg GK. Progressin of Unilateral Moyamoya Disease: A Clinical Series. Cerebrovascular Diseases. 2006;22:109–115.
5. Houkin K, Abe H, Yoshimoto T, Takahashi A. Is "Unilateral" Moyamoya Disease Different From Moyamoya Disease? Journal of Neurosurgery. 1996;85(5):772–776.
6. Uchino K, Johnson SC, Becker KJ, Tirschwell DL. Moyamoya Disease in Washington State and California. Neurology. 2005;65(6):956–958.
7. Gadgil N, Lam S, Pyarali M, Paldino M, Pan I-W, Dauser RC. Indirect Revascularization with the Dural Inversion Technique for Pediatric Moyamoya Disease: 20-Year Experience. Journal of Neurosurgery: Pediatrics. 2018;22(5):541–549.
8. Griessenauer CJ, Lebensburger JD, Chua MH, et al. Encephaloduroarteriosynangiosis and Encephalomyoarteriosynagiosis for Treatment of Moyamoya Syndrome in Pediatric Patients with Sickle Cell Disease. Journal of Neurosurgery. 2015;16(1):64–73.
9. Santoro C, Rocco FD, Kossorotoff M, et al. Moyamoya Syndrome in Children with Neurofibromatosis Type 1: Italian-French Experience. American Journal of Medical Genetics. 2017;173(6):1521–1530.
10. Koss M, Scott RM, Irons MB, Smith ER, Ullrich NJ. Moyamoya Syndrome Associated with Neurofibromatosis Type 1: Perioperative and Long-Term Outcome After Surgical Revascularization. Journal of Neurosurgery: Pediatrics. 2013;11(4):377–488.
11. Scott RM, Smith JL, Robertson R, Madsen JR, Soriano SG, Rockoff MA. Long-Term Outcome in Children with Moyamoya Syndrome after Cranial Revascularization by Pial Synangiosis. Journal of Neurosurgery. 2004;100(2):142–149.

12. Kim S-K, Cho B-K, Phi JH, et al. Pediatric Moyamoya Disease: An Analysis of 410 Consecutive Cases. Annals of Neurology. 2010;68(1):92–101.
13. Newman S, Boulter JH, Malcolm JG, Pradilla I, Pradilla G. Outcomes in Patients with Moyamoya Syndrome and Sickle Cell Disease: A Systematic Review. World Neurosurgery. 2020;135:165–170.
14. Hankinson TC, Bohman L-E, Heyer G, et al. Surgical Treatment of Moyamoya Syndrome in Patients with Sickle Cell Anemia: Outcome Following Encephaloduroarteriosynangiosis. Journal of Neurosurgery. 2008;1:211–216.
15. Ghosh PS, Rothner AD, Emch TM, Friedman NR, Moodley M. Cerebral Vasculopathy in Children with Neurofibromatosis Type 1. Journal of Child Neurology. 2013;28(1):95–101.

Figures

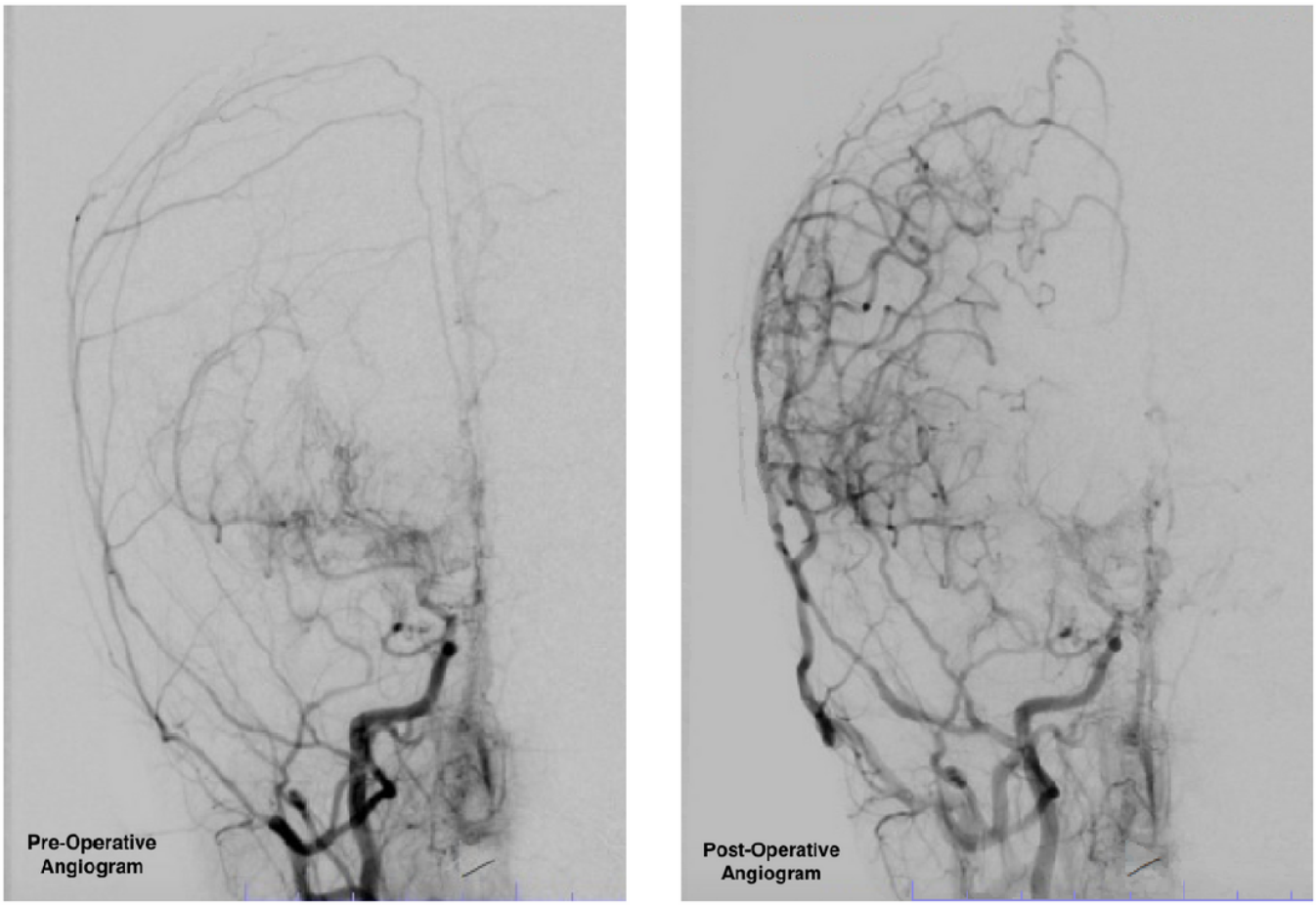

Figure 1

Legend not included with this version.