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Surgical Revascularization in North American Adults with Moyamoya Phenomenon: Long Term Angiographic Follow-Up

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Abstract

Background—North American and Asian forms of moyamoya have distinct clinical characteristics. Asian adults with moyamoya are known to respond better to direct vs. indirect revascularization. It is unclear whether North American adults with moyamoya have a similar long-term angiographic response to direct vs. indirect bypass.

Methods—A retrospective review of surgical revascularization for adult moyamoya phenomenon was performed. Pre-operative and post-operative cerebral angiograms underwent consensus review, with degree of revascularization quantified as extent of new middle cerebral artery (MCA) territory filling.

Results—Late angiographic follow up was available in 15 symptomatic patients who underwent 20 surgical revascularization procedures. In 10 hemispheres treated solely with indirect arterial bypass, 3 had 2/3 revascularization, 4 had 1/3 revascularization, and 3 had no revascularization of the MCA territory. In the 10 hemispheres treated with direct arterial bypass (8 as a stand alone procedure; 2 in combination with an indirect procedure), 2 had complete revascularization, 7 had 2/3 revascularization, and 1 had 1/3 revascularization. Direct bypass provided a higher rate of “good” angiographic outcome (complete or 2/3 revascularization) when compared to indirect techniques ($p = 0.0198$).

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Conclusions—Direct bypass provides a statistically significant, more consistent and complete cerebral revascularization than indirect techniques in this patient population. This is similar to that reported in the Asian literature, which suggests that the manner of presentation (ischemia in North American adults vs. hemorrhage in Asian adults) is likely not a contributor to the extent of revascularization achieved following surgical intervention.

Keywords

moyamoya; EDAS; EDAMS; STA-MCA; revascularization

INTRODUCTION

Moyamoya phenomenon refers to an uncommon pattern of cerebrovascular collateral formation that occurs in response to occlusive vasculopathies affecting the arteries of the circle of Willis. The name stems from the appearance of these collaterals on conventional catheter angiography; “moyamoya” translated from Japanese means “a hazy cloud like a puff of cigarette smoke.”[1] This phenomenon has been strictly classified as follows: 1) definite moyamoya disease when no underlying etiology is present and angiography reveals *bilateral* steno-occlusion of the distal internal carotid or proximal anterior/middle cerebral arteries and abnormal networks of collateral vessels (termed moyamoya collaterals) near the site of occlusion; 2) probable moyamoya disease when no underlying etiology is present and angiography reveals *unilateral* steno-occlusive changes and associated moyamoya collaterals; and 3) moyamoya syndrome when an underlying etiology such as sickle cell disease, radiation therapy, atherosclerosis, or autoimmune disease is present and angiography reveals unilateral or bilateral steno-occlusive changes and associated moyamoya collaterals.[2 3]

First described in 1957 by Shimizu and Takeuchi,[4] moyamoya disease is common in Japan and other Asian countries but has also been documented worldwide, including multiple reports from North America.[5] The Asian moyamoya phenotype is characterized by a bimodal age distribution (a large peak in the first decade of life and a smaller peak in the fourth decade of life), a minor female predominance (female:male ratio ~ 1.5:1), and a propensity for pediatric patients to present with ischemia and adult patients to present with hemorrhage.[6 7] In contrast, the North American moyamoya phenotype is characterized by a unimodal age distribution (primarily in the 3rd, 4th, and 5th decades of life), a major female predominance (female:male ratio ~ 3:1), and a predilection for patients to present with ischemia.[8]

Surgical interventional for cerebral revascularization is the mainstay of treatment for symptomatic patients with moyamoya phenomenon. While the efficacy of surgical therapy for moyamoya patients has yet to be proven in a randomized controlled trial, numerous large, well-documented case series strongly suggest that surgical revascularization for pediatric[9–12] and adult [13–15] patients presenting with ischemia likely affords clinical benefit. Whether a similar clinical benefit is realized in adult moyamoya patients presenting with hemorrhage is more controversial. The recent Japan Adult Moyamoya Trial found lower rates of recurrent bleeding, disabling stroke, or death in Asian moyamoya patients

presenting with intracranial hemorrhage randomized to bilateral superficial temporal to middle cerebral artery bypass instead of medical management.[16] However, the small study size of only 80 patients, a lower than expected surgical complication rate, and questions about the outcomes analysis, make the results difficult to generalize.[17]

Numerous surgical revascularization techniques have been developed and applied to the moyamoya patient population. These include indirect surgical techniques that have been shown to provide excellent angiographic and clinical results in pediatric moyamoya patients, [12–18] but less satisfactory results in adult moyamoya patients from Asia.[19] In fact, several studies have demonstrated that direct extracranial-intracranial arterial bypass is superior to indirect revascularization techniques for Asian adults with moyamoya.[13–15] These results raise the intriguing question whether the presenting symptomatology and neural milieu in Asian children with moyamoya (ischemia) vs. Asian adults with moyamoya (hemorrhage) may play a critical role in the angiographic response to surgical intervention. To date, however, the few studies that attempt to address this point have been limited by either only analyzing one form of surgical intervention,[20] or using imaging techniques other than the gold standard of digital subtraction catheter angiography (DSA).[21] Therefore, in the present study we sought to gain a better understanding of the angiographic and clinical response to direct vs. indirect revascularization in a North American series of adult moyamoya patients who presented primarily with cerebral ischemia.

MATERIALS AND METHODS

Patients

We identified via retrospective chart review all adult patients (18 years or older) with moyamoya phenomenon identified by DSA that underwent either direct or indirect surgical revascularization between 1996 and 2010 at our North American institution. Inclusion criteria included: 1) Pre-operative DSA that demonstrated unilateral or bilateral supraclinoid internal carotid artery or proximal middle cerebral artery steno-occlusion in addition to the presence of moyamoya collaterals, 2) direct or indirect surgical intervention, and 3) available late angiographic follow-up. A total of 27 patients underwent surgical revascularization during this time period. Three patients were excluded because pre-operative DSA was unavailable for review. Late angiographic follow-up was performed in 15 patients who become the subject of this report. These 15 patients underwent revascularization procedures on a total of 20 hemispheres, and mean time to late postoperative angiography was 15.2 months (Table 1). Patients were aged 20–57 at time of presentation (mean age = 37.6) and included 12 women and 3 men. There was one Asian patient in this series.

Surgical revascularization

Indirect revascularization was performed as previously described, using either encephaloduroarteriosynangiosis (EDAS) or encephaloduroarteriomyosynangiosis (EDAMS).[2–3] Direct revascularization was performed as previously described, consisting of superficial temporal artery-to-middle cerebral artery (STA-MCA) bypass.[2–3] In select cases, the STA-MCA bypass was performed with a concomitant EDAS or EDAMS.

Surgeries were performed by 4 different neurosurgeons in our department; the choice of procedure was at the discretion of the treating surgeon.

Angiographic follow-up

All patients in the series underwent pre-operative diagnostic DSA and also underwent follow-up post-operative DSA at various time intervals after revascularization. Angiograms were reviewed by consensus and were assessed for (a) degree of middle cerebral artery (MCA) territory revascularization (categorized as complete revascularization, 2/3 revascularization, 1/3 revascularization, or none); (b) presence of collateral vessels; and (c) patency of bypass if direct procedure performed. These parameters were assessed over time in cases where serial postoperative DSA was conducted.

Statistical Analysis

Angiographic results were dichotomized based on the degree of MCA territory revascularization. A “good” outcome was defined as one whose extent of revascularization ranged from complete to two thirds. Hemispheres where the revascularization of the territory was only 1/3 were considered a “poor” outcome. Each hemisphere was evaluated and classified independently. Univariate analysis assessing the affect of direct bypass on angiographic results was completed using Fisher’s Exact *t*-test. However, it is likely that the responses seen in a patient’s left and right hemisphere cannot be considered independent observations. Therefore, we further analyzed the data using a generalized linear model considering the patient as random effect, which accounted for the correlation between an individual’s hemispheres. All statistical computations were completed using SAS 9.1 (SAS Institute, Cary, NC), and significance was defined as $p < 0.05$.

RESULTS

Clinical Presentation

Eleven of fifteen patients in this series presented with ischemic symptoms (Table 1). Two patients presented with intracerebral hemorrhage, one of which also presented with accompanying intraventricular hemorrhage. Two patients presented initially with ischemic symptoms, and were referred to our institution after suffering an intracerebral hemorrhage. Preoperative DSA demonstrated bilateral disease in 14 patients and unilateral disease in 1 patient. Patients were categorized as having definite moyamoya disease (Patients 1, 2, 4–6, 8, 9, 11–15), probable moyamoya disease (Patient 7), or moyamoya syndrome (Patients 3, 10). Patient 7 was considered “probable” moyamoya disease because steno-occlusive arterial changes were unilateral rather than bilateral. Patients 3 and 10 were considered moyamoya syndrome due to lack of moyamoya collaterals (Patient 3) or presence of an underlying etiology (Patient 10).

Surgical Treatment

Indirect bypass—Indirect procedures were performed on 10 hemispheres in 9 patients. One of these patients (Patient 7) presented with hemorrhage and underwent a left-sided EDAS procedure; and one patient (patient 15) presented initially with ischemia and had a hemorrhagic event prior to undergoing left-sided EDAS. The other 7 patients (Patients 1, 2,

5, 7, 8, 9, 12) presented with ischemic symptoms and underwent a total of 3 EDAMS and 5 EDAS procedures.

Direct bypass—Eight isolated direct STA-MCA bypass procedures were performed on 8 hemispheres in 6 patients. Four of these patients presented with ischemic symptoms (Patients 3, 11, 12, 13), one patient presented with cerebral hemorrhage (Patient 4), and one patient presented initially with ischemic symptoms but was referred to our institution after a hemorrhagic event (patient 14).

Combined direct and indirect bypass—Two patients underwent combined direct and indirect bypass procedures consisting of STA-MCA bypass and a concomitant EDAMS (Patient 6) or EDAS (Patient 10). In both cases, direct procedures were performed prior to the indirect component. Both patients originally presented with ischemic symptoms.

Indirect bypass—Late follow-up angiograms on the 10 hemispheres treated with an indirect bypass procedure were obtained at a mean of 1.4 years following surgery. In the 4 hemispheres treated with an EDAMS procedure, EDAMS failed to produce complete revascularization in any hemisphere, but resulted in 2/3 revascularization of the MCA territory in 2 hemispheres, 1/3 revascularization of the MCA territory in 1 hemisphere, and no revascularization in 1 hemisphere. In the 6 hemispheres treated with an EDAS procedure, EDAS failed to produce complete revascularization in any hemisphere, but resulted in 2/3 revascularization of the MCA territory in 1 hemisphere, 1/3 revascularization of the MCA territory in 3 hemispheres, and no revascularization in 2 hemispheres (Table 2). An example of revascularization seen after an indirect procedure is demonstrated in Figure 1.

Out of the hemispheres presenting with ischemia, 2 showed 2/3 revascularization of the MCA territory, 4 showed 1/3 revascularization of the MCA territory, and 2 showed no revascularization. Of those presenting with hemorrhage, 1 showed 2/3 revascularization of the MCA territory and 1 showed no revascularization. In the 3 patients who underwent serial angiographic follow-up, 2 showed progressive MCA revascularization over time (Patients 5 and 6) and 1 showed no further MCA revascularization (Patient 8). No patient experienced postoperative ipsilateral ischemic or hemorrhagic stroke within a mean clinical follow-up interval of 3.3 years.

Direct bypass—Late follow-up angiograms on the 8 hemispheres treated solely with a direct STA-MCA bypass were obtained at a mean time of 11.3 months from surgery. Of these, 2 hemispheres showed complete revascularization of the MCA territory, 5 hemispheres showed 2/3 revascularization of the MCA territory, and 1 hemisphere showed 1/3 revascularization of the MCA territory (Table 2). An example of revascularization seen after a direct procedure is demonstrated in Figure 2.

Out of the hemispheres presenting with ischemia, 1 showed complete revascularization of the MCA territory, 4 showed 2/3 revascularization of the MCA territory, and 1 showed 1/3 revascularization of the MCA territory. Of those presenting with hemorrhage, 1 showed complete revascularization of the MCA territory and 1 showed 2/3 revascularization of the

MCA territory. No patient experienced post-operative ipsilateral ischemic or hemorrhagic stroke within a mean clinical follow-up interval of 2.3 years.

Combined direct and indirect bypass—Late follow-up angiograms on the 2 hemispheres treated with a combined direct and indirect revascularization procedure were obtained at a mean time of 1.2 years from surgery. One patient who presented with ischemia and was treated with combined STA-MCA bypass and EDAMS experienced 1/3 revascularization of the MCA territory at 9 days and 2/3 revascularization of the MCA territory at 16 months (Table 2). The majority of the delayed revascularization resulted from extracranial-intracranial indirect collateral vessel development via EDAMS rather than through the direct arterial bypass. One patient who presented with ischemia and was treated with a combined STA-MCA bypass and EDAS experienced 2/3 revascularization of MCA territory after 1 year, with virtually all flow supplied by EDAS indirect collaterals. No patient experienced post-operative ipsilateral ischemic or hemorrhagic stroke within a mean clinical follow-up interval of 3.0 years.

Statistical Results—Of those hemispheres undergoing direct revascularization using direct +/- indirect bypass, 9 of 10 (90%) were found to have a “good” angiographic outcome compared to 3 of 10 (30%) hemispheres in which only indirect bypass was used. In univariate analysis, the odds ratio of having a “good” angiographic outcome using direct bypass was 21 (95% CI 1.78 to 248.1) when compared to indirect techniques. This was statistically significant with $p = 0.0198$ (Fisher’s exact t -test). Using the generalized linear model accounting for the correlation between left and right hemispheres, the degree of revascularization was again found to be significantly higher in the direct bypass group compared to the indirect bypass group with an OR of 10.5 (95% CI 1.1 to 102.2) and $p = 0.0435$.

DISCUSSION

In this study, we assessed late angiographic response as well as clinical outcomes following direct and indirect surgical revascularization for a single institution series of North American adult patients with moyamoya. We found that while both direct and indirect procedures generally produced MCA revascularization, the proportion of patients in which a good angiographic outcome was seen was significantly higher in the direct bypass group (90%) when compared to the indirect group (30%). As expected, revascularization after indirect surgery took months to develop. Interestingly, the ultimate angiographic response achieved following direct surgical bypass resulted from a combination of direct flow via bypass as well as indirect augmentation via progressive development of indirect meningeal-pial collaterals. Our analysis also demonstrated that, irrespective of the mode of surgical treatment (indirect vs. direct), no patient experienced subsequent ipsilateral stroke or hemorrhage at long-term follow-up (mean 3.0 years). Together, these data provide insight into the long-term angiographic response as well as clinical outcome following surgical treatment of North American adult moyamoya population and suggest 1) surgical revascularization in this patient population is an effective means for improving perfusion to the affected hemisphere and reducing the risk of subsequent neurologic events; and 2) direct surgical revascularization provides more robust and consistent angiographic results.

As has been documented by several authors including ourselves,[8 22–26] North American adult patients with moyamoya phenomenon have distinct clinical characteristics as compared to the more extensively studied Asian adult population. One of the most prominent distinctions appears to be the manner of patient presentation. Multiple studies from the Asian literature demonstrate that most commonly adult-onset moyamoya disease presents with cerebral hemorrhage.[1 2 6 27] For example, Houkin and colleagues noted that 24/35 Japanese patients (68.6%) with adult moyamoya disease presented with cerebral hemorrhage.[14] In contrast, several recent studies show that North American adult moyamoya patients are much more likely to present with cerebral ischemia rather than hemorrhage. For example, we recently examined a larger group of adult patients with moyamoya phenomenon from our North American institution and noted 24/34 patients (70.6%) presented with symptoms of cerebral ischemia, whereas only 7/34 patients (20.6%) presented with hemorrhage.[8] Furthermore, it appears that classic moyamoya disease is less common in adult patients from North America vs. Asia.[8] Together, these clinical characteristics strongly suggest that moyamoya phenomenon in North American adults is a distinct clinical entity and that the natural history and response to treatment needs to be specifically examined in this unique population.

Although our study of 20 surgically treated hemispheres in 15 patients is somewhat limited due to small patient number and its retrospective nature, it is the first to specifically examine long-term angiographic results following direct vs. indirect bypass surgery in North American adult moyamoya patients. Several important observations were made. First, we found that direct surgical bypass procedures produced consistent revascularization of the MCA territory in all patients, with a statistically significant difference in the number of “good” outcomes when compared with indirect bypass. Second, we found that the revascularization achieved following direct bypass resulted from both direct reperfusion via the bypass itself as well as from the progressive development of extracranial-intracranial collateral vessels over time. This observation is important because some surgeons may be reluctant to perform an STA-MCA bypass when steno-occlusive changes effectively isolate the frontal from the temporal MCA vascular bed (Figure 3A). Our results suggest that this should not be a concern, as direct bypass procedures were observed to produce broad MCA revascularization via both direct and indirect pathways. Third, we found that indirect surgical procedures produced significant but incomplete revascularization of the MCA territory in most but not all patients, that this revascularization developed over many months, and that EDAMS procedures tended to produce more robust angiographic response as compared to EDAS procedures (Table 2).

These results are significant in that previous comparisons between revascularization procedures for moyamoya phenomenon have come exclusively from the Asian literature. It is often stated that indirect revascularization procedures are (a) more successful in children than in adults and (b) provide less overall angiographic revascularization than direct bypass procedures.[6 14 19 28 29] Although not conclusive due to the non-randomized and retrospective study design, many surgeons utilize these reports to guide surgical management of their patients with moyamoya phenomenon. However, due to the aforementioned substantial differences in the nature of moyamoya phenomenon in North American vs. Asian adults, conclusions from the Asian literature regarding the efficacy of

direct vs. indirect bypass procedures for the management North American adults should be drawn with caution. For example, it is plausible that the presence of an ischemic stimulus—as one would expect in the majority of pediatric and North American adults, but not in Asian adults—might greatly impact the degree of revascularization achieved following indirect procedures. Results from our study, however, suggest that despite the greater presence of ischemic stimuli in North American adults, angiographic response following surgical revascularization was similar to that reported in Asian adults. Specifically, direct surgery appeared to provide more consistent and more complete MCA revascularization than indirect procedures.[14] We did note that the development of indirect collaterals contributed significantly to the overall revascularization following direct bypass procedures alone or combined with indirect procedures, which contrasts with at least one study in the Asian literature. Specifically, Houkin et al.[19] showed that the contribution of indirect bypass in combined direct and indirect surgical revascularization was poor. It is possible that the higher incidence of ischemic stimuli in North American adults accounts for this particular finding.

CONCLUSIONS

Moyamoya phenomenon in the North American adult population appears to be a distinct clinical entity from that in the Asian adult population. Long-term post-operative angiographic follow-up demonstrates a statistically significant improvement in degree of revascularization favoring direct bypass over indirect bypass. This is similar to results previously reported in the Asian literature. There were no cases associated with long-term ipsilateral stroke or hemorrhage. Future studies in larger patient populations will be critical to generalize these findings in the North American adult moyamoya population, and to better delineate the relationship between long-term angiographic and clinical outcome.

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References

1. Suzuki J, Takaku A. Cerebrovascular “moyamoya” disease. Disease showing abnormal net-like vessels in base of brain. *Arch Neurol*. 1969; 20(3):288–99. [PubMed: 5775283]
2. Fukui M. Guidelines for the diagnosis and treatment of spontaneous occlusion of the circle of Willis (‘moyamoya’ disease). Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan. *Clin Neurol Neurosurg*. 1997; 99 (Suppl 2):S238–40. [PubMed: 9409446]
3. Zipfel GJ, Fox DJ Jr, Rivet DJ. Moyamoya disease in adults: the role of cerebral revascularization. *Skull Base*. 2005; 15(1):27–41.10.1055/s-2005-868161 [PubMed: 16148982]
4. Takeuchi K, Shimizu K. Hyopoplasia of the bilateral internal carotid arteries. *Brain Nerve (Tokyo)*. 1957; 9:37–43.
5. Yonekawa Y, Kahn N. Moyamoya disease. *Adv Neurol*. 2003; 92:113–8. [PubMed: 12760172]
6. Srinivasan J, Britz GW, Newell DW. Cerebral revascularization for moyamoya disease in adults. *Neurosurg Clin N Am*. 2001; 12(3):585–94. ix. [PubMed: 11390316]
7. Wakai K, Tamakoshi A, Ikezaki K, et al. Epidemiological features of moyamoya disease in Japan: findings from a nationwide survey. *Clin Neurol Neurosurg*. 1997; 99 (Suppl 2):S1–5. [PubMed: 9409395]

8. Hallemeier CL, Rich KM, Grubb RL Jr, et al. Clinical Features and Outcome in North American Adults With Moyamoya Phenomenon. *Stroke*. 2006
9. Karasawa J, Touho H, Ohnishi H, et al. Long-term follow-up study after extracranial-intracranial bypass surgery for anterior circulation ischemia in childhood moyamoya disease. *J Neurosurg*. 1992; 77(1):84–9. [PubMed: 1607976]
10. Kinugasa K, Mandai S, Kamata I, et al. Surgical treatment of moyamoya disease: operative technique for encephalo-duro-arterio-myo-synangiosis, its follow-up, clinical results, and angiograms. *Neurosurgery*. 1993; 32(4):527–31. [PubMed: 8474642]
11. Goda M, Isono M, Ishii K, et al. Long-term effects of indirect bypass surgery on collateral vessel formation in pediatric moyamoya disease. *J Neurosurg*. 2004; 100(2 Suppl Pediatrics):156–62. [PubMed: 14758943]
12. Scott RM, Smith JL, Robertson RL, et al. Long-term outcome in children with moyamoya syndrome after cranial revascularization by pial synangiosis. *J Neurosurg*. 2004; 100(2 Suppl Pediatrics):142–9. [PubMed: 14758941]
13. Nakashima H, Meguro T, Kawada S, et al. Long-term results of surgically treated moyamoya disease. *Clin Neurol Neurosurg*. 1997; 99 (Suppl 2):S156–61. [PubMed: 9409428]
14. Houkin K, Kamiyama H, Abe H, et al. Surgical therapy for adult moyamoya disease. Can surgical revascularization prevent the recurrence of intracerebral hemorrhage? *Stroke*. 1996; 27(8):1342–6. [PubMed: 8711799]
15. Okada Y, Shima T, Nishida M, et al. Effectiveness of superficial temporal artery-middle cerebral artery anastomosis in adult moyamoya disease: cerebral hemodynamics and clinical course in ischemic and hemorrhagic varieties. *Stroke*. 1998; 29(3):625–30. [PubMed: 9506603]
16. Miyamoto S, Yoshimoto T, Hashimoto N, et al. Effects of extracranial-intracranial bypass for patients with hemorrhagic moyamoya disease: results of the Japan Adult Moyamoya Trial. *Stroke*. 2014; 45(5):1415–21. 10.1161/STROKEAHA.113.004386 [PubMed: 24668203]
17. Derdeyn CP. Direct bypass reduces the risk of recurrent hemorrhage in moyamoya syndrome, but effect on functional outcome is less certain. *Stroke*. 2014; 45(5):1245–6. 10.1161/STROKEAHA.114.004994 [PubMed: 24668205]
18. Isono M, Ishii K, Kamida T, et al. Long-term outcomes of pediatric moyamoya disease treated by encephalo-duro-arterio-synangiosis. *Pediatr Neurosurg*. 2002; 36(1):14–21. pne36014 [pii]. [PubMed: 11818741]
19. Houkin K, Kuroda S, Ishikawa T, et al. Neovascularization (angiogenesis) after revascularization in moyamoya disease. Which technique is most useful for moyamoya disease? *Acta Neurochir (Wien)*. 2000; 142(3):269–76. [PubMed: 10819257]
20. Dussick JR, Gonzalez NR, Martin NA. Clinical and angiographic outcomes from indirect revascularization surgery for Moyamoya disease in adults and children: a review of 63 procedures. *Neurosurgery*. 2011; 68(1):34–43. discussion 43. 10.1227/NEU.0b013e3181fc5ec2 [PubMed: 21150753]
21. Amin-Hanjani S, Singh A, Rifai H, et al. Combined direct and indirect bypass for moyamoya: quantitative assessment of direct bypass flow over time. *Neurosurgery*. 2013; 73(6):962–7. discussion 67–8. 10.1227/NEU.0000000000000139 [PubMed: 23949274]
22. Cloft HJ, Kallmes DF, Snider R, et al. Idiopathic supraclinoid and internal carotid bifurcation steno-occlusive disease in young American adults. *Neuroradiology*. 1999; 41(10):772–6. [PubMed: 10552029]
23. Peerless SJ. Risk factors of moyamoya disease in Canada and the USA. *Clin Neurol Neurosurg*. 1997; 99 (Suppl 2):S45–8. [PubMed: 9409404]
24. Numaguchi Y, Gonzalez CF, Davis PC, et al. Moyamoya disease in the United States. *Clin Neurol Neurosurg*. 1997; 99 (Suppl 2):S26–30. [PubMed: 9409400]
25. Chiu D, Shedden P, Bratina P, et al. Clinical features of moyamoya disease in the United States. *Stroke*. 1998; 29(7):1347–51. [PubMed: 9660385]
26. Kelly ME, Bell-Stephens TE, Marks MP, et al. Progression of unilateral moyamoya disease: A clinical series. *Cerebrovasc Dis*. 2006; 22(2–3):109–15. CED20060222_3109 [pii]. 10.1159/000093238 [PubMed: 16685122]

27. Suzuki J, Kodama N. Moyamoya disease--a review. *Stroke*. 1983; 14(1):104–9. [PubMed: 6823678]
28. Kawaguchi S, Okuno S, Sakaki T. Effect of direct arterial bypass on the prevention of future stroke in patients with the hemorrhagic variety of moyamoya disease. *J Neurosurg*. 2000; 93(3):397–401. [PubMed: 10969936]
29. Asfora WT, West M, McClarty B. Angiography of encephalomyosynangiosis and superficial temporal artery to middle cerebral artery anastomosis in moyamoya disease. *AJNR Am J Neuroradiol*. 1993; 14(1):29–30. [PubMed: 8427106]

Figure 1.

Pre- and post-operative DSA following indirect surgical revascularization demonstrates progressive improvement in MCA territory supply over time. (A) Pre-operative DSA demonstrates right-sided moyamoya phenomenon. B–F: (B) 1 year after surgery, early phase. (C) 1 year after surgery, late phase. (D) 3 years after surgery, early phase. (E) 3 years after surgery, late phase. (F) Annotation of panel (D).

Figure 2.

Pre- and post-operative DSA following direct surgical revascularization demonstrates direct vascularization of the MCA territory concomitant with the development of spontaneous indirect collaterals. (A) Pre-operative DSA demonstrates left-sided moyamoya phenomenon. (B) 4 months after surgery, early phase common carotid injection. (C) 4 months after surgery, late phase common carotid injection. (D) Annotation of panel (B).

Figure 3.

Direct bypass to an isolated temporal branch resulting in robust indirect collateral flow to frontal territory. (A) Pre-operative DSA showing M1 occlusion with moyamoya collaterals reconstituting an isolated frontal branch. Severe stenosis of the A1 segment is also present. Twelve months after surgery, lateral DSA demonstrates abundant direct and indirect anastomoses after STA-MCA bypass that results in delayed but substantial revascularization of frontal branches as well (B, C, and D, early middle and late, respectively; B is annotation of B–D).

Table 1

Patient characteristics and outcomes for treated hemispheres

Patient	Age presenting/sex	Presenting symptoms	Preoperative angiogram findings	Interval from most recent angiogram to surgery	Surgical procedure	Interval to postoperative angiogram	Postoperative angiographic findings	Clinical follow-up interval per hemisphere	Postoperative ipsilateral stroke/hemorrhage?
1	48/F	Ischemia	<u>LCCA</u> : Suzuki Stage 3 - M1 occlusion and ICA/A1 stenosis	5 weeks	EDAMS (left)	6 months	<u>LCCA</u> : No change in pattern of disease; EDAMS collaterals fill 1/3 of MCA territory	4.8 years	No
			<u>RCCA</u> : Suzuki Stage 3 – ICA stenosis, M1 and A1 occlusion				<u>RCCA</u> : No change in pattern of disease; no procedure		
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : Increased pial collaterals to right ACA; no procedure		
2	53/F	Ischemia	<u>LCCA</u> : Suzuki Stage 5 – ICA occlusion	8 weeks	EDAS (left)	6 months	<u>LCCA</u> : No change in pattern of disease; EDAS collaterals fill 1/3 of MCA territory	0.9 years	No
			<u>RCCA</u> : Suzuki Stage 3 – ICA/M1/A1 stenosis				<u>RCCA</u> : No change in pattern of disease; no procedure		
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : No change in pattern of disease; no procedure		
3	38/F	Ischemia	<u>LCCA</u> : Suzuki Stage 5 - ICA occluded at OA; A1/M1 occlusion	5 weeks	STA-MCA bypass (left)	3 months	<u>LCCA</u> : No change in pattern of disease; STA-MCA bypass fills 2/3 of MCA territory	1.2 years	No
			<u>RCCA</u> : Suzuki Stage 5 – ICA occluded, A1/M1 occlusion				<u>RCCA</u> : No change in pattern of disease; no procedure		
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : No change in pattern of disease; no procedure		
4	37/M	Hemorrhage	<u>RCCA</u> : Suzuki Stage 3 – ICA/M1/A1 stenosis	9.5 months	STA-MCA bypass (right)	7 months	<u>RCCA</u> : No change in pattern of disease; STA-MCA bypass and extensive MMA and other ECA to pial collaterals fill 3/3 MCA territory	6.4 years	No
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : No change in pattern of disease; no procedure		
			<u>LCCA</u> : Suzuki Stage 1; ICA stenosis				<u>LCCA</u> : Fewer right A2 → right MCA pial collaterals; no procedure		
5	31/F	Ischemia	<u>LCCA</u> : Suzuki Stage 5 – ICA stenosis, M1 occlusion with ACA → MCA pial collaterals	7.3 weeks	EDAMS (left)	7 months (#1), 21 months (#2)	<u>LCCA</u> : #1 A1 occlusion; EDAMS collaterals fill 1/3 of MCA territory; #2 No change in pattern of disease; EDAMS collaterals fill 2/3 of MCA territory	4 years	No
			<u>RCCA</u> : Suzuki Stage 2 – ICA/M1 stenosis			15 months (angiogram #2 above)	<u>RCCA</u> : #2 No change in pattern of disease. No EDAMS collaterals noted.		
			<u>LCCA</u> : Suzuki Stage 5 – ICA stenosis, A1/M1 occlusion; MMA → pial collaterals				<u>LCCA</u> : #1 No change in pattern of disease STA-MCA bypass and EDAMS collaterals fill 1/3 of MCA territory; #2 EDAMS collaterals fill 2/3 of MCA territory		
6	20/F	Ischemia	<u>RCCA</u> : Suzuki Stage 5 – ICA stenosis, A1/M1 occlusion; MMA → pial collaterals	6.9 weeks	EDAMS (right)	3 months (#1), 18 months (#2)	<u>RCCA</u> : #1 No change in pattern of disease. #2 No change in pattern of disease; EDAMS collaterals fill 2/3 of MCA territory	6.3 years	No
			<u>LCCA</u> : Suzuki Stage 5 – ICA stenosis, A1/M1 occlusion; MMA → pial collaterals				<u>LCCA</u> : #1 No change in pattern of disease STA-MCA bypass and EDAMS collaterals fill 1/3 of MCA territory; #2 EDAMS collaterals fill 2/3 of MCA territory		
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : Increased pial collaterals to right ACA; no procedure		
7	23/M	Hemorrhage	<u>LCCA</u> : Suzuki Stage 3 – ICA stenosis, A1/M2 occlusion	9.3 weeks	EDAS (left)	17 months	<u>LCCA</u> : No change in pattern of disease; no EDAS collaterals noted	5.5 years	No
			<u>RCCA</u> : No disease				<u>RCCA</u> : No disease		
			<u>VA</u> : Bilateral pial collaterals				<u>VA</u> : Increased pial collaterals to right ACA; no procedure		

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Patient	Age presenting/ sex	Presenting symptoms	Preoperative angiogram findings	Interval from most recent angiogram to surgery	Surgical procedure	Interval to postoperative angiogram	Postoperative angiographic findings	Clinical follow-up interval per hemisphere	Postoperative ipsilateral stroke/hemorrhage?
8	34/F	Ischemia	<u>RCCA</u> : Suzuki Stage 4 – ICA/M1/A1 occlusion <u>LCCA</u> : Suzuki Stage 3 –ICA stenosis, M1 stenosis, ACA patent with pial collaterals to bilateral MCA territory <u>VA</u> : Bilateral pial collaterals	7.7 weeks	EDAS (right)	12months (#1), 19 months (#2)	<u>RCCA</u> : #1 No change in pattern of disease; EDAS collaterals fill 1/3 of MCA territory, #2 No change in pattern of disease; EDAS collaterals fill 1/3 of MCA territory <u>LCCA</u> : #1 Increased M1 stenosis; no procedure; #2 No change in pattern of disease; no procedure <u>VA</u> : #1 No change in pattern of disease; no procedure; #2 No change in pattern of disease; no procedure <u>LCCA</u> : Interval M1 occlusion; no EDAS collaterals noted <u>RCCA</u> : Interval M1 occlusion; no procedure	1.8 years	No
9	32/F	Ischemia	<u>RCCA</u> : Suzuki Stage 3 – ICA/A1/M1 stenosis <u>LCCA</u> : Suzuki Stage 3 – ICA/M1 stenosis, A1 occlusion <u>VA</u> : Bilateral pial collaterals	4.9 weeks	EDAS (left)	42 months	<u>RCCA</u> : Interval M1 occlusion; no EDAS collaterals noted <u>RCCA</u> : Interval M1 occlusion; no procedure	3.8 years	No
10	43/M	Ischemia	<u>VA</u> : Bilateral pial collaterals <u>LCCA</u> : Suzuki Stage 3 – ICA/A1 stenosis/M1 occlusion <u>RCCA</u> : A1 small-hypoplastic <u>VA</u> : Left pial collaterals	12.9 weeks	STA-MCA bypass with EDAS (left)	1 day (#1), 12 months (#2) 30 months (#3)	<u>VA</u> : No change in pattern of disease; no procedure <u>LCCA</u> : #1 No change in pattern of disease; STA-MCA bypass fills 1/3 of MCA territory; #2 Left A1 stenosis worse; STA-MCA bypass and EDAS collaterals fill 2/3 MCA territory; #3 Similar to #2 <u>RCCA</u> : #1 A1 small, retrograde ACA filling from MCA collaterals; #2 increased A1 flow, no disease; #3 unchanged <u>VA</u> : #1 Increase in pial collaterals from left PCA→MCA and left PCA→ACA; no procedure; #2 and #3 No change	1.1 years	No
11	55/F	Ischemia	<u>LCCA</u> : Suzuki Stage 4 – ICA/M1/A1 occlusion <u>RCCA</u> : Suzuki Stage 3 – ICA stenosis, M1/A1 occlusion <u>VA</u> : Bilateral pial collaterals	5 months 6 months	STA-MCA (left) STA-MCA (right)	13 months 12 months	<u>LCAA</u> : No change in pattern of disease; STA-MCA bypass and MMA and other ECA collaterals fill 3/3 of MCA territory <u>RCCA</u> : Interval ICA occlusion; STA-MCA bypass and MMA and other ECA collaterals fill 2/3 of MCA territory <u>VA</u> : No change	2.7 years 2.6 years	No No
12	45/F	Ischemia	<u>LCCA</u> : Suzuki Stage 3 – ICA/M1/A1 occlusion <u>RCCA</u> : Suzuki Stage 3 – ICA/A1 stenosis, M1 occlusion <u>VA</u> : Bilateral pial collaterals	11 weeks 5 months	STA-MCA (left) EDAS (right)	16.5 months 11.5 months	<u>LCAA</u> : No change in pattern of disease; STA-MCA bypass and MMA and other ECA collaterals fill 2/3 of MCA territory <u>RCCA</u> : interval A1 occlusion; MMA and other ECA collaterals fill 1/3 of MCA territory. <u>VA</u> : No change	2.2 years 1.8 years	No No
13	22/F	Ischemia	<u>VA</u> : Bilateral pial collaterals <u>LCCA</u> : Suzuki Stage 2 – ICA/M1/A1 stenosis <u>RCCA</u> : Suzuki Stage 2 – ICA stenosis, <u>VA</u> : Bilateral pial collaterals	2 months 2 weeks 1 month 1 weeks	STA-MCA (left) STA-MCA (right)	13 months 14 months	<u>LCCA</u> : Interval A1 and M1 stenosis, STA-MCA bypass and MMA and other ECA collaterals fill 1/3 of MCA territory <u>RCCA</u> : Interval M1 occlusion, increased A1 stenosis. STA-MCA bypass and MMA and other ECA collaterals fill 2/3 of MCA territory <u>VA</u> : Bilateral pial collaterals	1.2 years 1.3 years	No No

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Patient	Age presenting/ sex	Presenting symptoms	Preoperative angiogram findings	Interval from most recent angiogram to surgery	Surgical procedure	Interval to postoperative angiogram	Postoperative angiographic findings	Clinical follow-up interval per hemisphere	Postoperative ipsilateral stroke/hemorrhage?
14	27/F	Ischemia/hemorrhage	<u>LCCA</u> : Suzuki Stage 5 – ICA/A1 stenosis, M1 occlusion <u>RCCA</u> : Suzuki Stage 5 – ICA/M1 stenosis, A1 occlusion <u>VA</u> : Bilateral pial collaterals	4 weeks	STA-MCA (right)	1 day (#1), 12 months(#2)	<u>RCCA</u> : #1 not patent, no collateral flow; #2 Patent STA-MCA bypass and other ECA collaterals filled 2/3 of MCA <u>LCCA</u> : #1 Not done; #2 no change <u>VA</u> : no change	1.1 year	No
15	57/F	Ischemia/hemorrhage	<u>LCCA</u> : Suzuki Stage 4 – ICA/A1 stenosis, M1 occlusion, A2 occlusion. Large MMA to pial collaterals supplying 1/3 MCA <u>RCCA</u> : Suzuki Stage 3 – ICA stenosis, M1/A1 occlusion <u>VA</u> : Bilateral pial collaterals	1 day	EDAS (left)	12 months	<u>LCCA</u> : no change in pattern of disease. STA enlarged with 2/3 MCA supply <u>RCCA</u> : no change <u>VA</u> : no change	1.1 year	No

Table 2
Number of Treated Hemispheres Demonstrating Degree of MCA Revascularization on Late Angiographic Study

	None	1/3	2/3	Complete
Indirect Bypass	3	4	3	0
Direct Bypass	0	1	5	2
Combined Direct & Indirect	0	0	2	0