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Indirect revascularization for nonmoyamoya intracranial arterial stenoses: clinical and angiographic outcomes

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Abstract

Object—Symptomatic intracranial arterial stenoses have a high rate of recurrent stroke despite medical and endovascular treatments. The authors present clinical and angiographic quantitative outcomes of indirect revascularization for patients with symptomatic intracranial stenosis.

Methods—Patients treated for symptomatic intracranial arterial stenosis by indirect revascularization were included. The patient population comprised those in whom medical management had failed and for whom endovascular therapy was unsuitable or had failed. Patients underwent encephaloduroarteriosynangiosis (EDAS) with or without bur holes. Preoperative and postoperative angiograms were evaluated for change in caliber of extracranial blood vessels (superficial temporal artery [STA] and middle meningeal artery [MMA]) and for evidence of neovascularization.

Results—Thirteen patients underwent EDAS. Ischemic symptoms ceased within the follow-up period in all patients, returning in a delayed fashion in only 2. No other patients had recurrent TIAs or strokes after the initial postoperative period. Donor blood vessels increased in size relative to preoperative sizes in all but 1 case (average increase of 52% for proximal STA [$p = 0.01$], 74% for midpoint of STA [$p = 0.01$], and 84% for the MMA [$p = 0.02$]). In addition, 8 of 11 patients demonstrated direct spontaneous anastomoses from extracranial to middle cerebral artery branches, and all patients demonstrated angiographic evidence of vascular blush and/or new branches from the STA and/or MMA.

Conclusions—Indirect revascularization appears to be a safe and effective method to improve blood flow to ischemic brain due to intracranial arterial stenosis. Neovascularization and enlargement of the branches of the ECA were observed in all patients and correlated with improvement in ischemic symptoms. Indirect revascularization is an option for patients in whom medical therapy has failed and who are not suitable for endovascular treatment.

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Disclosure

Author contributions to the study and manuscript preparation include the following. Conception and design: Gonzalez, Saver, Dusick. Acquisition of data: Gonzalez, Dusick. Analysis and interpretation of data: Gonzalez, Dusick. Drafting the article: Dusick. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Gonzalez. Statistical analysis: Dusick. Study supervision: Gonzalez.

Keywords

encephaloduroarteriosynangiosis; stroke; indirect revascularization; cerebral ischemia; intracranial arterial stenosis; intracranial atherosclerosis; vascular disorders

Of the 900,000 cases of stroke or TIA that occur each year in the US, approximately 90,000 (10%) are caused by intracranial arterial stenosis.²¹ Symptomatic intracranial arterial stenosis carries one of the highest rates of recurrent stroke despite medical therapy, with annual recurrence rates for ischemic stroke reported in the WASID trial as high as 15% in the aspirin arm. The incidence of recurrent stroke can be even higher in some high-risk groups, as high as 25% in African Americans and females.^{5,25,26}

Despite improvement in the technical success of endovascular angioplasty and stenting, the clinical results of stenting have been disappointing. In fact, the SAMM-PRIS trial was recently stopped early because of disappointing results.¹⁸ This study aimed to compare the safety and efficacy of intensive medical therapy plus stenting with intensive medical therapy only in preventing stroke (<http://clinicaltrials.gov/ct2/show/NCT00576693>).⁴ After only 59% (451 of 764) of the planned patients had been enrolled, the study was stopped early because 14% of patients treated with angioplasty and stenting experienced stroke or died within the first 30 days after enrollment, compared with 5.8% of patients treated with medical therapy alone. This included 5 stroke-related deaths within 30 days of enrollment, all in the stent arm. The rate of stroke and death in the medical arm was also quite significant (12.2% of patients in 1 year). Additionally, analysis of subgroups of this population and that of the WASID trial reveal that the presence of poor collateral circulation is associated with a 6-fold increase in risk of stroke.¹⁴

In general, the surgical options for these lesions have been considered limited. In particular, direct revascularization techniques with bypass surgery, as addressed in the EC/IC Bypass Study Group⁷ and more recently in the COSS trial,¹⁹ have not demonstrated improved clinical outcomes compared with best medical management in terms of subsequent risk for stroke. The EC/IC Bypass Study Group found that patients with intracranial arterial stenosis, rather than complete occlusion, can actually fare worse after bypass.^{3,7} The sudden change in flow dynamics across the lumen of stenosis can lead to stasis of flow and may precipitate thrombosis or distal emboli originating from the stenotic segment. This area of thrombosis can propagate and/or embolize, occluding lenticulostriate arteries in the region and/or causing distal emboli and resulting cerebral infarction. The more recent COSS trial aimed to determine if EC-IC bypass could reduce subsequent ischemic stroke compared with medical management alone in patients with carotid artery occlusion and misery perfusion as determined by PET scanning criteria. Like the SAMM-PRIS trial, this study was also stopped early because it failed to provide an overall benefit in terms of the 2-year stroke recurrence rate compared with best medical management. Despite good patency of grafts and improvement in PET oxygen extraction fraction in the patients who underwent bypass, the perioperative stroke rate (within 30 days) was still 15%, not significantly different from that in the earlier EC/IC Bypass Study Group. The 2-year stroke and death rate in the surgical arm was not significantly better than that in the nonsurgical arm (21% vs 23%, respectively [$p = 0.7$]).

Indirect revascularization techniques have been used in moyamoya disease for many years with success in adults and children.^{1,6,15–17,22–24,27} These techniques have the advantage of being less technically demanding, of obviating the need for temporary occlusion of cerebral vessels, and of allowing gradual development of revascularization only where the brain demands it. There is very little literature exploring the use of these procedures in cases of

symptomatic, nonmoyamoya intracranial arterial stenosis due to atherosclerosis or of unknown etiology and their potential role in enhancing collateral perfusion. The only series in the literature using indirect revascularization for intracranial atherosclerotic disease largely treated patients with complete angiographic occlusion of the internal carotid artery and/or MCA, but not individuals with symptomatic stenosis.¹⁰

To directly address this gap in the literature, we present our experience with using indirect revascularization in adult patients who had symptomatic intracranial arterial stenoses. Our detailed characterization of this experience includes clinical outcomes as well as quantitative angiographic changes after indirect revascularization.

Methods

Patient Population

All patients treated for unilateral symptomatic intracranial stenosis by indirect revascularization techniques at our center were identified. Children and adult patients with bilateral disease consistent with a diagnosis of classic moyamoya disease were excluded. Clinical and imaging records were then reviewed retrospectively.

Thirteen patients were identified who underwent unilateral EDAS over a 9-year period (Table 1). Twelve of these 13 patients had simultaneous bur holes with duroplasty synangiosis (frontal or frontal and parietal). The mean patient age in our cohort was 38 years (range 25–61 years), and there were 9 women and 4 men. The median follow-up was 54 months (range 7–97 months), and all patients had follow-up angiograms at least 6 months after the indirect revascularization procedure (only 11 patients had both preoperative and follow-up angiograms available for review at the time of this retrospective study). Clinical outcomes are presented as a primary end point of stroke or death at last follow-up and a secondary end point of persistent or recurrent TIAs at last follow-up. The UCLA Institutional Review Board approved this study.

Preoperative Evaluation

Patients presenting with symptoms of cerebral ischemia, either TIAs or prior cerebral infarction, and with angiographic evidence of intracranial arterial stenosis not suitable for endovascular angioplasty or stenting, or individuals with failed stenting with restenosis despite further angioplasty and/or restenting, were considered for some form of revascularization. Patients presenting with such symptoms were routinely evaluated using both brain MRI and digital subtraction cerebral angiography. Magnetic resonance imaging or CT perfusion studies are now also routinely performed to evaluate for cerebral perfusion deficits, although earlier patients did not have these studies routinely included as part of their workup. All patients with preoperative perfusion studies did have a documented perfusion deficit consistent with their symptoms. Patients were considered for EDAS if they had recent ischemic symptoms (TIAs and/or nondisabling strokes within 30 days of treatment). Only patients in whom a hemodynamic etiology was suspected were considered, based on the distribution of MRI abnormalities (such as watershed distribution of ischemic lesions), the correlation of symptoms with postural changes or hypotension, and the absence of findings suggestive of embolisms on transcranial Doppler ultrasonography studies or MRI.

Most patients with symptomatic extracranial stenotic or occlusive arterial disease are treated by endovascular techniques, carotid endarterectomy, or arterial bypass into the intracranial circulation. However, because of the concern of potentially precipitating complete occlusion with direct bypass by flow reversal in the case of intracranial arterial stenosis, indirect revascularization has been favored at our center.

Intraoperative Monitoring, Anesthetic Considerations, and Surgical Technique

The general care and surgical technique applied to these patients is similar in most respects to the treatment of patients with moyamoya disease.⁶ In brief, in all cases of indirect revascularization, intraoperative electroencephalographic monitoring is used to monitor for any changes associated with hypotension that may occur during anesthesia. Anesthesia management is requested to keep strict control of blood pressure to avoid hypotension, maintaining the systolic blood pressure above 120 mm Hg, generally in the 120– to 140–mm Hg range for the duration of the procedure. Higher limits may be set in patients who are typically hypertensive, typically with a systolic blood pressure 20% above their baseline level. Hyperventilation is avoided to prevent vasoconstriction associated with hypocapnia. Systemic hypothermia or barbiturates are not used for neuroprotection, given that there is no period of temporary occlusion of any intracranial blood vessels as there would be in direct revascularization procedures.

The technique of EDAS has been well described in the literature, including the specific surgical nuances of the technique used by our group (Fig. 1).⁶ Of special note, because the importance of the MMA has been recognized in our moyamoya disease series, special attention is paid to construct the dural opening in a manner that preserves as many of the MMA branches as possible. Bipolar cautery of the dura mater is kept to a minimum, and the 2 layers of the dura are also gently peeled apart at the opening, removing as much of the avascular inner layer as possible. We believe that this more directly approximates the vascular outer layer to the underlying brain, promoting neovascularization. The arachnoid of the subjacent brain is also widely opened using microsurgical technique. Scrupulous surgical technique is necessary to prevent injuries of the small cortical vessels and to reduce the need for excessive hemostasis. However, the STA is not sutured to the pia mater as has been described as pial synangiosis by Adelson and Scott¹ and Scott et al.²³ The adventitia of the STA is sutured to the edges of the dura prior to replacing the bone flap. The superior and inferior ends of the craniotomy are left with large openings to reduce kinking of the entry and exit points of the STA. The inner table of the bone flap can also be trimmed to reduce excessive compression of the artery.

When additional bur holes are performed, the dura is also opened carefully and the underlying arachnoid is opened under microscopic visualization. Titanium plates that completely cover the bur hole are avoided. They are either left open or a linear plate is used as a bridge to support the scalp and avoid cosmetic deformity while allowing room for scalp vessels to grow into the underlying brain.

Of note, all patients receive aspirin (325 mg daily) during and after surgery. Patients are not given double antiplatelet agents (clopidogrel).

Clinical Analysis

The records of all patients were reviewed to define the primary end point of stroke and death at last follow-up and the secondary end point of persistent TIAs at last follow-up. Ischemic stroke was defined as a new focal neurological deficit of sudden onset, lasting at least 24 hours. Computed tomography or MRI confirmation of stroke is routinely performed if this diagnosis is suspected. A TIA was defined as a transient new focal neurological deficit of sudden onset, lasting less than 24 hours, and not associated with CT or MRI abnormalities.

Angiographic Analysis

Eleven patients had preoperative and postoperative (at least 6 months postsurgery) angiograms available for review. On the preoperative images, the location and degree of arterial stenosis were noted, as was evidence of collateral circulation.^{11–13} Digital calipers or

a computerized measuring tool were used to take measurements of 4 structures on the lateral angiographic projection of the ECA injection: the anteroposterior diameter of the sella turcica, the width of the proximal STA just distal to its bifurcation, the STA at its midpoint between the bifurcation and the convexity, and the MMA at its largest intracranial portion (just distal to the foramen spinosum) (Fig. 2).

The same structures (sella turcica, proximal STA, middle STA, and MMA) were all measured at the same locations on the follow-up angiograms at least 6 months postprocedure. Additionally, the arteries and bur holes were examined for the presence of a vascular blush, new branches, and spontaneous anastomoses to the intracranial circulation.

All angiogram measurements were performed in duplicate by 2 independent observers experienced in reading angiograms. The average of each pair of measurements was used for subsequent calculations. The use of this methodology provides an objective quantitative assessment of the change in collateral flow.

Statistical Analysis of Angiographic Measurements

To correct for differences in magnification between angiograms, the blood vessel measurements were normalized by comparison with a fixed structure (the sella turcica). The artery widths are thus presented as a vessel/ sella turcica ratio. Preoperative and postoperative ratios were compared to determine the degree and direction of change in vessel size.

A paired-samples Student t-test was used to compare average pre- and postoperative vessel size ratios for each vessel location. Test/retest consistency of measurements was evaluated by Spearman correlation testing between the 2 sets of measurements.

Results

Clinical Presentation and Clinical Results

All patients suffered TIAs or nondisabling strokes within 1 month prior to surgery and had intracranial arterial stenosis of 70% or more documented by angiography. Five of the 13 patients treated presented only with a history of TIAs. The remaining 8 patients had a documented case of prior cerebral infarction as well as episodes of TIAs. However, there were no large infarctions that involved an entire vascular territory or hemisphere. One patient had been previously treated by endovascular stenting but suffered rapid restenosis at that site.

All patients had symptoms that could be clinically correlated with cerebral ischemia of the brain in the territory of involved vessels. Ischemic symptoms included contralateral motor weakness (10 patients), sensory dysfunction (9 patients), language dysfunction including aphasia and/or dysphasia (5 patients), visual loss (2 patients), and/or cognitive decline and memory loss (1 patient who also had aphasia and motor weakness). None of the patients had only nonspecific symptoms such as headache. There were no patients with crescendo TIAs.

In only 3 patients could a definitive etiology of intracranial atherosclerosis be determined. In 1 patient, the area of stenosis looked like a healed area of arterial dissection. This same patient also had a history of idiopathic thrombocytopenic purpura. The remaining 9 patients were considered to have a vasculopathy of unknown etiology after a comprehensive stroke workup did not reveal any other abnormality. Five of these 9 patients had risk factors for atherosclerosis, including hypertension, diabetes mellitus, hyperlipidemia, and a history of Cushing disease. Three others had a history of migraine headaches.

Within the follow-up period, no patient (0%) reached the primary end point of stroke or death (Table 2). Regarding persistent or recurrent TIAs at last follow-up, 11 (84.6%) of 13 patients had long-term resolution of their ischemic symptoms. Two patients had a delayed return of TIAs (15.4% secondary end point). In 1 patient the return of TIAs occurred more than 4 years postoperatively. This patient returned to the operating room for an additional large bur hole/craniectomy anterior to the EDAS site and has done well after that procedure with no return of symptoms. The other patient's TIAs resolved for only about 1 year and returned. This patient went on to undergo EC-IC bypass at an outside hospital, which has resulted in a reduction, but not elimination, of her TIA occurrences.

Regarding immediate postoperative results, no patient suffered hemorrhagic complications. Three patients continued to have TIAs after surgery, but all ceased by 3 months. One of these patients only had mild TIAs for 2 weeks after surgery and another had TIAs for up to 3 weeks. The third patient continued having TIAs for 3 months. None of these patients suffered infarction, and these TIAs ceased after this initial posttreatment period and have not returned through the follow-up period (range of 17–40 months follow-up in these 3 patients). Besides the 2 patients with delayed return of symptoms, no other patients in this series had recurrent TIAs and no patients had new strokes at follow-up, either clinically or on imaging. All patients' functional levels are the same or better than preoperatively.

Quantitative Angiographic Results

Postoperatively, of 11 patients with both pre- and postoperative angiography available to review, the donor blood vessels increased in size relative to the preoperative size in all but 1 patient (Figs. 2 and 3 and Table 3). They increased in size an average of 52% for the proximal STA ($p = 0.01$), 74% for the midpoint of the STA ($p = 0.01$), and 84% for the MMA ($p = 0.02$). One patient had a reduction in size of the donor blood vessels postoperatively, decreasing by 18.6%, 28.4%, and 16.5%, respectively. The etiology of this reduction in vessel size was not evident. Of note, this patient did well clinically and did not have return of ischemic symptoms during the follow-up period.

All patients demonstrated angiographic evidence of either vascular blush and/or new visible branches from the STA and MMA. In addition, 8 (73%) of 11 patients demonstrated direct spontaneous anastomoses from extracranial branches to MCA branches (5 with just STA-to-MCA anastomoses and 3 with both STA- and MMA-to-MCA anastomoses) (Fig. 4). Three patients did not develop direct anastomoses but did have increased branching and vascular blush from one or both arteries and an increase in vessel size. Test/retest statistics comparing the 2 independent observers' angiographic measurements demonstrated strong correlation between the measurements (Spearman $\rho = 0.99$ and $p < 0.001$).

Of 8 patients with frontal bur holes that could be evaluated on postoperative angiography, 4 demonstrated neovascularization at the bur hole, from enlarged or new branches of the STA and/or MMA, including one with a direct anastomosis from the MMA to the MCA branch. Of 6 patients with parietal bur holes that could be evaluated, only 1 demonstrated appreciable revascularization at this bur hole. The other 5 had only trace vascularity or none visible at this location.

Of note, 2 patients did not have postoperative angiograms available to review (1 of the studies was old and could not be found and 1 was from an outside hospital). However, the reports for both patients stated that qualitatively there was improved perfusion in the area of the EDAS. However, the studies could not be directly reviewed and measurements could not be taken for this study.

Complications

There were no major surgical complications in this series (Table 4). Only 1 patient had a wound dehiscence over a bur hole that required a revision of the skin closure. One patient with no history of seizures had transient focal seizures several days after the procedure, which resolved fully with antiepileptic medication. One patient had transient hyponatremia that resolved spontaneously.

Discussion

Indirect Revascularization for Treatment of Intracranial Ischemic Disease

The optimal treatment of intracranial arterial stenosis has not been fully elucidated.^{2,20} Even with maximal medical therapy, symptomatic intracranial arterial stenosis has a high recurrent stroke rate (as high as 15% in 2 years and as high as 25% in high-risk groups).^{5,25,26} Most of these recurrent strokes are ipsilateral and nonlacunar, and many are disabling.⁸ Surgical and endovascular treatment options have failed to improve outcomes. Of the subgroups treated in the EC/IC Bypass Study Group, patients with intracranial stenosis consistently fared worse after bypass.⁷ It is our hypothesis that the competitive flow immediately introduced by the bypass can precipitate stasis of flow and thrombosis at the location of the stenosis. It is possible that thrombosis can occlude lenticulo-striate arteries, propagate or cause distal emboli, leading to new neurological deficits in the acute phase after revascularization. These findings have been reported by other authors as well.³ Because of this concern with treating intracranial arterial stenosis, we have avoided using direct bypass in these cases.

More recently, both SAMMPRIS, comparing endovascular angioplasty and stenting to medical management, and COSS, comparing surgical bypass to medical management, were stopped early because they failed to prove a benefit over best medical management.^{18,19} Therefore, there are no surgical or endovascular treatments that can currently be recommended based on the outcomes of these trials. Although our series cannot be compared directly to either trial as the patient populations varied somewhat, these prior studies help to emphasize the importance of this clinical problem and the lack of good treatments at this time.

Even with best medical management, many patients with intracranial arterial stenosis remain symptomatic, and the recurrent stroke rate is unacceptably high. In the most recent studies comparing interventional procedures or surgery with best medical therapy, the recurrent stroke rate in the medically treated arms is exceptionally high. In SAMMPRIS, 5.8% and 12.2% of medically treated patients experienced a stroke or died within 30 days and 1 year of enrollment, respectively. In addition, a study of the effects of poor collaterals in the WASID population with intracranial arterial stenosis revealed that the presence of poor collaterals increased by 6-fold the risk of stroke in the compromised vascular territory (no collaterals or poor vs good, 30% vs 5%, HR 6.05 [95% CI 1.41–25.92]; $p = 0.0056$, log-rank test).¹⁴ It is clear that these patients are in dire need of better options of treatment and that enhancing collateral circulation may play a significant role in reducing the risk of stroke.

We have favored indirect revascularization for those symptomatic patients in whom other treatments failed. The procedure is technically less demanding than direct bypass and avoids the period of temporary occlusion of intracranial arteries that is inherent to bypass. We believe that it offers a robust revascularization that develops gradually, avoiding the potential problems of direct bypass. In our series, all patients initially improved clinically. All patients' ischemic symptoms improved, and only 2 patients later experienced return of ischemic symptoms, which required further workup and treatment. As has been noted in series of indirect revascularization for moyamoya disease, these techniques do not provide

immediate flow to the ischemic brain. Therefore, patients may continue to experience TIAs in the immediate postoperative period, as was noted in 3 of the patients in our series. While infarction during this time period is theoretically possible, we did not observe any instances in this series.

While there is quite extensive experience in the literature using these techniques for patients with moyamoya disease, reports of indirect revascularization for intracranial atherosclerotic steno-occlusive disease are scarce. To our knowledge, Komotar et al.¹⁰ has reported the only series in the literature, in which they examined 12 symptomatic patients with primarily intracranial arterial occlusion treated by indirect revascularization (11 with EDAS with or without bur holes and 1 with only bur holes). The patients in this series did not fare well, with 5 patients demonstrating decreased perfusion on follow-up imaging despite STA patency and 10 patients suffering new infarctions or TIAs during the follow-up period, although only 5 of the patients had infarctions in the hemisphere ipsilateral to the treatment. Only 2 of these infarctions occurred after 6 months postoperatively. There are noticeable differences that can be pointed out between this study and ours. Most importantly, the series by Komotar et al.¹⁰ treated primarily patients with complete intracranial occlusion (in what appears to be 11 of the 12 patients), 2 cases of which were due to dissection of the artery. Therefore, their population represents a different group of patients with intracranial vascular disease from that presented here and is therefore not directly comparable.

Angiographic Patterns of Indirect Revascularization

As we have previously demonstrated with indirect revascularization for moyamoya disease,^{6,27} we found that the STAs and MMAs in almost all patients enlarged by a significant degree after surgery. While some of the STA enlargement may be due to exposing the artery and dissecting it free from its fascial connections, the proximal intracranial MMA is never exposed or manipulated at surgery. Therefore, these enlargements in the artery diameters likely indicate a compensatory growth in response to an increased hemodynamic demand due to cerebral neovascularization from the branches of the ECA. We also observed vascular blush into the pial vessels of underlying brain in the selective ECA injections; new or enlarged branches; and/or spontaneous, direct EC-IC anastomoses in all patients.

Study Limitations

This study is limited by the relatively small number of cases, its retrospective nature, and the variability of patient etiologies. The findings of this study potentially apply to the treatment of a subset of patients with intracranial atherosclerotic disease: those with symptomatic intracranial arterial stenoses due to atherosclerosis or vasculopathy of unknown etiology for which medical treatments have failed to control symptoms.

This study did evaluate changes in cerebral blood flow anatomically (in terms of angiographic changes), which is currently considered the gold standard for the anatomical evaluation of collateral flow.^{9,11,13} However, although we now routinely perform perfusion MRI in these patients, it was not done in a consistent way throughout this series, and most patients did not have both pre- and postoperative perfusion studies for comparison. Additionally, in the past, perfusion MRI has lacked the ability to make quantitative comparisons between studies over time in one individual patient. This lack of a quantitative measure of cerebral blood flow and how it changes after these procedures is a limitation of this series. We are working to refine protocols using arterial spin labeling and dynamic susceptibility contrast that allow more precise, quantitative MRI perfusion assessment so that we can prospectively follow changes in blood flow after indirect revascularization.

Conclusions

Indirect revascularization appears to be a safe and effective means to improve blood flow to ischemic brain due to intracranial nonmoyamoya stenotic disease. After surgery, enlargement of the branches of the ECA and visible neovascularization of the underlying brain appears to correlate with improvement in ischemic symptoms. In cases in which best medical management has failed, these and other revascularization procedures should be considered in the treatment of intracranial arterial stenoses. Indirect revascularization has benefits in that it is easier to perform than bypass, does not require temporary occlusion of intracranial blood vessels, and is not as likely to precipitate thrombosis and embolism that can occur with sudden changes in flow dynamics.

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Abbreviations used in this paper

COSS	Carotid Occlusion Surgery Study
ECA	external carotid artery
EC-IC	extracranial-intracranial
EDAS	encephaloduroarteriosynangiosis
MCA	middle cerebral artery
MMA	middle meningeal artery
SAMM-PRIS	Stenting Versus Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis
STA	superficial temporal artery
TIA	transient ischemic attack
WASID	Warfarin-Aspirin Symptomatic Intracranial Disease

References

1. Adelson PD, Scott RM. Pial synangiosis for moyamoya syndrome in children. *Pediatr Neurosurg*. 1995; 23:26–33. [PubMed: 7495663]
2. Arenillas JF. Intracranial atherosclerosis: current concepts. *Stroke*. 2011; 42(1 Suppl):S20–S23. [PubMed: 21164126]
3. Awad I, Furlan AJ, Little JR. Changes in intracranial stenotic lesions after extracranial-intracranial bypass surgery. *J Neurosurg*. 1984; 60:771–776. [PubMed: 6707746]
4. Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *N Engl J Med*. 2011; 365:993–1003. [PubMed: 21899409]
5. Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertz-berg VS, Frankel MR, et al. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. *N Engl J Med*. 2005; 352:1305–1316. [PubMed: 15800226]
6. Dusick 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; 68:34–43. [PubMed: 21150753]

7. EC/IC Bypass Study Group. Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke. Results of an international randomized trial. *N Engl J Med*. 1985; 313:1191–1200. [PubMed: 2865674]
8. Famakin BM, Chimowitz MI, Lynn MJ, Stern BJ, George MG. Causes and severity of ischemic stroke in patients with symptomatic intracranial arterial stenosis. *Stroke*. 2009; 40:1999–2003. [PubMed: 19407228]
9. Higashida RT, Furlan AJ, Roberts H, Tomsick T, Connors B, Barr J, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke*. 2003; 34:e109–e137.
10. Komotar RJ, Starke RM, Otten ML, Merkow MB, Garrett MC, Marshall RS, et al. The role of indirect extracranial-intracranial bypass in the treatment of symptomatic intracranial atheroocclusive disease. Clinical article. *J Neurosurg*. 2009; 110:896–904. [PubMed: 19199456]
11. Liebeskind DS. Collateral circulation. *Stroke*. 2003; 34:2279–2284. [PubMed: 12881609]
12. Liebeskind DS. Imaging the future of stroke: I. Ischemia. *Ann Neurol*. 2009; 66:574–590. [PubMed: 19938071]
13. Liebeskind DS, Cotsonis GA, Saver JL, Lynn MJ, Cloft HJ, Chimowitz MI, et al. Collateral circulation in symptomatic intracranial atherosclerosis. *J Cereb Blood Flow Metab*. 2011; 31:1293–1301. [PubMed: 21157476]
14. Liebeskind DS, Cotsonis GA, Saver JL, Lynn MJ, Turan TN, Cloft HJ, et al. Collaterals dramatically alter stroke risk in intracranial atherosclerosis. *Ann Neurol*. 2011; 69:963–974. [PubMed: 21437932]
15. Matsushima T, Inoue T, Ikezaki K, Matsukado K, Natori Y, Inamura T, et al. Multiple combined indirect procedure for the surgical treatment of children with moyamoya disease. A comparison with single indirect anastomosis and direct anastomosis. *Neurosurg Focus*. 1998; 5(5):e4. [PubMed: 17112207]
16. Matsushima T, Inoue T, Suzuki SO, Fujii K, Fukui M, Hasuo K. Surgical treatment of moyamoya disease in pediatric patients—comparison between the results of indirect and direct revascularization procedures. *Neurosurgery*. 1992; 31:401–405. [PubMed: 1407421]
17. Matsushima Y, Aoyagi M, Fukai N, Tanaka K, Tsuruoka S, Inaba Y. Angiographic demonstration of cerebral revascularization after encephalo-duro-arterio-synangiosis (EDAS) performed on pediatric moyamoya patients. *Bull Tokyo Med Dent Univ*. 1982; 29:7–17. [PubMed: 6961966]
18. National Institutes of Health. Clinical Alert: Angioplasty combined with stenting plus aggressive medical therapy vs. aggressive medical therapy alone for intracranial arterial stenosis: NINDS stops trial enrollment due to a higher risk of stroke and death in the stented group. Bethesda, MD: US National Library of Medicine; April 2011 (http://www.nlm.nih.gov/databases/alerts/intracranial_arterial_stenosis.html) [Accessed April 12, 2012]
19. Powers, WJ.; Clarke, WR.; Grubb, RL., Jr; Videen, TO.; Adams, HP., Jr; Derdeyn, CP. International Stroke Conference 2011. Los Angeles: 2011. Results of the Carotid Occlusion Surgery Study (COSS). (Abstract)
20. Qureshi AI, Feldmann E, Gomez CR, Johnston SC, Kasner SE, Quick DC, et al. Consensus conference on intracranial atherosclerotic disease: rationale, methodology, and results. *J Neuroimaging*. 2009; 19(Suppl 1) 1S–10S.
21. Sacco RL, Kargman DE, Gu Q, Zamanillo MC. Race-ethnicity and determinants of intracranial atherosclerotic cerebral infarction. The Northern Manhattan Stroke Study. *Stroke*. 1995; 26:14–20. [PubMed: 7839388]
22. Sainte-Rose C, Oliveira R, Puget S, Beni-Adani L, Boddaert N, Thorne J, et al. Multiple bur hole surgery for the treatment of moyamoya disease in children. *J Neurosurg*. 2006; 105(6 Suppl):437–443. [PubMed: 17184074]
23. Scott RM, Smith JL, Robertson RL, Madsen JR, Soriano SG, Rockoff MA. Long-term outcome in children with moyamoya syndrome after cranial revascularization by pial synangiosis. *J Neurosurg*. 2004; 100(2 Suppl Pediatrics):142–149. [PubMed: 14758941]
24. Starke RM, Komotar RJ, Connolly ES. Optimal surgical treatment for moyamoya disease in adults: direct versus indirect bypass. *Neurosurg Focus*. 2009; 26(4):E8. [PubMed: 19335134]

25. Waddy SP, Cotsonis G, Lynn MJ, Frankel MR, Chaturvedi S, Williams JE, et al. Racial differences in vascular risk factors and outcomes of patients with intracranial atherosclerotic arterial stenosis. *Stroke*. 2009; 40:719–725. [PubMed: 18832745]
26. Williams JE, Chimowitz MI, Cotsonis GA, Lynn MJ, Waddy SP. Gender differences in outcomes among patients with symptomatic intracranial arterial stenosis. *Stroke*. 2007; 38:2055–2062. [PubMed: 17540969]
27. Yamada I, Matsushima Y, Suzuki S. Childhood moyamoya disease before and after encephalo-duro-arterio-synangiosis: an angiographic study. *Neuroradiology*. 1992; 34:318–322. [PubMed: 1528443]

Fig. 1. Illustration showing the EDAS revascularization. The donor artery is placed close to the superficial brain arteries. A network of collaterals forms between the donor artery and the adjacent brain vessels without a surgical anastomosis.

Fig. 2.

Case 13. Angiograms obtained in a 61-year-old woman with a history of hypertension, diabetes, and hypercholesterolemia who presented with recurrent TIAs and stroke and a near complete occlusion of the distal left internal carotid artery. She had previously undergone endovascular stenting that rapidly restenosed. **A:** The measurements of the STA and MMA were normalized to a fixed landmark, the anteroposterior extent of the sella turcica, to account for differences in magnification and allow comparison of pre- and postoperative angiograms. **B and C:** Angiographic demonstration of increased vessel size after indirect revascularization. Preoperative (B) and postoperative (C) selective ECA injections demonstrating an increase in size of the STA (*white arrows*) and MMA (*black arrows*). Direct filling of cortical MCA branches can be seen.

Fig. 3. Graphs demonstrating the change in the corrected measurements for the STA proximally (A), at its midpoint (B), and for the MMA (C) pre- and post-EDAS. The *asterisks* indicate the patient whose vessels decreased in size after surgery, the values on the y axis represent the size ratio (STA/sella turcica or MMA/sella turcica).

Fig. 4.

Angiograms of spontaneous direct anastomoses from branches of the ECA to intracranial vessels in 6 patients. In each example, the cortical branches of the MCA fill directly from a selective ECA injection. CCA = common carotid artery.

TABLE 1

Demographics and surgical procedures of 13 patients *

Parameter	Value
no. of patients	13
age (yrs)	
mean	38
range	25–61
F/M	9:4
FU (mos)	
median	54
range	7–97
no. w/ EDAS	13
no. w/ bur holes	12

*
FU = follow-up.

TABLE 2

Summary of results for 13 patients who underwent unilateral EDAS *

Case No.	Age (yrs), Sex	Presenting Sx	% Change in Size				Direct Anastomoses	Last FU (mos)	End Point [†]	
			Proximal STA	Midpoint STA	MMA				Primary	Secondary
1	43, F	TIA's & stroke [‡]	40.8	16.4	47.8		no	87	no	yes, return of Sx at 4 yrs postop
2	33, M	TIA's only	-18.6	-28.4	-16.5		yes	67	no	no
3	31, M	TIA's & stroke [‡]	10.3	33.7	14.2		no	72	no	no
4	46, F	TIA's & stroke [‡]	NA [§]	NA	NA		NA	59	no	no
5	35, M	TIA's & stroke [‡]	13.4	25.3	33.7		yes	97	no	no
6	27, F	TIA's only	153.2	195.5	41.5		yes	76	no	no
7	25, F	TIA's only	34.2	17.8	54.2		no	54	no	yes, return of Sx at 1 yr postop
8	37, F	TIA's & stroke [‡]	94.2	99.6	117.2		yes	40	no	no
9	37, F	TIA's only	NA [§]	NA	NA		NA	24	no	no
10	42, F	TIA's & stroke [‡]	31.5	105.7	30.2		yes	7	no	no
11	39, M	TIA's only	59.1	65.8	218.1		yes	22	no	no
12	35, F	TIA's & stroke [‡]	23.3	27.2	23.7		yes	17	no	no

* NA = not available; Sx = symptoms.

[†] Primary end point is defined as stroke or death at last follow-up, and secondary end point is defined as persistent TIAs at the last follow-up.

[‡] Nondisabling stroke of the corresponding vascular territory.

[§] These follow-up angiograms were reported to demonstrate "improved collaterals," but images were not available for measurement.

TABLE 3

Measurements of change in vessel size in 6 hemispheres *

Vessel	V/ST Ratio		% Change	p Value
	Preop	Postop		
STA (proximal)	0.12 ± 0.04	0.18 ± 0.07	52.0	0.01
STA (midpoint)	0.11 ± 0.03	0.19 ± 0.08	74.0	0.01
MMA	0.11 ± 0.04	0.18 ± 0.09	84.0	0.02

* V/ST Ratio = ratio of the vessel diameter to the anteroposterior diameter of the sella turcica.

TABLE 4

Surgical complications in 3 of 13 patients

Complication	No. of Cases
surgical	
bur hole wound dehiscence	1
medical	
transient focal seizures	1
Mild transient hyponatremia	1