Is Extracranial-Intracranial Bypass Surgery Effective in Certain Patients?

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KEYWORDS

• Aneurysm • Blood flow • Extracranial-intracranial bypass • Ischemia

Cerebral revascularization can be performed through a variety of extracranial-intracranial (EC-IC) bypass operations, using several different donor and recipient vessels, interposition grafts, and anastomotic techniques. The choice of bypass option is dependent on many factors, including the goals of the operation and the availability and accessibility of particular donor and recipient vessels. Potential indications for EC-IC bypass fall into two major categories: (1) flow replacement, in the treatment of complex aneurysms or tumors that require vessel sacrifice and (2) flow augmentation, for treatment of cerebral ischemia. The effectiveness of EC-IC bypass for these indications is reviewed in this article.

EXTRACRANIAL-INTRACRANIAL BYPASS FOR FLOW REPLACEMENT IN PLANNED VESSEL SACRIFICE

Definitive management of giant or complex aneurysms may require sacrifice of the parent vessel. Permanent occlusion of the internal carotid artery (ICA) is used successfully to treat inoperable intracranial aneurysms.[1,2] Similarly, complete excision of skull base tumors occasionally requires resection of a major vessel. Although carotid sacrifice may be tolerated, ischemia and subsequent stroke can occur in up to 30% of patients.[1] Studies evaluating cerebral perfusion during carotid ligation show that patients who have signs of ischemia demonstrate a 25% or greater decrease in blood flow during carotid ligation, whereas patients who do not have ischemia have less than 25% decrease in blood flow.[3] Applying this criterion before permanent carotid ligation shows that the incidence of ischemia can be reduced to 7%, with a rejection rate of 39%.[4] Some patients, therefore, are unable to provide adequate collateral flow ipsilateral to ICA occlusion and are candidates for EC-IC bypass to prevent ischemic complications from carotid sacrifice. Fusiform or complex aneurysms of distal vessels, such as the middle cerebral artery (MCA) or its branches, typically also require revascularization using bypass techniques, as collaterals to such terminal vessels are inadequate in the acute setting to avert stroke.

Selective Revascularization

Selection criteria

In the current era, tolerance to carotid sacrifice is evaluated most frequently using the endovascular balloon occlusion test (BOT), during which the response to temporary carotid occlusion is evaluated. The tolerance to occlusion is based on several criteria consisting of neurologic, radiographic, electrophysiologic, perfusion, and provocative testing. Neurologic criteria are the primary modality of evaluation, consisting of continuous monitoring of patients for symptoms or signs of cerebral

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ischemia during a period of 20 minutes. This is supplemented with electrophysiologic monitoring with the use of electroencephalography or evoked potentials.[5] Radiographic features, such as the degree of cross filling from the communicating arteries and the speed of venous filling in the affected hemisphere, can be used to assess adequacy of collaterals.[6,7] Perfusion imaging with modalities, such as xenon CT and single photon emission CT (SPECT), can be used to assess collateral reserve further.[8–11] Although these modalities are used to identify asymmetric perfusion deficits during BOT, patients who have symmetric cerebral perfusion still may have the potential for ischemic complications.[10–13] The potential for false negatives during BOT in patients who subsequently develop ischemia after permanent occlusion has led to the use of provocative hypotensive challenge,[14] which additionally can be combined with SPECT[15,16] to improve the predictive value of the BOT.

Provocative testing is used for those patients who tolerate the initial segment of BOT, by providing an additional hypotensive challenge. This is induced for a 20-minute period, using intravenous infusion of sodium nitroprusside to decrease mean arterial pressure gradually 20% to 30% from baseline levels. If patients maintain normal neurologic status during this phase of testing, an intravenous injection of ^{99m}Tc–hexamethylpropylene amine oxime (HMPAO) is performed during the hypotensive phase. SPECT imaging is performed after removal of the catheter and stabilization of the patient, within 2 hours of ^{99m}Tc-HMPAO injections. SPECT images are analyzed for asymmetric distribution of the tracer and hypoperfusion ipsilateral to BOT. A significant decrease in perfusion or asymmetric perfusion in the hemisphere ipsilateral to ICA occlusion constitutes a failure of BOT.

Extracranial-intracranial bypass strategies

Patients who fail BOT require revascularization before carotid sacrifice. The results of BOT in addition to intraoperative assessment can help determine the strategy for revascularization. Failure of the BOT based on clinical criteria suggests that a high flow bypass is necessary. If failure of the BOT is based on provocative testing, a lower flow bypass may be adequate. Intraoperatively, the flow in the distal ICA or the MCA trunk can be measured with a quantitative flow probe before and after temporary carotid occlusion to measure the flow deficit directly. The bypass then can be tailored accordingly to the flow replacement needed (**Figs. 1** and **2**). The superficial temporal artery (STA) may provide adequate flow replacement dependent on its carrying capacity, which can be measured by its cut flow (the free flow through the cut end of the dissected vessel).[17] If the STA cannot provide adequate carrying capacity for a high flow bypass, an interposition graft

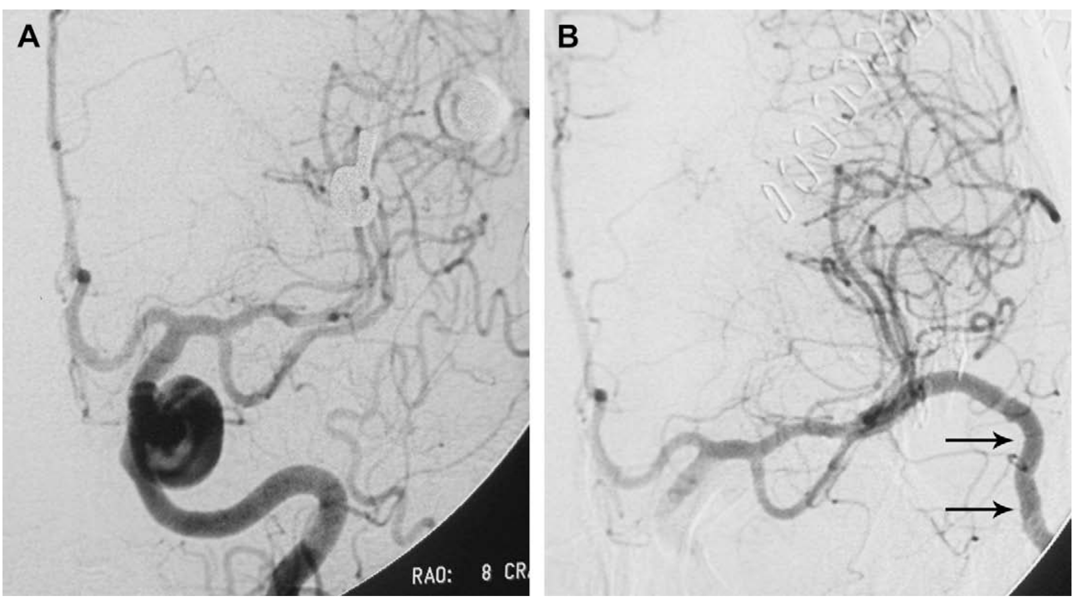

Fig. 1. Symptomatic cavernous carotid aneurysm. (*A*) Antero-posterior (AP) carotid angiogram demonstrating the aneurysm. The patient failed BOT clinically and underwent vein graft EC-IC bypass from the cervical carotid to the MCA with subsequent proximal occlusion of the ICA. (*B*) AP angiogram postoperatively demonstrating the patent vein bypass (*arrows*) filling the MCA and anterior cerebral artery territories.

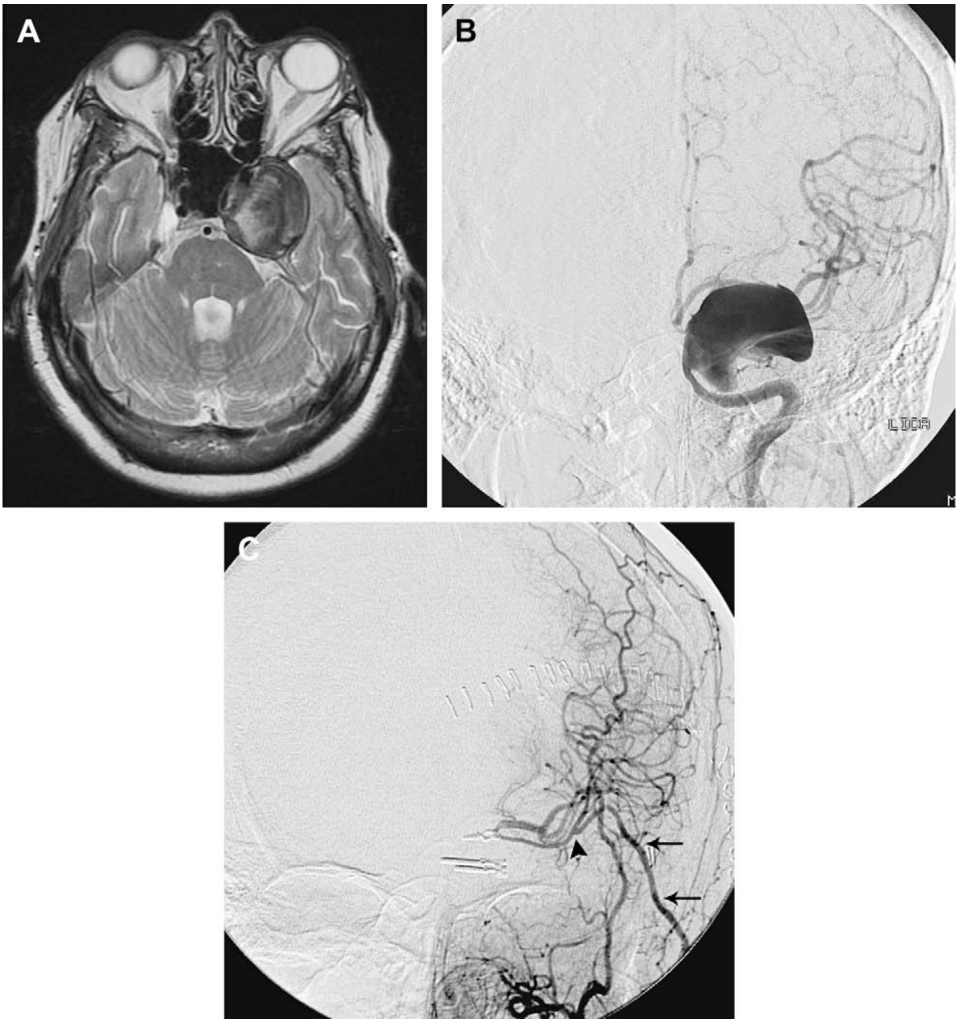

Fig. 2. Symptomatic giant partially thrombosed cavernous carotid aneurysm. (*A*) Axial T2-weighted MRI demonstrating the partially thrombosed aneurysm. (*B*) Partial filling of the aneurysmal sac is demonstrated on the anteroposterior carotid angiogram. The patient passed BOT clinically but demonstrated hypoperfusion in the left hemisphere on SPECT during the hypotensive challenge. Intraoperatively, a flow deficit of 15 mL/min was measured in the MCA trunk. The STA flow was found to be adequate to replace this deficit, and the patient underwent STA-MCA bypass with trapping of the aneurysm. (*C*) AP postoperative angiogram demonstrates excellent filling of the MCA territory via the STA (*arrows*) through the patent anastomosis (*arrowhead*).

using saphenous vein or radial artery anastomosed to the cervical carotid can be used.

Universal Revascularization

EC-IC bypass as a routine adjunct to vessel sacrifice is proposed as an alternative to selective revascularization.[18] The potential benefits from this approach are avoidance of any risks associated with the BOT procedure itself and avoidance of potential delayed cerebral ischemia. Additionally, the risk of de novo aneurysm formation, which can be associated with the hemodynamic consequences of vessel sacrifice on the contralateral circulation, could be reduced by performing EC-IC bypass routinely in all such cases. Alternatively, the selective revascularization strategy avoids the potential risks associated with bypass in patients who pass the BOT. Additionally, a majority of ischemic events after carotid sacrifice likely are embolic and would not be prevented by universal revascularization. The issue of de novo aneurysms may be most relevant in young patients, where an EC-IC bypass to reduce the long-term risk of future aneurysms may be warranted.

EXTRACRANIAL-INTRACRANIAL BYPASS FOR FLOW AUGMENTATION IN ISCHEMIA

Cerebral revascularization using EC-IC bypass continues to evolve as an option in the setting of cerebral ischemia. Although the EC-IC bypass study published in 1985[19] failed to demonstrate the efficacy of bypass over medical management for anterior circulation occlusive disease, the study preceded effective cerebral blood flow (CBF) testing. Currently, the potential use of STA-MCA bypass for ischemia in the setting of carotid occlusion is being re-evaluated by the Carotid Occlusion Surgery Study (COSS), which stratifies patients as candidates for surgery only if they demonstrate hemodynamic impairment.[20] The Japanese EC-IC Bypass Trial (JET) also is rigorously evaluating bypass to treat cerebrovascular occlusive disease.[21]

Extracranial-Intracranial Bypass for Anterior Circulation Ischemia

Atherosclerotic disease

The use of EC-IC bypass for treatment of anterior circulation cerebral ischemia dropped markedly after the unfavorable results of the randomized multicenter EC-IC bypass trial reported in 1985.[19] The trial failed to demonstrate benefit from surgical revascularization in patients who had carotid occlusive disease. Patients who had occlusive cerebrovascular disease not amenable to carotid endarterectomy in the setting of transient ischemic attack (TIA) or minor stroke were included for investigation. A total of 1377 patients of this type were randomized to best medical therapy or best medical therapy plus EC-IC bypass. Bypass patency of 96% was demonstrated with a low surgical risk of 3%. During an average follow-up of 55.8 months, however, EC-IC bypass conferred no benefit in regards to stroke risk.

Subsequent analysis of the EC-IC bypass trial methodology and results have raised shortcomings in the study design and implementation and suggest that universal abandonment of cerebral revascularization for cerebral ischemia is likely not warranted.[22,23] One of the primary drawbacks of the trial was the lack of selection criteria based on hemodynamic evaluation beyond the presence of anatomic disease. No objective physiologic criteria were used to differentiate patients in regards to hemodynamic compromise, and many of the patients may have had ischemic events resulting from embolic phenomenon or small vessel disease, which would not be expected to respond to the flow augmentation provided by bypass surgery. Subsequent studies demonstrate that careful evaluation of patients who have occlusive cerebrovascular disease can identify a subgroup with severe compromise in cerebrovascular reserve capacity, who are at higher risk for stroke,[24–29] and who may be reasonable candidates for revascularization.

In addition to the lack of hemodynamic selection criteria, the EC-IC bypass trial was criticized for selection bias. A review of the centers participating in the study revealed that a large number of patients, more than enrolled in the study, underwent surgery outside the trial.[23] This suggests that patients who were perceived to be most in need of bypass were not enrolled and underwent surgery, perhaps diluting any beneficial effect of the surgery in enrolled patients. With the concerns regarding the methodology of the trial and a greater understanding of the importance of assessing cerebral hemodynamic factors, interest in revascularization has re-emerged in recent years. Neurosurgeons have continued to perform EC-IC bypass for ischemic indications in selected patients,[30,31] and a randomized trial, COSS, to address the usefulness of STA-MCA bypass in patients who are symptomatic and who have unilateral carotid occlusion currently is underway.[20,32]

Hemodynamic assessment Identifying patients who have greater likelihood of benefiting from flow augmentation relies on identification of diminished cerebrovascular reserve in the affected arterial territory by physiologic CBF testing. There is a multitude of imaging modalities aimed at assessing adequacy of cerebral perfusion: positron emission tomography (PET), xenon CT, SPECT, transcranial Doppler (TCD), CT, and magnetic resonance (MR) perfusion modalities.[33] Each modality has relative advantages and disadvantages, but the premise for these methods is to identify those patients suffering from hemodynamic compromise as the source of ischemic symptoms. Degrees of cerebral hemodynamic impairment can be classified into two basic categories, designated as stage 1 and stage 2 hemodynamic compromise. Stage 1 compromise refers to autoregulatory vasodilation, which occurs to maintain normal CBF by reducing vascular resistance. As perfusion pressure decreases further, the capacity for maintaining normal blood flow by autoregulatory vasodilation is overcome and CBF decreases; the brain compensates by increasing the extraction of oxygen from the blood to maintain normal cerebral oxygen metabolism, referred to as stage 2 compromise.

Stage 1 compromise can be inferred by quantifying perfusion parameters, such as CBF and cerebral blood volume (CBV), with an increase in

CBV or CBV/CBF ratio reflecting autoregulatory vasodilation. Such quantitative measurements can be made reliably only with PET, as also is the case with the assessment of increased oxygen extraction fraction, which defines stage 2 compromise (also referred to as misery perfusion). Parameters indicating misery perfusion are correlated with increased stroke incidence after carotid occlusion,[24] and PET, therefore, has emerged as the gold standard predictive and quantitative tool for assessing critical hypoperfusion. Demonstration of misery perfusion (stage 2 hemodynamic failure) by PET in patients who have carotid artery occlusion is associated with a 30% 2-year stroke risk[24] and this subgroup now forms the basis for the multicenter randomized COSS trial currently in progress to examine the usefulness of EC-IC bypass in reducing stroke risk.[20] PET, however, is not a universally available imaging modality.

Identification of the presence and degree of autoregulatory vasodilation (stage 1 compromise) also can be assessed with the use of paired blood flow measurements, with the initial measurement obtained at baseline, and the second after a vasodilatory stimulus, such as acetozolamide, hypercapnea, or physiologic tasks, such as hand movement. The response to the vasodilatory stimulus reflects cerebrovascular reserve capacity and can be graded as a reduced, absent, or paradoxic reduction compared with baseline, referred to as steal phenomenon. Paired measurements can be obtained using a variety of modalities: SPECT, xenon CT, TCD, MR, and CT perfusion,[33] and correlations with stroke risk are described.[25–29] MR perfusion studies and technique of functional imaging looking for changes in the blood oxygen level–dependent (BOLD) signal with physiologic tasks[34,35] are promising modalities. These qualitative tools are useful to assess unilateral disease but generally are inadequate in patients who have bilateral or global pathology. There are no studies to compare the relative accuracy of each of these modalities, although the challenge tests all are based on a similar premise of identifying loss of cerebrovascular reserve.

Selection criteria In recent years, the use of bypass for anterior circulation ischemia in selected patients has been reported.[30,31,36] In general, the indications for STA-MCA bypass for purposes of flow augmentation (**Fig. 3**) are as follows:

- Symptoms, stroke, or TIA concordant with radiographic findings
- Failure of maximal medical therapy
- Compromised cerebrovascular reserve as demonstrated by any of the variety of perfusion imaging studies.
- Lack of major medical comorbidities

The ongoing COSS trial in the United States is assessing whether or not high-risk patients who have carotid occlusion and are selected based on demonstrable compromise of cerebral hemodynamic reserve may benefit from EC-IC bypass. Additionally, the JET study[21] is assessing the usefulness of bypass in patients who have carotid occlusion and intracranial anterior circulation disease with hemodynamic impairment.

Outcome assessment Assessment of the usefulness of EC-IC bypass in cerebral ischemia is an issue that requires well-controlled randomized studies with defined selection criteria, as is underway with the COSS trial.[20] Although stroke risk is the outcome of greatest interest, surrogate markers of success, such as bypass patency, improvement in hemodynamic compromise, and other endpoints, such as changes in cognitive function, also are of paramount interest.

Radiographic measures of blood flow and perfusion provide an adjunctive indication of bypass success, and establishing improvement in perfusion postoperatively is an important step in verifying that the bypass has performed the goal of augmenting flow adequately. Small studies support improvement in PET-measured misery perfusion after bypass.[37,38] Several studies also have incorporated paired blood flow measurements into the postoperative evaluation of patients after revascularization with bypass. Whereas some report improvement in hemodynamic parameters after bypass,[31,39–43] others find improvement only in a subset of patients[30,44,45] or early improvement that was not long lasting.[46–48] Improvements may be most prominent in patients who have the greatest degree of compromise preoperatively and are seen more often in cerebrovascular reserve rather than in resting CBF.[39,43,44] Furthermore, changes in the postoperative setting are difficult to interpret definitively without comparison to similar nonoperated patients, given that even spontaneous improvement in hemodynamic parameters are described,[49,50] occurring presumably as a result of collateral formation.

Ultimately, the success of the revascularization procedure is judged by its ability to favorably influence the natural history and stroke risk of the underlying cerebrovascular occlusive disease, an issue currently being addressed by prospective randomized studies, COSS[20] and JET, in the United States and Japan, respectively.

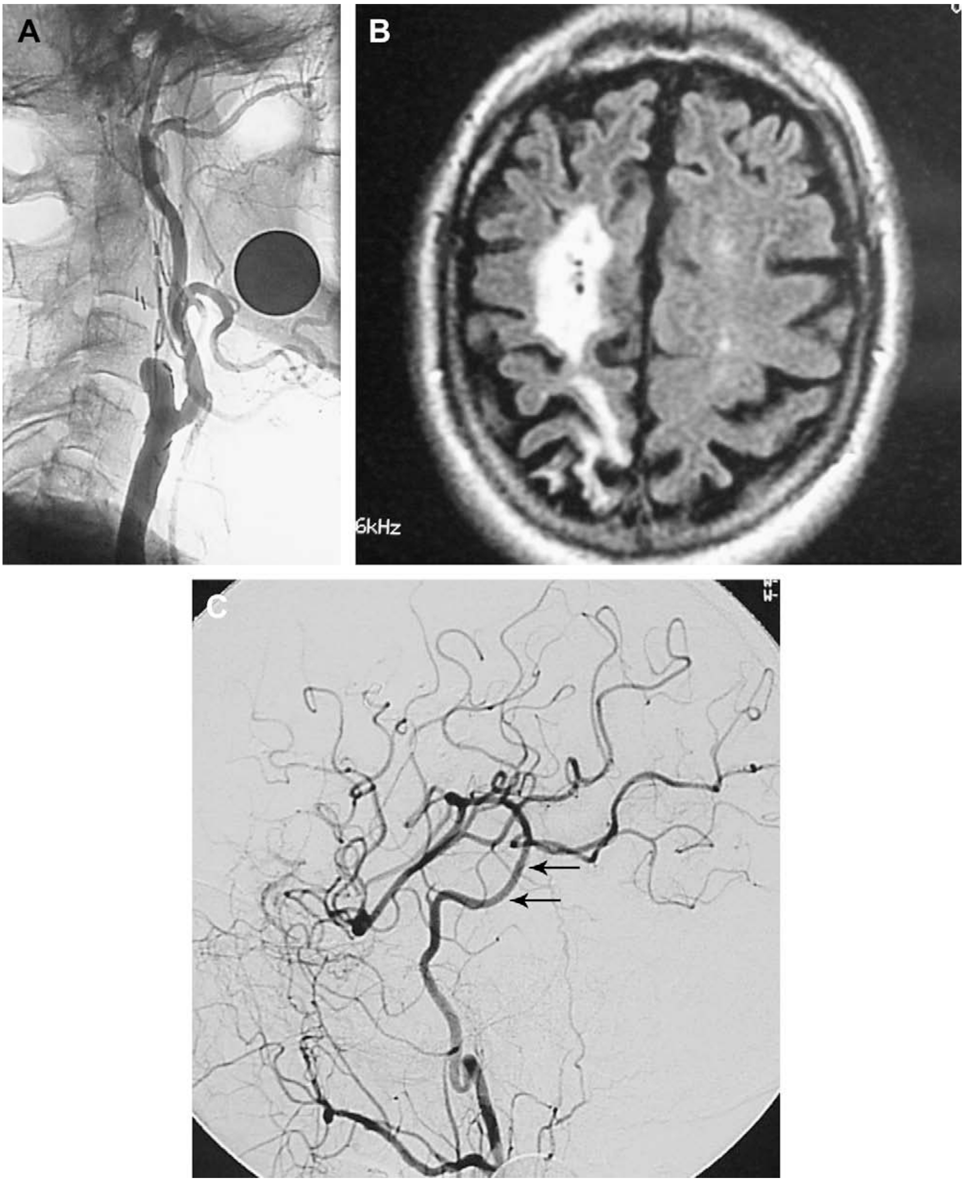

Fig. 3. Right carotid occlusion after a prior carotid endarterectomy presenting with stroke. (*A*) Lateral carotid angiogram demonstrates the occluded ICA. (*B*) Axial MRI demonstrates a typical watershed area stroke in the right hemisphere despite medical therapy. Perfusion testing with xenon CT confirmed loss of cerebrovascular reserve in the right hemisphere, and the patient underwent right STA-MCA bypass. (*C*) Postoperative lateral angiogram demonstrating excellent filling of the MCA territory by the widely patent STA bypass (*arrows*).

Moyamoya disease

Moyamoya disease is a well-described entity characterized by progressive stenosis and occlusion of the supraclinoid ICA and its branches, affecting primarily a pediatric population and resulting in stroke. Basal collateral vessels form, with a classic angiographic appearance of a "puff of smoke," from which the name of the disease entity arises.[51] These fragile collaterals, especially in the less common adult population, can be a source of hemorrhagic presentation of the disease rather than the ischemic presentation described more classically in the afflicted pediatric population.

Medical therapy for symptomatic moyamoya disease largely is ineffective. Consequently, surgical revascularization has become the primary modality of treatment for patients who have this disease for reducing the incidence of ischemic stroke and TIA. Many series report the efficacy of revascularization in this syndrome,[52–55] using either the technique of indirect revascularization using onlay grafts, direct EC-IC bypass using STA-MCA anastomosis, or a combination of both strategies.[56,57]

Indirect bypass using the technique of encephaloduroarteriomyosynangiosis (EDAMS) involves laying the STA, the dura, and the temporalis muscle over the brain surface, where these donor structures serve as a source of often exuberant collateralization to the brain surface over the course of 3 to 6 months. This technique demonstrates its best results in the pediatric population,[54] whereas in adults, direct STA-MCA bypass seems to offer greater benefit.[57] Direct bypass offers the advantage of immediate flow augmentation (**Fig. 4**), providing earlier relief of ischemic symptoms[58] but can be challenging in the pediatric population given the small size of donor and recipient vessels. The good results with indirect bypass in the pediatric group favor this approach in children.

The efficacy of revascularization for the treatment of hemorrhagic moyamoya disease is less clear. Reports support a trend toward reduced rebleeding rates[59–61] and also seem to indicate that direct STA-MCA anastomosis rather than indirect bypass is the most effective strategy.[62] Assessment of the effectiveness of direct bypass for hemorrhagic moyamoya disease is underway in Japan, with a prospective randomized trial addressing this issue (the Japan Adult Moyamoya Trial).[63]

Extracranial-Intracranial Bypass for Posterior Circulation Ischemia

The use of bypass for revascularization in the setting of posterior fossa ischemia is less studied than anterior circulation disease because of the relative prevalence of the conditions, the availability and evolution of endovascular techniques for treatment of vertebrobasilar stenosis, and the relatively higher morbidity and technical complexity of posterior circulation revascularization. Existing series indicate, however, the feasibility of various EC-IC bypass options to the posterior circulation, including occipital artery to posterior inferior cerebellar artery (OA-PICA), STA to posterior cerebral artery (PCA), and STA to superior cerebellar artery bypasses (**Fig. 5**).

Symptomatic vertebrobasilar disease (VBD), particularly if it affects intracranial vessels, carries a high stroke risk, averaging 10% to 15% per year despite medical therapy.[64,65] Therefore, patients presenting with refractory vertebrobasilar insufficiency (VBI), despite maximal medical therapy and intracranial occlusive VBD not amenable to

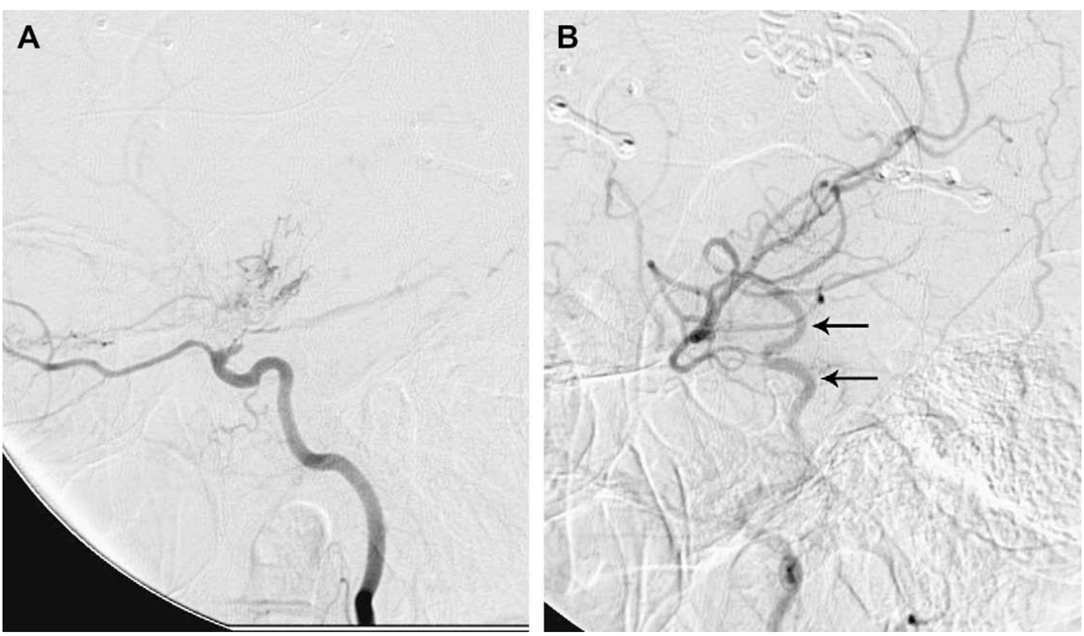

Fig. 4. Moyamoya disease presenting with TIAs. (*A*) Lateral carotid angiogram demonstrating supraclinoid ICA occlusion with a fine network of basal vessels. Patient underwent STA-MCA bypass. (*B*) Postoperative lateral angiogram demonstrating revascularization of the MCA territory via the STA graft (*arrows*).

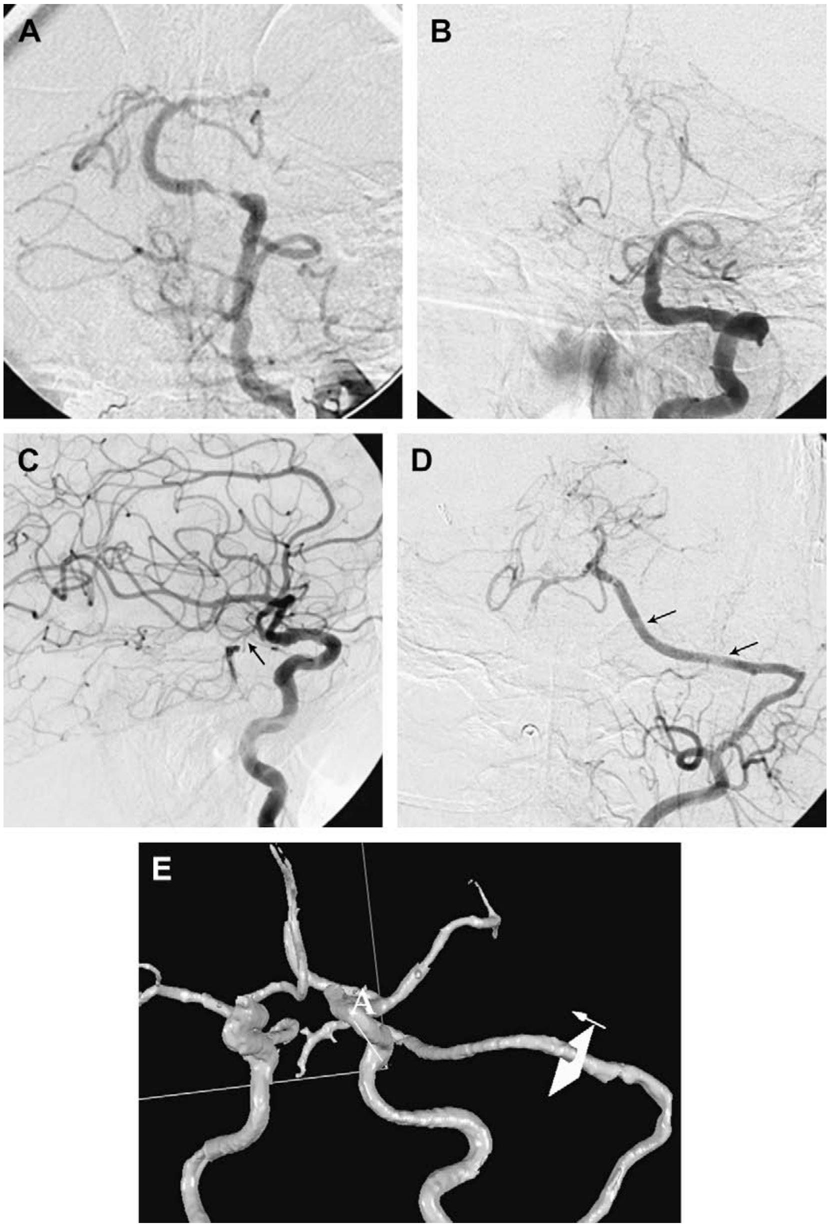

Fig. 5. Vertebrobasilar occlusive disease presenting with refractory VBI. (*A*) AP vertebral angiogram demonstrating a severe stenosis of the left vertebral artery. The right vertebral artery was occluded. While awaiting consideration of endovascular intervention, the patient experienced new deficits. (*B*) AP vertebral angiogram demonstrated progression of the stenosis to full occlusion. (*C*) Lateral carotid angiogram demonstrated minimal filling of the posterior circulation through a small posterior communicating artery (*arrow*). The patient was recurrently symptomatic and required hypertensive therapy. To avoid further strokes, he underwent a STA-PCA bypass using an interposition vein graft. (*D*) AP external carotid angiogram demonstrating the graft (*arrows*) and filling of the top of the basilar and its branches. (*E*) Postoperative quantitative MR angiography demonstrating anterograde flow in the bypass (*arrow*) measuring 70 mL/min. A, anterior.

endovascular angioplasty and stenting, are potential candidates for posterior circulation EC-IC bypass. Overall, surgical revascularization of the posterior circulation carries a higher risk and lower patency rates than seen with anterior circulation bypass. Patency rates for OA-PICA bypass range from 88% to 100%, with mortality rates averaging 4% in various series.[66] In a review compiled from several series of 86 bypasses using STA or vein to the SCA or PCA, patency rates were found to be in the 78% to 90% range, with mortality averaging 12%[66,67] and a serious morbidity of 20%. Although these series show improvement in symptoms in subsets of patients, the morbidity and mortality associated with such revascularization attempts, specifically for the posterior circulation, have introduced caution when entertaining these treatment options, particularly for patients in poor medical and neurologic condition. Nonetheless, advances in microsurgical and anesthetic technique since the publication of such series and improvements in perioperative neurointensive care management do allow posterior circulation revascularization to be undertaken successfully in selected patients who do not have other options for management.

SUMMARY

The role of surgical revascularization for patients who have ischemic disease remains controversial. Despite the previous EC-IC bypass trial that failed to demonstrate the benefit from STA-MCA bypass compared with medical therapy, there is mounting evidence that the procedure should be considered in selected patients. Bypass remains a mainstay of treatment in moyamoya disease and in flow replacement in the setting of planned vessel sacrifice.

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