Investigación clínica

Bypass surgery for the prevention of ischemic stroke: current indications and techniques

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ABSTRACT

Introduction: Although most ischemic strokes are thromboembolic in origin and their management is endovascular or medical, some are haemodynamic in origin and their management may be surgical. We reviewed bypass indications, patient selection and surgical techniques used in our current practice.

Methods: Extracranial-intracranial (EC-iC) bypass with superior temporal artery-to-middle cerebral artery (STA-MCA) bypass, high-flow interposition grafts and reconstructive techniques were used to treat patients with symptomatic ischemia.

Results: During a 13-year period, 152 bypasses were performed for ischemia in 129 patients. Specific diagnoses included: (1) internal carotid artery (iCA) occlusion (58 bypasses); (2) MCA occlusion and, rarely, high-grade MCA stenosis (22 bypasses); (3) vertebrobasilar atherosclerotic steno-occlusive disease (2 bypasses); (4) moyamoya disease (65 bypasses); and (5) ischemic complications after aneurysm treatment (5 bypasses). Of the 152 bypasses, 137 were conventional STA-MCA bypasses. Fourteen patients had high-flow bypasses that included 4 "double-barrel" STA-MCA bypasses, 6 bypasses with interposition grafts to the cervical carotid artery, 2 subclavian artery-to-MCA bypasses, 1 MCA-to-posterior cerebral artery (PCA) bypass and 1 aorto-carotid bypass. The bypass patency rate was 96.1%.

Conclusions: Bypass surgery for the prevention of ischemic stroke is safe and elegant techniques have been developed. Patients with athero-occlusive disease, ischemic symptoms and haemodynamic insufficiency have significant risk of stroke if managed medically or left untreated. However, surgical intervention lacks supporting evidence from the recent Carotid occlusion Surgery Study (CoSS). Patients will be caught in a difficult position between a dismal natural history and an unproven surgical intervention. Clinicians must individualise their management until additional data are published or further consensus develops.

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**Cirugía de bypass para la prevención del ictus isquémico: indicaciones y técnicas actuales**

**RESUMEN**

**Introducción:** Aunque la mayoría de los accidentes cerebrovasculares isquémicos son de origen tromboembólico y su tratamiento son endovasculares o médico, algunos son de origen hemodinámico y su manejo puede ser quirúrgico. Hemos revisamos las indicaciones del bypass en el infarto isquémico, la selección de pacientes y las técnicas quirúrgicas utilizadas en nuestra práctica actual.

**Métodos:** Bypasses extra-intracraneales (EC-iC) de la arteria temporal superficial a arteria cerebral media (STA-MCA), bypasses de alto flujo con interposición de injertos y técnicas de reconstrucción se utilizaron para el tratamiento de pacientes con isquemia sintomática. Durante un periodo de 13 años, 152 bypasses fueron realizados por isquemia en 129 pacientes. Los diagnósticos específicos incluyeron: a) oclusión de la arteria carótida interna (ICA) (58 bypasses); b) oclusión de la arteria cerebral media y, raramente, la estenosis de alto grado de la misma (22 bypasses); c) ateroesclerosis esteno-oclusiva del sistema vertebrobasilar (2 bypasses); d) enfermedad de moyamoya (65 bypasses), y e) complicaciones isquémicas tras el tratamiento del aneurisma (5 bypasses). Ciento treinta y siete fueron bypasses convencionales de STA-MCA. Catorec pacientes tenían bypass de alto flujo que incluyó 4 «double-barrel» bypass de STA-MCA, 6 bypasses con injertos de la arteria carótida cervical, 2 de arteria subclavia a arteria cerebral media, un bypass de arteria cerebral media a arteria cerebral posterior, y un bypass aortocarotídeo. La tasa de permeabilidad de las anastomosis fue del 96,1%.

**Conclusions:** La cirugía de bypass para la prevención del ictus isquémico es segura y se han desarrollado técnicas elegantes para ésta. Los pacientes con enfermedad atero-oclusiva, síntomas de isquemia e insuficiencia hemodinámica tienen un riesgo importante de accidente cerebrovascular si se manejan mediante o no se tratan. Sin embargo, la intervención quirúrgica carece de evidencia científica que la respalde desde el reciente Carotid Occlusion Surgery Study (COSS). Los pacientes se ven atrapados en una situación difícil entre una historia natural pobre y una intervención quirúrgica sin evidencia. Los médicos deben individualizar el manejo de estos pacientes hasta que se publiquen datos adicionales o se desarrolle un mayor consenso.

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**Introduction**

Ischemic stroke is the third leading cause of death and disability in the developed countries and a significant public health problem. Most strokes are thromboembolic in origin, resulting from clot blocking blood flow in an intracranial artery. Stroke patients can be treated pharmacologically with intravenous tissue plasminogen activator (tPA) if they present within 4.5 hours of symptom onset. Stroke patients with large artery occlusions can be treated with a variety of endovascular techniques in addition to intravenous thrombolysis. Currently available options include intra-arterial thrombolitics, mechanical thrombolysis, and/or embolectomy with devices such as the Merci retrieval system or the Penumbra device. The vast majority of ischemic stroke intervention for ischemic stroke caused by thromboembolism from atherosclerotic plaque in a symptomatic cervical internal carotid artery with high-grade stenosis (70%-99%).

However, some ischemic strokes are due to more chronic conditions that progressively diminish cerebral blood flow in the absence of compensatory collateral circulation. Bypass surgery is a surgical intervention for these ischemic strokes that are hemodynamic rather than thromboembolic. Yasargil and Donaghy introduced the superficial temporal artery-to-middle cerebral artery (STA-MCA) bypass in 1969 and initiated the practice of bypass surgery. Extracranial-intracranial (EC-IC) bypass revascularizes ischemic brain by redirecting blood flow from the scalp through this low-flow surgical conduit. Bypass surgery evolved with the development of high-flow bypasses that use saphenous vein grafts or radial artery grafts to connect cervical carotid donor arteries with intracranial recipient arteries. The latest development is intracranial-intracranial (IC-IC) bypasses that use reconstructive techniques and donor arteries that are entirely intracranial. A pathological segment in a diseased artery can be excised and the artery reconstructed with an end-to-end reanastomosis; a compromised artery can be reimplanted on an adjacent artery to restore blood flow; an
in situ bypass brings adjacent arteries together with a side-to-side anastomosis that preserves flow in both donor and recipient arteries, and short interposition grafts between intracranial donor arteries eliminate the need for long grafts and additional exposure in the neck. Although bypass techniques are applicable to complex aneurysms whose treatment might require deliberate occlusion of an afferent or efferent artery, these techniques are not as applicable to symptomatic ischemia. Some patients have ischemic symptoms that are hemodynamic in origin, and bypass surgery can be beneficial in these patients.

Here we reviewed our clinical experience to examine indications, patient selection, and surgical techniques of bypass for ischemic stroke. We also review the latest scientific evidence on this controversial topic.

Methods

The study was approved by the Institutional Review Board and conducted in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations. The prospectively maintained database for the Vascular Neurosurgery Service at the University of California, San Francisco was searched for patients who had bypass surgery for ischemia. Patients who had bypass surgery as part of their treatment for aneurysms or skull base tumors were not included. Medical records, radiographic studies, operative reports, and intraoperative photographs were reviewed. Neurological outcomes were assessed, but are the subject of a separate report.

Surgical techniques

STA-MCA bypass

STA-MCA bypass is by far the most common bypass for stroke patients. The patient is positioned supine and with the head turned 90 degrees to align the lateral convexity parallel to the floor. The course of the STA is mapped with a Doppler flow probe and the posterior limb is usually selected. The anterior limb is used only when the posterior limb is too small. The microscope is used to dissect the STA from zygoma to the superior temporal line. The artery is left in continuity and vasodilated with papaverine extraluminally. Temporalis muscle is divided under the STA and mobilized to each side. Alternatively, temporalis can be flapped anteriorly to expose directly over or in the Sylvian fissure for a larger recipient artery. A small craniotomy is made by working under the STA and staying below the superior temporal line. Dura is opened in flap that preserves middle meningeal arteries if they have developed collateral circulation.

MCA vessels exiting the Sylvian fissure are inspected under the microscope and a recipient artery is selected with suitable size and accessibility. The STA is transected, stripped of its adventitia, cut at a 60 degree angle, and spatulated with an axial incision in the arterial wall. After the patient is placed into propofol-induced EEG burst suppression, the recipient artery is trapped between temporary clips, arteriotomized, and flushed with heparinized saline. Two 10-0 sutures are placed on either end of the arteriotomy to approximate the STA and MCA. Running continuous sutures are placed from one end of the arteriotomy to the other, then tightened and tied. The opposite wall is sutured similarly. The temporary clips are removed and hemostasis is achieved with fibrillar Nu-Knit packing. Indocyanine green videoangiography confirms the patency of the bypass.

The closure must avoid compromising flow in the bypass. The dural closure should not constrict the STA as it passes through. A small passageway for the STA is rongeured from the bone flap. Temporalis muscle is closed loosely around the graft, and galea sutures and skin staples are placed carefully to avoid pinching the graft.

Posterior circulation bypasses

Posterior circulation bypasses augment flow to the basilar apex using the STA as the donor artery and either superior cerebellar artery (SCA) or PCA as the recipient artery. The SCA is accessible through a subtemporal approach that elevates the temporal lobe to expose the tentorial incisura. The PCA is accessible through a pretemporal approach that mobilizes the temporal lobe posterolaterally to expose the oculomotor nerve and the crural cistern. Either artery can be used as a recipient when they communicate with the basilar apex, but a hypoplastic P1 PCA segment or a fetal PCA contraindicate the use of the PCA. PCA offers a large-caliber, thick-walled recipient. The caliber of SCA is approximately half that of PCA, and a duplicated SCA has an even smaller caliber.

The depth of these bypasses makes them technically demanding, and an orbitozygomatic-pterional approach increases exposure and maneuverability at the depths of a narrow surgical corridor. The patient is positioned supine the head turned 30 degrees for pretemporal exposure and 60 degrees for subtemporal exposure. The STA is harvested as described above, but at least 8 cm of artery are harvested to reach the anastomotic depth. After completing the orbitozygomatic-pterional exposure, the Sylvian fissure is widely split under the microscope to expose MCA, ICA, and PCA. Bypasses to the SCA do not require a Sylvian fissure split, and instead require temporal lobe retraction and dissection of the arachnoid in the tentorial incisura. Either artery can be used as a recipient when they communicate with the basilar apex, but a hypoplastic P1 PCA segment or a fetal PCA contraindicate the use of the PCA. PCA offers a large-caliber, thick-walled recipient. The caliber of SCA is approximately half that of PCA, and a duplicated SCA has an even smaller caliber.

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High-flow bypasses

Athero-occlusive disease is variable and multifocal. Traditional donor arteries like the STA may be involved with the pathology,
compromised by pathology in proximal arteries, or sacrificed by previous surgery. In these rare cases, alternative bypasses are needed. Bypasses with interposition grafts like saphenous vein or radial artery have higher flow than traditional EC-IC bypasses. The cervical carotid artery is an accessible donor artery, with anastomotic sites on the ICA, ECA, and common carotid artery (CCA). The ICA is used when a patent stump is available and collateral circulation from the ECA must be preserved. ECA is used when the cerebral circulation is critically dependent on ICA flow and temporary ICA or CCA occlusion during the anastomosis would be poorly tolerated. CCA is used when the carotid bifurcation is high-riding and exposure is compromised by the mandible. High-flow bypasses connect the ICA, ECA, or CCA with the MCA, typically along the M2 segment distal to the lenticulostrate arteries originating from the M1 segment. The distal end-to-side anastomosis between the MCA and the graft is performed first to preserve the mobility of the graft during this more difficult anastomosis. 9-0 monofilament nylon is used because of the thicker walls of both the recipient artery and the graft. The graft is tunneled under the skin anterior to the ear down to the neck incision. The proximal anastomosis can either be end-to-end or end-to-side, depending on the donor artery and the need to preserve distal flow in the donor artery. 7-0 prolene suture is used for anastomoses with the carotid artery.

A similar bypass can be constructed for high-flow bypasses to the posterior circulation. The PCA is preferred over SCA because its caliber matches that of the bypass graft. The distal end-to-side anastomosis is performed before the proximal anastomosis in the neck. This bypass requires a wide Sylvian fissure split, and therefore the M2 MCA is already exposed. A shorter bypass alternative is the MCA-PCA bypass, which uses the MCA as the donor site rather than the cervical carotid artery. This bypass is entirely intracranial (IC-IC), spares the patient a cervical incision, and requires only a short radial artery graft. Shorter grafts generally have higher long-term patency rates than longer grafts to the neck. Radial artery is generally preferred over saphenous vein because it is an arterial structure and it has superior handling, and the radial artery is always long enough for IC-IC grafts.

When the patency of cervical carotid arteries is compromised by disease, a more proximal donor artery is needed. The subclavian artery can be accessed through a supraclavicular incision and serve as a proximal donor. The distance to the recipient site is much longer than with other high-flow bypasses involving the cervical carotid artery, and therefore saphenous vein interposition grafts are typically required.

### Results

During a 13-year period between 1997 and 2010, 152 bypasses were performed for ischemia in 129 patients, which included 80 women and 49 men with a mean age of 47.2 years (range 9 months to 80 years). Patients presented with athero-occlusive disease that resulted in chronic, low cerebral blood flow accompanied by episodes of ischemic symptoms (transient ischemic attack (TIA) or stroke.

Bypass surgery was indicated in patients with 5 distinct conditions: (1) extracranial atherosclerotic occlusive disease (ICA occlusion, 58 bypasses); (2) intracranial atherosclerotic steno-occlusive disease (MCA occlusion and, rarely, high-grade MCA stenosis; 22 bypasses); (3) vertebralbasilar atherosclerotic steno-occlusive disease (2 bypasses); (4) moyamoya disease (65 bypasses); and (5) ischemic complications after aneurysm treatment, when bypass was not a pre-planned part of therapy (5 bypasses) (Table 1). Ischemic complications after aneurysm treatment included: supraclinoid ICA occlusion to treat an angioplasty-induced carotid-cavernous fistula, following endovascular coiling of a ruptured MCA aneurysm (Fig. 1); false negative balloon test occlusion and subsequent TIA or strokes after carotid sacrifice (immediately after treatment in one patient and delayed in one patient); and one flow-related aneurysm formation and rupture after Takayasu’s arteritis-related bilateral CCA and unilateral vertebral artery occlusion.

Of the 152 bypasses, 137 were conventional STA-MCA bypasses. Bilateral STA-MCA bypasses were performed in 23 patients, of whom 22 had moyamoya disease. Temporalis muscle was laid down on the brain surface as an adjunct in 27 of these 137 patients.

Fourteen patients had other high-flow bypasses (Table 2). Four of these patients had “double-barrel” STA-MCA bypass that used both anterior and posterior limbs of the STA and two MCA anastomoses. 6 patients had high-flow bypasses with interposition grafts to the cervical carotid artery. 2 patients had subclavian-MCA bypasses. One MCA-PCA bypass was performed in one patient with unilateral vertebral artery occlusion, a hypoplasic contralateral vertebral artery, no

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<th>Table 1 – Bypasses for ischemic stroke or TIA performed at the University of California, San Francisco, between 1997 and 2010</th>
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<td>Diagnosis</td>
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<td>MCA occlusion/stenosis</td>
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<th>Table 2 – High-flow bypasses for ischemic stroke or TIA performed at the University of California, San Francisco, between 1997 and 2010</th>
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<tr>
<td>Doubled-Barrel STA-MCA bypass</td>
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Figure 1 – Case example, iatrogenic supraclinoid carotid occlusion. This 57 year-old woman presented with subarachnoid hemorrhage, as seen on (A) axial computed tomography scan. (B) Catheter angiography revealed a right MCA aneurysm (right ICA injection, lateral view). (C) The aneurysm was coiled endovascularly without complication. (D) She developed symptomatic vasospasm one week later (right ICA angiogram, lateral view). (E) The ICA perforated during angioplasty and caused a carotid-cavernous fistula that was treated with balloon occlusion of the ICA (F). She had a small right PCoA and a small A1 anterior cerebral artery, and awoke with a hemiparesis. An ICA-MCA bypass was performed immediately. (G) Despite severe vasospasm in the recipient MCA, (H) the distal end-to-side anastomosis was completed. (I) After completing the proximal end-to-end anastomosis in the neck, (J) indocyanine green videoangiography confirmed patency of the bypass intraoperatively. (K) Postoperative angiography (right CCA injection, lateral view) also confirmed bypass patency. Her vasospasm and hemiparesis resolved and she made a good recovery.

Figure 2 – Case example, vertebrobasilar ischemia. This 57 year-old man with hypertension, hypercholesterolemia and diabetes presented with symptoms of vertebrobasilar ischemia. (A) MRI (T1-weighted image, axial view) demonstrated a small medullary stroke and (B) angiogram demonstrated complete occlusion of the left vertebral artery in the neck (left subclavian artery injection, anteroposterior view). (C) The right vertebral artery had a high-grade atherosclerotic stenosis just proximal to joining the vertebrobasilar junction (right vertebral artery injection, anterior-oblique view), with slow filling of the distal basilar circulation. The posterior communicating arteries were absent bilaterally (not shown). A MCA-PCA bypass was performed to revascularize the distal posterior circulation. (D) Through a right orbitozygomatic approach, the P2 segment of the PCA was exposed deep and lateral to the carotid bifurcation, lateral to the oculomotor nerve and medial to the tentorial edge. (E) The radial artery graft was anastomosed to the P2 segment with a 9-0 continuous suture and (F) then to the frontal M2 segment, creating an IC-IC bypass. (G) Postoperative angiogram (right internal carotid artery injection, anterior oblique view) showed a patent right MCA-PCA bypass graft that filled the basilar apex and posterior circulation retrograde.

posterior communicating artery collateral, and diminutive STA donor arteries (Fig. 2). One aorta-to-CCA bypass was performed in a 1 year-old child with complete occlusion of both carotid arteries and both vertebral arteries, and blood-pressure dependent hemiparesis (Fig. 3).

Autologous saphenous vein grafts were used in 5 patients. Radial artery grafts were used in 4 patients. Allograft saphenous vein was used in one patient whose supraclinoid ICA occluded during angioplasty/stenting and could not be reopened. Her saphenous veins had been harvested for previous coronary bypass surgery and her STA was diminuitive on that side.
Figure 3 – Case example, Occlusion of the great vessels. This 10 month-old boy presented with right hemiparesis. Magnetic resonance imaging demonstrated acute ischemia in the left MCA territory (diffusion-weighted images, [A] coronal and [B] axial views). (C) Catheter angiography (aortic injection, anteroposterior view) revealed severe obliterative arteriopathy of the great vessels originating from the aortic arch. Cerebral blood flow was reconstituted by collaterals from the anterior spinal artery to the vertebral arteries, and from intercostal and cervical arteries to the left CCA. Delayed phase of the angiogram showed filling of the right carotid circulation via anterior communicating artery and the basilar circulation via the posterior communicating artery. The patient's hemiparesis resolved and he was successfully weaned from pressor agents. His bypass remained patent at 1-year follow-up.

Bypass patency rate was 96.1%. Six patients (3.9%) had graft occlusions, and patency was re-established in 4 patients with surgical revision.

Discussion

Indications for bypass in stroke patients

CT and MR imaging

In addition to the diagnosis of an underlying athero-occlusive lesion, the presence of ischemic tissue that is at risk for stroke, but still salvageable, is another important indication for bypass surgery. Brain tissue ischemia cannot be imaged directly but can be inferred from conventional imaging. A large stroke on CT or MR imaging contraindicates bypass surgery if it involves the entire territory of the affected artery because this brain tissue is not salvageable and revascularization could precipitate hemorrhagic conversion of an acute infarction. Bypass candidates have significant areas of ischemia that can be rescued by revascularization. Watershed infarcts that occur in the areas between vascular territories, such as between MCA and anterior cerebral artery (ACA) territories or between MCA and posterior cerebral artery (PCA) territories, are commonly seen in patients with athero-occlusive disease and hemodynamic insufficiency.

Furthermore, internal watershed infarcts that occur at the gray matter-white matter junction between superficial and deep perforators of the MCA (such as the centrum semiovale) may be more suggestive of hemodynamic insufficiency than cortical watershed infarcts. These areas lie in the distal outreaches of the ICA territory and therefore are most vulnerable to low perfusion pressures.

Angiography

Catheter angiography defines a patient's underlying athero-occlusive disease, but also compensatory collateral circulation. An intact circle of Willis can compensate for a carotid occlusion with cross-filling from the contralateral ICA through the anterior communicating artery (ACoA) and from the vertebrobasilar circulation through the posterior communicating arteries (PCoAs). Retrograde flow in the ophthalmic arteries can provide collateral circulation from the external carotid arteries (ECAs). Leptomeningeal or pial collaterals can be recruited over the cerebral convexity connecting PCA and MCA territories as well as ACA and MCA territories. Other less common sources of collateral
circulation include: anterior, middle, and posterior meningeal arteries in the dura mater connecting to cortical arteries; ACA-PCA connections through a “limbic loop,” extracranial connections between ECA or vertebral artery branches and the distal ICA; and anterior spinal artery collateralizing the vertebrobasilar circulation. Well developed collateral circulation can compensate for severe athero-occlusive disease, whereas the absence of collateral circulation may make surgical bypass an important option\textsuperscript{15,16}. Angiography distinguishes occlusion from stenosis, the latter being amenable in some cases to endovascular intervention with angioplasty, stenting, or both.

**Hemodynamic studies**

The above indications are clinical, diagnostic, and radiographic guidelines for selecting patients for bypass surgery. However, none directly measures the complex relationship between cerebral blood flow and brain metabolism that determines tissue ischemia and stroke risk. The ability to identify mismatches between blood supply and brain demand facilitates patient selection and increases the likelihood of a benefit to those who undergo bypass surgery\textsuperscript{12,17-22}. Conversely, the failure to assess hemodynamic insufficiency as part of patient selection might render bypass surgery ineffective. The multi-center EC-IC Bypass Trial randomized 1377 patients to surgical or medical therapy and found no significant difference in stroke rates in surgical and medical patients (31% and 32%, respectively)\textsuperscript{23}. Stroke patients were entered into this study based on clinical and angiographic criteria, without differentiating between hemodynamic and thromboembolic etiology and without assessing hemodynamic insufficiency. Therefore, the negative results reflect the study’s design rather than just the efficacy of bypass surgery.

Advances in neuroradiology since the EC-IC Bypass Trial have enabled the assessment of cerebral hemodynamics and chronic ischemia. Xenon-enhanced CT is one method of measuring cerebral blood flow before and after the administration of acetazolamide, inhaled CO\textsubscript{2}, or breath-holding\textsuperscript{24}. Acetazolamide (Diamox\textsuperscript{®}) inhibits carbonic anhydrase, thereby increasing CO\textsubscript{2} in the blood. Hypercapnia vasodilates cerebral arteries and increases cerebral blood flow. Patients with hemodynamic insufficiency have arteries that are maximally vasodilated, dysautoregulated, and cannot respond to increases in CO\textsubscript{2}. Therefore, dysautoregulated arteries cannot compete with normal arteries during acetazolamide challenge, and Xe-CT demonstrates a “steal” phenomenon: minimal increases or paradoxical decreases in cerebral blood flow in ischemic brain due to diversion of blood flow to normal brain.

Positron emission tomography (PET) measurement of oxygen extraction fraction (OEF) is another method of assessing cerebral hemodynamics and chronic ischemia\textsuperscript{24,25}. When arteries maximally vasodilate in response to inadequate blood flow, cells respond by extracting more oxygen from circulating blood. According to the St. Louis Carotid Occlusion study, patients with ischemic territories and increased OEF had a 2-year stroke risk of 26.5%, compared to 5.3% in patients with normal OEF. Furthermore, OEF normalizes after EC-IC bypass surgery\textsuperscript{26,27}.

However, if measurements of hemodynamic insufficiency are necessary, then they should be simple, quick, and easily obtainable. PET is cumbersome (limited facilities produce the radiotracers and conduct PET/OEF testing) and costly (an estimate $20,000 per quality-adjusted life-year\textsuperscript{22}). Even Xe-CT measurements with acetazolamide challenge are cumbersome because xenon is not readily available. Perfusion CT (PCT) or perfusion MR imaging may be alternative techniques that are simple, quick, and accessible. PCT has been used to select patients presenting with acute ischemic stroke because it provides physiological information about the ischemic penumbra\textsuperscript{28,29}. PCT imaging uses a bolus injection of iodinated contrast and spiral CT imaging during the passage of the contrast bolus through the brain. Perfusion maps show parameters including: time to peak (TTP, the time between the first arrival of contrast intracranially and its peak concentration), mean transit time (MTT, the average time for blood to travel through a volume of brain), cerebral blood flow (CBF), and cerebral blood volume (CBV). In acute stroke, ischemic penumbra has increased TTP and MTT, relatively normal CBV due to vasodilation and recruitment of collateral flow, and decreased CBF. In contrast, infarcted brain has increased TTP and MTT, but CBV and CBF are both decreased. The identification of ischemic but salvageable penumbra may encourage stroke intervention, regardless of time from stroke symptoms, and studies of this approach are underway.

PCT may be similarly useful in selecting patients for bypass surgery. In a study that compared PET and PCT results in our COSS patients, we found agreement between MTT on PCT and OEF on PET\textsuperscript{29}. Surprisingly, increased OEF correlated with increased MTT better than with decreased CBF. The value of MTT was also observed in our head trauma patients, where increased MTT correlated with decreased brain tissue oxygen tension measured with parenchymal oxygen probes.

Therefore, summarizing all the above, our current algorithm for surgical selection identifies patients with symptomatic lesions, no significant infarction in the involved vascular territories, and poor collateral circulation on angiography. PCT imaging then identifies hemodynamic insufficiency as increased MTT, near normal CBV, and decreased CBF. This algorithm might be a practical alternative to PET and Xe-CT studies (Fig. 4).

**Current status of scientific evidence**

Our bypass experience demonstrates that bypass surgery has a role in the management of some ischemic diseases, but the published scientific evidence is confusing and some times contradictory. A systematic review of the literature published in 2009 showed that patients with severe hemodynamic insufficiency, as measured by vascular reactivity to CO\textsubscript{2} (stage I hemodynamic failure) or by PET/OEF (stage II hemodynamic failure), are at increased risk of stroke than those with mild disease. In addition, this review showed that patients with severe hemodynamic insufficiency respond better to surgery than those with mild disease. Bypass surgery in patients with severe hemodynamic insufficiency
stage I (no reactivity to CO2 or steal phenomenon) had a 54% reduction in stroke risk relative to the natural history. In those with hemodynamic failure stage II (decreased OEF), the authors conclude that bypass must be beneficial since no strokes were reported after surgery during a mean follow-up period of 18 months.

The Japanese EC-IC Bypass Trial (JET) used vasoreactivity to acetazolamide challenge as a criterion for eligibility. Patients with symptomatic ICA or MCA occlusion or high-grade stenosis (>70%) with small or no brain infarct were randomized to bypass surgery or medical treatment. Eligible patients had diminished regional cerebral blood flow in the ipsilateral MCA territory (<80% of the control value) and diminished acetazolamide reactivity (<10%). Preliminary results in 206 patients showed a statistical significant decrease in stroke rate in the surgical group at 2 years, indicating that bypass surgery benefits patients with hemodynamic insufficiency and that discriminating patient selection is necessary. However, these promising results were reported in the interim analysis of the study, and the final results have never been published, for unknown reasons.

The Carotid Occlusion Surgery Study (CoSS) used PET and OEF to identify patients with hemodynamic insufficiency and examine the protective effect of bypass surgery. This prospective, randomized, multi-center trial was stopped when interim analysis failed to demonstrate a difference between surgical and medical groups. CoSS was a well-designed study and its results are impossible to ignore. on the one hand, high rates of graft patency (98% at 30 days and 96% at 2 years) demonstrate that bypass surgeons are highly proficient and achieved excellent technical results. in addition, bypass improved OEF from 1.25 to 1.10, indicating a significant increase in perfusion to ischemic brain. on the other hand, 19 surgical patients experienced ischemic strokes, 14 in the perioperative period and 5 in the follow-up period (21% ischemic stroke rate overall). The 23% ischemic stroke rate in the non-surgical group was not statistically different from the surgical group and much better than expected. These more favorable outcomes were attributed to increased use of statins. However, some data from this study has already evoked some criticism. for example, reported perioperative stroke rate of the participating surgeons was 7.5% before CoSS vs the 15% reported during the trial. This doubling of the stroke rate deserves further scrutiny. Furthermore, a morbidity-mortality rate no higher than 8% would mean a benefit with revascularization, which makes this change in perioperative stroke rate an important issue. The difficulties associated with PET imaging may have affected CoSS enrollment. Patients may have been excluded from the trial because of the impossibility of moving them out of the intensive care or out of the hospital to the PET facility. it’s possible that these patients might have benefited from bypass surgery, but were excluded from the trial.

All these studies paint a confusing and contradictory picture of bypass surgery for stroke. They demonstrate that revascularization is safe, with less than 5% risk of operative morbidity and mortality, and greater than 95% bypass patency. They also demonstrate that a high degree of selectivity is necessary to achieve beneficial results with bypass surgery. Evidence proving a benefit from bypass surgery may be lacking, but it is clear that untreated patients with severe hemodynamic insufficiency fare poorly. Furthermore, COSS results have not been published yet and conclusions should not be made until additional long-term results are analyzed.
Conclusions

Bypass surgery for the prevention of ischemic stroke is controversial. Safe and elegant techniques have been developed and refined to augment cerebral blood flow, but efficacy data have been contradictory. Patients with athero-occlusive disease, symptomatic ischemia, and hemodynamic insufficiency have significant risk of stroke if managed medically or left untreated. However, surgical intervention lacks of supporting evidence from COSS, which will have profound clinical and reimbursement ramifications. Patients will be caught in a difficult position between a dismal natural history and an unproven surgical intervention. Clinicians must individualize their management until additional data are published or further consensus develops.

REFERENCES
