Extracranial-Intracranial Arterial Bypass for Treatment of Occlusion of the Internal Carotid Artery

Robert L. Grubb, Jr, MD

Address
Department of Neurological Surgery, Washington University School of Medicine, Campus Box 8057, 660 South Euclid Avenue, St. Louis, MO 63110-1093, USA.
E-mail: grubbr@nsurg.wustl.edu

Current Neurology and Neuroscience Reports 2004, **4:**23–30
Current Science Inc. ISSN 1528–4042

Extracranial-intracranial arterial bypass was frequently utilized in the 1970s and early 1980s to treat patients with atherosclerotic occlusive carotid arterial lesions not amenable to extracranial arterial revascularization procedures. After a large randomized trial reported in 1985 that there was no benefit of surgery in these patients, the procedure was generally abandoned as a treatment for symptomatic atherosclerotic cerebrovascular disease. In the past two decades, multiple studies have shown that patients with impaired cerebral hemodynamics distal to an occlusive cerebrovascular lesion have a significantly increased risk of subsequent stroke. Two new randomized, controlled clinical trials of extracranial-intracranial arterial bypass in patients with symptomatic atherosclerotic occlusive cerebrovascular disease that are using cerebral hemodynamic criteria for patient selection are currently in progress. At the present time, extracranial-intracranial arterial bypass should not be performed on these patients outside of a clinical trial.

Introduction

A significant number of atherosclerotic lesions responsible for brain ischemia involve arteries or arteries at sites inaccessible to extracranial surgical approaches [1–3]. Although many of these atherosclerotic lesions are hemodynamically insignificant and produce ischemic symptoms due to embolization from diseased intima, others can obstruct blood flow to the brain. The development of sophisticated microvascular surgical techniques led to the development of extracranial-intracranial (EC/IC) arterial bypass procedures, which have been applied to patients in an attempt to prevent stroke by improving the hemodynamic status of the circulation distal to a diseased vessel. Approximately 730,000 initial or recurrent strokes occur each year in the United States. Complete carotid artery occlusion is found in 10% to 15% of patients presenting with carotid artery territory stroke or transient ischemic attack (TIA) [4,5]. This results in an estimated 61,000 first-ever strokes and 19,000 TIAs annually in the United States that are associated with complete carotid artery occlusion. In 12 prospective follow-up studies (mean duration of 45.5 months) of angiographically documented symptomatic carotid artery occlusion in 1261 patients, investigators found an overall annual risk of subsequent stroke of 7% and an annual risk of stroke ipsilateral to the occluded carotid artery of 5.9% [6]. These risks persist even with the use of platelet-inhibitory drugs and anticoagulant therapies.

Extracranial-Intracranial Bypass Techniques

In 1951, Fisher [7] proposed an EC/IC arterial bypass to increase brain blood flow in patients with symptoms caused by complete carotid artery occlusion. Jacobsen and Suarez [8] in 1960 described microsurgical techniques that allowed the anastomosis of blood vessels 2 mm in diameter. In 1963, Woringer and Kunlin [9] sutured a saphenous vein graft from the cervical internal carotid artery (ICA) to the intracranial ICA. Donaghy [10] and Yasargil [11] performed a series of anastomoses between the superficial temporal artery (STA) and the middle cerebral artery (MCA) in dogs in the microsurgical laboratory at the University of Vermont in 1965. The first successful STA-MCA bypass procedures in patients were performed independently by Yasargil [12] in Zürich, Switzerland on October 30, 1967 and by Donaghy in Burlington, VT on October 31, 1967 [10].

Following the initial development of this procedure, various types of EC/IC arterial anastomoses have been performed for atherosclerotic carotid artery disease. These include direct anastomosis of a branch of the external carotid artery (ECA) to a branch of the ICA circulation intracranially, placement of an interposition vein or arterial graft between the extracranial and intracranial carotid artery circulation, and an indirect anastomosis between ECA branches and the pial circulation of the brain surface. Indirect anastomoses between ECA branches and the brain circulation occur from the gradual development of microvascular collateral chan-

nels between a vascularized tissue (usually muscle or omentum) surgically placed on the surface of the brain, and the pial circulation. These indirect procedures are rarely used to treat brain ischemia due to atherosclerotic occlusive disease. They are mainly used to treat progressive ischemia due to moyamoya disease.

Extracranial-Intracranial Arterial Bypass of the Internal Carotid Artery Circulation

The most frequent EC/IC arterial bypass procedure used in the treatment of cerebral ischemia due to atherosclerotic carotid artery occlusive disease has been the STA-MCA cortical branch anastomosis. The operation is performed by anastomosis of the frontal or parietal branch of the STA to distal (M3) branch of the MCA exiting the posterior Sylvian fissure [12–14]. Because of the relatively small size of the anastomoses with this procedure, EC/IC arterial bypasses using the STA as a donor vessel can usually be carried out with no more than 30 to 45 minutes occlusion of the donor and recipient arteries, obviating the need for systemic anticoagulation.

When the STA is not an adequate donor vessel, an interposition graft, using the saphenous vein, radial artery, or a synthetic vascular substitute (such as Gore-Tex [W.L. Gore, Newark, DE]) can be performed, usually between the external or common carotid artery (CCA) and a large, proximal (M2) branch of the MCA or the intracranial ICA [18]. These high-flow bypasses routinely deliver a flow of 75 to 175 mL/min. These procedures are technically more difficult and have a higher rate of complications compared with an STA-MCA cortical branch anastomosis. Long saphenous vein grafts have a lower long-term patency rate compared with the STA-MCA cortical branch anastomosis. The Mayo Clinic reported patency rates of 86% at 1 year, 82% at 5 years, and 73% at 13 years for long saphenous vein bypass grafts to the carotid and vertebrobasilar circulations [15].

Major postoperative complications can occur with EC/IC arterial bypass procedures [16,17]. These are most often ischemic or hemorrhagic cerebral events. Ischemic events may be embolic, secondary to graft occlusion, or hemodynamic in origin [16]. Hemorrhagic complications can occur secondarily to intraparenchymal hemorrhage caused by a sudden, large increase of blood flow to an area of chronic brain ischemia or from poor suturing techniques causing leakage from an anastomosis [18]. Intraparenchymal hemorrhages are more common with EC/IC bypass procedures with a large volume of flow.

The Extracranial-Intracranial Arterial Bypass Trial

In the 1970s and early 1980s, EC/IC arterial anastomosis was widely performed for atherosclerotic occlusive disease. An international, multicenter randomized trial conducted between 1977 and 1985 tested the ability of the operation to reduce the rate of subsequent stroke among patients with symptomatic atherosclerotic lesions of the ICA or MCA [19]. Patients who had experienced TIAs or minor strokes in the carotid artery distribution within the previous 120 days were eligible for the study. The patients were divided into groups based on the radiologic site of the lesion: occlusion of the ICA, intracranial stenosis of the ICA, occlusion of the M1 segment of the MCA, and stenosis of the M1 segment of the MCA. There were 1377 patients entered into the trial, with 714 patients assigned to best medical care (aspirin) and 663 assigned to best medical care with the addition of a STA-MCA cortical branch anastomosis. The largest subgroup of patients in this trial had complete occlusion of the ICA. The patients were followed for an average of 55.8 months. The 30-day perioperative morbidity and mortality rate was 12.2%. There was a major stroke rate of 4.5% and a mortality rate of 1.1%. However, there was an average delay from randomization to surgery of 9 days, and one third of the perioperative morbidity and mortality occurred in patients prior to surgery. There was a major stroke rate of 2.5% and a mortality rate of 0.6% during surgery and in the subsequent 30 days. The postoperative bypass patency rate was 96%. The study showed no benefit of surgery. Separate analyses in patients with different angiographic lesions did not identify a subgroup with any benefit from surgery. Based on the results of this trial, EC/IC arterial bypass was generally abandoned as a treatment for symptomatic atherosclerotic cerebrovascular disease.

During the time that this study was being conducted, an additional 2572 patients had an EC/IC bypass performed outside of the study. This led to the suggestion that patients who had surgery outside of the trial were ones who naturally would have done better with the procedure. However, 52 centers in the trial that did not operate on patients outside of the study had their results analyzed separately. These patients, who represented 87% of the subjects enrolled in the study, also had no benefit from the surgical procedure [20,21]. The EC/IC bypass trial was also criticized for failing to identify and separately analyze the subgroup of patients with reduction in cerebral perfusion pressure (CPP) in whom surgical revascularization might be more beneficial [22–24]. At the time the trial was conducted, there was no reliable and proven method for identifying a subgroup of patients in whom cerebral hemodynamic factors were of primary pathophysiologic importance. In addition, STA-MCA bypass was criticized for not providing adequate augmentation of blood flow to restore cerebral hemodynamics to normal. This led to the development of other surgical revascularization strategies. The relative importance of hemodynamic and embolic factors in these patients remains unclear [25,26]. These patients may suffer stroke from hemodynamic insufficiency distal to the carotid occlusion or from emboli arising from multiple sources. Because EC/IC arterial bypass is unlikely to provide protection from embolic stroke, its efficacy in preventing stroke should be greatest in those patients in whom hemodynamic factors are important in the pathogenesis of cerebral infarction.

Assessment of Cerebral Hemodynamics

The hemodynamic status of the human circulation can be indirectly assessed in vivo with a variety of different imaging techniques. These methods are not interchangeable as they rely on different physiologic mechanisms to infer the presence of hemodynamic compromise. Measurements of cerebral blood flow (CBF) alone are inadequate for this purpose because they cannot distinguish reduced CBF caused by the hemodynamic effects of arterial occlusive disease from compensatory physiological reductions in CBF caused by the reduced metabolic demands of damaged tissue. Thus, it is necessary to rely on indirect assessments based upon the compensatory responses made by the brain to progressive reductions in cerebral perfusion pressure. When CPP is normal (Stage 0 hemodynamic impairment), CBF is closely matched to the resting metabolic rate of the tissue. As a consequence of this resting balance between flow and metabolism, the oxygen extraction fraction (OEF) of the brain shows little regional variation. Moderate reductions in CPP have little effect on CBF. Vasodilation of arterioles reduces cerebrovascular resistance, thus maintaining a constant CBF (Stage 1 hemodynamic impairment). This phenomenon is known as cerebrovascular autoregulation. As a consequence of arteriolar vasodilation, the intravascular cerebral blood volume (CBV) is often elevated, although this has been an inconsistent finding. With more severe reductions in CPP, the capacity for compensatory vasodilation is exceeded and autoregulation fails. CBF begins to decline, but a progressive increase in OEF now maintains cerebral oxygen metabolism and brain function (Stage II hemodynamic impairment) [27,28]. This more severe form of cerebral hemodynamic failure has also been termed "misery perfusion" [29].

Two basic approaches have been used to assess regional cerebral hemodynamics in humans. The first approach is based on detecting Stage I autoregulatory vasodilation by either measuring CBF and CBV or by determining if there is reduced responsiveness of CBF to a vasodilatory stimulus. A variety of vasodilatory stimuli have been used, including hypercapnia, acetazolamide, and physiologic tasks such as hand movement [25,28]. Normally, each of these vasodilatory stimuli will produce a robust increase in CBF. Failure of this augmentation is interpreted as evidence of pre-existing autoregulatory vasodilation (Stage I hemodynamic failure). The second approach is based on detecting increases in regional OEF (Stage II hemodynamic failure) [25,28,30,31]. In comparison with the use of vasodilatory stimuli or CBV measurements, interpretation of increased OEF does not require any inferences about hemodynamic status because it is the direct measurement of a pathophysiologic response. Measurement of OEF currently is only possible with positron emission tomography (PET). The correlation between the CBF response to vasodilatory agents and increased OEF has been somewhat variable and inconsistent [26]. It is not possible at this time to identify a non-PET method for assessing OEF that has sufficient proven sensitivity and specificity for a substitute method.

Cerebral Hemodynamics and Stroke Risk

Multiple methodologies have been used to assess the impact of cerebral hemodynamics on the pathogenesis and treatment of stroke (Table 1). In many of these reports, follow-up information about patients studied with these techniques has been limited and not sufficient to make definitive conclusions. Stage I hemodynamic compromise was found to have an increased stroke risk in seven studies, and three studies did not find an association. Yonas *et al.* [24] tested cerebrovascular reserve in 41 patients with ICA occlusion by paired CBF measurements obtained with the stable xenon/computed tomography (CT) scanning method, with the cerebral vasodilatory agent acetazolamide given intravenously 20 minutes prior to the second study. The patients were retrospectively determined to have normal or impaired cerebral hemodynamics (based on the vascular territory found to have the lowest cerebral vasoreactivity) and a relatively low baseline CBF. During a mean follow-up of 24 months, there were no ipsilateral strokes in the 25 patients with ICA occlusion with normal cerebral hemodynamics, whereas five of 16 patients with ICA occlusion and impaired cerebral hemodynamics suffered a subsequent ipsilateral stroke (31% stroke risk). These authors subsequently classified these patients and 23 additional patients into two groups based on a paradoxical response to acetazolamide [32]. They were followed for a mean of 19.6 months. In the second group (with the more severe impairment of cerebral vasoreactivity), eight of 38 patients with occlusion of the ICA had a subsequent ipsilateral stroke (21% stroke risk). Another longitudinal study tested the cerebrovascular reserve capacity in 85 patients with ICA occlusion using transcranial Doppler sonography [33]. Forty-six patients were asymptomatic. MCA blood flow velocity and end-tidal P_{CO_2} were monitored during steady states of normocapnia, hypercapnia induced by breathing 5% CO_2 in 95% O_2, and hypocapnia produced by voluntary hyperventilation. The patients were prospectively classified into three groups based on the results of the CO_2 reactivity studies and followed for a mean of 38 months. In the group with normal CO_2 reactivity, there were no strokes. Three of 26 patients with moderate impairment of CO_2 reactivity had an ipsilateral stroke (12%) and two patients had a contralateral stroke. In the group with more severe impairment of CO_2 reactivity, five of 11 patients (45%) had an ipsilateral stroke and two patients had a contralateral hemisphere stroke. There was no significant relationship between patients with and without a history of neurologic symptoms at the time the ICA occlusion was discovered. This is puzzling because the prognosis of asymptomatic carotid occlusion is relatively benign [34]. These same authors later reported 86 patients with carotid artery occlusion who were followed for variable periods of time (Table 1) [35].

Vernieri *et al.* [36] followed 65 patients with occlusion of the carotid artery prospectively for a median follow-up of 24 months. Forty-two patients were symptomatic (22 with stroke and 20 with TIA) and 23 patients were asymptomatic. Cerebral hemodynamics were studied with transcranial Doppler

Table 1. Cerebral hemodynamics and stroke risk

Study	Design	Patients, *n*	Follow-up, *mo*	Technique	Patients with cerebral vasoreactivity, *n* (ipsilateral annual stroke risk, %)		
					Normal impairment	Moderate impairment	Severe impairment
Powers *et al.* [42] / 1989	Retrospective	30	12	PET CBV/CBF and OEF	9 (11)	21 (0)	
Hasegawa *et al.* [43] / 1992	Prospective	51	18.5	SPECT CBF Acetazolamide	31 (0)	20 (0)	
Kleiser and Widder [33] / 1992	Prospective	85*	38	Transcranial Doppler CO_2 reactivity	48 (0)	26 (7)	11 (24)
Widder *et al.* [35] / 1994	Prospective	86*(111†)	19	Transcranial Doppler CO_2 reactivity	48† (1)	37† (1)	26† (8)
			31.7				
Yonas *et al.* [24] / 1993	Retrospective	41*	24	Xenon-CT CBF Acetazolamide	25 (0)	16 (16)	
Webster *et al.* [32] / 1995	Retrospective	64*	19.6	Xenon-CT CBF Acetazolamide	26 (0)	38 (13)	
Yokota *et al.* [40] / 1998	Prospective	105	32.5	SPECT CBF Acetazolamide	50 (4)	55 (4)	
Vernieri *et al.* [36] / 1999	Prospective	42*	24	Transcranial Doppler Breath-holding index	9 (0)	33 (12)	
Kuroda *et al.* [38] / 2001	Prospective	77	18.4	SPECT CBF Acetazolamide	39 (0.6)	27 (2)	11 (23.7)
			43.9				
			48.7				
Ogasawara *et al.* [39] / 2002	Prospective	70	24	SPECT CBF Acetazolamide	47 (1)	23 (17)	
Yamauchi *et al.* [44] / 1996	Prospective	40	12	PET OEF	33 (6)		7 (57)
Yamauchi *et al.* [45] / 1999	Prospective	40	60	PET OEF	33 (3)		7 (11)
Grubb *et al.* [46] / 1998	Prospective	81*	31.5	PET OEF	42 (3)		39 (13)

*Only internal carotid artery occlusion patients.
†Number of cerebral hemispheres.
CBF—cerebral blood flow; CBV—cerebral blood volume; CT—computed tomography; OEF—oxygen extraction fraction; PET—positron emission tomography; SPECT—single photon emission computed tomography.

ultrasonography and cerebrovascular reactivity to apnea was calculated with the breath-holding index (BHI) in the MCAs. During the follow-up period, eight of the 33 symptomatic patients with an abnormal BHI had a stroke ipsilateral to the occluded carotid artery (12.2% annual ipsilateral stroke risk). None of the symptomatic patients with a normal BHI had a subsequent ipsilateral stroke. Only one of the 23 asymptomatic patients had a subsequent ipsilateral stroke. Another prospective study examined 48 patients who had ICA occlusion with bilateral transcranial Doppler ultrasonography of the MCAs [37]. Cerebrovascular reactivity was tested by having the patients breathe 8% CO_2. During the follow-up period (mean, 1.71 years), there were five ipsilateral strokes. The authors concluded that impaired reactivity to 8% CO_2 was a significant predictor of ipsilateral stroke. Kuroda *et al*. [38] prospectively followed 77 patients with symptomatic occlusion of the ICA or MCA for an average follow-up period of 42.7 months. Cerebrovascular reserve capacity was tested by using xenon-133 single photon emission computed tomography (SPECT) to make paired regional CBF measurements with acetazolamide given intravenously 15 minutes prior to the second study. The annual risk of total and ipsilateral stroke was 35.6% and 23.7%, respectively, in patients with severe cerebral hemodynamic impairment, 3.85% and 2%, respectively, in patients with moderate cerebral hemodynamic impairment, and 3.8% and 0.6%, respectively, in patients with normal cerebral hemodynamics. Ogasawara *et al*. [39] prospectively followed 70 patients with symptomatic occlusion of the ICA or MCA for 24 months or until a recurrent stroke or death occurred. Regional cerebrovascular reactivity to acetazolamide was calculated with xenon-133 SPECT. Recurrent ipsilateral strokes occurred in eight of the 23 patients (17.4% annual risk), with reduced regional cerebrovascular reactivity distal to an occluded ICA or MCA and in three of 47 patients (1.2% annual risk) with normal regional cerebrovascular reactivity.

The largest and most methodologically sound study that did not demonstrate a relationship between Stage I impairment of cerebral hemodynamics and the risk of subsequent stroke was a prospective study reported by Yokota *et al*. [40]. One hundred and five symptomatic patients with unilateral occlusion or severe stenosis of the ICA or proximal MCA confirmed by cerebral angiography were entered into the study. Each patient had a qualitative SPECT study of cerebral perfusion using N-isopropyl-P-[iodine-123]-iodoamphetamine (IMP) and measurement of cerebrovascular reactivity using acetazolamide. Fifty-five patients had an abnormal cerebral vasoreactivity response to acetazolamide and 50 patients had a normal response. During the follow-up period (mean, 32.5 months), 13 patients had a stroke, 11 died, 16 had surgical cerebral revascularization procedures (nine EC/IC bypasses and seven carotid endarterectomies), and 11 were lost to follow-up. There was no significant difference in the rate of subsequent stroke in the two groups. However, Ogasawara *et al*. [41] measured cerebrovascular reactivity to acetazolamide in the MCA territory in 70 patients with symptomatic ICA or MCA occlusion, using two different methodologies in all of the patients. CBF percent change was obtained quantitatively with xenon-133 SPECT, and an asymmetry index (AI) percent change was obtained qualitatively with iodine-123–IMP SPECT. The patients were divided into two groups within each SPECT methodology (normal or decreased CBF percent change and normal or decreased AI percent change) and were followed for up to 5 years. Cumulative stroke recurrence-free survival rates for patients with decreased CBF percent change were significantly lower compared with those with a normal CBF percent change. There was no significant difference in cumulative stroke recurrence-free survival rates between patients with decreased AI percent change and those with normal AI percent change. These findings indicate that these two SPECT methodologies do not always identify the same patients as having hemodynamic compromise.

A small longitudinal, retrospective study using PET measurements of the CBV/CBF ratio and OEF followed 30 medically treated patients with carotid artery occlusion or intracranial arterial stenoses for 1 year [42]. In 21 patients with increased CBV/CBF ratios distal to a stenotic or occluded artery, no ipsilateral ischemic strokes occurred. One of nine patients with normal cerebral hemodynamics had an ipsilateral ischemic stroke. Another small prospective study followed 51 patients with asymptomatic and symptomatic carotid artery and intracranial artery stenoses and occlusions for 1.5 years [43]. Each patient had a SPECT study of cerebral perfusion using iodine-123–IMP and measurement of cerebrovascular reactivity using acetazolamide. Twenty patients had impaired cerebrovascular reactivity. No patient had a stroke during the follow-up period.

A positive association of Stage II cerebral hemodynamic compromise and stroke risk has been found by two groups. In these studies, the finding of increased OEF increased the subsequent risk for ipsilateral stroke. A small longitudinal study performed PET measurements of regional rCBF, rCBV, rOEF, and $rCMRO_2$ in 40 patients with symptomatic occlusion or intracranial stenosis of the ICA or MCA treated medically [44]. Patients had either normal or increased OEF based on the absolute mean hemispheric value of OEF in the symptomatic cerebral hemisphere. At 1 year following the PET studies, five of seven patients with increased OEF had developed a stroke (four ipsilateral) and four of 33 patients with normal OEF had developed a stroke (two ipsilateral). In a subsequent study by these authors, a 5-year follow-up of these 40 patients was reported [45].

The strongest evidence of an association of cerebral hemodynamic impairment and stroke was seen in the St. Louis Carotid Occlusion Study [46]. This was a blinded, prospective study to test the hypothesis that increased OEF in the cerebral hemisphere distal to complete carotid artery occlusion was an independent predictor of the subsequent risk of stroke in symptomatic medically treated patients. PET measurements of rCBF, rCBV, $rCMRO_2$, and OEF were carried out. Patients with left/right OEF ratios outside the normal range

were categorized as having Stage II hemodynamic compromise in the hemisphere with higher OEF. Eighty-one patients were followed for a mean of 31.5 months. Thirty-nine patients had Stage II hemodynamic failure (increased OEF) in the hemisphere ipsilateral to the occluded carotid artery and 42 did not. There were no subjects with bilateral carotid occlusion with increased OEF. There were no significant differences between the two groups in baseline risk factors or subsequent medical treatment. Arteriographic collateral circulation did not permit distinction between the two groups. In the 39 subjects with increased OEF, there were 12 total and 11 ipsilateral strokes (13.3% annual risk). In the 42 subjects with normal OEF, there were three total and two ipsilateral strokes (2.7% annual risk). In the multivariate analysis of multiple risk factors, only younger age and Stage II hemodynamic failure were significant predictors of both all stroke and ipsilateral ischemic stroke.

Cerebral Hemodynamics and Extracranial-Intracranial Arterial Bypass Surgery

Multiple studies with PET have demonstrated postoperative improvement of cerebral hemodynamics by STA-MCA bypass surgery [26]. Improvement in impaired cerebral vasoreactivity to CO_2 or acetazolamide and return of hemispheric OEF ratios to normal has been reported following EC/IC bypass for atherosclerotic occlusive cerebrovascular disease [26]. Although EC/IC arterial bypass has been recommended for symptomatic patients with appropriate cerebrovascular lesions in which hemodynamic impairment has been demonstrated, no results of prospective studies of patients with occlusion of the ICA and increased OEF or impaired cerebral vasoreactivity to CO_2 or acetazolamide randomized to medical treatment or EC/IC arterial bypass, with other risk factors for stroke controlled, have been reported. Thus, the long-term benefit of using impaired cerebral hemodynamics in the selection of patients for EC/IC arterial bypass to prevent stroke remains unproven at this time.

Conclusions

The results of medical treatment of Stage II patients in the St. Louis Carotid Occlusion Study [46] were poor and comparable with those reported for medically treated patients with symptomatic severe carotid stenosis [47]. Surgical procedures that improve cerebral hemodynamics, such as EC/IC arterial bypass, would seem to be a logical treatment for these patients. However, in the absence of an empiric trial, it cannot be assumed that the stroke risk in patients operated upon would be equal to that in patients with normal OEF, nor can it be assumed that the morbidity and mortality due to surgery would be outweighed by any subsequent reduction in stroke risk. The large multicenter, randomized trial of EC/IC Bypass surgery conducted from 1977 to 1985 showed no benefit of surgery in preventing subsequent stroke [19]. At the time that this trial was conducted, there was no reliable and proven method for identifying a subgroup of patients in whom cerebral hemodynamic factors were of primary pathophysiologic importance. It is now established that such a subgroup can be identified with modern neuroimaging techniques and, furthermore, that they are at high risk for subsequent stroke when treated medically. However, in the absence of an empirical trial, it cannot be assumed that surgery would be of benefit in this subgroup of patients. The morbidity and mortality due to surgery and the long-term stroke risk in patients who were operated upon are not known at this time. For these reasons, EC/IC arterial bypass surgery should not be performed on those patients outside of a clinical trial at the present time.

Two new randomized, controlled clinical trials of EC/IC arterial bypass in patients with symptomatic atherosclerotic occlusive cerebrovascular disease that use hemodynamic criteria for patient selection are currently in progress. The Japanese EC/IC Bypass Trial [48••] has completed enrollment and final results are expected in 2004. This study enrolled patients with TIA or minor stroke occurring within 3 months of study entry who had unilateral or bilateral ICA or MCA occlusion or severe stenosis due to atherosclerotic disease and evidence of hemodynamic impairment distal to the vascular lesion. Cerebral hemodynamics were measured by baseline CBF and CBF changes after acetazolamide administration, primarily with the use of iodine-123–IMP SPECT. The Carotid Occlusion Surgery Study (COSS) [49,50••] is currently enrolling subjects at 28 sites in the United States. Patients with unilateral internal carotid artery occlusion who have had ipsilateral hemispheric symptoms for 120 days are eligible to undergo PET measurements of OEF to determine if they qualify. The trial covers the costs of PET and surgery. Further information regarding COSS can be obtained online at http://dmchost.public-health.uiowa.edu/coss/.

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