

NEUROSCIENCES AND NEUROANAESTHESIA

Carotid artery disease: stenting vs endarterectomy

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Key points

- Carotid endarterectomy is a standard intervention for carotid artery stenosis, while angioplasty/stenting is gaining acceptance.
- General and regional anaesthetic techniques are equally effective for CEA; CAS is performed under sedation.
- It is important to optimize cerebral blood flow and minimize myocardial stress during these procedures.

Summary. Several multicentre, randomized trials have validated the efficacy of carotid endarterectomy (CEA). Comparative randomized trials are also currently developing insight into the role of carotid angioplasty and stenting (CAS), and identifying factors for optimal patient selection. Although these interventions are aimed at embolic stroke prevention, anaesthetic management might prevent the subset of strokes that are haemodynamic in nature by maintaining tight physiological control. The perioperative risk of myocardial events is increased in this population. Hence, preoperative attention to cardiovascular disease, hypertension, renal insufficiency, and diabetes mellitus might reduce neurological and cardiovascular complications. During carotid artery cross-clamping, the risk of cerebral ischaemia can be decreased by maintaining normal to high perfusion pressure. Although there is no demonstrable advantage of a specific anaesthetic technique for patients undergoing CEA, it is imperative that cerebral blood flow is optimized, that there is minimal cardiac stress, and that anaesthetic recovery is rapid. Carotid angioplasty and stenting is performed under light sedation with antithrombotic therapy and vigilance for bradycardia and hypotension. Tight haemodynamic control remains a priority in the immediate postoperative period for both interventions.

Keywords: anaesthesia; angioplasty, balloon; carotid stenosis; endarterectomy, carotid; stroke

Carotid artery atherosclerosis is a major cause of neurological morbidity and mortality. Medical, surgical, and endovascular therapies aim to reduce the risk of stroke by relieving stenosis and preventing thromboembolism. This review focuses on current data guiding patient care and anaesthetic management for carotid endarterectomy (CEA) and for carotid angioplasty and stenting (CAS).

Epidemiology

There are about 800 000 strokes and 300 000 transient ischaemic attacks (TIAs) each year in the USA and, with an estimated 144 000 deaths each year, stroke is the third leading cause of death.¹ Worldwide, stroke is the second leading cause of death after ischaemic cardiac disease, representing ~10% of all deaths per year (5.4 million deaths).² Carotid stenosis is responsible for ~20% of strokes in the adult population.³ Data from large trials and observational studies suggest that the rate of stroke associated with a significant ipsilateral carotid artery stenosis is 1–2% per year.⁴ With 6 million stroke survivors and an age-dependent prevalence of asymptomatic carotid artery disease as high as 7.5%, carotid artery disease is a significant anaesthetic issue for patients over 50 yr of age.⁵

The aetiology of stroke from vascular disease varies among ethnic groups. Ischaemic stroke in non-Hispanic whites is more commonly due to extracranial carotid artery disease or cardiogenic embolism, whereas in African Americans, intracranial thromboembolic disease is more likely. Below age 75, stroke incidence is higher in males than in females but is higher in females after age 85.¹

Pathophysiology of carotid atherosclerosis: anatomic considerations for endarterectomy

Carotid artery disease is typically the result of atherosclerosis at the bifurcation of the common carotid artery or in the origins of either the internal or the external carotid artery. Cholesterol deposits in the endothelium and underlying smooth muscle of the artery are accompanied by cellular proliferation of the surrounding fibrous and smooth muscle tissues to form atheromatous plaque (Fig. 1). Large plaque that extends into the lumen of the artery not only reduces blood flow but also presents an irregular surface prone to thrombus formation. Plaque instability and rupture create thromboembolic debris and lead to neurological injury. Plaque ulceration and thrombosis are associated with

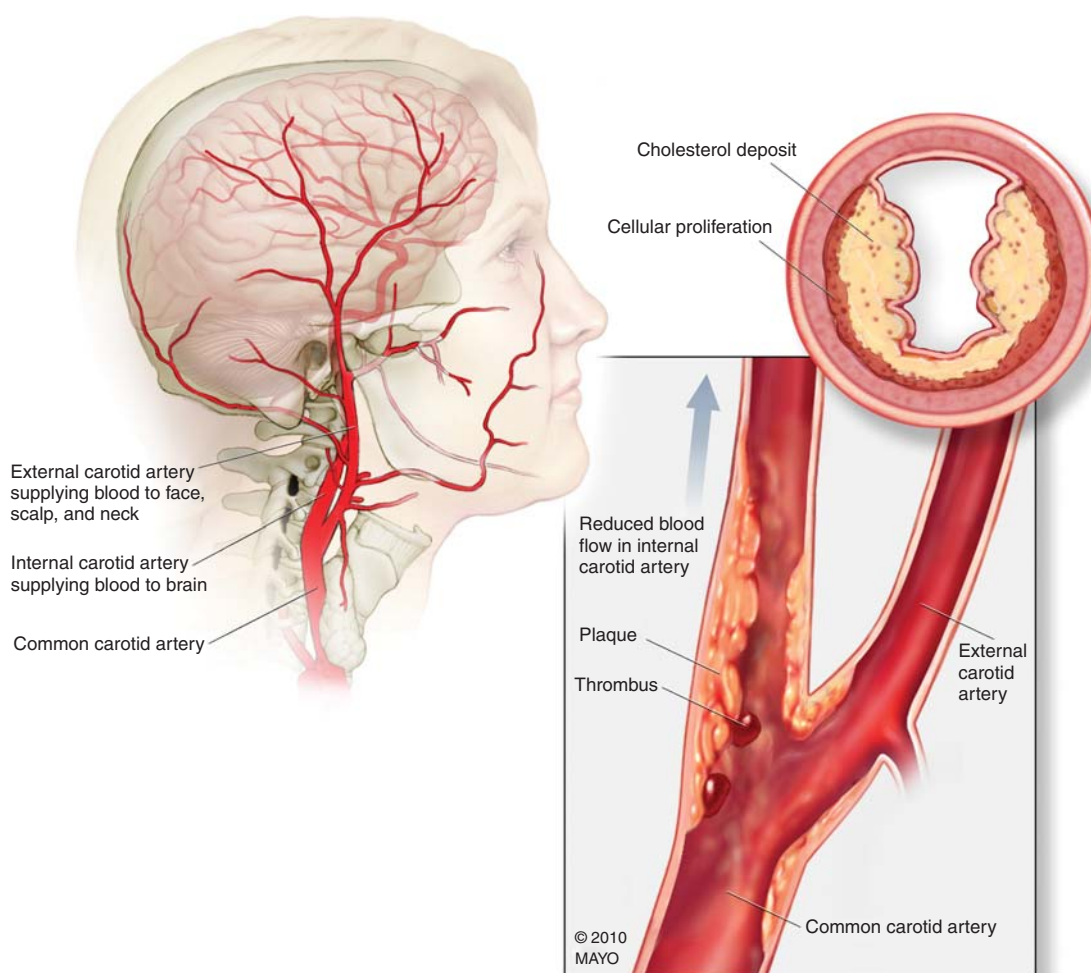


Fig 1 Carotid artery disease: atheromatous plaque at the bifurcation of the carotid artery. Plaque, a result of cholesterol deposit and cellular proliferation, reduces the arterial lumen, alters blood flow, and promotes thrombus and embolus formation.

neurological symptoms, independent of the degree of stenosis.⁶

During periods prone to ischaemia, including intra-operative arterial cross-clamping, collateral flow is critical for cerebral blood flow (CBF) compensation and a major determinant of the severity of the ischaemic insult. Other factors include plaque morphology, duration of hypoperfusion, characteristics of the embolus, and cerebral vaso-reactivity (cerebrovascular reserve, or the capacity for vasodilation). These influences determine the clinical outcome which ranges from mild (TIA, reversible ischaemic neurological deficit, and homonymous hemianopsia) to severe (completed stroke).⁷ The principal pathways of collateral flow are the Circle of Willis, extracranial anastomotic channels, and leptomeningeal communications that bridge watershed areas between major arteries.^{8, 9} Figure 2 illustrates the under-appreciated collateral circulation between internal and external carotid arteries.

Less frequently, ischaemic events are associated with hypoperfusion through the stenosed artery.¹⁰ The gradual reduction

of blood flow distal to a developing plaque produces changes in cerebral haemodynamics in three phases as blood flow is diminished.¹¹ Moreover, it is also possible to have both hypoperfusion and thromboembolic phenomena.

Diagnosis of carotid artery stenosis

Clinical examination and imaging determine the need for intervention. Major symptoms of carotid artery disease include changes in vision, headache, speech, or facial and extremity weakness. Signs suggestive of carotid artery disease include a high-pitched bruit at the origin of the internal carotid artery, an increase in size and pulsation of the ipsilateral superficial temporal artery, and changes in the retinal examination. Patients with a history of prior stroke or TIA have an increased risk of recurrent perioperative stroke. Confirmation of carotid artery disease and assessment of the degree of stenosis are achieved by vascular imaging.

The degree of stenosis of the carotid artery is determined by one of several methods. Angiography is considered highly

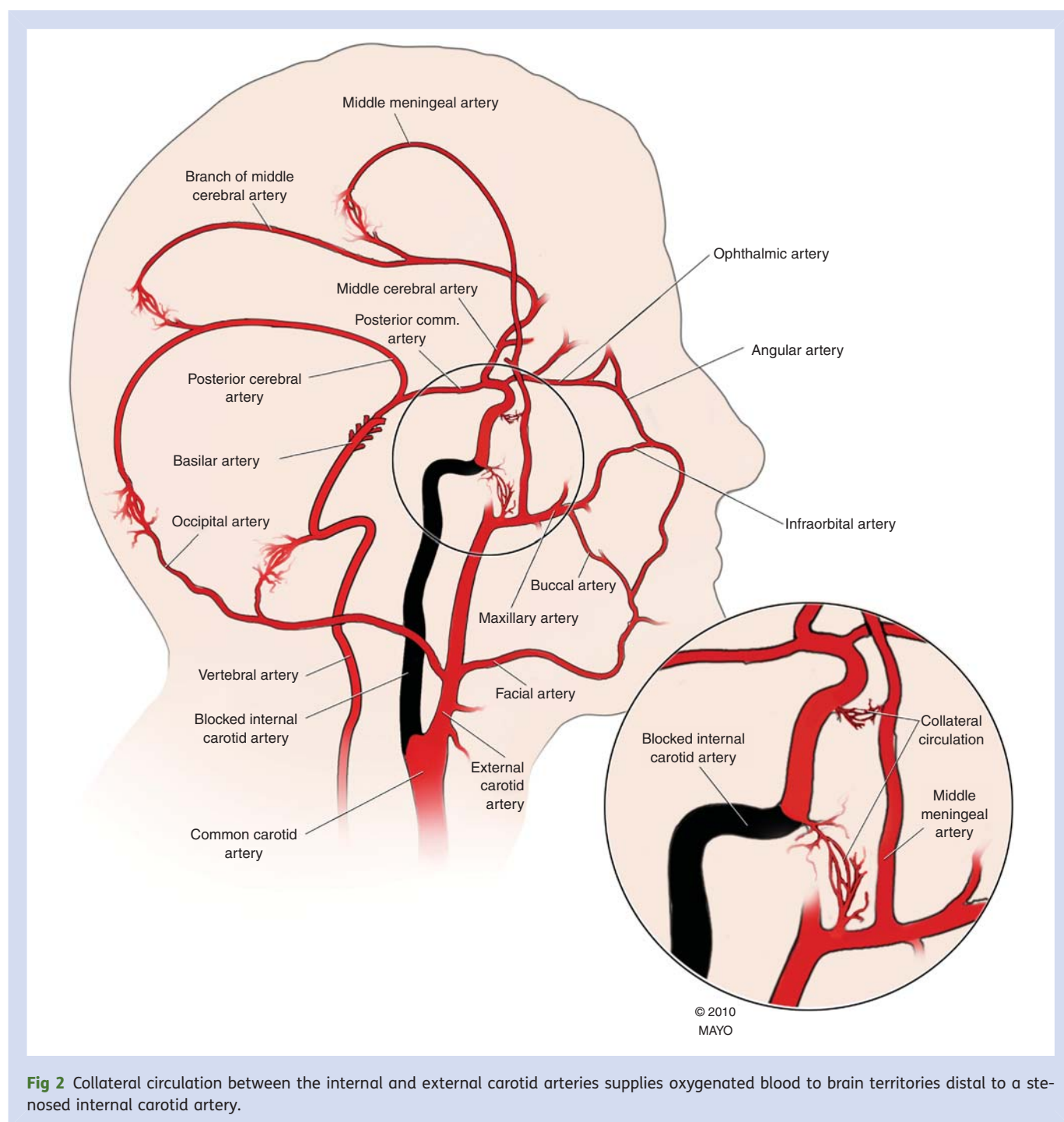


Fig 2 Collateral circulation between the internal and external carotid arteries supplies oxygenated blood to brain territories distal to a stenosed internal carotid artery.

accurate, and large trials of carotid stenosis therapy rely on angiographic measurements.^{12 13} However, most patients evaluated for carotid artery disease undergo non-invasive tests such as duplex ultrasonography, or sometimes computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). Duplex ultrasound imaging is safe, quick, and considered reliable, although accuracy can vary by users and factors that affect flow velocities, such as contralateral disease, can cause artificial elevations of velocity and alter measurements.^{14 15} The accuracy of CTA

and MRA is comparable with duplex ultrasonography and such imaging has the added ability to identify plaque morphology, which can be helpful in planning CEA or CAS.¹⁶

Medical therapy of carotid artery disease

Medical therapy to prevent stroke encompasses a combination of non-invasive therapies directed at correcting modifiable risk factors. Mainstays of medical therapy include antithrombotic, antihypertensive, dyslipidaemic,

antiarrhythmic, and diabetic agents. Current management also entails ongoing education, physician monitoring, and the support of healthy lifestyle choices including diet modification, reduction of alcohol intake, exercise prescription, and smoking cessation. The protective effect of comprehensive medical intervention alone for patients with asymptomatic carotid stenosis has not been measured, although it might equal that of endarterectomy in this population and is less costly.^{17 18}

Surgical therapy for carotid artery disease

CEA was first performed in 1954 as a treatment for occlusive carotid artery disease.¹⁹ Efficacy data on CEA were limited until the 1990s. Analysis of three trials demonstrated that endarterectomy is of greatest benefit in patients with >70% stenosis of the carotid artery and has a marginal benefit in symptomatic patients with 50–69% stenosis.^{12 13 20 21} Early surgery is associated with increased benefits compared with delayed surgery.²² Benefit from surgery was greatest in men, those ≥ 75 yr of age, and patients undergoing CEA within 2 weeks of their last ischaemic event and declined with greater delay.²³ The ACAS trial demonstrated a small benefit for CEA in addition to medical therapy for asymptomatic patients with >60% stenosis compared with medical therapy alone.²⁴ However, a recent review suggests that current medical management alone provides stroke protection in asymptomatic patients equivalent to that of CEA and medical therapy in the trials above.¹⁷ Indeed, the potential benefit of CEA in asymptomatic patients is lost if periprocedural complication rates are >2.7–3.1%.⁴ Moreover, for patients with carotid stenosis <50%, there was no significant benefit from surgery.²¹

The operation itself involves cross-clamping of the common carotid artery before arterial incision and plaque extraction. Neurological changes during cross-clamping, either in the patient (if awake) or changes in neurophysiological monitoring, might warrant placement of a temporary shunt from the common to the internal carotid artery, although criteria for selective shunt placement are not clearly defined.^{25 26} Complications of shunting include air embolus, atheroembolus, arterial dissection, malposition, and product malfunction.^{27 28}

Endovascular therapy for carotid artery disease

Endovascular carotid artery angioplasty and stenting for the prevention of stroke is still evolving as a treatment modality. It is selectively used as an alternative to CEA and is gaining in popularity, although concerns about its efficacy and appropriate target population remain.

Stenting and angioplasty involve the intra-arterial introduction of a catheter via guidewire and the deployment of a balloon, with or without stent, to expand the lumen of the carotid artery (Fig. 3). Angiography before and after CAS is shown in Figure 4. The approach was developed in the 1980s, after the earlier introduction of endovascular

therapy for the limb, renal and coronary arteries. Balloon angioplasty for carotid artery disease was rarely used before the 1990s, as outcomes were plagued by poor long-term patency of the carotid artery and by periprocedural embolization of debris causing neurological deficits.

The addition of intraluminal stents increased patency duration but outcomes were still inferior to CEA. Further technological innovations included crush-resistant nickel–titanium stents to extend long-term patency, and double balloon or emboli-protection devices for embolic stroke prevention.^{29 30} Carotid artery stenting and angioplasty are not universally advocated because of the excellent results usually achievable by CEA.^{12 13 20 24 31}

Advantages of CAS include that it is quicker and less invasive than CEA. It is almost always performed under light sedation or monitored anaesthesia care rather than general anaesthesia. Medical conditions that pose a significant risk for surgery are an indication for CAS.²² Myocardial infarction (MI), cranial nerve injury, wound infection, and venous thromboembolism are unlikely. Perioperative hypertension (HTN) is largely avoided and cervical haematoma causing airway compromise and cranial nerve injury are not concerns after CAS. Stenting and angioplasty are often performed when endarterectomy is technically difficult such as in patients with challenging cervical anatomy, restenosis after CEA or radiation in the cervical area. Lesions that are either high (above the level of the mandible) or low (below the clavicle) are more amenable to CAS than CEA.³² Carotid artery stenting and angioplasty have been used after arterial dissection and for conditions such as fibromuscular hyperplasia and Takayasu's arteritis.^{4 33} Neither women nor men have a discernibly higher rate of stroke or death from CAS.³⁴ Although advanced age was initially thought to be an indication for such a procedure, largely due to the avoidance of general anaesthesia, data to the contrary have recently been reported. Periprocedural risk of stroke and death occurred at markedly higher rates in older subjects (defined as octogenarians) in a recent meta-analysis and in two large trials: SPACE, and in the lead-in phase and final results of the Carotid Revascularization with Endarterectomy or Stent Trial (CREST).^{35–37} Costs incurred by CAS and CEA are comparable.³³

A majority of published trials acknowledge the dependence of outcomes on the experience, skill, or credentialing of the operator. According to American Heart Association guidelines for secondary prevention of stroke, 'CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4–6%, similar to that observed in trials of CEA and CAS'.²² Results from a trial that included CAS operators with limited experience showed a risk of stroke or death of 12.1%.³⁸ The lead-in phase of the recent CREST trial included comparative outcomes of physicians according to speciality training. Neuro-radiologists had the lowest event rate per 100 procedures at 1.6, whereas the next best physician group, cardiologists, had 3.9 events per 100 procedures. Event rates of the highest groups were over four-fold higher than that of the

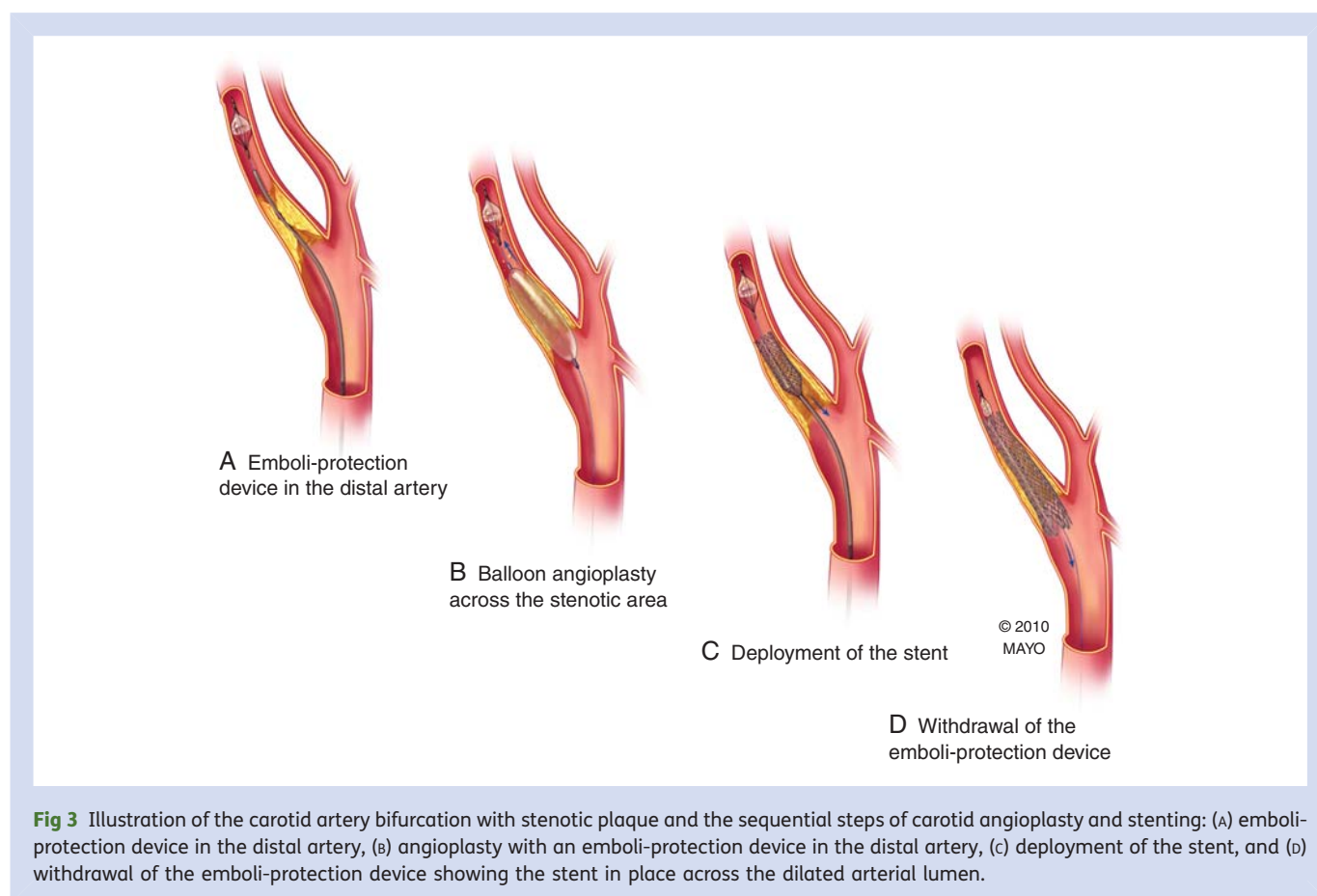


Fig 3 Illustration of the carotid artery bifurcation with stenotic plaque and the sequential steps of carotid angioplasty and stenting: (A) emboli-protection device in the distal artery, (B) angioplasty with an emboli-protection device in the distal artery, (C) deployment of the stent, and (D) withdrawal of the emboli-protection device showing the stent in place across the dilated arterial lumen.

lowest group.³⁹ Evidence appears to support the intuitive concept that expertise affects outcomes.

The primary limitation for performing CAS is unfavourable anatomy.¹⁶ Unfavourable aortic arch types, vascular anomalies such as bovine anatomy, proximal and distal tortuosity, and other specific arterial lesions can reduce success with this approach.^{40 41} The addition of CTA or MRA to the traditional Doppler ultrasonography might improve patient selection and thereby avoid the risks of angiography for patients judged to be poor candidates for CAS. More accurate imaging has also been suggested to improve the assessment of the degree of carotid stenosis (and to determine whether medical or procedural therapy is indicated), to help decide operative technique and choice of device, and to increase efficiency in the interventional suite.¹⁶ Poor candidates for CAS also include patients with incomplete collateral circulation or so-called isolated hemispheres who are intolerant of the reversal of flow. Other contraindications to CAS include intolerance to endovascular treatment such as significant contrast allergy. Endarterectomy is recommended for candidates suitable for either CAS or CEA.²²

In an effort to prevent embolic stroke, the leading procedural complication of CAS, three approaches to emboli-protection device development have been pursued. These include devices for distal occlusion, proximal occlusion, and, most commonly, distal filtration.^{32 42} The overall efficacy of

protection devices is controversial. Retrospective data from the CREST lead-in phase included some procedures done before the introduction of distal protection and presented a reduced rate of imaging lesions in patients without distal protection during CAS.⁴³ Non-randomized data from the Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial led investigators to stop unprotected CAS early due to a nearly quadrupled 30 day rate of stroke without protection.⁴⁴ Consensus opinion strongly advocated filter device-use in 2004 and asserted that randomized trials would be unethical.^{45 46} However, in a prospective randomized trial, Barbato and colleagues⁴⁷ found no reduction in ischaemic lesions when filter devices were used. This was followed by a non-randomized substudy of the large International Carotid Stenting Study (ICSS) trial that showed the rate of new ischaemic lesions in filter-protected patients to be twice the rate of unprotected patients.⁴⁸ These data also suggest that subclinical lesions detected on imaging might serve as surrogate markers for new neural deficits, including stroke, for use in future investigations.

Several recent large randomized clinical trials have compared outcomes of CAS and CEA.^{30 36 49–53} Rates of stroke and death for each are summarized in Table 1. The recently reported CREST trial demonstrated non-inferiority of CAS compared with CEA.⁵³



Fig 4 Still frames from an angiogram of the carotid bifurcation in a patient with internal carotid stenosis of 85% (A). After dilation and stent placement (B), there is 15% residual stenosis. (Courtesy of Harry J. Cloft M.D., Ph.D.).

Table 1 Rate of stroke and death after comparative trials of CEA vs carotid angioplasty and stenting. *Stroke or death at 30 days plus ipsilateral stroke or death from neurological causes within 31 days to 1 yr. **EVA-3S data are per-protocol, not intention-to-treat

Trial (yr)	Rate of stroke and death (%)		Observation period
	CEA	CAS	
CAVATAS ⁴⁹ (2001)	9.9	10.0	30 days
SAPPHIRE ³⁰ (2004)	8.4	5.5	1 yr*
CaRESS ⁵⁰ (2005)	13.6	10.0	1 yr
SPACE ³⁶ (2006)	6.3	6.8	30 days
EVA-3S ^{44**} (2006)	6.1	11.7	6 months
ICSS ⁵² (2010)	4.7	8.5	120 days
CREST ⁵³ (2010)	4.7	6.4	4 yr

One of the earliest randomized controlled trials demonstrating non-inferiority of CAS with the use of an emboli-protection device compared with CEA (SAPPHIRE) included both symptomatic (30%) and asymptomatic (70%) patients.³⁰ The total rates of death, stroke, or MI within 30 days, or death or ipsilateral stroke within a year occurred in 20 stent patients and 32 endarterectomy patients (30 day risk: 8.5% for CAS, 12.6% for CEA, $P=0.004$

for non-inferiority). Most of the risk reduction found in the stenting group was due to the lower rate of MI.³⁰ After this report, the FDA approved CAS for symptomatic carotid artery stenosis.¹⁰

Other completed randomized trials report less favourable results for CAS. The EVA-3S investigation was prematurely stopped after an unexpectedly high incidence of 30 day complications was observed after CAS.^{44 51} Likewise, the ICSS included 1713 symptomatic patients and reported a higher risk of stroke and death in its stenting group at 120 days (Table 1).⁵² Longer-term follow-up of patency has yet to be reported. Subgroup analysis suggested amaurosis fugax to be one neurological deficit for which CAS might be favoured based on the risk of stroke or death, whereas a recent stroke or TIA favoured endarterectomy as the preferred treatment.⁵² Approximately 13% of the patients also underwent magnetic resonance imaging as part of a non-randomized substudy of ICSS. New ischaemic lesions were observed more frequently in CAS patients than in those treated with CEA [odds ratio (OR), 5.21; 95% confidence interval (CI), 2.78–9.79; $P<0.0001$].⁴⁸

The CREST trial [funded by The National Institute of Neurological Diseases and Stroke (NINDS)] recently compared CEA with CAS in 2502 patients with severe stenosis, both symptomatic and asymptomatic ($\geq 70\%$ by ultrasonography or $\geq 50\%$ by NASCET angiography criteria).⁵³ The primary

Table 2 Key points of anaesthetic management of CEA vs carotid angioplasty and stenting

	Carotid endarterectomy	Carotid angioplasty/stenting
Indications	In symptomatic patients, CEA is indicated if stenosis is >70%; and for selected patients if the stenosis is 50–69%. In asymptomatic patients, the indications are controversial	In patients eligible for CEA, CAS is indicated if anatomy is unfavourable for CEA; recurrent laryngeal nerve injury on the ipsilateral side; possibly co-morbidities
Preoperative concerns	Hypertension, coronary artery disease, diabetes mellitus, renal insufficiency, active neurological process	Similar
Anaesthetic technique	No proven advantage to a single technique. However, when using a general anesthetic technique, nitrous oxide should be discontinued before shunt placement or reperfusion	Minimal sedation, heparin administration and ACT management, anti-platelet therapy, pre-emptive or rescue anticholinergic medication, external pacing available, protamine available
Cerebral monitoring	Neurological status in the awake patient and the electroencephalogram may be close to a 'gold standard'. Transcranial Doppler has the advantage of the ability to detect cerebral emboli	Neurological status (awake)
Postoperative concerns	Haemodynamic stability, myocardial ischaemia, neurological status, hyperperfusion syndrome, wound haematoma, cranial nerve dysfunction	Haemodynamic stability, neurological status, hyperperfusion syndrome, myocardial ischaemia

median follow-up period was 2.5 yr (up to 4 yr). Clinical durability was similar during this period, with rates of ipsilateral stroke of 2.0% after CAS and 2.4% after CEA. A meta-analysis of randomized trials just before CREST showed a pattern of increased periprocedural risk with CAS, but no difference in 'intermediate-term' effects vs CEA.⁵⁴ No difference was found in the composite endpoint of stroke, MI, or death. However, the 30 day stroke rate was higher after CAS (4.1% vs 2.3% for CEA), whereas MI was more frequent after CEA (2.3% vs 1.1% after CAS). A major finding was that octogenarians carry a significantly higher risk of periprocedural stroke and death (12.1%). The reason behind this is not clear as results of this trial were adjusted to account for possible confounding factors such as symptom status, the degree of carotid stenosis, the use of anti-embolic devices, gender, and the presence of distal arterial tortuosity. Unfavourable arterial anatomy and unstable plaque morphology in older patients could explain the increased risk of atheroemboli during catheter-wire manipulation.¹⁶ Furthermore, an attempt to differentiate between periprocedural stroke and MI in terms of impact on quality of life 1 yr later demonstrated that stroke was more devastating to health status than was MI.

Finally, it is helpful to recall that publication bias is naturally present regarding new procedures and industry-generated devices such as for CAS. The Wallstent trial, examining stent use in symptomatic patients, is one example. This study was stopped early for safety concerns because of excessive complications in the angioplasty and stent-placement arm. The data went unpublished, but were presented at a medical meeting.³⁸ Unpublished trial data are difficult to obtain but can temper enthusiasm in data interpretation.

The anaesthetic technique for CAS involves minimal sedation along with activated clotting time (ACT) management. Anticoagulation helps prevent thromboembolic complications. After a baseline ACT, a small heparin bolus is

administered i.v. to achieve an ACT of approximately twice normal (250–300 s). Protamine should be immediately available to treat haemorrhage, although it is not routinely used for the reversal of anticoagulation at the end of the case. Often an oral anti-platelet drug (ticlopidine, clopidogrel, or abciximab) is also given. In patients with heparin-induced thrombocytopenia, direct thrombin inhibitors can be used.⁵⁵ The key points when managing a patient for CAS are summarized in Table 2.

Distension of the carotid artery and stimulation of the baroreceptor often causes significant bradycardia and hypotension. Cerebral hyperperfusion can also develop. Pre-emptive or rescue anticholinergic medication (atropine or glycopyrrolate) typically prevents this complication, although external pacing should be available. Vigilance for signs of thromboembolism, dissection, transient ischaemic episode, and stroke must be maintained and appropriate supportive care administered.

Preoperative evaluation of the patient with carotid artery disease

The incidence of medical complications is about 10% after CEA and less after CAS. Complications are associated with coexisting HTN, coronary artery disease, diabetes mellitus, and renal insufficiency. Preoperative evaluation should focus on identifying these conditions and optimizing modifiable risk factors when possible.

Carotid artery disease is not only a risk factor for stroke, but is also a manifestation of systemic vascular disease and ischaemic cardiac disease.^{4 56} Severe correctable coronary artery disease was found in 28% of the patients undergoing CEA in one study.⁵⁷ Another CEA trial was stopped because MI occurred in 26% of those in the surgical arm without aspirin.⁵⁸ Hence, preoperative evaluation of the cardiovascular system routinely includes an electrocardiogram and clinical assessment of function.

If a patient has both severe coronary artery disease and severe carotid artery stenosis, the dilemma emerges whether coronary artery revascularization should be combined with CEA or whether one should precede the other. Although studies have demonstrated that a combined technique can be done safely at centres of excellence, such results might not be widely reproducible.^{59–61} Because there are no randomized trial data on the subject, decisions should be based on careful review of the individual patient's condition, giving consideration to the experience of the surgeons and the record of the institution.

HTN warrants preoperative attention as it is associated with a greater incidence of neurological deficit after CEA.⁶² The incidence of both postoperative hypotension and HTN is greater in patients with uncontrolled HTN before operation. In a multicentre study, diastolic HTN (>110 mm Hg) was a predictor of adverse events.⁶³ Although it seems reasonable that arterial pressure should be controlled before surgery, there is an absence of prospective data to confirm this logic. A reasonable recommendation would be to delay elective surgery if the systolic arterial pressure is >180 mm Hg or the diastolic pressure is >100 mm Hg in a patient without anxiety or pain.⁶⁴

The use of anti-platelet therapy in the perioperative period is supported by growing research. On the basis of randomized controlled trial data, the use of aspirin is recommended unless contraindicated.^{4 65} Relatively newer medications (e.g. ticlopidine, clopidogrel, and dipyridamole) were likewise found to be significantly protective against stroke in a Cochrane Collaboration review of randomized trials.⁶⁶ Blood loss and occurrence of cervical haematoma have not been found to differ significantly from placebo.⁶⁷ In a large observational study by the Vascular Study Group of Northern New England, preoperative anti-platelet therapy was shown to protect against stroke and death (OR, 0.4; 95% CI, 0.2–0.9; $P=0.02$) after CEA.⁶⁸ Although currently there are no randomized trial data comparing anti-platelet agents or defining their effects on neurological outcomes, perioperative single-agent therapy is recommended for patients undergoing endarterectomy.

Although diabetes mellitus is a known risk factor for cardiovascular complications, data indicate that CEA can be performed safely in patients with diabetes.^{69 70} Patients with renal insufficiency have an overall increased risk for stroke, death, and cardiac morbidity associated with CEA.⁷¹ Table 2 includes the key points of preoperative assessment for CEA and CAS.

Anaesthetic management for endarterectomy

Monitoring

Routine monitoring should include electrocardiography, pulse oximetry, and intra-arterial arterial pressure monitoring. In patients with poor ventricular function or myocardial ischaemia, more advanced monitoring can be considered.

Cerebral monitoring for ischaemia is meant to signal impending neurological deficit and allow intervention to

prevent stroke. No special cerebral monitor is required in awake patients with regional anaesthesia. When general anaesthesia is used, it is prudent to monitor the brain during cross-clamping of the carotid artery, although no difference in stroke rate has been convincingly demonstrated with the use of any specific monitoring technique.^{72–75}

EEG is more commonly used than somatosensory-evoked potentials (SSEPs) for electrophysiological monitoring during CEA. The 16-channel EEG is a sensitive indicator of inadequate cerebral perfusion of the cortex. Intraoperative neurological complications have been shown to correlate well with EEG changes indicative of ischaemia.^{74 76} Ipsilateral or bilateral attenuation of high-frequency amplitude or development of low-frequency activity during carotid cross-clamping is indicative of inadequate cerebral perfusion. Increasing changes in the EEG represent greater degrees of ischaemia, the most severe of which is an isoelectric waveform.⁷⁷ Computer-processed EEG methods have also been found to be useful.^{78 79} Temperature and arterial pressure changes may produce waveforms that mimic ischaemia.

Most studies suggest that SSEPs are useful for monitoring cerebral perfusion during cross-clamping and have similar or superior sensitivity and specificity to conventional EEG.^{80–82} Stable anaesthesia must be maintained to minimize the influence of anaesthetics on SSEP amplitude. In general, a >50% reduction in amplitude of the cortical component is considered a significant indicator of inadequate cerebral perfusion. In contrast to conventional EEG, SSEPs monitor the cortex and the subcortical pathways in the internal capsule, an area not reflected in cortical EEG.⁸²

Transcranial Doppler (TCD) can be used to measure blood flow velocity in the middle cerebral artery during CEA and followed as an indicator of CBF.^{83–90} Ischaemia is considered severe if mean velocity after clamping is 0–15% of pre-clamp value, mild if 16–40%, and absent if >40%.⁸² TCD has been shown to be beneficial not only for the detection of intraoperative cerebral ischaemia, but also in detecting malfunctioning shunts and identifying high-velocity states associated with hyperperfusion.^{84 85 87–89 91–93} TCD can be useful in diagnosing the cause of postoperative stroke, carotid artery occlusion, vs haemorrhage.⁸³ TCD is the only monitoring tool that is capable of detecting microemboli.^{83 90 93 94} However, it is difficult to distinguish between gaseous and particulate emboli. It is generally assumed when monitoring before arteriotomy or after carotid artery closure that embolic signals represent particulate matter. In the presence of an open vessel, discrimination between particulate vs air sources of emboli is not straightforward. In general, air emboli produce a greater intensity of signal due to greater reflection and backscattering of ultrasound waves.⁹⁵ The frequency of emboli has been positively correlated with postoperative cognitive dysfunction.^{90 93} Technical and anatomical challenges can limit accurate interpretation in some cases.⁸³

The use of stump pressure as a monitor is based on the concept that perfusion pressure is an important determinant of CBF. It follows that directly monitoring arterial pressure in

the 'stump,' or clamped end, of the distal internal carotid artery, would reflect collateral CBF. Stump pressures, however, are neither sensitive nor specific.²⁵ When stump pressure was compared with EEG monitoring, 6% of the patients demonstrated ischaemic EEG changes despite stump pressures in excess of 50 mm Hg.⁹⁶ On balance, extreme values (<25 or >60 mm Hg) are useful indicators of the state of the cerebral circulation, but not intermediate values.^{97 98}

Near-infrared spectroscopy (NIRS) is a non-invasive continuous monitoring technique that measures transcranial regional cerebral oxygen saturation. Although measurement is straightforward and values show a significant change from baseline during cross-clamping, NIRS largely reflects localized venous oxygen saturation at the frontal lobes. It is highly variable from patient to patient and poorly related to neurological injury.⁹⁹ Owing to low sensitivity and specificity, NIRS should not be used as the sole determinant of ischaemia.¹⁰⁰ Table 2 summarizes the key points of monitoring for CEA and CAS.

Anaesthetic technique

No compelling advantage has been demonstrated with any single anaesthetic regimen. Accordingly, a technique that optimizes brain perfusion, minimizes myocardial stress, and allows for a rapid recovery is recommended. General anaesthesia is preferred in patients with anatomy or pathology that could make surgical conditions difficult. One underappreciated caveat concerns the use of nitrous oxide. It is very difficult to place a shunt in the carotid artery or to release the carotid artery cross-clamp, without exposing the distal cerebral circulation to air. Accordingly, it is recommended that, if used, nitrous oxide be discontinued before these events.

Sevoflurane and desflurane have been shown to result in quicker extubation times and recovery profiles after CEA compared with isoflurane with no significant differences in perioperative cardiac morbidity.¹⁰¹ Propofol and opioids can be associated with better haemodynamic stability than isoflurane, and remifentanyl/propofol might have less evidence of myocardial ischaemia than isoflurane/fentanyl.^{101–103} In one study, raising systemic arterial pressure using phenylephrine resulted in greater myocardial ischaemia than when lightened anaesthesia was used.¹⁰⁴

A regional technique for CEA requires anaesthesia of cervical nerves 2–4. Superficial cervical plexus block, deep cervical plexus block, epidural anaesthesia, local, and combinations of these techniques have all been used successfully. Cervical plexus blocks do not provide coverage for the angle of the mandible which is innervated by the trigeminal nerve. The ipsilateral phrenic nerve is often affected by cervical plexus block, although the clinical effect is insignificant unless severe respiratory compromise or contralateral diaphragmatic paresis is present.¹⁰⁵ Vigilance for signs of local anaesthetic toxicity should be maintained. Although important complications are infrequent, one study reported near-toxic levels of local anaesthetic in approximately half

of the patients receiving deep and superficial cervical plexus blocks.¹⁰⁶ Patients with redundant neck tissue can feel discomfort in adjacent, unanaesthetized areas if aggressive surgical retraction is necessary.

The choice of technique depends on consideration of the advantages and disadvantages of each and on physician experience and patient preference. The principal advantage of regional anaesthesia is continuous sensitive monitoring of neurological function.¹⁰⁷ Regional techniques have also been associated with decreased shunting requirements and lower costs.^{108–112} Other potential advantages of a regional technique include avoidance of potential postoperative cognitive decline, health-related quality of life and cancer recurrence possibly associated with general anaesthesia.¹¹³ Although patient satisfaction with regional techniques is high, disadvantages include the unpredictable risk of patient agitation or distress and poor access to the airway.^{114 115} Seizure, unconsciousness, or stroke can occur in association with carotid artery cross-clamping. It is impractical to administer pharmacological cerebral protection to the awake patient. Nonetheless, it is rare that a regional technique must be converted to general anaesthesia (2–6% of cases).¹⁰

Several non-randomized reports describe contrasting haemodynamic patterns for CEA under regional vs general anaesthesia. Arterial pressure under regional anaesthesia tends towards HTN during cross-clamping and hypotension afterwards and in the postoperative period. In contrast, under general anaesthesia, relative hypotension is observed intraoperatively followed by postoperative HTN.^{64 116} Other data tracking specific variables show that although arterial pressure is more stable and vasopressor requirements are reduced with a regional technique, a higher incidence of tachycardia and increased blood levels of catecholamines occur in comparison with general anaesthesia.^{109 111 115 117}

Regardless of technique, intraoperative haemodynamic management deserves special attention. Atheromatous plaque reduces cerebral perfusion pressure and interferes with baroreceptor sensitivity and cerebrovascular responsiveness.¹¹⁸ Given that long-standing essential HTN is a near-ubiquitous co-morbidity, intraoperative arterial pressure management can be challenging. The prevention of arterial pressure lability is achieved by anticipating stimuli and using small doses of therapeutic drugs. The goal before and after arterial cross-clamping is normotension, and arterial pressure should, in general, be mildly elevated from baseline (~20%) during cross-clamping. Haemodynamic instability can persist into the postoperative period and is more prominent in patients with bilateral carotid artery plaque and greater baroreflex dysfunction.¹¹⁹

Until recently, non-randomized studies suggested that the use of a regional technique were associated with reductions (~50%) in the odds of stroke, death, MI and pulmonary complications.¹²⁰ However, in 2008, Lewis and colleagues published the results of the GALA trial in which 3526 patients were randomized to undergo CEA with either general

or regional anaesthesia. They observed no differences between groups in the incidence of stroke, MI or death.¹²¹ Similarly, a large Cochrane review reported no difference in stroke or death between the two techniques.¹²² The key points of anaesthetic management for CEA are included in Table 2.

Modalities of cerebral protection

Cerebral protection from ischaemia can be approached by surgical means, by manipulation of physiology, or by administration of specific anaesthetics. Surgical stroke prevention involves the placement of a shunt to maintain CBF during cross-clamping. Although it can reduce the incidence of ischaemic stroke, a shunt entails the risks of embolization and carotid intimal dissection, among others, and limits surgical exposure. Most often a shunt is placed selectively on the basis of cerebral monitoring rather than routinely. There is insufficient evidence from randomized controlled trials to support or refute the use of routine or selective shunting during CEA.²⁶ At surgical closure, a patch angioplasty technique rather than primary closure of the artery might confer reduced rates of restenosis and ipsilateral stroke, although this evidence is not strong.¹²³

The management of physiological parameters can influence outcomes. Specific parameters include temperature, glucose, arterial pressure, blood rheology, and arterial carbon dioxide tension. The beneficial effect of mild hypothermia on cerebral ischaemia has been well studied in other contexts.^{124–126} Although hypothermia has appeal for CEA, the associated risks of bleeding, infection, and myocardial stress preclude a great deal of the benefit.^{127–128} Nor is the therapeutic sequence of cooling and warming practical for a case lasting 1.5–2 h, although it has been reported.¹²⁹ Thus, the routine employment of hypothermia is not recommended for patients undergoing CEA. Conversely, hyperthermia should be avoided.

Hyperglycaemia should probably be avoided. This is accomplished by eliminating glucose-containing i.v. solutions and by treating hyperglycaemia with small doses of insulin. Data reveal conflicting outcomes however. When hyperglycaemia is present, a more severe neurological injury results.^{130–131} Long-term changes in cognitive function have also been associated with elevated glucose.¹³² At the same time, other research shows glucose to be neuroprotective *in vitro* and *in vivo*.^{133–134} The molecular mechanism remains largely unexplained.¹³⁵

Induced systemic arterial HTN therapy might be indicated. During ischaemia, autoregulation is impaired and CBF is dependent on perfusion pressure. Augmenting systemic arterial pressure should increase collateral perfusion, increasing flow to the area of ischaemia. HTN therapy decreases injury in animals; however, clinical efficacy is not definitively established in humans.^{136–139} Nevertheless, there is evidence of an ischaemic arterial pressure threshold in patients with stroke; above this threshold neurological symptoms subsided, and below this threshold neurological symptoms were

manifest.¹⁴⁰ Thus, it is advisable to maintain normal-to-high arterial pressure in most situations.

Using haemodilution to improve CBF is based on the rationale that CBF is inversely related to haematocrit. Although the optimal haematocrit during cerebral ischaemia seems to be about 30%, the clinical data are not compelling.¹⁴¹ Regarding arterial carbon dioxide tension, normocarbica is the goal in order to maintain normal cerebral perfusion, and hypocarbica should be avoided.

Cerebral protection by anaesthetics refers to evidence of reduction in the size of focal ischaemic brain injury when a specific agent is used. In general, most anaesthetics, with the exception of etomidate, have been shown to be protective against such focal insults.^{142–146} Ischaemic injury has been found to be a dynamic process in which neurones continue to die long after the insult and that anaesthetic protection might be of limited duration.¹⁴⁷ Although controversial, recent data have identified detrimental effects of anaesthetics on global cognitive function (possibly by triggering apoptosis, inducing β -amyloid formation, and/or affecting neurotransmitter systems such as *N*-methyl-D-aspartate glutamate receptors).^{148–152} Nonetheless, in the context of intraoperative focal ischaemia, anaesthetic agents have been shown to reduce the degree of brain injury.

During temporary focal ischaemia, there is evidence that barbiturate therapy reduces the degree of permanent neurological injury.^{142–144–153} Dosing that produces EEG burst suppression is not necessary to achieve the effect.¹⁵⁴ If a barbiturate or other protective agent is to be used, it would be best infused before temporary carotid artery cross-clamping during endarterectomy. Significant cardiovascular depression and delayed emergence must be weighed against the degree of potential protection.

Among volatile anaesthetics, isoflurane is the most commonly described. Isoflurane has been shown to confer protection of a similar order to barbiturates, although the effect is transient, lasting up to 7 days but not seen at 14 days in rodent models.^{142–144–155–156} General anaesthesia with isoflurane and sevoflurane is associated with a lower critical CBF (that at which EEG evidence of ischaemia is present) compared with halothane and enflurane.^{157–158} Overall, isoflurane likely delays, but does not prevent, the development of cerebral infarction.

Owing to its short duration of action, haemodynamic profile, and metabolic properties, etomidate has been used during neurovascular procedures. However, there is evidence in animals that etomidate worsens ischaemic injury, whereas thiopental improves injury.¹⁴² Accordingly, etomidate is not recommended for use as a cerebral protectant. Although many laboratory models have produced positive results for propofol, the evidence is not as extensive as that for barbiturates.^{145–159–161} Early studies in animals suggest that dexmedetomidine is neuroprotective.^{162–163} Although controversial, in human volunteers, dexmedetomidine decreases CBF but does not increase the incidence of shunt placement during awake CEA.^{146–164–166}

Complications of endarterectomy

Endarterectomy has an inherent risk of perioperative stroke, precisely the event it is meant to avert. Differences in accuracy of diagnosis, definition of stroke, study design, and other factors lead to a wide range in reported risk, from 1% to 20%.¹⁶⁷ Authors of the CREST trial reported a 2.3% incidence of periprocedural or ipsilateral stroke within 30 days of operation.⁵³ One-quarter of perioperative strokes associated with CEA occur during the procedure, of which the large majority are embolic. Far fewer strokes are the result of low CBF, due to low systemic pressure and contralateral disease, poor collateral circulation, or reduced cerebrovascular reserve.^{168 169} Rarer still, haemorrhagic stroke accounts for 5% of perioperative strokes.¹⁷⁰ Haemorrhage is usually ipsilateral and can occur as a result of suddenly increased perfusion pressure and CBF in a patient with prior severe stenosis and altered autoregulation.

The risk of stroke after CEA is most strongly associated with an active neurological process before surgical intervention. Other factors reported to increase neurological risk include hemispheric vs retinal TIA, recurring neurological events, male gender, an emergent procedure for stroke-in-evolution, ipsilateral ischaemic lesion on computerized tomography, contralateral carotid occlusion, poor collateral circulation, impaired consciousness, and an irregular or ulcerated plaque.^{123 169} Risk might also be associated with the presence of midline brain shift and the level of consciousness.¹⁷¹ One author has suggested that the stroke/death rate might be related to the ASA physical class status if surgery is performed in the first 3 weeks after a stroke.¹⁷²

Cardiovascular complications after CEA occur most often in patients with symptomatic cardiac disease. MI, defined by Q-wave criteria on electrocardiogram, occurs in <2% of the cases.⁶⁷ It must be noted that many trials do not publish a definition of MI, or include elevated cardiac enzymes in the term, which can overestimate the incidence. Nonetheless, MI is the major cause of perioperative and long-term mortality after CEA and represents almost half of the major adverse events associated with carotid revascularization in asymptomatic patients.^{67 169 173 174} Congestive heart failure, dysrhythmias, and angina also occur perioperatively.

HTN is common and should be treated promptly. Excessively elevated arterial pressure confounds efforts to prevent myocardial stress and other complications such as wound haematoma and neurological complications. Although exact parameters are not supported by data, a systolic pressure of <160 mm Hg is often the goal.⁶⁴ Hypotension is less common and can result from residual anaesthetic, anti-hypertensive therapy, or baroreceptor hypersensitivity, although more serious causes should be ruled out.

Post-endarterectomy or CAS cerebral hyperperfusion is more commonly ipsilateral than bilateral. The clinical syndrome occurs most frequently after intervention (either

CEA CAS) for a severely stenosed artery in the setting of exhausted cerebrovascular reserve and altered autoregulation. Slower in onset than stroke, hyperperfusion occurs a few days after treatment. The syndrome consists of cerebral oedema and headache and can include intracerebral haemorrhage, focal neurological signs, and/or epileptic seizures. Diagnosis is made by brain imaging and angiography, which help distinguish hyperperfusion from similar presentations associated with cerebral vasoconstriction.¹⁷⁵

Death is a not a remote concern. Overall mortality for CEA is reported at 1.3–1.8% in two large systematic reviews, in which the highest rate was 15%.^{167 176} Table 1 shows a range of reported rates for stroke and death combined.

Other complications include cranial and peripheral nerve damage. Although such injuries are usually minor or transient, permanent disability does rarely occur. Wound infection, haematoma, and pneumonia also occur rarely. The key postoperative concerns for CEA and CAS are summarized in Table 2.

Conclusions

Although there is no demonstrable advantage of a specific anaesthetic technique for patients undergoing CEA, it is imperative that CBF is optimized, that myocardial stress is minimized, and that anaesthetic recovery is rapid. Carotid angioplasty and stenting is usually performed under light sedation with antithrombotic therapy and vigilance for bradycardia and hypotension. Tight haemodynamic control remains a priority in the immediate postoperative period for both interventions.

Conflict of interest

None declared.

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