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Carotid endarterectomy

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Carotid endarterectomy (CEA) is performed to prevent embolic stroke in patients with atheromatous disease at the carotid bifurcation. There is now substantial evidence to support early operation in symptomatic patients, ideally within 2 weeks of the last neurological symptoms. Thus, the anaesthetist may be faced with a high risk patient in whom there has been limited time for preoperative preparation. The operation may be performed under local or general anaesthesia. The advantages and disadvantages of both are explored in this review. Carotid shunting may offer a degree of cerebral protection, but carries its own risks and has not been proved to reduce morbidity and mortality. The use of carotid shunts is based on clinical judgement, awake neurological monitoring, and the use of monitors of cerebral perfusion. There is no ideal monitor of cerebral perfusion in the patient receiving general anaesthesia. Both the intraoperative and postoperative periods may be witness to dramatic haemodynamic changes that may compromise the cerebral or myocardial circulations. In particular, postoperative hypotension may compromise both myocardial and cerebral perfusion, and severe hypertension can cause cerebral hyperperfusion. There is as yet limited evidence to guide the management of these problems. In summary, CEA can yield significant benefit, but those with the most to gain from the operation also present the greatest challenge to the anaesthetist.

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Carotid endarterectomy (CEA) is a prophylactic operation. It is performed in patients who are at risk of stroke from emboli arising from atheromatous plaque at the carotid bifurcation. Although atheroma at this site can cause marked carotid stenosis, CEA is not performed to relieve stenosis, but is undertaken in patients. Timely CEA can substantially reduce the risk of disabling or fatal stroke, but if this benefit is to be realized it is essential that the risks of surgery do not outweigh the subsequent reduction in the risk of stroke. This article reviews the perioperative management of patients undergoing CEA.

Evidence of the need for CEA

The indications for CEA in various circumstances were recently reviewed by the American Academy of Neurology.[11] There are two groups of patients to consider: symptomatic patients who have active plaque giving rise to emboli that enter the cerebral circulation and cause transient ischaemic attacks (TIAs) and reversible ischaemic neurological deficits, and asymptomatic patients who have demonstrable disease at the carotid bifurcation but no history of a recent neurological event attributable to this lesion.

There is unequivocal evidence to support CEA in symptomatic patients with >70% carotid stenosis in the relevant carotid territory. This is based particularly on two large studies, the North American Symptomatic Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST), both of which compared surgery with best medical treatment.[19 69] The data from these and the smaller Veteran's Affairs Trial were combined in a meta-analysis by Rothwell and colleagues.[80] For patients with a carotid stenosis of 70% or more there was absolute risk reduction for the combined outcome of perioperative death or subsequent stroke more than 5 yr of 16% yielding a number needed to treat of 6.3. The benefit in patients with 50–69% stenosis was less marked with an absolute risk reduction of 4.6% more than 5 yr and a number needed to treat of 22. CEA was not beneficial to symptomatic patients with 30–49% stenosis or near carotid occlusion, and was harmful in symptomatic patients with <30% stenosis.

Patients with asymptomatic carotid disease with >50% stenosis are a different population to patients with 'active' plaque that is discharging emboli into the cerebral circulation. There are data to support CEA in asymptomatic patients but they are less robust than those supporting the operation for patients with symptoms. The asymptomatic carotid artery stenosis (ACAS) study was halted after a 2.7 yr median follow-up because of a projected 5.9% absolute reduction in

the risk of ipsilateral stroke at 5 yr.[20] Although the results of this study were encouraging, the very low perioperative stroke and death rate of 2.3% was not supported by more recent studies. The asymptomatic carotid surgery trial (ACST) recruited patients with a carotid artery diameter reduction of at least 60% on ultrasound and no symptoms in the previous 6 months. This study showed a net reduction of 5.4% in the combined outcome of stroke within 5 yr and death within 30 days of surgery.[65] The benefits were mainly seen in younger patients and were uncertain for patients older than 75 yr. The American Academy of Neurology document makes the point that there is a significant difference between the primary endpoint of the ACAS and ACST studies.[11] ACAS took ipsilateral stroke as the primary endpoint, whereas ACST included contra-lateral and vertebrobasilar strokes. If ACST analysis was limited to ipsilateral stroke, the absolute benefit would be reduced.

CEA should be performed sooner rather than later in symptomatic patients. A pooled analysis of data from NASCET and ESCT demonstrated that the greatest absolute risk reduction for ipsilateral stroke, any stroke, and death within 30 days of surgery was found in patients who underwent surgery within 2 weeks of their last event.[81] This decrease in benefit from surgery was significantly more rapid in women than in men. The benefit of early surgery is explained by the natural history of carotid plaque in symptomatic patients. In a study conducted by Harrison and Marshall,[35] 66% of patients undergoing CEA within 4 weeks of their most recent event had thrombus overlying the carotid stenosis compared with 21% of patients waiting for a longer period. Plaque morphology studies have shown that patients with recent symptoms are more likely to have acute plaque disruption, spontaneous embolization, overlying thrombus formation, and abnormal levels of metalloproteinases within the plaque.[68] Ideally, patients presenting with a suspected TIA should have undergone investigation and, if appropriate, surgery within 2 weeks of presentation. At present, this goal is far from being achieved in the UK. The 2004 Royal College of Physicians Sentinel Stroke Audit found that only 50% of patients had undergone a duplex scan within 12 weeks of presentation, let alone surgery.[68 83]

The best care of a patient with a progressing stroke of less than 24 h duration is less clear. The American Academy of Neurology review identified four studies that examined this issue.[11] Three of the studies found benefit from surgery, but one reported a postoperative stroke and death rate of 20%. The best management of this difficult clinical problem remains unclear.

Anatomy

The brain receives its blood supply from four major arteries. Eighty-to-ninety per cent of the cerebral blood supply is delivered via the two internal carotid arteries with the majority of the remainder coming from the vertebrobasilar system. The carotid arteries and basilar artery unite to form the Circle of Willis at the base of the brain. This ring of arteries offers the brain considerable protection against the occlusion of one or another vessel, but its presence should not lead to clinical complacency. The Circle of Willis is incomplete in 15% of normal people and in patients with cerebrovascular disease one or more of the vessels within the circle maybe occluded by atheromatous plaque.

Operation

After careful surgical exposure, the external, internal, and common carotid arteries are cross-clamped so that the carotid bifurcation is isolated from the circulation. The artery is opened and the plaque removed. Most often this is done through a longitudinal incision and the artery is patched upon closure as this reduces the incidence of re-stenosis. The operation of eversion CEA in which the internal carotid artery is transected and turned inside out to remove the plaque is used by some surgeons. Whichever technique is used care must be taken to remove all of the debris from the intimal surface of the artery to prevent postoperative emboli occurring.

Shunting

During the course of the operation, a shunt may be inserted. There are a number of different types of carotid shunt but all are essentially a length of plastic tubing to carry the blood from the common carotid to the internal carotid artery, so maintaining blood flow during the course of surgery. Although at first sight this may seem to be a useful technique to maintain cerebral blood flow in those patients who have a contralateral carotid stenosis or a compromised Circle of Willis, it is not an entirely benign intervention. Acute complications of shunt insertion include air or plaque embolization, intimal tears, and carotid dissection. There is an associated risk of local complications including haematoma, nerve injury, infection, and late carotid restenosis. For all these risks, flow through the shunt may be inadequate to meet cerebral oxygen requirements.

Practice varies widely between surgeons; some routinely insert shunts in all patients, whereas others eschew their use altogether. A middle way is a policy of selective shunting based on one or another monitor of cerebral function or blood flow. The technologies used to monitor for cerebral ischaemia are discussed below. There are limited high quality data to guide practice. The issue is made complex by the number of different options to be compared. Studies may compare a policy of shunting *vs* not shunting, shunting *vs* selective shunting based on the use of a cerebral monitor, or selective shunting *vs* not shunting. Bond and colleagues[6] systematically reviewed the

evidence for and against shunting. They found only three studies that were sufficiently rigorous for inclusion in a systematic review. In two studies comparing routine shunting with no shunting there was no significant difference in the rate of all strokes, ipsilateral stroke, or death up to 30 days after surgery.[28 88] However, these studies suffered from flaws of methodology and reporting. A third trial compared shunting on the basis of EEG monitoring and carotid pressure measurement with pressure measurement alone.[23] There was no significant difference between the risk of ipsilateral stroke between the two groups. Bond and colleagues suggest that further trials of various methods of monitoring are not justified until the efficacy of shunting is established. This is perhaps too simplistic a statement. They do concede that a systematic review of the sensitivity and specificity of the various forms of monitoring would be appropriate to inform any trial of selective shunting.

Perioperative complications

The two most feared major perioperative complications of CEA are cerebrovascular accident and myocardial infarction. The pooled data from the NASCET, ESCT, and Veteran's Administration Trial provide an insight into the incidence of cerebrovascular accident after CEA.[80] Data are presented on 3248 patients who underwent surgery. Of 35 deaths (1.1%) within 30 days of surgery, 20 deaths were from operative strokes. Two hundred and twenty-nine patients suffered the combined outcome stroke or death within 30 days of surgery.

The data from the Cochrane Collaboration meta-analysis of regional *vs* general anaesthesia for CEA also provide valuable information on the overall incidence of adverse events. In this analysis, there were 195 deaths within 30 days of surgery among 17 703 patients, a death rate of 1.1%. There were 564 strokes within 30 days of surgery among 16 835 patients, an incidence of any stroke of 3.4%. Twenty-six studies including 13 547 patients reported on the combined outcome of any stroke or death within 30 days of surgery. There were 604 events in the pooled data giving an event rate of 4.5%. Twenty-two studies reported on the occurrence of myocardial infarction within 30 days of surgery. There 323 postoperative myocardial infarctions were reported in a total of 14 773 patients, a myocardial infarction rate of 2.2%. It is not clear what proportion of these myocardial infarctions was fatal.[78]

Although carotid cross-clamping is a major haemodynamic challenge to the cerebral circulation, the majority of strokes after surgery are due to embolization or thrombosis. In a review of 38 neurological events that occurred in 2024 patients who had undergone CEA, the causes of neurological events included intraoperative clamping ischaemia in 5 patients (13.2%); thromboembolic events in 24 (63.2%); intracerebral haemorrhage in 5 (13.2%); and deficits unrelated to the operated artery in 4 (10.5%).[79] The majority of perioperative events become manifest within 8 h of surgery. In a retrospective review of 771 CEAs, 26 patients developed a neurological deficit after surgery. Nineteen of the neurological deficits were diagnosed in the operating theatre or recovery room and a further five within 8 h of surgery.[92]

Patients with carotid artery disease have a high incidence of severe coronary artery disease. Hertzer and colleagues[39] reported coronary angiography data on 1000 patients being considered for major vascular surgery, including 295 patients presenting with cerebral vascular disease. Twenty-six per cent of the patients with cerebrovascular disease had coronary artery disease sufficiently severe that they were considered to be potential candidates for coronary artery surgery.[39] It is unsurprising that patients undergoing CEA are at risk of preoperative myocardial injury. The pooled meta-analysis data discussed earlier rank myocardial infarction second to stroke as a complication of endarterectomy with rates of 3.4 and 2.2%, respectively. Data on perioperative cardiac troponin release indicate that considerably more patients suffer asymptomatic perioperative myocardial injury. In a study comparing CEA with carotid stenting, 13% of patients undergoing CEA had detectable cardiac troponin I release into the circulation.[66] This silent cardiac troponin release cannot be regarded as clinically irrelevant. The association between asymptomatic perioperative troponin release after major vascular surgery and a worsened intermediate and long-term prognosis is well established.[48 51]

CEA may also be associated with cranial nerve injury, bleeding and airway swelling and oedema. Ballotta and colleagues reported cranial nerve deficits in 25 out of 200 patients who underwent CEA. There were 11 hypoglossal, 8 recurrent laryngeal, 2 superior laryngeal, 2 marginal mandibular, and 2 greater auricular nerve injuries. Many, if not all of these injuries, can be attributed to surgical traction. All nerve dysfunctions were transient, with all but four nerves recovering completely within 6 months.[5] The operation is performed on an artery imbedded among vascular tissues, and postoperative bleeding, leading to a neck haematoma, airway compression, and respiratory compromise are possible. Patients should be monitored for this in the immediate postoperative period. If there is evidence of respiratory compromise, the clips should be removed from the neck wound to decompress the airway and the patient taken back to theatre immediately. This is a setting in which the use of local anaesthesia has the benefit that surgery can proceed at once.

Anaesthesia

CEA may be carried out under regional or general anaesthesia. The impact of the choice of anaesthesia on the outcome of this operation has been extensively studied. A

systematic review by Tangkanakul and colleagues[102] of the impact of the type of anaesthesia on outcome from CEA was published in 2000 and was updated by Rerkasem and colleagues[78] in 2004. Data were reported from seven randomized trials involving 554 operations and 41 nonrandomized studies involving 25 622 operations. The authors of the review had significant concerns about the quality of several of the nonrandomized studies. A meta-analysis of the nonrandomized studies showed that the use of local anaesthetic was associated with significant reductions in the odds of death from all causes (OR 0.67, 95% CI 0.46–0.97), stroke (OR 0.56, 95% CI 0.4–0.70), stroke or death (OR 0.61, 95% CI 0.48–0.77), myocardial infarction (OR 0.55, 95% CI 0.39–0.79), and pulmonary embolism within 30 days of surgery (OR 0.31, 95% CI 0.15–0.63). A meta-analysis of the randomized studies showed that the use of local anaesthetic was associated with a reduction in the risk of local haemorrhage within 30 days of surgery, but there was no evidence of a reduction in the odds of operative stroke.[78 102] However, the trials were small and in some studies intention-to-treat analyses were not possible. A large-scale study of general anaesthesia *vs* local anaesthesia (GALA) is currently in progress.

Local and regional anaesthesia

CEA may be performed under either a superficial cervical plexus block or combined deep and superficial cervical plexus block. The techniques for performing these blocks have been described elsewhere.[96] Many practitioners use both blocks together while others choose to use a superficial block alone. Patients should be told to report any discomfort because the surgeon can supplement the block with local anaesthetic infiltration.

Stoneham and colleagues[95] compared superficial cervical plexus block alone with combined deep and superficial block in a randomized controlled trial and found them to be comparable with regard to the amount of local anaesthetic supplementation given by the surgeon. However, patients in whom paraesthesia was elicited during placement of the deep block required less lidocaine supplementation and those in the deep block group were less likely to require analgesia during the first 24 h after the operation.

Anatomical considerations suggest that a superficial block alone might not be expected to block all the relevant nerves for CEA. Dye injection studies performed in cadavers suggest a communication between the deep and superficial cervical spaces such that local anaesthetic may be able to spread from a superficial cervical plexus block to the deep structures so long as the injection is made beneath the investing fascia of the neck and is not only s.c.[74] The hazards of deep cervical plexus block include injection into the CSF with consequent brainstem anaesthesia, arterial injury and intra-arterial injection, and phrenic nerve paralysis resulting in respiratory distress.[10] The deep block should not be performed in anticoagulated patients.

CEA under cervical epidural anaesthesia is well described and does provide good operating conditions. However, it is associated with a significant risk of major anaesthetic complications. In a series of 394 patients who underwent endarterectomy under cervical epidural anaesthesia, serious complications included dural puncture in two patients, epidural venepuncture in six patients, and respiratory muscle paralysis in three patients.[7]

General anaesthesia

While the use of local anaesthesia has the merit that it allows direct neurological monitoring of the conscious patient, general anaesthesia also has laudable qualities. Patients can find CEA under regional anaesthesia stressful. They must lie still with their head turned to one side for 90 min or more and the positioning of the drapes may be profoundly unpleasant for a claustrophobic patient.

The operation may be performed with a laryngeal mask airway and a laryngeal mask may be inserted if there is a need to convert from regional to general anaesthesia as described in what follows. However, access to the airway during surgery can be difficult and, with the head turned to one side, it is the view of this author that the definitive airway control offered by endotracheal intubation is to be preferred.

There are no data to favour any particular general anaesthetic technique. It may be argued that sevoflurane is the volatile agent of choice for neuroanaesthesia.[17] Desflurane has been shown in an animal model to cause marked vasodilation, increasing cerebral blood volume, and thence intracranial pressure.[40] Although both sevoflurane and isoflurane can provide rapid recovery, sevoflurane produces less vasodilation than isoflurane at the same depth of anaesthesia.[41] However, these considerations regarding intracranial pressure are of more importance in the setting of intracranial surgery than in an extracranial operation such as CEA. The effect of anaesthetic agents on cerebral blood flow and metabolism are perhaps more important. At concentrations of up to 1.0 MAC, sevoflurane produces concomitant reductions in cerebral metabolic blood flow and cerebral metabolic rate. At concentrations above this there is evidence of increases in regional cerebral blood flow.[64] A study conducted by Kaisti and colleagues using positron emission tomography showed that a concentration of 1.0 MAC of sevoflurane reduced regional cerebral blood flow in all areas. At a concentration of 1.5 MAC there was evidence of increased regional blood flow in the frontal cortex, thalamus, and cerebellum.[44] Static autoregulation is well maintained in patients receiving 1.2 MAC of sevoflurane.[12] There is evidence that dynamic autoregulation is impaired even with concentrations of volatile anaesthetic agents <1.0 MAC, although this effect

is more marked with isoflurane than with sevoflurane.[73 101] The response of the cerebral circulation to carbon dioxide is maintained with sevoflurane.[3]

Nitrous oxide should be avoided if possible. It increases the cerebral metabolic rate and produces a concomitant increase in middle cerebral artery blood flow velocity (MCAv). It causes increases in cerebral blood flow in the presence of both the volatile anaesthetic agents and propofol.[50 57 99] Cerebral vascular reactivity to carbon dioxide is maintained with sevoflurane alone, but is impaired when nitrous oxide is added to sevoflurane.[100]

Anaesthesia may also be maintained using propofol and the merits of this drug for neurosurgical anaesthesia have been closely argued in a recent review.[32] Propofol produces comparable reductions in cerebral blood flow and metabolic rate in contrast to the flow metabolism decoupling that is reported with higher concentrations of sevoflurane.[43] While cerebral autoregulation is impaired with sevoflurane, it is preserved under propofol–remifentanil anaesthesia.[14] During carotid cross-clamping, ipsilateral cerebral blood flow depends upon perfusion across the Circle of Willis. This may be affected by haemodynamic changes on the contralateral side. In a recently published study, internal carotid artery pressure (stump pressure) was monitored during propofol and sevoflurane anaesthesia. Internal carotid artery pressure on the site of surgery was lower with sevoflurane and this was attributed to the vasodilation induced by this drug.[61] Conti and colleagues compared two different propofol infusion regimes for total i.v. anaesthesia for CEA. Patients received a propofol infusion with a target effect site concentration of either 1.2 or 2.4 μg litre^{-1} and a remifentanil infusion. The remifentanil infusion was adjusted to maintain haemodynamic stability and a bispectral index of between 40 and 60. Patients receiving the higher dose of propofol displayed greater haemodynamic stability, and the authors concluded that a hypnotic, rather than an opiate-based regime, was to be preferred in this setting.[26]

Both the volatile anaesthetic agents and propofol may offer a degree of neuroprotection. There is experimental evidence to support neuronal protection from isoflurane, although this appears to be age-dependent and is not seen in tissues from older animals.[112] In an *in vitro* study, Payne and colleagues[75] have also demonstrated preconditioning and neuronal protection with sevoflurane. A neuroprotective effect of propofol has been demonstrated in an animal model, but was not seen in an *in vitro* study using a hippocampal slice preparation.[18 22] There are also some data to support post-insult neuroprotection (post-conditioning) by anaesthetic drugs.[9] The experimental anaesthetic agent, xenon appears to hold out the possibility of both pre- and post-insult neuroprotection.[16 55]

The experimental evidence for neuroprotection poses a dilemma for the anaesthetist in the setting of awake CEA performed under local anaesthesia. If the patient develops a neurological deficit upon cross-clamping, is it appropriate to institute general anaesthesia to protect the brain? It is the view of this reviewer that there is insufficient evidence to support this approach. Any theoretical benefit of neuroprotection is offset by being able to demonstrate neurological recovery on shunt insertion and the opportunity to undertake further manoeuvres such as raising the arterial pressure if such recovery is not seen. If the patient does not make a full recovery despite such interventions it may then be appropriate to institute general anaesthesia, but otherwise anaesthesia should be induced for clinical indications such as agitation or airway compromise.

Neurological monitoring

A key decision for all involved in the operation of CEA is whether or not a shunt is to be inserted. In the awake patient, the anaesthetist should remain in constant verbal contact with the patient during and after cross-clamping. This should consist of more than simply asking the patient if they feel alright. It is appropriate to check frequently that the patient is orientated in time and place and can perform simple mental tasks such as counting backwards from 100. The patient should be asked to demonstrate that they can move the side of their body contralateral to surgery. If the patient's hand is under the drapes, a squeaky toy or a fluid filled bag connected to a pressure transducer may be placed in their hand before surgery and they can be asked to squeeze this regularly. If the patient becomes confused and restless, stops responding to commands, or simply ceases to communicate, these are all signs of cerebral ischaemia and shunt insertion is indicated.

When the patient is under general anaesthesia, the decision as to whether or not to perform shunting is more difficult. Some surgeons always insert a shunt in these circumstances while others may only shunt patients with severe bilateral disease. A number of techniques and monitors are available to assist with this decision. These are well reviewed by O'Conner and Tuman.[71] None of the monitors of cerebral ischaemia is perfect.

Stump pressure

Once the common and external carotid arteries are clamped, the pressure measured in the internal carotid artery reflects the perfusion pressure transmitted around the Circle of Willis. This is the stump pressure. A number of thresholds for the stump pressure, ranging between 25 and 70 ml of mercury, have been proposed below which shunting would be appropriate.[2] Studies in patients who underwent surgery under general anaesthesia suggest stump pressure to be specific but not sensitive at identifying patients who develop EEG changes consistent with cerebral ischaemia upon carotid cross-clamping.[34 62] A study by Hans and colleagues using awake neurological monitoring in patients undergoing surgery under regional

anaesthesia also demonstrated a low false positive rate but a high false negative rate for monitoring using stump pressure. A stump pressure of 50 mm Hg had a sensitivity 29.8% and a specificity 98.6% for the prediction of neurological changes necessitating shunt placement. For a stump pressure of 40 mm Hg, the values were sensitivity, 56.8%; specificity, 97.4%.[33] Because of the effects of anaesthetic agents on the cerebral vasculature, it cannot be assumed pressure thresholds established under regional anaesthesia are applicable in the setting of general anaesthesia.

EEG

Both the raw and the processed EEG have been used for neurological monitoring during CEA. There is no doubt that the EEG is affected by cerebral ischaemia but the technique suffers from many limitations. The EEG signal reflects only cortical events and does not disclose ischaemia in deeper structures. The raw EEG is difficult to interpret. Its monitoring in real-time requires considerable skill and experience. The processed EEG, for example the compressed spectral array, is easier to interpret but considerable information is lost during its conversion to a processed format.[31 47] Unfortunately, the BIS monitor is not suitable for cerebral monitoring in this setting as it primarily detects frontal lobe activity and cannot be relied upon to detect localized changes elsewhere in the brain.[15]

Somatosensory evoked potentials

Somatosensory evoked potentials (SSEPs) offer theoretical advantages over the EEG for cerebral ischaemia monitoring. This type of monitoring examines not only the cortex but the deeper structures of the brain. Stimulation from a peripheral nerve passes through first- and second-order neurones and brainstem synapses before evoking a response in the somatosensory cortex. Unfortunately, this theoretical promise is not borne out by clinical studies. SSEPs certainly demonstrate the presence of cerebral ischaemia, but are no more specific or sensitive than the EEG.[36 46] However, they may be superior in patients whose baseline EEG is not easily interpretable because of a previous stroke.[56] It should be borne in mind that the volatile anaesthetic agents can reduce the amplitude of SSEPs.[91]

Near infrared spectroscopy

Near infrared spectroscopy (NIRS) gives a value for regional cerebral oxygenation (rSO_2) which is a composite measure of arterial venous and capillary oxygenation, although the predominant influence is the venous blood.[89] Carotid cross-clamping produces a decrease in rSO_2.[86] Unfortunately, this change is not consistently related to changes in other measures of cerebral blood flow.[71] Studies of NIRS indicate that it has a high negative predictive value for cerebral ischaemia, but poor specificity and positive predictive value. In a study of patients undergoing CEA under regional anaesthesia, Samra and colleagues[87] found that a reduction of 20% in rSO_2 on cross-clamping had a 66% false positive rate for the detection of cerebral ischaemia, but a 97.4% negative predictive value. Grubhofer and colleagues examined the reliability of NIRS for detecting significant reductions in MCAv measured by TCD and again found a high false positive rate for NIRS.[27] Decreases in rSO_2 of more than 13% identified two patients who required shunting; however, this threshold would have indicated unnecessary shunting in seven patients, a false positive rate of 17%. A number of factors account for the limitations of NIRS in carotid surgery.[71] The sensors are placed over the frontal lobes and so are not ideally positioned for detecting reductions in middle cerebral artery blood flow. The signal may be contaminated by the blood flow in extracranial tissues and by the effects of ambient light. Changes in rSO_2 may be related to redistribution of cerebral blood flow during anaesthesia rather than the effects of cross-clamping. There is no well-defined 'normal' range for rSO_2 during surgery and the change in rSO_2 during a carbon dioxide challenge differs between two commercially available monitors.[111] Finally, there is not a well-defined biologic zero and studies in dead subjects give an average rSO_2 value of 51%, compared with a value of 68% in normal controlled subjects.[89]

Transcranial Doppler

Transcranial Doppler relies on the fact that the thin petrous temporal bone provides an acoustic window that allows ultrasound visualization at the middle cerebral artery. A probe is placed on the petrous temple bone and the skilled operator is able to detect the Doppler signal generated by blood flow in the middle cerebral artery. TCD may be used to monitor both cerebral haemodynamics and the occurrence of emboli.

A marked reduction in MCAv on cross-clamping has been taken as an indication for shunting. In a review published by the International Transcranial Doppler Collaborators in 1992, a persistent reduction in mean MCAv on cross-clamping to between 0 and 15% of the baseline value was found to be strongly associated with postoperative stroke.[29] The author proposed that patients with such marked reductions in MCAv would benefit from shunt insertion. Although a reduction in MCAv is often taken to be an indication for shunt insertion in current practice, in this study shunting was not found to be beneficial in patients with a reduction in MCAv to between 16 and 40% of baseline. More recently, McCarthy and colleagues reported that a mean MCAv of <30 cm s^{-1}, a clamp/pre-clamp ratio of MCAv of <0.6, or a reduction of mean MCAv more than 50% were not reliable methods for

the detection of cerebral ischaemia and the identification of patients requiring shunting.[59]

Unlike the other monitors discussed, TCD is able to detect emboli. The majority of perioperative neurological events are embolic or thrombotic rather than haemodynamic in nature and gaseous or particulate emboli can be detected in more than 90% of patients undergoing CEA.[25] Gaseous emboli, seen at shunt opening and during restoration of flow, are not generally associated with adverse clinical outcomes. However, significant particulate embolization correlates with deterioration in cognitive function after CEA, postoperative ischaemic events, and evidence of new lesions on brain MRI.[1 25 53 67] On the basis of these findings, some workers advocate the use of an incremental Dextran-40 infusion in patients having frequent microemboli on postoperative TCD monitoring.[52]

TCD monitoring is undoubtedly operator-dependent. It suffers from the limitations that the probe has to be placed relatively near to the surgical site and may impede the operator, especially if it needs constant adjustment, and an acoustic window may not be found in between 10 and 20% of subjects.

Management of cerebral ischaemia

The primary intervention in the event of the patient developing evidence of cerebral ischaemia upon carotid cross-clamping is the insertion of a shunt. It is appropriate to maintain the mean arterial pressure perhaps 20% above the preoperative level to maintain the perfusion pressure across the Circle of Willis. Transcranial Doppler studies suggest that an augmented arterial pressure is also needed to maintain an adequate blood flow through a surgical shunt.[37] Both induced hypocarbia and hypercarbia have been proposed as means of augmenting ipsilateral cerebral blood flow.[4 38] Both are fraught with risk. Hypocarbia may cause ipsilateral vasoconstriction and extend the area of cerebral ischaemia. Hypercarbia may produce contralateral vasodilatation and cause a steal phenomenon.[8] Based on current evidence, normocarbia is the best policy. It is certainly appropriate to administer supplemental oxygen to the patient, and it has been suggested that in some cases this may be sufficient to reverse the cerebral ischaemia.[97]

Cardiovascular management

The majority of patients presenting for CEA suffer from hypertension. A systematic review of 36 studies by Rothwell and colleagues[82] found a significant association between a preoperative systolic blood pressure or >180 mm Hg and postoperative stroke or death. Wong and colleagues found a significant association between a postoperative systolic blood pressure >220 mm Hg and postoperative stroke or death. A preoperative systolic blood pressure of >160 mm Hg was also a risk factor for postoperative hypertension.[109] It would seem to be wise to control marked hypertension before surgery, where possible, for example systolic blood pressures that are consistently above 180 mm Hg of mercury. However, while cerebral autoregulation can be expected to adjust to the lower arterial pressure, the time course of this adaptation is unclear.[98] If the patient is subjected to anaesthesia and surgery before the cerebral circulation has adapted to the new arterial pressure, there could be an increased risk of stroke. The greatest benefit is seen from CEA if the operation is performed soon after presentation.[81] There are also concerns that lowering the arterial pressure in patients with bilateral carotid stenosis may compromise cerebral perfusion. Although an association between poorly controlled arterial pressure and stroke has been demonstrated, no study has demonstrated that reducing the arterial pressure does indeed reduce operative risk. At present the best advice that can be offered is that it is reasonable to take the time to achieve good control of the arterial pressure in patients who have a preoperative systolic blood pressure consistently above 180 mm Hg, who do not have severe bilateral disease, and are not having frequent neurological events. It is probably appropriate to proceed to surgery even in the presence of marked hypertension in the patient who has severe bilateral disease and is having frequent TIAs. This is an area where further research is needed.

By the very nature of their carotid disease, patients presenting for CEA are arteriopaths and are likely to have extensive atheromatous disease. The patient presenting for CEA is at significant risk of perioperative myocardial ischaemia and infarction. Anaesthesia should be conducted carefully with a view to haemodynamic stability. Direct arterial pressure and five-lead ECG monitoring should be used and two ECG leads (usually II and V5) should be displayed. Automated ST-segment analysis should be used if available.

Haemodynamic changes

Cardiovascular lability in hypertensive patients undergoing anaesthesia and surgery is a well-documented problem. These patients are prone to episodes of hypotension and hypertension in the intraoperative period.[13 24] These problems are especially marked in patient undergoing CEA. Carotid cross-clamping is frequently associated with a marked increase in arterial pressure. CEA combines the haemodynamic effects of anaesthesia with those of surgical manipulation of the carotid bifurcation. Rerkasem and colleagues[78] identified four studies that compared the haemodynamic changes seen in patients undergoing CEA under regional and general anaesthesia. In all four trials, arterial pressure decreased in the GA group after induction of anaesthesia. Three of the four trials found an increase in arterial pressure in the local anaesthesia group on

carotid cross-clamping. In the fourth study, by McCarthy and colleagues,[60] pre-clamp mean arterial pressure was significantly lower in GA patients than LA patients but post-clamp mean arterial pressure did not differ from pre-clamp pressure in either group.

Both postoperative hypertension and hypotension are common after CEA. O'Conner and Tuman[71] suggested that hypertension is seen in 25–58% of patients after endarterectomy and hypotension in 8–10% of patients. However, the frequency of such cardiovascular perturbations is difficult to quantify because different studies use different definitions of hypotension and hypertension and studies frequently report the number of episodes of hypo- or hypertension rather than the numbers of patients with each condition.[78] It has been suggested that postoperative hypertension is more common after eversion endarterectomy.[63]

Postoperative hypertension can plausibly be explained by a reduction in sensitivity of the carotid baroreceptor reflex although a small study conducted by Yakhou and colleagues[110] that included 10 patients undergoing CEA showed no change in the carotid baroreflex response after CEA. In contrast, a spectral analysis study of the impact of CEA on arterial pressure control in a group of 60 patients suggested that surgery is associated with an acute deterioration in carotid baroreflex sensitivity.[93] The same group was able to confirm this finding in a further study in a group of 80 patients. This study compared patients with unilateral and bilateral carotid artery disease.[70] Baroreflex sensitivity was reduced after surgery, presumably because of the mechanical injury caused by surgery. Patients with bilateral disease had a more marked response to direct stimulation of the carotid sinus than those with unilateral disease and this was attributed to sensitization of the baroreflex response to compensate for the dysfunction of the contralateral side. After surgery, patients with bilateral disease had a more marked deterioration in baroreflex function. A study by Timmers and colleagues[105] suggests that this baroreflex dysfunction persists after surgery.

In the patient with postoperative hypotension, the anaesthetist may feel caught between the head and the heart. On one hand, the low systolic and mean arterial pressure may compromise myocardial perfusion and indeed predispose to internal carotid artery thrombosis. On the other, raising the arterial pressure across a carotid artery which is now no longer partially occluded by a stenosis may lead to excessive increases in cerebral perfusion. The conventional treatment in this setting is to render the patient normotensive with the use of fluids and vasopressors. It seems reasonable to suggest that transcranial Doppler monitoring should be used if available to monitor MCAv in patients who are given vasopressors for postoperative hypotension, especially patients who had severe bilateral stenosis or marked hypertension before surgery and so may be prone to hyperperfusion.

In patients with marked hypertension, the appropriate clinical course of action is more clear cut, there is a concern that marked hypertension may injure both the heart by inducing myocardial ischaemia and the head by causing cerebral hyperperfusion, and arterial pressure reduction is appropriate. The particular agent to be used can be at the discretion of the clinician. Unusually, for neurological practice this is a setting in which the use of vasodilators may be appropriate.

Anticoagulation and antiplatelet management

Current recommendations are that all patients with carotid artery disease should be on between 75 and 325 ml of aspirin on a regular basis. Aspirin should be continued through the perioperative period. There are currently insufficient data to give robust recommendations with regard to other antiplatelet agents in the perioperative setting.[11]

Heparin is administered in the intraoperative period before cross-clamping to reduce the risk of thromboembolic complications. A fixed dose of heparin may be given, often 5000 units, or dosing may be weight-based. A fixed dose regimen is associated with a wide dose range per kilogram of body weight and with a wide variation in the intraoperative activated clotting times (ACT). A study of fixed dosing with 5000 units of heparin found an association between neck haematoma and intraoperative ACT, but the only neck haematoma that required reoperation occurred in a patient with an ACT of more than 400 s. Although performance on neuropsychometric tests did not appear to be statistically influenced by heparin dosing or the degree of ACT elevation, there was a trend for deficits to be associated with lower heparin doses. The authors concluded that weight-based heparin dosing may reduce the incidence of complications such as haematoma formation or decline on neuropsychometric tests and may result in more predictable ACT values, but no statistically compelling clinical advantage could be demonstrated. On the basis of these findings they suggested that either weight-based or fixed dosing is acceptable.[76] There is evidence that the antiplatelet action of aspirin is reduced during the intraoperative period after the administration of heparin and it has been suggested that this may account for some perioperative thromboembolic events.[107] Despite this, there is no evidence to support the use of high dose aspirin in the perioperative period. The ACE study found lower incidences of stroke, death, and myocardial infarction within 30 days and 3 months of surgery in patients taking 81 or 325 mg of aspirin than in those taking 650 or 1300 mg.[103]

It has been suggested that the use of protamine may be associated with an increased incidence of stroke.[21 54 58] These findings are based on a small number of events. However, protamine administration does appear to reduce wound drainage and the risk of haematoma. Two retrospective studies did not find an association between protamine administration and adverse outcome in CEA.[30 49]

Data from 2800 patients enrolled in the GALA study also support the safety of protamine (M.J. Gough, personal communication). It should be borne in mind that some patients presenting for CEA may subsequently be candidates for coronary artery by-pass grafting and therefore face a repeat exposure to protamine.

Cerebral blood flow and autoregulation

CEA is associated with an acute increase in cerebral blood flow and middle cerebral artery velocity as measured by transcranial Doppler. In a TCD study of symptomatic and asymptomatic patients undergoing CEA pulsatility index, cerebrovascular reactivity and flow acceleration were all lower in the symptomatic patients before surgery. After surgery there was an increase in flow velocity and an improvement in all TCD variables in both symptomatic and asymptomatic patients.[104]

Dynamic cerebral autoregulation is impaired in patients with carotid artery disease and improves after CEA.[77 108] Marked increases in middle cerebral artery velocity in association with increases in mean arterial pressure in symptomatic patients, have been taken as markers of disordered static autoregulation after surgery.[42 72] The immediate changes in static cerebral autoregulation after surgery are of direct relevance to the perioperative haemodynamic management of patients. On the one hand, if patients with poor cerebral autoregulation show little improvement immediately after surgery, the arterial pressure should not be allowed to rise unduly in the postoperative period. On the other, if autoregulation is intact, the arterial pressure should be controlled with a view to the needs of the coronary circulation. Further studies of the immediate changes in static autoregulation after surgery would be of value.

Hyperperfusion syndrome

Between 1 and 3% of patients develop very dramatic increases in cerebral blood flow with middle cerebral artery blood flow velocities more than 100% above the preoperative value. These patients develop the constellation of symptoms known as the hyperperfusion syndrome with ipsilateral headache, hypertension, seizures, and focal neurological deficits. If not treated properly it can result in cerebral oedema, intracerebral or subarachnoid haemorrhage, and death. Important risk factors for hyperperfusion syndrome include diminished cerebrovascular reserve, preoperative hypertension, recent ipsilateral non-haemorrhagic stroke, previous ischaemic cerebral infarction, surgery for a >90% ipsilateral carotid artery stenosis, intraoperative ischaemia or emboli, postoperative hypertension, and hyperperfusion lasting more than several hours after CEA.[106] The arterial pressure should be aggressively reduced and target arterial pressures lower than in other groups of patients with symptoms of cerebral oedema may be appropriate. Scozzafava and colleagues[90] recently described a systolic blood pressure target of between 90 and 140 mm Hg in this setting. It has been proposed that cerebral hyperperfusion occurs in those patients who were maximally vasodilated before surgery because their cerebral perfusion was limited by a tight carotid stenosis. Cerebral perfusion pressure is restored after surgery, but the cerebral vasculature remains paretic and they are unable to vasoconstrict.[85] There are certainly data to suggest an association between impaired carbon dioxide reactivity and an increased risk of stroke in the non-operative setting.[94] Although it is known that carbon dioxide reactivity improves in the months after surgery, further studies conducted in the immediate postoperative period would be of value.[84] An alternative explanation is that hyperperfusion represents a reperfusion syndrome. Karapanayiotides and colleagues[45] have described MRI findings that are consistent with this hypothesis.

Conclusion

CEA is a valuable operation which has a firm evidence base and can reduce the incidence of stroke in vulnerable patients. However, much work still remains to be done; the benefits of surgery in asymptomatic patients require further study. It remains unclear if general or local anaesthesia offer particular benefits in this setting and the results of the GALA study will shed light on this. Changes in cerebral vascular reactivity and autoregulation after surgery in the immediate postoperative period require further delineation as these may help to dictate perioperative haemodynamic management. The management of postoperative haemodynamic instability and hyperperfusion requires study, as the anaesthetist may be pulled between the conflicting haemodynamic needs of the head and the heart. The optimal management of the patients with severe hypertension presenting for urgent surgery remains unclear as does the best anaesthetic management of patients undergoing surgery after a very recent TIA. This is especially important if there is increasing evidence to support early surgery in patients with symptomatic carotid disease. CEA is a prophylactic operation which only yields benefit if the risks of surgery are less than the risks of medical management. The anaesthetist has an important role in controlling perioperative risk in CEA.

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