**Introduction**

There are about 800,000 strokes and 300,000 transient ischemic attacks each year in the United States; and, with an estimated 144,000 deaths each year, stroke is the third leading cause of death. With six million stroke survivors and an age-dependent prevalence of asymptomatic carotid artery disease as high as 7.5%,

Medical therapy for stroke is directed at prevention by correcting modifiable risk factors, and by utilizing antiplatelet/anticoagulant/fibrinolytic agents for patients whom have suffered cerebral ischemia of atherothrombotic origin. A stroke occurs due to occlusive or hemorrhagic conditions. Occlusive cerebrovascular disease can be thrombotic, embolic, or stenotic in origin. Performing an accurate history and physical examination should identify nearly all significant neurological symptoms.

Patients with a history of prior stroke or transient ischemic attack have an increased risk of recurrent perioperative stroke. Major symptoms of carotid artery disease include changes in vision, headache, changes in 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, increase in size and pulsation of the ipsilateral superficial temporal artery, and changes in the retinal examination. Confirmation of carotid artery disease is achieved by vascular imaging which may include ultrasound, MR angiography, or catheter angiography.

Presently, there is insufficient information to establish guidelines regarding the timing of surgery following an ischemic episode. Data suggests there is a small but real increase in morbidity if surgery is performed shortly after the onset of symptoms. Risk may be associated with the presence of a low density lesion on CT scan, vascular territory of the infarct, brain shift, and level of consciousness. One author has suggested that the stroke/death rate may be related to ASA physical class status if surgery is performed in the first three weeks following a stroke.

**Carotid Artery Revascularization**

Carotid endarterectomy (CEA) was introduced in 1954 as treatment for occlusive carotid artery disease. Efficacy data on CEA was limited until the 1990s. Analysis of three trials has demonstrated that CEA has a marginal benefit in symptomatic patients with 50%-69% stenosis of the carotid artery, and was of greatest benefit in patients with >70% stenosis. The ACAS trial demonstrated a marginal benefit for CEA in asymptomatic patients with >60% stenosis.

Stenting and angioplasty of the carotid artery (CAS) has been performed for almost two decades. Potential advantages of this technique include avoiding cranial nerve damage, wound hematoma, and general anesthesia. In addition, stenting and angioplasty is utilized for patients who present a technical surgical challenge (e.g., post radiation, restenosis after previous CEA, and surgically inaccessible lesions) or have severe cardiovascular disease. The anesthetic technique for this procedure involves minimal sedation and ACT management. This procedure can cause severe bradycardia and hypotension, and can result in cerebral hyperperfusion. Although the frequency of CAS has been increasing while CEA has been decreasing, it is unclear whether CAS offers an advantage over CEA (see Table 1, the recently reported CREST trial demonstrated non-inferiority of CAS as compared to CEA). There are approximately 140,000 carotid artery interventions performed each year. As anesthesiologists are infrequently involved in the care of CAS, the remainder of this handout will focus on managing the patient for CEA.

**Anatomic/Physiologic Considerations**

Carotid artery disease is typically the result of atherosclerosis at the bifurcation of the common carotid artery or the origin of the internal carotid artery. Ischemia is most often embolic in origin but may also have a hemodynamic basis. There are three phases of the response of various cerebral variables to progressive carotid artery disease (see Figure 1). During ischemia, collateral flow is a cornerstone of cerebral blood flow (CBF) compensation. The principal pathways of collateral flow are the Circle of Willis, extracranial anastomotic channels, and leptomeningeal communications that bridge "watershed" areas between major arteries. During CEA, the risk of Ischemia is related to the dependency of the cerebral circulation on the ipsilateral internal carotid artery, and the cerebrovascular reserve of the contralateral hemisphere.
Table 1 - stroke and death rate following comparative trials of CEA versus CAS. (*stroke, death and myocardial infarction)

<table>
<thead>
<tr>
<th>Study</th>
<th>CEA (%)</th>
<th>CAS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAVATAS-2001</td>
<td>9.9</td>
<td>10.0</td>
</tr>
<tr>
<td>SAPPHIRE-2004</td>
<td>8.4</td>
<td>5.5</td>
</tr>
<tr>
<td>CARESS-2005</td>
<td>3.6</td>
<td>2.1</td>
</tr>
<tr>
<td>SPACE-2006</td>
<td>6.3</td>
<td>6.8</td>
</tr>
<tr>
<td>EVA-3S-2006</td>
<td>3.9</td>
<td>9.6</td>
</tr>
<tr>
<td>ICSS-2010*</td>
<td>5.2</td>
<td>8.5</td>
</tr>
<tr>
<td>CREST-2010*</td>
<td>6.8</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Figure 1. Relative changes in CBV (cerebral blood volume), CBF, and OEF (oxygen extraction fraction) in relation to progressive hemodynamic changes in cerebral perfusion (phase I → phase II → phase III.)

Preoperative Concerns
CEA has an inherent risk of perioperative stroke and cardiovascular events. Approximately ¼ of strokes associated with CEA occur intraoperatively; and about ⅓ of these stroke are hemodynamic versus embolic in origin. In symptomatic patients, there is a 6.5% rate of stroke and death associated with CEA; while the reported stroke and death rate for patients with asymptomatic disease is 2.3%. The risk for stroke following CEA is most strongly associated with an active neurologic process prior to surgical intervention. Other factors which have been reported to increase neurological risk include:

- hemispheric versus retinal transient ischemic attack
- an urgent procedure
- a left sided procedure
- ipsilateral ischemic lesion on computerized tomography
- contralateral carotid occlusion or poor collaterals
- impaired consciousness
- an irregular or ulcerated ipsilateral plaque

In general, carotid artery disease should be considered a manifestation of systemic disease. Medical complications occur about 10% of the time after CEA and are associated with the following:

- Hypertension (HTN)-the incidence of a neurologic deficit is greater in patients with postoperative HTN, and the incidence of both postoperative hypotension and HTN is greater in patients who have uncontrolled HTN preoperatively. In a multicenter study, diastolic HTN (>110 mmHg) was found to be a predictor of adverse events. Although it seems reasonable that blood 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 blood pressure is >180/110 mmHg in a patient without anxiety or pain.
Cardiac-a cardiac assessment is indicated in patients who present for CEA. An ECG should be routine; and more advanced tests are often indicated.

Diabetes-data indicate that CEA can be performed safely in patients with diabetes.\textsuperscript{15,17}

Renal insufficiency-patients with renal insufficiency have an overall increased risk for stroke, death, and cardiac morbidity, associated with CEA.\textsuperscript{18}

Monitoring

Basic Monitoring-this should include basic ASA monitoring and intra-arterial blood pressure monitoring. In patients with poor ventricular function or myocardial ischemia more advanced monitoring may be considered.

CNS Monitoring-no special cerebral monitor is required in awake patients with regional anesthesia. When general anesthesia is employed, physiological considerations dictate that 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 a specific monitoring technique.\textsuperscript{19-22}

Electrophysiological Monitoring: The 16-channel EEG remains a sensitive indicator of inadequate cerebral perfusion. Intraoperative neurologic complications have been shown to correlate well with EEG changes indicative of ischemia.\textsuperscript{21,23} Ipsilateral or bilateral attenuation of high frequency amplitude or development of low frequency activity seen during carotid cross-clamping is indicative of inadequate cerebral perfusion. The computer-processed EEG and somatosensory evoked potential (SSEP) have also been found to be useful.

Most studies suggest that SSEPs are useful for monitoring cerebral perfusion during cross-clamping and has similar or superior sensitivity and specificity to conventional EEG.\textsuperscript{26-28} Stable anesthesia must be maintained to minimize the influence of anesthetics on the SSEP amplitude. In general, >50% reduction of amplitude of the cortical component is considered to be a significant indicator of inadequate cerebral perfusion. In contrast to conventional EEG, SSEP monitors the cortex as well as the subcortical pathways in the internal capsule, an area not reflected in the cortical EEG.

Measurement of Stump Pressure: Since one important determinant of CBF is perfusion pressure, it seems reasonable to assume that the distal arterial pressure in the ipsilateral hemisphere during carotid occlusion would provide some indication of collateral CBF. Stump pressure involves direct measurement of the retrograde internal carotid artery pressure following occlusion of the more proximal common and external carotid arteries. Stump pressures are neither sensitive nor specific. When stump pressure was compared to EEG monitoring, 6% of patients demonstrated ischemic EEG changes despite stump pressures in excess of 50 mmHg.\textsuperscript{29} On balance, extreme values (<25 mmHg or >60 mmHg) are useful indicators of the state of the cerebral circulation, but not intermediate values.\textsuperscript{30,31}

Transcranial Doppler (TCD): TCD\textsuperscript{32-40} has been utilized as a monitoring tool by measuring blood flow velocity in the middle cerebral artery during CEA. Ischemia is considered severe if mean velocity after clamping is 0-15% of preclamped value, mild if 16-40% and absent if > 40%.\textsuperscript{28} TCD has been shown to be beneficial not only for detection of intraoperative cerebral ischemia,\textsuperscript{32-35} but also in detecting malfunctioning shunts,\textsuperscript{36} and identifying high velocity states associated with hyperperfusion,\textsuperscript{37-39} as well as emboli detection.\textsuperscript{40-42} The frequency of emboli has been positively correlated with postoperative cognitive dysfunction.\textsuperscript{40,41}

Anesthetic Management

No compelling advantage has been demonstrated with any anesthetic regimen, and accordingly, a technique that optimizes brain perfusion, minimizes myocardial stress, and allows for a rapid recovery is recommended. General anesthesia is preferred in patients with anatomy/pathology that may make the surgical conditions difficult. One caveat that is often not appreciated regards 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 prior to the above events.

Sevoflurane and desflurane have been shown to result in quicker extubation times and recovery profiles after CEA, compared to isoflurane, with no significant perioperative difference in cardiac morbidity. Propofol and narcotics may be associated with better hemodynamic stability than isoflurane, and remifentanil/propofol may have less evidence of myocardial ischemia than isoflurane/fentanyl.\textsuperscript{43-45}
A regional technique for CEA requires anesthesia of cervical nerves 2-4. Superficial cervical plexus block, deep cervical plexus block, epidural anesthesia, straight local, and combinations of these techniques have all been used successfully. Until recently, non-randomized studies suggested that the use of a regional technique may be associated with reductions (approximately 50%) in the odds of stroke, death, myocardial infarction and pulmonary complications. However, in 2008, Lewis et al\textsuperscript{46} published the results of the GALA trial in which 3526 patients were randomized to undergo their CEA with either general or regional anesthesia. They observed no between groups difference in the incidence of stroke, myocardial infarction or death.

**Modalities of Cerebral Protection**

**Surgical:** a shunt is placed to maintain CBF during cross-clamping. Most often, placement of the shunt is dependent on the data of a cerebral monitor. A shunt entails the risks of embolization and carotid intimal dissection, and limits surgical exposure. There is insufficient evidence from randomized controlled trials to support or refute the use of routine or selective shunting during CEA.\textsuperscript{47}

**Physiologic:**

1. **Hypothermia:** much has been studied about the beneficial effect of mild hypothermia on cerebral ischemia. Although hypothermia has appeal for CEA, the therapeutic sequence of normothermia→hypothermia→normothermia is not a simple maneuver that one turns on or off. Accordingly, is the concern that if hypothermia is employed as a cerebral protectant for CEA, many patients may suffer from shivering during recovery, and a consequent increase in myocardial oxygen consumption which may precipitate myocardial ischemia. Thus, routine employment of hypothermia is not recommended for patients undergoing CEA. Conversely, hyperthermia should be avoided.

2. **Hyperglycemia:** should be avoided and treated when possible. This is accomplished by eliminating glucose-containing intravenous solutions, and by treating hyperglycemia with small doses of insulin. If hyperglycemia is present, a more severe neurologic injury results. This may be due to higher tissue lactate levels.

3. **Hypertension:** during ischemia, autoregulation is impaired and CBF is dependent on perfusion pressure. Augmenting arterial blood pressure should open collateral vessels, effecting an increase in flow to the area of ischemia. Hypertensive therapy has consistently decreased injury in animals; however, the clinical efficacy is not definitively established. Nevertheless, there is evidence of an ischemic blood pressure threshold in patients with stroke.\textsuperscript{48} i.e., above this threshold neurologic symptoms subsided, and below this threshold neurologic symptoms were manifest. Thus, it is advisable to maintain normal to high arterial pressure in most situations.

4. **Hemodilution:** using hemodilution to improve CBF is dependent upon the rationale that CBF is inversely related to hematocrit. Although the optimal hematocrit during cerebral ischemia seems to be about 30%, the clinical data are not compelling.

5. **Carbon Dioxide:** normocarbia should be the goal.

**Anesthetics:**\textsuperscript{43-45,49-55}

1. **Barbiturates:** as a whole, the evidence does not support the use of barbiturates as a cerebral protectant for permanent focal ischemia. However, during transient focal ischemia there is evidence to support barbiturate therapy. One point for barbiturates is just prior to carotid artery cross-clamping; however significant cardiovascular depression and delayed awakening can occur.

2. **Volatile Anesthetics:** general anesthesia with isoflurane and sevoflurane is associated with a lower critical CBF (that at which EEG evidence of ischemia was present) compared to halothane and enflurane.\textsuperscript{49,50}

3. **Etomidate:** because of its short duration of action, hemodynamic profile, and metabolic properties etomidate has been used during neurovascular procedures. However, there is evidence in animals that etomidate worsens ischemic injury while thiopental improves injury.\textsuperscript{52} Accordingly, etomidate is not recommended for use as a cerebral protectant.

4. **Propofol:** although many laboratory models have produced positive results, the amassed database is not as large as that for barbiturates.

5. **Dexmedetomidine:** early studies in animals suggest that dexmedetomidine is neuroprotective. Although controversial, it should be pointed out that in human volunteers dexmedetomidine decreases CBF but does not increase the incidence of shunt placement during awake CEA.\textsuperscript{53-55}
The Postoperative Period
The objective is a smooth and prompt emergence with optimal systemic and cerebral hemodynamics. Concerns in the immediate postoperative period include:

1. HTN—may occur as a result of damage or local anesthesia to the carotid sinus or its nerve and is profound in 20% of patients in the immediate recovery period. Patients who have systolic HTN are at greater risk of developing a neurologic deficit than those patients who remain normotensive. HTN may worsen neurologic outcome by exacerbating the hyperperfusion syndrome with resultant intracerebral hemorrhage.56

2. Hyperperfusion—is most likely to occur in patients with high grade carotid artery stenosis who develop >100% increase in CBF after CEA.56,57 Normotension should be maintained in patients at risk for hyperperfusion.

3. Hypotension—after the removal of atheromatous plaques, increased stimulation to baroreceptors may result in bradycardia and hypotension. Regional anesthesia may be associated with a higher incidence of postoperative hypotension while general anesthesia is more often associated with postoperative hypertension.

4. Myocardial Infarction—the most frequent cause of morbidity and mortality.

5. Stroke—most often embolic in origin.

6. Bleeding—airway obstruction has been attributed to neck hematoma that is worsened by hypertension. Soft tissue swelling with edematous supraglottic mucosal folds compromising the airway also occurs in patients after CEA.58,59

7. Cranial Nerve Injury—occurs in approximately 10% of patients.13 Damage to the recurrent laryngeal nerve may compromise protective reflexes as well as cause airway obstruction. Bilateral injuries can result in upper airway obstruction (beware in patients with preexisting neck surgery).

8. Carotid Body Damage—results in reduced ventilatory response to hypoxemia and hypercapnia. Patients undergoing second-side CEA merit close observation.

9. CNS Dysfunction—there appears to be an association with CEA, per se, and post-operative CNS dysfunction—without regard to the anesthetic regimen.60

Conclusions
Several multicenter, randomized, trials have validated the efficacy of CEA. Approximately one third of perioperative strokes are hemodynamic in nature. It is reasonable that tight physiologic management might affect this subset of patients. Most strokes however, are embolic in nature. Patients who have undergone CEA have increased risk of a perioperative myocardial event. There is no demonstrable advantage of a specific anesthetic technique for patients undergoing CEA. Whichever anesthetic technique is employed, it is imperative that CBF is optimized, there is minimal cardiac stress, and that anesthetic recovery is rapid. During the cross-clamp period, the risk of ischemia may be decreased by maintaining normal to high perfusion pressure. Additional concerns in the immediate postoperative period are tight hemodynamic control. The key points when managing a patient for CEA are summarized in Table 2.

Table 2—key points of anesthetic management of CEA.

**Indications**
In symptomatic patients, CEA is indicated if stenosis is >70 percent; and for selected patients if the stenosis is 50-69 percent. In asymptomatic patients, the indications are controversial.

**Preoperative Concerns**
Hypertension, coronary artery disease, diabetes mellitus, renal insufficiency, active neurologic process.

**Anesthetic Technique**
No proven advantage to a single technique. However, when using a general anesthetic technique nitrous oxide should be discontinued prior to shunt placement or reperfusion.

**Cerebral Monitoring**
Neurologic 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.

**Postoperative Concerns**
Hemodynamic stability, myocardial ischemia, neurologic status, hyperperfusion syndrome, wound hematoma, cranial nerve dysfunction.
References
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