Anesthetic Issues and Perioperative Blood Pressure Management in Patients Who Have Cerebrovascular Diseases Undergoing Surgical Procedures

W. Scott Jellish, MD, PhD
Department of Anesthesiology, Loyola University Medical Center, 2160 South First Avenue, Building 103–Room 3114, Maywood, IL 60153, USA

Perioperative assessment of patients with cerebrovascular disease

Cerebrovascular disease is the third leading cause of death in developed countries today. It also is associated with a higher risk of morbidity in patients who have cardiovascular disease, diabetes, and hypertension. Cerebrovascular disease is produced by pathologic processes that occur in blood vessels of the brain, which are caused from structural derangement (dissections or rupture), embolic events, diminished perfusion, stenosis, or increases in blood viscosity.

Patients who have cerebrovascular disease present a unique challenge for anesthesiologists involved in the surgical management of these patients. Not only must practitioners be concerned with physiologic changes that occur from surgery and plan an anesthetic to control for blood loss and cardiovascular stability, but also brain perfusion and protection from cerebral ischemia must be considered in the anesthesia assessment. Preoperative evaluation should address three key points: (1) Does the physical status of a patient increase the risk of mortality and morbidity during the operation? (2) What concurrent disease processes and medications influence the intraoperative and postoperative course? and (3) Which immediate medical actions would be beneficial to increase the chances of a successful outcome?

When anesthesiologists assess surgical risk, the fact-finding methods include adequate history, physical examination, and, finally, as directed by the history and physical examination, confirmatory laboratory tests. Particular attention should be focused on risk factors for atherosclerosis and
commonly encountered atherosclerotic diseases, such as coronary artery and peripheral vascular disease. Questions directed toward neurologic impairment, loss of vision, or changes in vision that could be suggestive of cerebrovascular insufficiency or embolic phenomenon must be ascertained.

Patients who have symptoms associated with vascular insufficiency or who come to an operating room with a history of stroke or transient ischemic attacks (TIAs) are at an even higher risk of intraoperative morbidity from the procedure. Besides a carotid etiology for TIAs, more than half of these patients could have emboli from cardiac origin, ulcerated lesions of the aortic arch, arteritis, hypercoagulable states, small vessel disease, or other nonvascular problems that cause reduced cerebral perfusion.

Vertebrobasilar disease, manifested by symptoms, such as dizziness, vertigo, ataxia, and drop attacks, must be confirmed by ruling out other causes, such as arrhythmias, intracranial tumors, and multiple sclerosis. Unlike carotid artery disease, whose symptoms primarily are the result of thromboembolism, vertebrobasilar insufficiency is believed caused mainly by inadequate blood flow to the distal vertebral and basilar arteries. Thus, anesthesiologists should pay close attention to the preoperative blood pressure to determine the range at which patients function and try to maintain that pressure within 10% of preoperative baseline to assure adequate cerebral perfusion throughout surgery.

Intraoperative concerns—physiologic parameters

Blood pressure control

Protecting the brain during surgery is a key consideration of anesthesiologists for patients who have known cerebral insufficiency. The type of surgery performed along with patients’ cardiovascular status are key concerns when considering neuroprotective strategies. One of the prime considerations is the maintenance of cerebral perfusion pressure (CPP) during the surgery. Deliberate augmentation of systemic arterial blood pressure may be an effective means of maintaining or improving blood flow [1]. In the intraoperative period it is used to increase collateral perfusion during temporary interruption of cerebral blood flow (CBF) with carotid endarterectomy or aneurysm surgery [2]. It also is used to treat cerebral vasospasm and maintain perfusion in patients who have suspected thromboembolic strokes or cerebral insufficiency [3,4]. Intraoperative deliberate hypertension carries some systemic risk. An important point is to determine how the blood pressure will be augmented. Intravascular volume may be increased with either colloids or crystalloids, or vascular resistance can be enhanced pharmacologically. The latter method probably is the most reliable, but vasopressors should be used only in patients whose cardiac status and left ventricular functions are maximized. The use of deliberate hypertension theoretically is sound. In the setting of an acute
reduction in CPP (hypotension, carotid clamping, vasospasm, and so forth), augmenting systemic arterial pressure provides a steeper pressure gradient across stenotic inflow channels and opens collateral pathways. It is believed that patients who have fluctuating deficits, proximal large vessel stenosis, occlusion, or a known diffusion/perfusion mismatch are most likely to respond to induced hypertension or at least maintenance of the preanesthetic blood pressure [5]. Trials using phenylephrine-induced hypertension in patients who have MRI diffusion deficits find improvement in outcomes after maintenance of blood pressure at elevated levels [6]. Adequate CPP must be maintained at approximately 60 mm Hg or higher in individuals who are chronically hypertensive and whose autoregulatory curve is right shifted (Fig. 1). Drummond, however, determined that the lower pressure limit for autoregulation is far from clear and may be much greater than the 50 to 60 mm Hg noted for normal patients [7]. In choosing the ideal CPP for patients who have known cerebrovascular insufficiency, it is perhaps best to maintain patients at their historical baseline or slightly above. If blood pressure intentionally is elevated above baseline with pressors, attention should be given to monitoring cardiovascular status, because many patients also are at risk for myocardial ischemia. Elevated blood pressure increases cardiac oxygen demand because of increased afterload and myocardial work. This manifests particularly in patients whose pressures are supplemented with phenylephrine while under inhalational general anesthesia. Smith and colleagues demonstrate echocardiographic wall motion abnormalities indicative of transmural ischemia in patients under deep general anesthesia whose blood pressure was supplemented with phenylephrine [8]. They believe that increased afterload and circulatory blood flow changes in the heart combine to produce transmural ischemia and do not recommend pharmacologic supplementation of blood pressure with this agent.

By contrast, hypotension is shown to be deleterious to ischemic patients or those who have symptoms of cerebral vascular insufficiency. Hypotension

![Fig. 1. Cerebrovascular autoregulation in healthy, chronic hypertension, and acute ischemia.](Fig_1.png)
can increase infarction volume and should be avoided in patients who have suffered a stroke. Hypotension also is demonstrated to be one of the most important contributors to poor outcome in patients who have sustained head injury.

Other cerebrovascular disease states also may benefit from augmentation of blood pressure during surgery. The effect of temporary arterial occlusion, during carotid endarterectomy, is minimized with blood pressure augmentation. This also is described for temporary carotid occlusion during skull base surgery [9]. Many investigators believe that moderate increases in systemic arterial blood pressure during carotid occlusion should be done on all patients. Others believe, however, that selective use of pressors, based on identification of cerebral ischemia using an electroencephalogram (EEG), may be better [10].

During ablation of cerebral aneurysms, a mild to moderate increase in blood pressure is recommended during temporary clip application, because it can increase collateral perfusion to affected areas through willisian channels, pial-to-pial collaterals, or leptomeningeal pathways and blunts the effects of the momentary drop in blood supply. The usefulness of increased perfusion pressure in these circumstances is dependent on the state of the blood vessels operated on, the patency of the circle of Willis, and the presence or absence of significant collateral circulation.

Finally, augmentation of blood pressure after aneurysm clipping is purported to be beneficial in preventing or reducing possible vasospasm. A good deal of information is available about the use of hypertension, along with hypervolemia and hemodilution, to control delayed cerebral ischemia from vasospasm [11,12]. Most anesthesiologists who are involved with cerebral aneurysm surgery are adept at increasing intravascular volume and raising blood pressure to reduce the risk of vasoplastic ischemia. The impact of such therapy, however, is controversial [13]. The timing of the induced hypertension is crucial in determining efficacy of treatment. Triple-H therapy is recommended, but this is based on uncontrolled studies that demonstrate deficit resolution and improved outcomes. Most controlled trials do not demonstrate efficacy and results are equivocal [14]. Regional CBF measurements do not always indicate a uniform increase during deliberate hypertension. Darby and coworkers observed increases in regional CBF not related directly to the degree of hypertension [15]. They also noted a decline in regional CBF in some vascular areas. Aggressive prophylactic hypertensive therapy and volume expansion have been recommended for many years in all patients who have aneurysms, even though the incidence of clinical vasospasm occurs only in 20% to 30% of patients who have aneurysmal bleeds [16]. Cardiovascular consequences of deliberate hypertension are well documented during vasospasm and a greater number of anesthesiologists believe that monitored volume expansion is safer than pharmacologic augmentation, which may be used to treat only the most symptomatic vasospasm.
Glucose control

Hyperglycemia is noted to be detrimental in the neurosurgical population, especially if there is a risk of intraoperative cerebral ischemia. In the normal brain that is perfused adequately, glucose is metabolized aerobically. During ischemic periods, which could occur with hypotension or with inadequate perfusion, glucose is metabolized via glycolysis, with lactic acid produced as a byproduct of metabolism. This acidosis could contribute to significant neuronal necrosis should perfusion remain low [17]. In long-term outcome studies, hyperglycemia is shown to be an independent predictor of poor outcome in patients who have focal ischemic injury [18].

In patients at risk for cerebral ischemia during surgery, treatment includes management of physiologic stress, avoidance of glucose-containing fluids, and treatment of hyperglycemia with volume expansion and insulin. Insulin benefits the brain during diminished perfusion by reducing glucose concentration. It also has a cerebroprotective effect that is glucose independent. Blood glucose concentrations should be maintained in the normoglycemic range as long as there is risk for cerebral ischemia. If an ischemic event occurs during surgery, blood glucose increases of as little as 40 mg/dL may result in worsened outcomes [19]. Thus, no patient should have persistent blood glucose concentrations in excess of 250 mg/dL. Efforts should also be made to avoid excessive hypoglycemia during tight control of blood glucose levels. The adverse effect of hypoglycemia on the brain has tempered an aggressive approach to the control of hyperglycemia. Recommendations for tight control of glucose for prevention of ischemic damage are between 80 and 110 mg/dL. The incidence of hypoglycemia with tight control is noted to be approximately 5%. Thus, more centers have opted to begin to control glucose levels with insulin/glucose infusions. Blood sugars are targeted between 100 and 180 mg/dL to reduce central nervous system (CNS) injury during surgery if cerebral ischemia occurs while safeguarding from the real risk of hypoglycemia should glucose levels fall during aggressive control.

Cerebrospinal fluid pH, CO₂ modulation, and oxygenation

Manipulation of arterial CO₂ tension is a potent means to affect CBF and cerebral blood volume. Hyperventilation often is used intraoperatively to produce brain relaxation and decrease intracranial hypertension. One concern about significant hypocapnia in patients who have ischemic intracranial disease is whether or not blood flow reduction enhances injury. Laboratory investigations show that hypocapnia can decrease CBF significantly in an ischemic brain [20]. Thus, during general anesthesia in patients who have a history of diminished brain perfusion, hyperventilation usually is avoided.

In patients who are acidic and those who have head trauma, reversal of cerebral lactic acidosis may be accomplished by the intravenous administration of sodium bicarbonate. Systemic alkalinization may improve brain pH,
nicotinamide adenine dinucleotide (NADH) redox state, and regional CBF. The intraoperative administration of alkalinizing agents may be a useful adjunct to enhance cerebral protection when there is a risk of ischemia [21].

Patients who have compromised cerebral circulation also are shown to have significantly lower tissue Po2 with increased Pco2 and decreased pH. This is because of decreased O2 delivery and CO2 clearance. Recent studies using a multiparameter sensor (Paratrend 7 Biomedical Sensor, High Wycombe, United Kingdom) demonstrate that tissue Pco2 increases above 60 mm Hg and pH decreases to less then 7.0 when Paco2 is below 20 mm Hg (Fig. 2) [22]. In patients who have a history of diminished cerebral perfusion, the use of 100% O2 during anesthesia is recognized as a method to avoid hypoxia and acidosis in brain tissue. Elevation of the inspired fraction of O2 (Fio2) results in higher tissue levels than expected of dissolved O2 in the blood [23]. In a small study in humans who have unruptured nonspastic cerebral aneurysms, hyperoxia caused only a limited increase in tissue oxygenation in regions distal to temporary vascular clips [24]. Even though normobaric hyperoxygenation is shown to be of limited efficacy in increasing O2 levels in the brain during treatment of focal ischemia, there is increasing support for its use.

Body temperature

Every anesthesiologist knows the supposed benefits of hypothermia for cerebral protection, especially if there is a risk of hypoperfusion or ischemia. The protection afforded by intraischemic mild hypothermia is attributed to the reduction in glutamate, glycine and dopamine release, inhibition of protein kinase C, and possible reduction in free radical triggered lipid peroxidation. This reduction in deleterious events and relative preservation of cellular function may be the result of the reduction in cerebral metabolism that retards and diminishes the primary synergists of the ischemic cascade. In the setting of focal ischemia, hypothermia reduces infarction size while hyperthermia increases infarction volume markedly. For every 1°C decrease

Fig. 2. Tissue Po2, Pco2, pH, and temperature sensor. A microporous polyethylene tube that is gas and ion permeable covers the sensor tip. The void between the active sensors is filled with acrylamide gel containing phenol red. The CO2 sensor includes a barrier, which is CO2 but not ion permeable. The oxygen sensor is a Clark electrode using silver wires. The pH and CO2 sensors contain fiberoptic elements.
in temperature, cerebral metabolism is reduced by 5% to 7%. Therefore, a reduction in temperature from 37°C to 34°C produces a 15% to 20% reduction in cerebral metabolism. Mild hypothermia is accomplished easily in a cold operating room and, provided that the surgery is long enough to promote active reheating, is neuroprotective in the setting of reduced CBF. Small studies of patients who have head trauma, cardiac arrest, and stroke suggest that neurologic deficits and mortality are reduced when mild to moderate hypothermia are used early after an insult. It seems reasonable that hypothermia, induced before the ischemic event, also reduces hypoxic brain injury. A recent pilot trial using intraoperative hypothermia (to 33°C) during neurovascular aneurysm surgery demonstrated that the use of mild hypothermia had no true beneficial affect on neurologic outcome [25]. In spite of the minimal benefit observed, its use in the operating room as a neuroprotectant still is advocated. Proponents argue that hypothermia is achieved easily in an operating room and is not accompanied by significant myocardial depression or arrhythmias. In addition, patients can be actively rewarmed once the risk of ischemia has subsided.

The data with regard to the application of mild hypothermia in survivors of cardiac arrest are even more positive. Induction of hypothermia to 32°C-34°C, after successful resuscitation from cardiac arrest, resulted in significantly better neurologic outcomes 6 months after arrest [26]. These studies demonstrate the clinical efficacy of hypothermia for purposes of reducing intraoperative ischemic injury and always should be a consideration in patients at risk for intraoperative cerebral injury. Temperature reduction in humans should be used with caution, because excessive decreases increase the likelihood of systemic side effects, such as cardiac dysfunction, coagulopathy, diminished cardiac output, and shivering.

Anesthetics as neuroprotectants

Anesthetic agents are known to reduce the brain’s requirement for energy. This reduction of cerebral metabolism coupled with suppression of seizures and sympathetic discharge provide strong support for these agents as neural protectants. In designing the anesthetic plan for patients at high risk for cerebral ischemia, it is useful to consider the relative degree of protection provided by various agents. Current investigation focuses on the effects of anesthetics on the pathophysiology of cerebral ischemia. There is general agreement that volatile agents, barbiturates, and propofol reduce ischemic neurologic injury after a short postischemic recovery period (Fig. 3).

Intravenous agents

Barbiturates are identified as the prototypic neuroprotective agent. They reduce electrical brain activity in a dose-dependant manner and preserve the concentration of adenosine 5-triphosphate. Studies demonstrate that in the
setting of global ischemia, such as cardiac arrest, barbiturates in high doses do not reduce ischemic injury [27]. They are found to be of value with focal ischemia that may be produced during episodes of diminished perfusion [28]. Thiopental loading is demonstrated to reduce postcardiopulmonary bypass neurologic deficits. In more controlled studies, where a temperature effect was negated, barbiturates provide some protection but not in proportion to their ability to suppress cerebral metabolic rate (CMR). Barbiturate-induced neuroprotection also may be attributed to the redistribution of blood that occurs to these peri-ischemic areas. Barbiturate neuroprotection also is attributed to sodium-channel and glutamate receptor blockade, inhibition of Ca$^{++}$ influx, reduced free radical formation, and potentiation of γ-aminobutyric acid (GABA)-ergic activity.

Propofol shares several properties with barbiturates. It can produce burst suppression of the EEG, reducing CMR and conserving ATP. Clinically, EEG burst suppression with propofol does not prove superior to sufentanil alone after open heart surgery as assessed by the incidence of postoperative neurocognitive dysfunction [29]. Propofol has a shorter half-life than thiopental, but it produces a similar degree of cardiovascular depression. Recent data from Bayona and colleagues suggest that propofol neuroprotection, like that of isoflurane, is not sustainable [30]. Laboratory evidence suggests, however, that in injuries that are mild, the neuroprotective efficacy of propofol is similar to that of volatile agents.

Etomidate is another anesthetic agent that frequently is used to induce anesthesia in patients who have hemodynamic compromise or impaired cerebral perfusion. The drug is not a potent vasodilator and does not have the cardiodepressant effects noted with some inhalational agents. Etomidate seems like the ideal neuroprotective drug. It reduces CMR, similar to
barbiturates, by 50% at EEG burst suppression and it is cleared rapidly from the blood. In moderate, incomplete global ischemia, etomidate is shown to delay loss of cerebral high-energy phosphates and accumulation of brain lactate [31]. Despite its ability to reduce CMR and ATP loss, it is noted to increase infarction size after experimental focal ischemia compared with isoflurane and thiopental. It is suggested that etomidate decreases microcirculation in tissue undergoing preinfarction depolarization by inhibition of nitric oxide synthetase [32]. Because of the present body of data, support for etomidate use during periods of intraoperative cerebral ischemia has diminished.

**Volatile anesthetics**

Inhalational anesthetics are another large group of drugs used routinely for anesthesia in patients at risk for cerebral ischemia. The main agents in use today, isoflurane, sevoflurane, and desflurane, can produce burst suppression at high dose. Isoflurane is shown to be neuroprotective in models of hemispheric focal and near complete ischemia. Sevoflurane and desflurane have similar properties. Studies demonstrate that this effect is short lived and neurons die of apoptosis. The precise mechanism by which volatile anesthetics reduce brain injury is not defined clearly. Many investigators have indicated that these agents can attenuate excitotoxicity by inhibiting glutamate release and postsynaptic receptor-mediated responses. Consistent with the neuroprotective role of isoflurane, intraoperative analysis of data from the Mayo Clinic indicates that isoflurane-anesthetized patients demonstrated fewer ischemic EEG changes during carotid surgery than patients anesthetized with enflurane [33]. All volatile agents vasodilate the brain while reducing EEG activity. Isoflurane has been used for many years as the anesthetic of choice for neurovascular procedures. Additionally, temporary aneurysm clipping under desflurane alters brain oxygenation less than with intravenous anesthesia, presumably because of improved collateral circulation.

Finally, other studies suggest the neuroprotective effect after isoflurane may not be long lasting because of a continued loss of neurons. This suggests that volatile anesthetics delay but do not prevent neuronal death. By delaying neuronal death, volatile agents increase the therapeutic window for the administration of other agents that have neuroprotective efficacy.

Other agents, used routinely by anesthesiologists, also can reduce neurologic injury with intraoperative ischemia. Opiates, such as fentanyl and benzodiazepines, are shown to reduce CMR and provide some aspect of peri-ischemic neural protection. Benzodiazepines decrease cerebral metabolism and blood flow by modulating postsynaptic responses to GABA and receptor-linked chloride channels. By increasing GABA receptor affinity, benzodiazepines are useful in reducing ischemic neuronal death. These agents and barbiturates are reported to have a similar efficacy after incomplete global ischemia but not after severe hypoxia [34]. Magnesium
administration is demonstrated to decrease the proportion of dead or disabled patients after stroke. The administration of magnesium after subarachnoid hemorrhage reduces the risk of delayed cerebral ischemia by 34% [35]. The mechanisms by which magnesium protects the brain include the reduction of presynaptic release of glutamate, blockade of N-methyl-D-aspartate (NMDA) receptors, smooth muscle relaxation improving perfusion, and blockade of calcium entry during ischemia.

**Intraoperative monitoring**

Patients who have cerebral vascular disease may be at an elevated risk for development of cerebral ischemia during surgery. Besides the obvious risks of ischemia associated with neurovascular procedures, such as carotid endarterectomy, cerebral aneurysm clipping, and arteriovenous malformation ablation, other surgical procedures also can produce cerebral ischemia if hypotension or a large amount of blood loss occurs with associated reduction in oxygen-carrying capacity and delivery. Close control of blood pressure is accomplished with the use of an indwelling arterial line where beat-to-beat perfusion pressure can be monitored. Cerebral perfusion also can be monitored by anesthesiologists with the use of intraoperative EEG. With the advent of computerized analysis of EEG activity by fast Fourier transform, conventional EEG epochs are separated into component sine and cosine signals, each having a calculated amplitude, frequency, and phase. This process results in a spectral display in which the power in pW of each component wave is plotted as a function of frequency [36]. Monitoring of computerized EEG before surgical manipulation provides a baseline that can be used to detect cortical ischemia and the need for shunting during carotid surgery [10]. EEG also is used to determine ischemic changes during cardiac surgery. A decline of more than 75% in total EEG power, from the postinduction baseline, predicts the development of new deficits. Bispectral index, a computerized transformation of EEG waveforms, recently has been noted also as an indicator of inadequate cerebral perfusion [37]. Typical EEG changes during cerebral ischemia are reported as a progressive slowing of the signal accompanied by a decrease in high-frequency activity and a generalized attenuation of voltage, resulting finally in isoelectricity. EEG slowing decreases the spectral edge frequency of the EEG, which correlates with a decreased BIS number. These same investigators found that a BIS value of less than 30 is an indication of EEG suppression and detects incidental ischemic brain insults [37].

Another monitor used for the detection of cerebral hypoperfusion during surgery is near-infrared cerebral oximetry (rSO₂). This technology is useful during open heart surgery, neurosurgical procedures and in patients who have head injury. Samra and colleagues [38] demonstrated that a change in rSO₂ after carotid cross clamping can be used as a trend monitor for the development of cerebral ischemia. It is not possible to specify an
absolute rSO₂ reading as the critical value below which cerebral ischemia develops. A decrease of greater than or equal to 20% from presurgical values has a high negative predictive value (if rSO₂ does not decrease, ischemia is unlikely), however, but a low positive predictive value for cerebral ischemia.

In conclusion, patients who have cerebrovascular disease and vascular insufficiency go to an operating room routinely for neurosurgical and non-neurosurgical procedures. The anesthetic priorities are to provide a still bloodless operative field while maintaining cardiovascular stability and normal renal function. Patients who have symptoms or a previous history of cerebrovascular disease are at increased risk of stroke, cerebral hypoperfusion, and intraoperative cerebral anoxia. The type of surgery performed, along with patients’ cardiovascular status, are key concerns when considering neuroprotective strategies. Optimization of patients’ current condition is important for a good outcome. This also includes optimization of patients’ cerebrovascular state and the ability to monitor neural function under anesthesia. Whether or not it is augmentation of blood pressure, tight glucose control, use of moderate hypothermia, or any combination of these therapies, the risks of each must be weighed against its perceived benefit in protecting neurons in the presence of perceived ischemia. Anesthetics themselves act as neuroprotectants and their use in conjunction with physiologic manipulations successfully can reduce neurologic injury caused from diminished perfusion and reduced oxygen delivery. The therapies listed above, coupled with the use of intraoperative neurophysiologic monitoring, which can function as a surrogate for identifying CNS ischemia, provide a mechanism to assure the safe and effective conduct of surgical care in patients in whom cerebral hypoperfusion is a real and significant risk.

References


[34] Siemkowicz E. Improvement of restitution from cerebral ischemia in hyperglycemic rats by pentobarbital or diazepam. Acta Neurol Scand 1980;61:368–76.


