Prevention of Ischemic Neurologic Injury With Intraoperative Monitoring of Selected Cardiovascular and Cerebrovascular Procedures: Roles of Electroencephalography, Somatosensory Evoked Potentials, Transcranial Doppler, and Near-Infrared Spectroscopy

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The United States Census estimates that there will be 40 million Americans ages 65 and older in 2010 [1]. The aging population undoubtedly will result in an increased occurrence of chronic diseases, such as cardiovascular (coronary and aortic) and cerebrovascular (carotid artery) diseases, which will lead to an increasing number of surgical and interventional procedures. The American Heart Association estimates that of 709,000 open-heart procedures performed in 2002, 515,000 were coronary artery bypass grafting (CABG) procedures [2]. Postoperative neurologic complications, including cerebral infarction and encephalopathy, occur in up to 15% of patients who undergo CABG surgery. In addition, neuropsychologic testing can document behavioral abnormalities in up to 70% of patients [3–11]. The risk of stroke after CABG can be predicted based on characteristics known before surgery [8,11–16]. Carotid endarterectomy (CEA) is the noncardiac vascular procedure performed most frequently, with 134,000 procedures performed...
in the United States in 2002. The complication rate after CEA should be maintained at an extremely low rate (between 5% and 6% for symptomatic and <3% for asymptomatic internal carotid artery [ICA] disease) by surgeons to maintain the beneficial effects of CEA over medical therapy [17]. The number of CEAs likely will increase because of aging of the population and the results of the Asymptomatic Carotid Atherosclerosis Study and the Asymptomatic Carotid Surgery Trial [17]. Neurologic injury is a significant problem during repairs of the ascending and transverse aortic arch repairs and during repairs of the acute type A aortic dissection [18,19]. For the acute type A aortic dissection, the incidence of focal neurologic injury ranges from 1% to 11% and is associated with increased early and late mortality [20–23]. In addition, postoperative confusion, agitation, or delirium, collectively known as temporary neurologic dysfunction, varies in incidence from 9% to 32% [24,25], with detrimental long-term consequences [26].

The occurrence of adverse neurologic outcomes after diverse cardiovascular and cerebrovascular procedures has fostered the development of methods to monitor the brain and cerebral circulation noninvasively in an attempt to identify electrophysiologic, hemodynamic, and other abnormalities that may be ameliorated by changes in operative technique or treatment. The ideal neuromonitoring system should provide continuous, real-time information about the cerebral circulation and cerebral function. Currently available functional neuromonitoring methods include electroencephalography (EEG) [27] and somatosensory evoked potentials (SSEP) [28], whereas circulatory/hemodynamic information can be provided by transcranial Doppler ultrasonography (TCD) [29,30] and near-infrared spectroscopy (NIRS) [30]. Each of these methods has advantages and disadvantages, and no one technique has perfect sensitivity, specificity, or discriminating value in a specific setting.

This article has two objectives. First, the capabilities of each noninvasive technique are described briefly. Second, data on the use of these techniques, often applied in combination, in the settings of CABG, CEA, and aortic surgery, are presented.

Noninvasive neuromonitoring methods

Electroencephalography

Cerebral ischemia produces neuronal dysfunction, leading to slowing of frequencies or reduced amplitude in the EEG tracing. These changes may be generalized (global ischemia) or regional (focal ischemia). The depth of ischemia is associated with the severity of EEG changes. EEG cannot assess the whole cerebral cortex, however, and is less reliable at assessing subcortical structures. In the setting of CEA, the focal EEG changes after cross clamping the carotid artery may be defined as none, mild (increase in theta waves <25% or decrease in amplitude >50%), moderate (increase of theta
waves >25% or increase of delta waves <25%), or severe (increase of delta waves >25%, severe flattening of amplitude or isoelectric curve). In patients who receive thiopental narcosis to induce burst suppression, only asymmetries between the hemispheres can be used [31].

**Somatosensory evoked responses**

Cerebral ischemia results in delay in the arrival of or reduction in amplitude of evoked responses, as measured by peak-peak amplitudes of the cervical potential N14-P18 and the primary cortical response N20-P25 from the postcentral region on the side that is operated on. Critical ischemia leading to cerebral hypoperfusion is assumed if the N20-P25 peak on the side operated on is not identifiable [32].

**Transcranial Doppler ultrasonography**

TCD uniquely measures local blood flow velocity (BFV) (speed and direction) in the proximal portions of large intracranial arteries [29], based on the assumption that the angle of insonation between the ultrasound beam and the direction of arterial flow is 0° to 30°. As long as fluctuations in arterial blood pressure and arterial CO₂ content are small, changes in flow velocity reflect changes in cerebral blood flow [33,34]. TCD monitoring of the middle cerebral artery (MCA) does not provide information about hemodynamic changes occurring in arteries that may serve as collateral pathways supplying ischemic brain. Hemodynamic compromise is inferred when there is reduction in mean flow velocities or when there is slow flow acceleration. In addition, TCD can detect cerebral microembolic signals, reflecting the presence of gaseous or particulate matter in the insonated cerebral artery. Particulate (solid or fat) or gaseous (gas or air) materials in flowing blood are larger and of different composition and, thus, have different acoustic impedance than surrounding red blood cells. The Doppler ultrasound beam, thus, is both reflected and scattered at the interface between the embolus and blood, resulting in an increased intensity of the received Doppler signal. Microembolic signals are detected in patients who have or do not have symptoms, in patients who have diverse cardiovascular or cerebrovascular diseases, and in patients undergoing a wide variety of surgical and interventional procedures. There often is considerable overlap of intensities and velocities corresponding to particles of different compositions and sizes. A completely accurate and reliable characterization of embolus size and composition, however, is not yet possible with current technology [29].

**Near-infrared spectroscopy**

In brain tissue, the venous oxygen saturation predominates (70%–80%), and cerebral oximetry relies on this fact. NIRS uses light optical spectroscopy in the near-infrared range to evaluate brain oxygen saturation by
measuring regional cerebral venous oxygen saturation (rCVOS) [30]. Assuming constant metabolism, the change of hemoglobin is directly proportional to the change of CBF. A reduction in rCVOS is believed to reflect the occurrence of cerebral ischemia. Clinical applications of cerebral oximetry have relied on relative changes expressed as percent deviation from baseline [30].

TCD can be used to localize the embolic source or monitor the effects of antithrombotic treatment in patients who have atherosclerotic cerebrovascular disease [35–39]. In patients who have high-grade carotid stenosis, sources of asymptomatic microembolic signals may include ulcerated plaques [40,41] and microscopic platelet aggregates and fibrin clots [42]. Asymptomatic cerebral microembolization is reported to be associated with an increased risk of further cerebral ischemia (odds ratio 8.10; 95% CI, 1.58–41.57) in this setting [40]. Recently, cessation of microembolic signal detection after institution or modification of antiplatelet but not anticoagulant therapy has been reported in patients who have arterioembolic cerebrovascular disease [40].

**Perioperative and periprocedural monitoring**

*Coronary artery bypass graft surgery*

During cardiopulmonary bypass (CPB), the brain is subjected to marked changes in systemic and cerebral hemodynamics, temperature, oxygenation, and hematocrit. Although the etiology and reversibility of neurologic injury after CABG are not understood completely, there is evidence that hypo- and hyperperfusion with consequent compromise of oxygen delivery and focal occlusion by microemboli or macroemboli may play a role [29,30].

TCD monitoring can show MCA BFV changes in all phases of the operation. Flow velocities decrease after induction of anesthesia and during initiation of CPB and increase during rewarming; changes correlate best with temperature and arterial CO₂ content [43,44]. Flow velocity changes typically remain within a relatively narrow range and do not correlate with neurologic complications [45]. During moderately hypothermic CPB, CO₂ reactivity generally is preserved, although impaired autoregulation can lead to dependence of MCA flow velocities on cerebral perfusion pressure [46]. Hypoperfusion and hyperperfusion are reported during the period of CPB [46–48]. The MCA BFV, typically in parallel with cerebral blood flow (CBF), typically decreases from a preoperative baseline after induction of anesthesia and during the first minutes of CPB [46,47]. Later in the procedure (after hypothermia is begun), hyperperfusion often is seen [44,48]. Given the lower metabolic demands of a hypothermic anesthetized brain, the presence of this dramatic increase in blood flow is suggestive of an uncoupling of flow and metabolism, excitotoxicity, or compensatory vasodilatation [48]. During rewarming, BFV is increased
to baseline levels or higher [47]. Rewarming increases CBF/CBFV to values similar to or even higher than CBFV levels during hypothermic anesthesia. Cerebral BFV changes correlate best with temperature and PaCO2 if vasoreactivity is intact [47]. The mechanism of these changes remains unclear. A sudden decrement in MCA CBFV on one side without change in blood pressure or other physiologic variables, however, may suggest a significant embolic event to the ipsilateral hemisphere [49]. There are no reports of correlations between changes in flow velocities or CO2 reactivity and neurologic outcome. There are no significant relationships between controllable intraoperative variables and in-hospital mortality [50], and there is no evidence that glucose concentration or minimum hematocrit is associated with major adverse events [51].

Macroemboli and microemboli may occur during CPB [52,53]. Cerebral microembolic signals of all types may be detected at all phases of the operation, especially during aortic cannulation, aortic cross-clamping, and clamp removal [54,55]. There is a significant correlation between the number of emboli detected by TCD and TEE [55]. Recent data suggest that distal aortic arch cannulation [56] or off-pump technique [57,58] may be associated with lower numbers of cerebral microemboli. TCD demonstration of the presence of microembolic signals led to the acceptance of membrane over bubble oxygenators during CPB [59,60]. More recent studies suggest that microemboli may occur most often during cardiopulmonary bypass [61], with greater numbers of microemboli associated with longer duration of CPB [62,63]. In this latter setting, neuropsychologic impairment may be associated with greater than 10 injections of air into the venous side of the CPB circuit by perfusionists [63,64]. Four other studies [54,60,65,66] suggest that high numbers of microembolic signals may be associated with postoperative neuropsychologic abnormalities. The level of the glial protein S100B, a marker of cerebral injury [67], is correlated with the number of microembolic signals during aortic cannulation and duration of CPB [68]. In addition, higher numbers of microembolic signals are observed in small numbers of patients who have stroke or who have longer lengths of hospital stay [69]. Quantification of subclinical embolic signals for more precise evaluation of embolic risk and delineation of an objective correlation between number of emboli and brain injury after CPB has not been done. Other data indicate, however, that the number of cerebral microemboli and changes in neuropsychologic function are not necessarily interrelated, suggesting that location of microemboli, systemic parameters, and other factors may be important [70]. Even though no comprehensible validated association between intraoperative emboli and perioperative stroke is reported, surgeons using TCD during CABG respond to the finding of emboli by applying preventive measures [71]. Anesthetic and surgical techniques slowly are modified in an attempt to reduce the numbers of emboli [64,71].

It has been shown that the trend changes in NIRS rCVOS seem to follow the changes in jugular bulb venous oxygen saturation (SjV̇O₂) in most
patients during CABG [72]. Low rCVOS values are believed to reflect the development of tissue hypoxia within susceptible regions of the cerebral cortex during the nonpulsatile perfusion of CPB. Rapid detection and correction of such episodes should help avoid regional hypoxia and attendant postoperative sequelae. Absolute saturation values are influenced by many variables, however, and normative values are not established. In addition, there is no “gold standard” technology with which NIRS can be compared.

Recent data suggest that low rCVOS values obtained during surgery are highly associated with postoperative frontal lobe dysfunction, cognitive declines, disorientation, and other clinical indices of prolonged recovery and extended postoperative length of stay (PLOS) [73,74]. A recent study evaluated the effect of intervention to improve rCVOS on postoperative outcome after CABG, where monitoring and maintaining rCVOS above 75% of baseline was associated with a decreased PLOS [74]. A recent prospective nonrandomized study [75] of consecutive high-risk patients undergoing CPB (monitored, n = 102, and nonmonitored, n = 43) was completed with monitoring of cerebral hemodynamics by TCD and NIRS. In this study, the majority of significant cerebral BFV and rCVOS changes were corrected by adjustment in perfusion and oxygenation directed toward maintaining BFV between 20 cm/s and 80 cm/s, and rCVOS remaining stable at baseline level or changes not exceeding 25% from baseline. There were no differences with respect to age, gender, risk factors across two groups or type of surgery, length of CPB, length of aortic cross-clamping, and so forth. There were significantly shorter POLS, however, in the hospital (8.5 days versus 14.2 days, \( P \leq .001 \)) and reduced percentage of postoperative neurologic complications (\( P \leq .001 \)) and renal dysfunction (\( P = .000 \)) among the monitored group than in the nonmonitored group. A more recent nonrandomized prospective study [76] in monitored (n = 256) versus nonmonitored (n = 410) patients using similar methods showed that monitored patients were significantly more likely to have prior CVA/TIA (32% versus 19%, \( P \leq .001 \)) and PVD (33% versus 25%, \( P \leq .02 \)) at baseline; less likely to suffer stroke (1% versus 4%, \( P \leq .01 \)), other neurologic complications, and postoperative renal failure; and more likely to have a shorter postoperative length of stay (5 days versus 6 days, \( P \leq .03 \)). These studies, however, were not randomized trials and also were limited by the absence of pre- and postoperative cognitive deficit evaluation.

Studies in much larger groups of patients are required to determine whether or not a prognostic relationship exists between alterations in cerebral oxygen saturation, adverse outcomes, and postoperative length of stay after CPBs. In addition, future randomized clinical trials will need to determine the most beneficial neuromonitoring techniques for decreasing the incidence of postoperative complications and shortening length of stay for patients who undergo CABG.
**Carotid endarterectomy**

The causes of stroke complicating CEA, both hemodynamic and embolic, recently have been reviewed [77,78]. The principal cause of stroke, particularly in the postoperative phase, is embolism from the operative site [78]. TCD monitoring of the ipsilateral MCA during CEA allows real-time monitoring of velocity changes in the basal cerebral arteries. Although a precise percent decrease in flow velocity from baseline or a velocity threshold that predisposes to cerebral ischemia has not been established, a large decrease in velocities intraoperatively is considered an indication for pharmacologic blood pressure augmentation, shunt placement, or repair of shunt kinking or thrombosis in the appropriate setting [79–81]. In addition, flow velocity changes during cross-clamping correlate with stump pressure measurements [79–81]. Reports of complementary intraoperative TCD monitoring in conjunction with EEG monitoring show that although there is high overlap between low MCA flow velocities and ipsilateral EEG slowing, neither technique alone may identify all candidates for shunting or prevent all strokes [82–85]. A recent meta-analysis of 3136 patients from 15 previous studies to examine the effect of SSEP’s monitoring on CEA outcome [86] suggests that SSEP changes are unreliable predictors of neurologic outcome and consequently provide unsuitable criteria for selective use of an intravascular shunt. TCD has the unique ability to detect microembolic signals that correspond to particulate matter or microbubbles. Hemodynamic changes after CEA include an improvement in MCA, ACA, and ophthalmic flow velocities; resolution of side-to-side MCA flow velocity asymmetries; and restoration of cerebrovascular reactivity to CO₂ or acetazolamide challenge [87–93]. Finally, increases in MCA flow velocities postoperatively to more than 150% of the preclamp values may identify the hyperperfusion syndrome and the risk of encephalopathy and intracerebral hemorrhage [94].

Not all ischemic events complicating CEA are accompanied by MCA velocity changes. The role of microembolic signals in the production of cerebral ischemia associated with CEA has been studied actively [78,95–107]. CEA monitoring with TCD can provide important feedback pertaining to hemodynamic and embolic events during and after surgery that may help surgeons take appropriate measures at all stages of the operation to reduce the risk of perioperative stroke. Microembolic signals occur most commonly during the dissection phase intraoperatively, during shunting and unclamping, during wound closure, and in the first few hours postoperatively [95–97,100,103,107]. The number of microembolic signals during dissection correlates best with new ischemic lesions seen on MRI [100] and postoperative cognitive deterioration [96]. The presence of more than 50 microembolic signals per hour during the early postoperative phase is reported to be predictive for the development of ipsilateral focal cerebral ischemia [98]. TCD-detected microembolic signals during dissection and wound closure, greater than 90% MCA velocity decrease at cross clamping and greater
than 100% pulsatility index increase at clamp release, are associated with intraoperative stroke [103]. In one report, a policy of quality control assessment (TCD monitoring and completion angioscopy) reduced the occurrence of intraoperative stroke substantially [104]. In another study [105], postoperative microembolic signals were significantly more common in women, patients not receiving antiplatelet therapy, and after left CEA.

Postoperative TCD monitoring may identify patients at risk for carotid thrombosis [96,98,102] or ipsilateral hemispheric ischemia who may benefit from variable dose intravenous dextran-40 therapy [99,107]. One recent study reports CEA with intraoperative TCD monitoring and completion angioscopy followed by 3 hours of TCD monitoring to guide selective dextran therapy in 500 consecutive patients at high risk of progressing to thrombotic stroke [108]. Overall, only 22 patients (4.4%) required dextran therapy. The rate of intraoperative stroke was 0.2% and no patient suffered a stroke as a result of postoperative carotid thrombosis. TCD also may be used to noninvasively monitor the effect of novel antiplatelet agents or antiplatelet regimens on the frequency of microembolic signals in symptomatic [109] or asymptomatic [110] patients preoperatively or in patients after CEA [111].

**Aortic arch surgery**

There are three main methods used for cerebral protection in aortic arch surgery: deep hypothermia (<20°C), total cerebral circulatory arrest (HCA), and selective brain perfusion (retrograde cerebral perfusion [RCP] or anterograde cerebral perfusion [ACP]) [30]. Deep levels of hypothermia and hypothermic circulatory arrest (HCA) are known to reduce the neurological injury associated with hypoxia. This protective mechanism is related to a decrease in metabolic rate in association with decreased temperatures and a simultaneous reduction in oxygen requirement by the neurons. RCP can provide blood flow and oxygen to the brain and may reduce ischemic damage. In addition, RCP can cool the brain homogeneously and maintain a low cerebral temperature. Recently, regional low-flow cerebral perfusion (RLFP) has gained increasing use as a perfusion technique to avoid or limit deep HCA [112]. The superiority of one or the other method, however, still is a matter of controversy. Part of the problem in determining the usefulness of the different techniques is the difficulty in monitoring CBF and metabolism in the operating room.

Inclusion of TCD as a continuous monitoring tool potentially is of great value because cerebral hypoperfusion and hyperperfusion are suggested as possible etiologic factors in brain injury during aortic arch surgery. The measurement of MCA BFV with TCD is practicable during ACP, RCP, and RLFP. Changes in MCA BFV are shown to help in evaluating cerebral perfusion and maintaining an adequate cerebral perfusion during CPB or hypothermic circulatory arrest with or without retrograde brain perfusion [18,19,73,112–118]. An experimental study [116]
shows that during HCA, RCP provides sustained retrograde blood flow in the MCA comparable to CPB. TCD also can provide optimal RCP with individual settings of pump flow [18] and may detect malperfusion and prompt corrective measures [19]. More specifically, MCA BFV adds valuable information to cerebral oxygen saturation data in guiding bypass flow during RLFP and its most important use may be prevention of cerebral hyperperfusion during periods of high rCVOS values [114]. In addition, TCD can provide a quantitative description of embolic processes and their magnitude and course. Information on the presence of cerebral emboli is useful for individual patient management (for instance, repair of an air leak) and general improvement of perfusion technique [20,117,118].

Two recent studies have examined the role of RCP during profound HCA as an adjunct for cerebral protection for repairs of the ascending and transverse aortic arch. In one study [18], transcranial power M-mode Doppler ultrasound was used to monitor 40 ascending and transverse aortic arch repairs during RCP. Mean RCP time was 32.2 ± 13.8 minutes. Mean RCP pump flow and RCP peak pressure for identification of cerebral blood flow were 0.66 ± 0.11 L/min and 31.8 ± 9.7 mm Hg, respectively. Retrograde flow during RCP was detected in 97.5% of cases (39 of 40 patients) with a mean CBFV of 15.5 ± 12.3 cm/s. In the study group, 30-day mortality was 10.0% (4 of 40 patients). The incidence of stroke was 7.6% (3 of 40 patients); the incidence of temporary neurologic deficit was 35.0% (14 of 40 patients). Thus, transcranial power M-mode Doppler ultrasound can provide optimal RCP with individualized settings of pump flow. RCP with continuous monitoring with TCD may extend the “safe” time for HCA, allowing ample opportunity to perform complicated cardiac and aortic operations with reduced risk of adverse neurologic events. A more recent prospective nonrandomized study [19] used power M-mode TCD to monitor patients undergoing repairs of acute type A aortic dissection under profound HCA and RCP. Patients in whom TCD monitoring was used to monitor CBFV and modify operative technique during repair (study group, n = 28) were compared with those without monitoring and modification (control group, n = 28). Power M-mode TCD monitoring altered operative cannulation and guided RCP flow in 28.5% (8/28) and 78.6% (22/28) of cases, respectively. Two patients presented with preoperative stroke, one in each group. One operative death occurred in each group. In-hospital mortality and the occurrence of new stroke were not significantly different between the two groups. Temporary neurologic dysfunction occurred less often in monitored patients (14.8% versus 51.8%, *P* = .008). These promising data suggest that prospective randomized studies are needed to determine if dedicated use of TCD during RCP decreases the occurrence of permanent neurologic complications and in-hospital mortality in patients undergoing aortic arch operations.
Summary

All neuromonitoring techniques, although imperfect, provide useful information for monitoring cardiothoracic and carotid vascular operations. They may be viewed as providing complementary information, which may help surgical technique and, as a result, possibly improve clinical outcomes. As of this writing, the efficacy of TCD and NIRS monitoring during cardiothoracic and vascular surgery cannot be considered established. Well designed, prospective, adequately powered, double-blind, and randomized outcome studies are needed to determine the optimal neurologic monitoring modality (or modalities), in specific surgical settings.

References


