Cerebral monitoring to optimize outcomes after cardiac surgery

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Purpose of review
Although significant achievements have been made in the perioperative care of patients undergoing cardiac surgery, adverse cerebral outcomes remain an ongoing concern. Multiple approaches have been utilized to address neurologic complications, though definitive therapeutic strategies are lacking. This review focuses on the various cerebral monitoring options that can be used in cardiac surgery to improve perioperative outcomes.

Recent findings
Prevention of adverse outcomes has shown promise, and central to this is the identification of conditions, through cerebral monitoring, which may put the brain at risk. Multimodal cerebral monitoring utilizing hemodynamics, temperature, electroencephalography, and near-infrared spectroscopy techniques allow for the manipulation of perioperative conditions aimed at improving cerebral outcome.

Summary
The use of a comprehensive cerebral monitoring strategy can optimize cerebral outcomes after cardiac surgery.

Keywords
brain, cardiac surgery, cardiopulmonary bypass, monitoring, outcome

Introduction
Adverse cerebral outcomes remain a continued problem in patients undergoing cardiac surgery [1–3]. Efforts to improve outcome have been made on many fronts and continue to be modified based on the evolving concepts of etiology and pathophysiology [4]. The early detection of clinical scenarios that may predispose a patient to brain injury is important in order to preempt the conditions that may increase injury. Historically, the brain has been considered somewhat of a black box, permitting few ‘windows’ through which one can assess its overall well being. However, recent developments are now changing this concept, and, increasingly, one is now able to gain access to this most important organ. It is only through the development of an integrated and comprehensive monitoring strategy that preventive interventions can be instituted.

Evidence-based medicine is clearly a laudable goal in all aspects of the care that we provide to our patients. Unfortunately, the evidence needed to support what we do is more often lacking than it is available [5]. A striking example of this is the various monitoring systems that we utilize during the care of our patients. Even those monitors whose use has been, and continues to be, designated as a ‘standard of care’ have never been brought into practice with the levels of evidence demanded by other therapeutics. For example, one can argue that the use of pulse oximetry, a mainstay in our practice, should be questioned if there is no evidence that it prevents adverse events [6]. Beneficial evidence from randomized, controlled, prospective trials, despite its decades long use, does not exist [7]. However, this somewhat flawed line of thinking obviously needs to be tempered with what has been intuitively discovered through widespread routine experience. However, other more recently available monitors are being required to demonstrate more robust links to improved outcomes.

This review addresses the background and rationale for a comprehensive monitoring strategy aimed at optimizing cerebral (and other) outcomes after cardiac surgery. Cerebral monitoring has undergone, and continues to undergo, considerable evolution in the past 10 years or so, with an increasing number of options for us to improve overall cerebral well being during surgery. With numerous depth of anesthesia monitors, multichannel electroencephalography (EEG), evoked potentials, jugular venous bulb saturation, and cerebral oximeters, along with what we standardly use for hemodynamic and temperature monitoring, we are increasingly faced with decisions as to when and whom we should monitor, and with what, and for how long. Without more evidentiary data to provide us better guidance, we run the risk of relying disproportionately on case reports and opinion for
In addition to optimizing hemodynamic and temperature modulation through the use of optimally monitoring these parameters, numerous other devices have been used to monitor the brain during both cardiac and non-cardiac surgery. For the most part, none have become widely accepted and technologies such as multichannel EEG, evoked potentials, transcranial Doppler (TCD), and jugular bulb saturation monitoring have infrequently come into routine use because of either logistical and technical difficulties, associated costs, or the overall lack of data suggesting any efficacy in enhancing patient outcome.

Transcranial Doppler
TCD monitoring has been variably used during cardiac surgery, utilizing velocity to assess the adequacy of CBF. In addition, it can detect and quantify embolic phenomena in the blood transiting the middle cerebral artery. As a research tool, it has proven to be useful to demonstrate the relationship between these emboli and cerebral outcomes (principally neurocognitive). In addition, there are reports outlining the potential utility of using TCD to monitor the hemispheric symmetry of CBF. One of the difficulties in using this device is its inconsistency in acquiring an uninterrupted signal. Often, the temporal window, which allows ultrasound access to the middle cerebral artery, is technically difficult to locate in up to

Temperature monitoring
The effect of temperature on cerebral injury has been reviewed elsewhere [15,16]. The benefits of hypothermia are related to its effect on lowering cerebral metabolic rate, but, equally important, it has significant effects on the inhibition of excitatory neurotransmitter release as well as other protective cellular mechanisms [17]. Although mild-to-moderate hypothermia during CPB has not been shown to have a sustained benefit on postoperative neurologic outcome [18], there are data that outline the detrimental effect of hyperthermia in the perioperative period. For example, in the cardiac surgery population, maximum postoperative temperature has been associated with greater postoperative cognitive dysfunction at 6 weeks [15]. Modern strategies for perioperative temperature management are directed towards preventing cerebral hyperthermia and its physiologic consequences. Slower rewarming rates have been shown to be associated with a lower incidence of postoperative cognitive dysfunction compared with faster rewarming rates with lower peak and mean intraoperative temperatures [19]. This may be due to temperature gradients between the bypass circuit, various monitoring sites, and the brain, which are more significant during rapid changes in temperature. Nasopharyngeal temperature has been shown to underestimate jugular venous temperature during rewarming on CPB, possibly exposing the brain to hyperthermia if this temperature gradient is not considered [20]. Nasopharyngeal and tympanic temperatures have been shown to be reasonable surrogates for brain temperature [21,22]; however, the limitations of these sites in their underestimation of brain temperature (specifically during rewarming) must be recognized.

Hemodynamic monitoring
Fundamental monitors for cardiac surgery include invasive hemodynamic monitoring of blood pressure (BP) and central venous pressure (CVP). The cause of perioperative brain injury in the cardiac surgery population is, at least in part, secondary to cerebral embolism, but hypoperfusion and subsequent ischemia–reperfusion injury also play a role [1]. Hypotension, defined by an overall low cerebral perfusion pressure (CPP), can occur due to low mean arterial pressure (MAP) or an elevated CVP. Given the equation CPP = MAP – CVP, aberrations in both these parameters can independently occur during cardiac surgery. There has been a great deal of interest in exploring the role of global hypoperfusion (secondary to low CPP) during cardiopulmonary bypass (CPB) and its role in postoperative neurologic injury. Although the evidence is not consistent in the cardiac surgery literature [3,8,9], global cerebral hypoperfusion (from low MAP) during CPB is thought to play some role in postoperative neurologic dysfunction, especially in the high-risk patient population such as the elderly [10]. However, global hypoperfusion alone is unlikely to lead to poor postoperative neurologic outcomes, but, when combined with other factors, may represent an additive insult [9]. For example, low CPP may exacerbate embolic insults to the brain through impairment of microembolism clearance [1], and also through impairment of pressure-dependent collateral perfusion.

Although most commonly low CPP is secondary to hypotension during CPB, avoiding elevations in CVP is also of importance in maintaining CPP [11,12]. Critical increases in CVP can occur during Trendelenburg positioning, lifting and rotation of the heart to access the posterior circulation, as well as with venous cannulation aberrations. If not recognized, critical reductions in CPP can occur, despite otherwise adequate MAP [13]. Similarly, when considering CPP and its potential implications in perioperative neurologic injury, one must also consider cerebral autoregulation and the effect of BP on cerebral blood flow (CBF). The cardiac surgery population often has chronic hypertension and may have impaired (i.e. rightward shifted) cerebral autoregulation and thus require a higher MAP to maintain CBF [14].

direction, clearly an inferior option compared with more evidence-based methods.
25% of patients and the signal may be unreliable [23]. TCD has not undergone the rigorous evaluation needed to determine whether it can guide interventions to unequivocally contribute to improved cerebral outcomes. However, it is frequently used in cases of aortic arch surgery to detect interruptions in carotid blood flow that can occur due to the complexities of the variable anatomical surgical techniques used in this procedure. However, it has not undergone widespread adoption or evaluation, and, with other more reliable techniques available (such as cerebral oximetry), it cannot be recommended confidently for use in this setting.

**Bispectral index**

Although not directly related to improving neurologic outcome, the bispectral index (BIS) remains a mainstay of brain monitoring in cardiac surgery. However, considerable debate has recently emerged concerning the utility of BIS monitoring and its role in the prevention of intraoperative awareness. Until recently, the weight of the evidence suggested that patients at higher risk for intraoperative awareness (such as cardiac surgery) would benefit from the use of BIS. Although not considered as a standard of care, the best evidence for the use of BIS in cardiac surgery comes from Myles et al. [24] in their landmark trial, demonstrating that the use of the BIS monitor in patients at high risk for awareness (including patients undergoing cardiac surgery) had an 82% reduction in the relative risk of awareness when a BIS target of less than 60 was used to tailor the administration of anesthetics. However, more recently, Avidan et al. [25] have cast serious doubt on this relationship with their own provocative study in 2000 patients, in which there was no additional advantage conferred by the BIS versus the use of end-tidal agent (ETAG) monitoring alone. Their study had two confirmed cases of awareness in patients randomized to BIS versus two cases in the ETAG group.

Independent of its direct application to awareness, the information provided with BIS, when integrated with other sources of information (such as the ETAG), can be used to help balance the anesthetic requirements with vasoactive therapies. It can be invaluable in titrating the balance of very complex intraoperative hemodynamic and anesthetic goals. For example, in previous years, when a patient developed intraoperative hypertension, additional hypnotic anesthetic agents were usually administered (beyond what could be considered necessary for otherwise adequate levels of anesthesia) with the intent of trying to reduce the perceived light anesthetic state of the patient, and thus modulate the patient’s BP. In essence, the side effects (i.e., hypotension) of volatile anesthetics were used to treat a hypertensive state not related to wakefulness. However, with additional information provided by the BIS, it appears that the hemodynamic perturbations seen during cardiac surgery often can be aptly treated with targeted vasodilator, vasopressor, and/or β-blocker therapies if the patient has an otherwise adequate anesthetic depth.

Furthermore, recent studies have raised concern about potential neurotoxic effects of anesthetic agents, particularly in the developing brain, with experimental models demonstrating that exposure to clinically relevant doses of anesthetic agents can cause neuronal cell death and apoptosis [26]. Although limited human studies exist, a recent retrospective, population-based birth cohort study by Wilder et al. [27] was able to show that children who were repeatedly exposed to anesthesia prior to the age of 4 years had an increased risk of learning disability proportional to the cumulative duration of anesthetic exposure. Although this effect seems to be on the developing brain, one may hypothesize that other ‘at-risk’ neurons, such as in the elderly may also be more susceptible to anesthesia-induced toxicity. Using the BIS to titrate anesthetic agents may avoid unnecessary increases in anesthesia levels and possible neurotoxicity.

**Multichannel electroencephalography**

The use of multichannel EEG has been described for decades as a means to monitor for the occurrence of adverse cerebral events, and thus to guide potential interventions [28]. Whereas there are many interesting anecdotal case reports outlining the utility of this particular monitor in detecting and avoiding major intraoperative catastrophes [29], there are almost no prospective trials, and certainly none large enough, that have objectively demonstrated its utility. However, single-channel and/or multichannel EEG monitoring is increasingly being used in deep hypothermic circulatory arrest (DHCA) for aortic reconstructive surgery [30]. In this particular subset of cardiac surgical procedures, it can be used to help determine the endpoint of brain cooling (i.e., EEG isoelectricity). Although an argument can be made for the current use of single-channel EEG monitoring (i.e. the unprocessed BIS signal) [31], the single-channel limitations of this monitor make it far inferior to multichannel monitoring which may detect residual activity in brain regions not monitored by the BIS. That said, there is no objective evaluation of using EEG isoelectricity as opposed to time as targets for cooling as a means to optimize brain outcome after DHCA. This area once again highlights the overall lack of evidence-based guidance for brain monitoring.

**Cerebral oximetry**

Cerebral oximetry using near-infrared spectroscopy (NIRS) has been available for more than a decade. In much the same way that a pulse oximeter can determine
peripheral arterial saturation, cerebral oximetry can similarly determine the saturation of the cerebral tissue; in essence, a compilation of both venous and arterial blood within the brain. Using wavelengths of both visible and near-infrared light, the differential absorption of this light by oxygenated and deoxygenated species of hemoglobin determines the overall saturation of the blood (a balance of arterial and venous, in approximately a 1:3 ratio) present within brain tissue.

The rationale for using cerebral oximetry developed from multiple sources, one example of which was data based on the relationship between jugular bulb desaturation and clinical outcome [32]. However, the invasiveness of jugular bulb saturation and other logistical difficulties have limited its use, making a noninvasive option that can capture some of the same information highly desirable. Cerebral oximeter devices were first used to focus on brain injury after cardiac surgery. As there had been well described patterns of brain injury in this area since the advent of cardiac surgery, to have a monitor to determine when these injurious events occurred was clearly advantageous. What followed in the literature was a logical time course and pattern with observational and anecdotal case reports of the use of these devices. However, it was not for many years after the initial utilization of these commercial devices in randomized controlled trials, utilizing a monitor-based interventional strategy, that the true utility of this cerebral oximetry did become apparent. Although there is a growing experience in the pediatric population [33], the largest studies have centered on the adult population and will remain the focus of the remainder of this review.

One of the first of many observational studies published was by Yao et al. [34], who reported the relationship between the degree of cerebral desaturation and functional brain outcome. Specifically, they examined the integral accounting for the amount of time and degree of cerebral desaturation as compared with the postoperative mini-mental status examination (MMSE) and other indices of frontal lobe function. What these investigators demonstrated was that the more severe the desaturation that the patients experienced, the more impaired their cognitive function was. The observations of the utility of oximetry continued with numerous published case reports, thus establishing an overall clinical utility of this device. Partly because of its fast signal response time, it rapidly became a user-friendly (as compared with invasive jugular venous saturation and tedious TCD) monitor of cerebral perfusion, in particular being excellent at interrogating the symmetry of perfusion across the brain. Without doubt, numerous catastrophic intraoperative events were avoided by the use of this device by the early recognition of perfusion abnormalities in the brain [35]. However, it has only been relatively recently that randomized controlled data specifically defining the utility of cerebral oximetry have been published. Murkin et al. [36] published a trial of 200 patients in which an interventional strategy was utilized to maintain the cerebral saturation signals within 75% of their baseline reading. This interventional strategy was based upon optimizing both oxygen supply and utilization in the brain. For example, following establishment of the baseline reading (an initial step in utilizing cerebral oximetry), the investigators instituted an interventional algorithm if the patient’s saturation dropped 20% from their baseline. This intervention included ruling out mechanical causes such as cannula malplacement or jugular venous impingement due to head position, and followed with techniques to optimize oxygen supply to the brain. For example, if patients were hypopcapnic, $\text{paCO}_2$ was returned to a normal level. In addition, the MAP was increased modestly and, also, there were increases in $\text{FiO}_2$. If these parameters failed to return the saturation to normal, and if there was significant anemia, the patients were transfused to improve oxygen carrying capacity. If these efforts to improve oxygen delivery failed, additional methods to suppress cerebral oxygen metabolism were used including administration of additional propofol and modest cooling. This management strategy has been further elucidated by Denault et al. [37] (Fig. 1).

Although the study by Murkin et al. [36] was not powered to precisely examine neurologic outcome (i.e. stroke), the results did demonstrate a trend toward the stroke reduction in patients who had the interventional algorithm. However, what was unique about the study was that not only was there a trend toward an improvement in neurologic outcome but also that there was an improvement in an overall organ outcome as identified by a reduction in major organ morbidity. Indeed, this study [37] described that the use of these technologies may have come full circle from only examining brain perfusion (as a means to improve neurologic outcome) to the point of monitoring the brain to use it as an index organ for overall organ function. In essence, because of the brain’s close proximity to the skin’s surface and its ability to be monitored by these technologies, it may be a better way to monitor overall organ perfusion.

More recently, Slater et al. [38] have also studied the use of cerebral oximetry in cardiac surgery. In their study, 265 patients undergoing CPB were randomized either to a group blinded to cerebral oximetry or to a group unblinded, with the aforementioned interventions utilized if cerebral saturation ($\text{rSO}_2$) dropped below 20% of baseline. Neurocognitive testing was performed preoperatively, prior to hospital discharge, and at 3 months. Although the incidence of neurocognitive dysfunction
was not decreased in the treatment group (59 versus 61%), they did find an overall correlation between prolonged cerebral desaturation below 50% and an increased risk of neurocognitive decline. An rSO2 desaturation score was calculated as the length of time each patient’s rSO2 was less than 50%. An rSO2 score more than 3000-second less than 50% was seen in 33% of patients with postoperative cognitive decline compared with 20% of patients with no decline ($P = 0.024$). When multivariate analyses were performed, the reduction in cognitive decline in the intervention group [odds ratio (OR) 0.81, 95% confidence interval (CI) 0.46–1.43] was not statistically significant ($P = 0.47$). The authors suggest that the failure to see treatment effect may have been the result of poor compliance with the protocol when an intraoperative rSO2 desaturation was encountered. Although the study was not specifically powered to study length of hospital stay, they found a significant correlation between prolonged rSO2 desaturation and hospital stay greater than 6 days (OR 2.71, 95% CI 1.31–5.60, $P = 0.007$), which may also add to the data that cerebral oximetry may be a surrogate marker for overall end-organ perfusion/oxygenation.

**Conclusion**

There is a general paucity of evidence-based data guiding us on our choices of whom to monitor, with what, when, and for how long. This data void can be seen as either a gap and weakness in our knowledge or as an opportunity to redefine how and why we practice as we do. However, considering this background limitation, the weight of the evidence suggests that an integrated cerebral monitoring strategy utilizing hemodynamic, temperature, BIS, and NIRS can optimize cerebral outcome in cardiac surgery.

**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:

* of special interest
** of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 119).


Cardiovascular anesthesia


This is the most recent and second randomized controlled trial that corroborates previous work demonstrating a relationship between cerebral desaturation events and adverse cerebral (and/or) outcomes after cardiac surgery. Although inconsistencies in adherence to a specific intervention algorithm likely contributed to the failure in the NIRS group to have an overall better outcome compared with the control group, there was a consistent association between all-group cerebral desaturation and poor neurocognitive outcome.