The Use of Absolute Cerebral Oximetry in Cardiovascular Surgery

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Introduction

Cerebral oximetry, based on near infrared spectroscopy (NIRS) technology, provides information on the availability of oxygen in brain tissue at risk during numerous pathological conditions.[1] Cerebral oximetry measures local concentrations of hemoglobin (oxy- and deoxy-), and regional cerebral tissue oxygen saturation ($SctO_2$) at the microvascular level (arterioles, venules, and capillaries only).[2,3,4] As a result, cerebral oximetry $SctO_2$ is a mixed oxygen saturation parameter which has a value between arterial (SaO_2) and jugular venous oxygen saturation ($SjvO_2$) under normal physiological conditions, therefore $SaO_2 > SctO_2 > SjvO_2$. Complementary to the arterial oxygen saturation (SaO_2) measured by pulse oximetry, $SctO_2$ reflects regional cerebral metabolism and the balance of local cerebral oxygen supply/demand. The advantages of cerebral oximetry are: 1) It provides $SctO_2$ values continuously and non-invasively at the bedside;[5] 2) $SctO_2$ is a sensitive index of cerebral hypoxia and/or cerebral ischemia[6,7] which is one of the main causes of brain injury in clinical settings[8,9].

The FORE-SIGHT™ Cerebral Oximeter (CAS Medical Systems) is significantly different from cerebral oximeters currently on the market. The FORE-SIGHT monitor was developed with the support of a series of Small Business Innovation Research Grants from the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institute of Health (NIH).[10] It is the only absolute cerebral oximeter cleared by the FDA[11] based on accuracy. The FORE-SIGHT Cerebral Oximeter, with its ability to provide absolute measurement makes it possible to establish threshold values for $SctO_2$ that can be used to guide clinical interventions.

FORE-SIGHT Cerebral Oximeter determined cerebral tissue oxygen saturation, $SctO_2$, is defined as the ratio of concentrations of HbO_2 and $Hb + HbO_2$ in the brain tissue, thus $SctO_2 = 100\% * HbO_2 / (Hb + HbO_2)$. The value of $SctO_2$ reflects a proportional mix of arterial and venous blood that can be calibrated from arterial and internal jugular venous blood[12]. It is estimated that the NIRS cerebral oximeter interrogated brain tissue microvasculature is about 70% venous and 30% arterial during most physiological conditions in humans based on Positron Emission Tomography (PET) studies[13]. In validation studies, FORE-SIGHT cerebral oximeter determined $SctO_2$ showed a strong correlation with the reference $SctO_2$ over the spectrum of pulse oximeter determined arterial oxygen saturation SpO_2 values between 70 and 100% from 18 subjects.[14,15] The bias and precision (1 standard deviation) for the FORE-SIGHT Cerebral Oximeter $SctO_2$ compared to reference $SctO_2$ derived from co-oximetry of arterial and jugular bulb blood was 0.18 ± 3.7 (1SD). The FORE-SIGHT Cerebral Oximeter, with its ability to provide absolute measurement of cerebral tissue oxygen saturation $SctO_2$, overcomes the limitations of previous cerebral oximeters.[16] Particularly, clinically relevant $SctO_2$ threshold values can be established with the FORE-SIGHT Cerebral Oximeter for physicians to provide tailored patient management[17]. It is known that $SjvO_2$ has a normal lower limit at ~45% and the upper limit at 70%.[18,19] The FORE-SIGHT $SctO_2$ is about 10% higher than $SjvO_2$ consistently over a wide range of oxygen saturation values. Therefore, the absolute FORE-SIGHT Cerebral Oximeter lower safe $SctO_2$ threshold is about **55%.**

The Need for Bedside Cerebral Oximetry

Monitoring brain oxygenation is critical in providing information used to guide patient management in many clinical situations.[20,21] Currently, brain oxygenation can be measured invasively by jugular bulb oximetry $SjvO_2$ or brain tissue pO_2 sensor.[22,23] Benefits of $SjvO_2$ monitoring include: a) improved outcome in physiologic management of head injury patients (370,000 cases/year, in the US);[24,25,26] b) detection of critical events when brain oxygenation could be compromised during cardiac surgery (800,000 cases/year worldwide)[27], and neurosurgery.[28] In some institutions, $SjvO_2$ monitoring is routinely applied in surgery of the aorta[29], and in neuro intensive care units.[30] Therefore, a bedside cerebral oximeter that can provide non-invasive measurement of cerebral oxygenation is highly desirable.

Despite decline in overall mortality after coronary artery bypass grafting (CABG) and valvular surgery with cardiopulmonary bypass (CPB), the rates of cognitive dysfunction have not improved.[31] In some reports, most patients had subtle signs of impaired cognitive performance, with incidences ranging from 60 to 80%.[32] There are two different forms of brain injury that may occur after CABG or thoracic aorta surgery: neurological dysfunction (ND) and neurocognitive dysfunction (NCD). ND is defined as clinically evident focal or global neurological injury resulting in stroke, hypoxic encephalopathy, transient ischemic attack, or stupor. NCD is defined as postoperative confusion, agitation, delirium, prolonged obtundation, or transient Parkinsonism. NCD occurs more frequently, affecting 40% to 80% of CABG/aortic surgery patients, depending on the method of detection.[33] While it is easy to diagnose post-operative ND, NCD is more subtle, and needs to be evaluated with a full battery of neurocognitive testing administered by trained professionals. Recent reports based on accurate neurocognitive testing before and after surgery have suggested that NCD can no longer be considered a benign self-limiting condition, but rather a long-lasting neurocognitive insult capable of reducing quality of life by impairing memory and fine motor function.[34]

The etiology of brain injury following cardiac surgery is still not completely understood and somewhat controversial. Some of the possible mechanisms include diffuse microembolization, cerebral hypoperfusion, and metabolic factors; the incidence of injury seems to be higher when CPB duration exceeds 70 minutes, and when there is rapid rewarming, particularly in the older surgical population.[35] Regardless of the immediate cause, such persistent cognitive dysfunction likely results from brain ischemia during surgery, which may be a result of focal arterial embolism,[36] global hypo-perfusion of the brain,[37] or an interaction of the two.[38]

Strategies for preventing arterial embolism and brain hypo-perfusion differ. To avoid arterial embolism during CPB, arterial line filters, intraoperative imaging, and careful manipulation by the surgeon are essential. On the other hand, diffuse hypo-perfusion of the brain can be avoided only by very careful planning: <u>if something goes wrong, the only hope is early detection and immediate restoration of adequate perfusion before irreversible brain damage develops. For this purpose, sensitive, real-time monitoring of brain ischemia during such surgical procedures is needed.[39] At the present time cerebral oximetry is the only feasible technology that monitors cerebral hypoxia and/or cerebral ischemia noninvasively and continuously.</u>

Cerebral oximeters provide information that other bedside brain monitors, such as electroencephalography (EEG) and transcranial Doppler (TCD), cannot offer. Other modalities, such as positron emission tomography (PET), perfusion CT, and magnetic resonance imaging (MRI) can provide detailed “snap shot” information about cerebral oxygenation, but cannot be used at the bedside. Since cerebral oximetry can provide an immediate indication of cerebral blood flow changes, oxygenation changes, it could find a wide range of applications in operating rooms (OR), in recovery rooms, as well as in intensive care units (ICU). In all of these situations, cerebral oximetry can be used to monitor the safety and efficacy of treatment interventions.

Why Absolute Cerebral Oximetry

<u>Current trend only cerebral oximetry may be inadequate:</u>

Previous cerebral oximeters on the market measure cerebral oxygenation as a <u>trend only</u>.[40] Some studies suggest that operative technique can be modified based on application of trend-only cerebral oximetry. Since these monitors measure trends only, a baseline first has to be established and cerebral oximetry values need to be maintained at or near preoperative baseline.[41,42] Another approach is to keep the cerebral oxygen saturation at levels within 20-25% of the anesthesia pre-induction value.[43,44] However, studies have shown that <u>seventy five percent of patients</u> undergoing coronary bypass have a significant impairment in baseline regional cerebral perfusion (rCP).[45] Other studies also demonstrated that patients undergoing cardiovascular surgery have a high prevalence of cerebral vascular disease in varying degrees.[46] In addition, abnormal preoperative rCP was found to be a strong indicator for post surgical decline in neuropsychologic testing.[47] These findings suggest that it is difficult to define a "normal" pre-induction baseline value for the trend only cerebral oximetry. A percentage drop based on the unreliable baseline value is more questionable to serve as a threshold for clinical intervention. In fact, studies have confirmed that while a trend only cerebral oximeter can detect adverse brain oxygenation by measuring the change in $SctO_2$ from a baseline value, it cannot provide accurate and reliable normal and threshold values of cerebral tissue oxygen saturation.[48,49,50,51,52,53,54]

<u>Absolute cerebral oximetry is essential for tailored patient management:</u>
There is an increasing amount of evidence that has demonstrated the need for a tailored patient management protocol as current approaches for managing flow, arterial blood pressure, and pH during cardiac surgery are based on studies that included few elderly or high-risk patients and predated many other contemporary practices[55]. For example, watershed-distribution stroke happens more frequently in patients undergoing cardiac surgery than in general stroke population (over 40% versus 2-5%, respectively).[56,57,58] Gottesman et. al., reported that mechanism of watershed stroke after cardiac surgery may include an intraoperative drop in blood pressure from a patient's baseline.[59] This suggests that following the standard protocol to maintain an optimal range for blood pressure during cardiac surgery is insufficient for some patients. We believe that what is needed, is an online monitor to evaluate the effect of blood pressure level as well as blood pressure change on the brain. Our own studies suggest that the FORE-SIGHT Absolute Cerebral Oximeter could be used for this tailored patient management approach. Readings of cerebral tissue oxygen saturation $SctO_2$ indicated that maintaining mean arterial blood pressure at 50-60 mmHg during hypothermic CPB is tolerated by most patients, but this level seems to be inadequate for certain patients.

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