Cerebral Hypoxia in Severely Brain-Injured Patients Is Associated with Admission Glasgow Coma Scale Score, Computed Tomographic Severity, Cerebral Perfusion Pressure, and Survival

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Background: The purpose of this study was to determine the relationship of cerebral hypoxia with admission Glasgow Coma Scale (GCS) score, brain computed tomographic (CT) severity, cerebral perfusion pressure (CPP), and survival in patients with severe brain injury.

Methods: CPP and noninvasive transcranial oximetry (Sto$_2$) were recorded hourly for 6 days in patients with a GCS score ≤ 8 (3,722 observations). CT score was derived from midline shift (0/1) plus abnormal cisterns (0/1) plus subarachnoid hemorrhage (SAH) (0/1) (range, 0–3).

Results: Brain CT results were as follows: shift, 10 (56%); abnormal cisterns, 14 (78%); SAH, 9 (50%); epidural hematoma, 2 (11%); subdural hematoma, 11 (61%); and contusion, 17 (94%). The incidences of Sto$_2$ < 60 were: GCS score 3–4, 26.5%; GCS score 5–7, 12.4%; and GCS score 8, 2.8% (p < 0.0001); CT score 2/3, 26.4%; and CT score 0/1, 10.0% (p < 0.0001); nonsurvivors 36.1%; and survivors 16.3% (p < 0.0001). For incidence of CPP < 70, the results were as follows: Sto$_2$ < 60%, 33% of observations; Sto$_2$ ≥ 60%, 10% of observations (odds ratio, 4.3; p < 0.01). Despite CPP ≥ 70, Sto$_2$ < 60 incidence was 16% of observations.

Conclusion: Cerebral hypoxia is common, even with CPP ≥ 70, and is associated with GCS score, CT scan severity, and mortality. Cerebral hypoxia is related to cerebral hypoperfusion. Additional studies may prove that Sto$_2$ monitoring will enhance the treatment of severe brain injury.

Key Words: Cerebral hypoxia, Glasgow Coma Scale score, Cerebral perfusion pressure, Computed tomographic scan score, Traumatic brain injury.


The primary objective after severe traumatic brain injury (TBI) is to maintain cerebral oxygen delivery (cerebral blood flow, Sa$_{O_2}$, and hemoglobin) at a level that meets intracranial neural tissue oxidative needs. The primary strategy to attain this goal is to decrease episodes of intracranial hypertension and optimize cerebral perfusion pressure (CPP).1–3

While using similar treatment strategies, cerebral oxygen alterations have been demonstrated in numerous studies describing patients monitored with jugular venous oxygen saturation (SjVO$_2$)4–14 and brain tissue partial pressure of oxygen (PbtO$_2$).11,14–23 Several relationships between cerebral oxygen delivery, cerebral metabolic rate of oxygen (CMRO$_2$), and SjVO$_2$ or PbtO$_2$ have been described. A desirable relationship is when cerebral oxygen delivery is adequate to maintain CMRO$_2$ and meet tissue oxygen requirements. A modest decrease in cerebral oxygen delivery may cause a decrement in SjVO$_2$ or PbtO$_2$; however, oxygen extraction is increased and CMRO$_2$ is adequate (compensated cerebral hyperperfusion).7 Elevated cerebral oxygen delivery can cause an increase in the SjVO$_2$ or PbtO$_2$ (cerebral hyperemia/cerebral hyperoxia).9 A good outcome is likely when CMRO$_2$ is maintained. When CMRO$_2$ is decreased secondary to inadequate cerebral oxygen delivery, SjVO$_2$ or PbtO$_2$ is likely to be decreased and outcome worsened (cerebral ischemia/cerebral hypoxia).24,25 Intracranial hypertension, systemic hypotension, hyperventilation, anemia, and seizures have been linked to episodes of cerebral hypoxia.10,11,13,24 If CMRO$_2$ is diminished secondary to infarcted tissue or decreased unloading of oxygen from hemoglobin (decreased oxygen extraction/cerebral hyperoxia), SjVO$_2$ or PbtO$_2$ may be increased and a poor outcome is likely.9

Our previous pilot study used a noninvasive cerebral oximeter, the INVOS 4100 system (Somanetics Corporation, Troy, MI), to investigate transcranial oxygen saturation (Sto$_2$) in severe TBI patients.26 The pilot study demonstrated an association between the StO$_2$ values and other measures of oxygenation (CPP, arterial oxygen saturation, and hemoglobin). The primary objectives of the current study were to establish the relationships between StO$_2$ and admission Glas-
grew Coma Scale (GCS) score, brain computed tomographic (CT) scan severity, CPP, and survival. A significant association between \( \text{StO}_2 \) and these clinically important variables would suggest that cerebral oximetry provides relevant data. A secondary objective was to determine the incidence of cerebral hypoxia with CPP \( \geq 70 \).

**PATIENTS AND METHODS**

**Patient Characteristics**

Patients were considered for study entry if they had blunt traumatic brain injury, an initial GCS score \( \leq 8 \), a brain CT scan that demonstrated a hemorrhagic lesion, and an age between 18 and 65 years. The institutional review board for human investigations approved the study.

**Patient Monitoring**

Patient monitoring began when the intracranial pressure (ICP) device was inserted and study consent was obtained. Each hour, ICP and mean arterial blood pressure (MAP) were monitored and recorded by the nursing staff. \( \text{StO}_2 \) was measured with the INVOS 4100 system. Self-adhesive skin patches, which contain a near-infrared light-emitting diode and two photodiode detectors to measure returning scattered light intensities, were applied to the patient’s left and right forehead. The skin patches were connected to cables that communicated with a computer and a near-infrared light generator. Near-infrared light entering the cerebral cortex is absorbed or scattered, some of which is passed back through the surface near the entry point. The majority of the near-infrared light attenuation is caused by absorption by hemoglobin. Because hemoglobin and oxymyoglobin have unique absorption profiles, the computer can calculate a ratio between them. This information is converted to a digital format and oxymyoglobin saturation is derived from these values. The \( \text{StO}_2 \) is then displayed in real time on the computer screen. At the end of each hour, the nurse recorded the left and right \( \text{StO}_2 \) on the vital sign flow sheet.

**Patient Interventions**

Routine clinical targets included the following: isotonic fluid administration at maintenance rates; hemoglobin, \( > 10 \) g/dL; \( \text{SpO}_2, > 92\% \); \( \text{PaCO}_2, 35 \) to \( 42 \) mm Hg; MAP, \( 80 \) to \( 90 \) mm Hg; head-of-bed elevation, 15 to 30 degrees; eutemia; CPP \( \geq 70 \) mm Hg; euolema or mild hypervolema; cardiac index, \( \geq 3.0 \) L/min/m\(^2\); serum osmolality, \( \geq 290 \) mOsm/kg; and serum lactate, \( \leq 2.5 \) mmol/L. Primary interventions for patients with ICP \( > 20 \) mm Hg included the following: brain CT scan to detect surgical lesions and the need for craniotomy, sedation when MAP is \( \geq 85 \) mm Hg, cerebrospinal (CSF) drainage, neuromuscular blockade for motor hyperactivity uncontrolled by sedatives or sedative-induced hypotension, mannitol (if serum osmolality is \( < 320 \) mOsm/kg, or earlier if cerebral edema was present), diuretics (for hyperosmolar serum and/o hypervolema), and modest hyperventilation (\( \text{Paco}_2, 31 \)–34 mm Hg).

Secondary interventions for recalcitrant intracranial hypertension included the following: brain CT scan to detect surgical lesions that require a craniotomy, alpha-agonist (dopamine \( \geq 8 \) \( \mu \)g/kg/min), Neo-Synephrine, or Levophed) to elevate MAP to a supranormal level, hypothermia, aggressive hyperventilation, barbiturate coma, and decompressive craniectomy. Interventions for systemic arterial hypotension included the following: (1) obvious vasodilation (capillary nail bed hyperemia or decreased systemic vascular resistance index), afterload augmentation with an alpha-agonist, and discontinuation of sedatives; (2) for obvious hypovolemia (low central venous pressure or pulmonary artery occlusion pressure, low cardiac index, or fluid input much less than fluid output), fluid-bolus administration (250 mL of normal saline over 20 minutes), pitressin for diabetes insipidus, or red blood cells for hemoglobin \( < 10 \) g/dL; and (3) for impaired cardiac contractility (cardiac index \( < 3.5 \) L/min/m\(^2\), or increased lactate and pulmonary artery occlusion pressure \( > 15 \) mm Hg), inotropic support. When the cause was unclear, combinations of the above recommendations were used.

The intensivists and neurosurgeons ordered interventions on the basis of hourly ICP and CPP values. The hourly \( \text{StO}_2 \) values did not influence treatment strategies.

**Data Collection**

General information included patient age, gender, Injury Severity Score, intracranial CT scan results for the first 24 hours (epidural hematoma, subdural hematoma, cerebral contusion or hematoma, midline shift \( > 3 \) mm, abnormal mesencephalic cisterns, subarachnoid hemorrhage), brain Abbreviated Injury Scale (AIS) score, initial GCS score, need for craniotomy, ICP device (intraventricular or parenchymal), and mortality outcome. Attending radiologists, blinded to each patient’s condition, provided brain CT scan interpretations. Poor outcome has been associated with abnormal cisterns,\(^{27-29}\) subarachnoid hemorrhage,\(^{27,29,30}\) and midline shift.\(^{27,31}\) A score was computed from the brain CT scan obtained in the first 24 hours: midline shift \( > 3 \) mm (0/1) plus abnormal mesencephalic cisterns (0/1) plus subarachnoid hemorrhage (0/1) (range, 0–3).

The ICP, MAP, and \( \text{StO}_2 \) values were recorded hourly for each of the six study days. If the ICP device was removed before the sixth study day, data collection was terminated. Day and hour values represented the period of time that had elapsed since the date and time of each patient’s injury. Because patients had a \( \text{StO}_2 \) probe placed over the left and right forehead, two readings were obtained for each patient (left frontal lobe and right frontal lobe) at each day and hour postinjury. All \( \text{StO}_2 \) values were paired with the patient’s ICP and MAP for a given day and hour, postinjury. CPP was calculated from the MAP and ICP values. The degree of frontal lobe injury was recorded according to an arbitrary scale: 0, no edema and no hemorrhage; 1, hemorrhage much less than one third of the frontal lobe volume and only mild or absent edema; 2, hemorrhage one third to two thirds of the...
Table 1: Glasgow Outcome Scale Results and Hospital Stay

<table>
<thead>
<tr>
<th>Death</th>
<th>No.</th>
<th>%</th>
<th>LOS (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent vegetative state</td>
<td>3</td>
<td>16.7</td>
<td>8.0 ± 4.4</td>
</tr>
<tr>
<td>Severe disability</td>
<td>2</td>
<td>16.7</td>
<td>33.7 ± 6.5</td>
</tr>
<tr>
<td>Moderate disability</td>
<td>2</td>
<td>11.1</td>
<td>23.5 ± 7.8</td>
</tr>
<tr>
<td>Good recovery</td>
<td>8</td>
<td>44.4</td>
<td>22.0 ± 7.4</td>
</tr>
</tbody>
</table>

LOS, length of stay (admission to discharge).

frontal lobe volume or moderate to severe edema without any hemorrhage; and 3, hemorrhage greater than two thirds of the frontal lobe volume or moderate to severe edema with any degree of hemorrhage. Yes or no values were recorded for interventions at each hour of each postinjury day: sedation (midazolam, lorazepam, propofol, low-dose barbiturates, or morphine within the previous 2 hours), CSF drainage (≥5 mL in the past 1 hour), mannitol (given within the previous 2 hours), neuromuscular blockade, and alpha-agonist administration (dopamine [≥8 μg/kg/min], Neo-Synephrine, or Levophed).

Statistical Analysis

Data entry and preliminary data analysis were conducted using EpInfo version 6.1 (Centers for Disease Control and Prevention, Atlanta, GA). Data were exported from EpInfo into SAS for windows version 6.11 (SAS statistical software, Cary, NC) for statistical analysis. Measurements were reported as the mean ± SD. Group frequencies were compared with the χ² or Fisher’s exact test. Multivariate logistic regression analysis was used to evaluate the effect of independent variables (e.g., CPP and Stco₂) on dichotomous dependent variables (e.g., mortality, CPP < 70, CT score 0/1 vs. 2/3). Level of statistical significance was set at p < 0.05 for all tests.

RESULTS

The admission GCS score was 3 to 4 in 11 patients (61.1%), 5 to 7 in 5 patients (27.8%), and 8 in 2 patients (11.1%). The mean admission GCS score was 4.7 ± 2.0. The mechanism of injury was motor vehicular crash in 10 patients (55.6%), fall (≥ 20 ft) in 3 patients (16.7%), assault in 2 patients (11.1%), pedestrian struck in 2 patients (11.1%), and motorcycle crash in 1 patient (5.6%).

Brain CT abnormality was cerebral hemorrhage in 17 patients (94.4%), subdural hematoma in 11 patients (61.1%), epidural hematoma in 2 patients (11.1%), abnormal cisterns in 14 patients (77.8%), midline shift in 10 patients (55.6%), and subarachnoid hemorrhage in 9 patients (50.0%). The brain AIS score was 4.6 ± 0.5.

Fifteen patients (83.3%) were men and 3 patients (16.7%) were women, and the age was 34 ± 10 years. The Injury Severity Score was 35 ± 7. An intraventricular ICP device was inserted in 7 patients (38.9%) and a nonintraventricular ICP device was placed in 11 patients (61.1%). A craniotomy was performed in 10 patients (55.6%). Three patients (16.7%) died. The Glasgow Outcome Scale results and hospital days of stay are described in Table 1. The intensive care unit length of stay for the 15 survivors was 23 ± 8 days.

Cerebral oximetry signal detection was attempted in all 18 patients. Of the 36 attempts (left and right forehead), 33 (91.7%) were successful. Signal failure was caused by cable dysfunction in one patient and unilateral forehead swelling/hematoma in two patients. A total of 3,722 Stco₂ hourly values were recorded during the six study days: Stco₂ < 60, 20.2%; Stco₂ 60 to 74, 48.6%; and Stco₂ ≥ 75, 31.2%.

Intracranial hypertension (ICP ≥ 20), cerebral hypoperfusion (CPP < 70), and cerebral hypoxia (Stco₂ < 60) incidence increased as the admission GCS score decreased (Table 2). The admission GCS score was independently associated with Stco₂ and CPP (p = 0.0001). The brain CT score was 0 in two patients (11.1%), 1 in five patients (27.8%), 2 in five patients (27.8%), and 3 in six patients (33.3%). Intracranial hypertension (ICP ≥ 20), cerebral hypoperfusion (CPP < 70), and cerebral hypoxia (Stco₂ < 60) incidence increased with higher CT scores (Table 3). The CT score 2/3 rate was higher in the patients with a poor outcome (death or severe

Table 2: Incidence of Intracranial Hypertension, Cerebral Hypoperfusion, and Cerebral Hypoxia by Admission GCS Score

<table>
<thead>
<tr>
<th>GCS Score</th>
<th>Patients</th>
<th>Observations</th>
<th>ICP ≥ 20 (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>CPP &lt; 70 (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Stco₂ &lt; 60 (%)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>2</td>
<td>432</td>
<td>0.0</td>
<td>4.2</td>
<td>2.8</td>
</tr>
<tr>
<td>5–7</td>
<td>5</td>
<td>936</td>
<td>21.2</td>
<td>13.5</td>
<td>12.4</td>
</tr>
<tr>
<td>3–4</td>
<td>11</td>
<td>2,354</td>
<td>32.6</td>
<td>17.7</td>
<td>26.5</td>
</tr>
</tbody>
</table>

ICP, intracranial pressure; CPP, cerebral perfusion pressure; Stco₂, transcranial oxygen saturation; GCS, Glasgow Coma Scale.

* χ² = 217.7, p < 0.0001.  
* χ² = 59, p < 0.0001.  
* χ² = 175, p < 0.0001.
vegetative state, six of six (100.0%) when compared with those with a better outcome (severe disability to good recovery, 5 of 12 (42.7%); \( p = 0.038 \)). The CT score was independently related to Stc_{O2} and CPP \( (p = 0.0001) \). Intracranial hypertension \( (ICP \geq 20) \), cerebral hypoperfusion \( (CPP < 70) \), and cerebral hypoxia \( (Stc_{O2} < 60) \) incidence increased in the dying patients (Table 4). Mortality was independently associated with Stc_{O2}, CPP, and admission GCS score \( (p = 0.0001) \). Cerebral hypoxia \( (Stc_{O2} < 60) \) was associated with a decrease in cerebral perfusion (Table 5). The Stc_{O2} < 60 incidence decreased and the Stc_{O2} \geq 75 incidence increased with frontal lobe injury (Table 6). Multivariate logistic regression analysis indicated that Stc_{O2} < 60 was independently associated with CPP < 70, brain CT score 2/3, decreasing frontal lobe abnormality score, and death \( (p = 0.0001) \).

The 15 patients with bilateral sensors accounted for 93.5% of the observations (3,480 of 3,722). Of the 1,740 paired readings, the left and right frontal lobe Stc_{O2} values differed > 5 in 718 observations (41.3%) and differed > 10 in 349 observations (20.1%). The incidence of left and right frontal lobe Stc_{O2} difference > 5 was greater in the dying patients (63.5% [231 of 364 observations]) when compared with the survivors (35.4% [487 of 1,376 observations], \( p < 0.0001 \); odds ratio, 3.2). The incidence of left and right frontal lobe Stc_{O2} difference > 10 was also higher in the dying patients (33.5% [122 of 364 observations]) when compared with the survivors (16.5% [227 of 1,376 observations], \( p < 0.0001; OR, 2.6 \) (Fig. 1).

A CPP \geq 70 occurred in 3,161 (84.9%) of the observations. Cerebral hypoxia \( (Stc_{O2} < 60) \) was found in 501 (15.9%) of these values. In the observations with CPP \geq 70, cerebral hypoxia was associated with an increased incidence of intracranial hypertension and a greater need for CSF aspiration, mannitol administration, and alpha-agonist assistance (Table 7).

### Table 3: Incidence of Intracranial Hypertension, Cerebral Hypoperfusion, and Cerebral Hypoxia by CT Score

<table>
<thead>
<tr>
<th>Patients</th>
<th>Observations</th>
<th>ICP ( \geq 20 ) (%)</th>
<th>CPP &lt; 70 (%)</th>
<th>Stc_{O2} &lt; 60 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT score 0/1</td>
<td>7</td>
<td>1,403</td>
<td>14.1</td>
<td>7.5</td>
</tr>
<tr>
<td>CT score 2/3</td>
<td>11</td>
<td>2,319</td>
<td>33.1</td>
<td>19.7</td>
</tr>
</tbody>
</table>

ICP, intracranial pressure; CPP, cerebral perfusion pressure; Stc_{O2}, transcranial oxygen saturation; CT, computed tomographic; CT score derived from abnormal cisterns (0/1) + midline shift (0/1) + subarachnoid hemorrhage (0/1); OR, odds ratio.

a OR, 3.0; \( p < 0.0001 \).
b OR, 3.2; \( p < 0.0001 \).

d OR, 3.2; \( p < 0.0001 \).

### Table 4: Incidence of Intracranial Hypertension, Cerebral Hypoperfusion, and Cerebral Hypoxia by Survival Status

<table>
<thead>
<tr>
<th>Patients</th>
<th>Observations</th>
<th>ICP ( \geq 20 ) (%)</th>
<th>CPP &lt; 70 (%)</th>
<th>Stc_{O2} &lt; 60 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lived</td>
<td>15</td>
<td>2,991</td>
<td>22.2</td>
<td>8.8</td>
</tr>
<tr>
<td>Died</td>
<td>3</td>
<td>731</td>
<td>41.0</td>
<td>40.8</td>
</tr>
</tbody>
</table>

ICP, intracranial pressure; CPP, cerebral perfusion pressure; Stc_{O2}, transcranial oxygen saturation; OR, odds ratio.
a OR, 2.4; \( p < 0.0001 \).
b OR, 7.1; \( p < 0.0001 \).
c OR, 2.9; \( p < 0.0001 \).

d OR, 7.1; \( p < 0.0001 \).

e OR, 2.9; \( p < 0.0001 \).

### Table 5: Increase in Cerebral Hypoperfusion with Cerebral Hypoxia

<table>
<thead>
<tr>
<th>Observations</th>
<th>CPP &lt; 70 (%)</th>
<th>CPP &lt; 65 (%)</th>
<th>CPP &lt; 60 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stc_{O2} \geq 60</td>
<td>2,970</td>
<td>10.4</td>
<td>4.9</td>
</tr>
<tr>
<td>Stc_{O2} &lt; 60</td>
<td>752</td>
<td>33.4</td>
<td>23.3</td>
</tr>
</tbody>
</table>

CPP, cerebral perfusion pressure; Stc_{O2}, transcranial oxygen saturation; OR, odds ratio.
a OR, 4.3; \( p < 0.0001 \).
b OR, 5.9; \( p < 0.0001 \).
c OR, 6.2; \( p < 0.0001 \).

d OR, 4.3; \( p < 0.0001 \).

e OR, 5.9; \( p < 0.0001 \).

### Table 6: Stc_{O2} Increases with Frontal Lobe Injury

<table>
<thead>
<tr>
<th>Frontal Lobe Score</th>
<th>Observations</th>
<th>Stc_{O2} \leq 60 (%)</th>
<th>Stc_{O2} &gt; 75 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1,785</td>
<td>26.2</td>
<td>25.1</td>
</tr>
<tr>
<td>1</td>
<td>1,200</td>
<td>18.0</td>
<td>35.6</td>
</tr>
<tr>
<td>2</td>
<td>737</td>
<td>9.4</td>
<td>38.9</td>
</tr>
</tbody>
</table>

Stc_{O2}, transcranial oxygen saturation.
a \( \chi^2 = 123; p < 0.0001 \).
Stco₂ readings in our study, others have noted in studies of severe TBI patients differences between left and right SjvO₂. The association of asymmetry with death in our study also suggests that Stco₂ values reflect cerebral oxygenation. The clinically relevant level of Stco₂ < 60 found in our study is slightly higher than the critical levels described in severe TBI patients undergoing SjvO₂ monitoring: ≤ 55, < 55, and < 50. The slightly higher clinically significant saturation value in our study supports the notion that Stco₂ reflects intracranial mixed arteriovenous oxyhemoglobin saturation. The variation in Stco₂ levels according to the degree of frontal lobe injury in our study also suggests that the Stco₂ values reflect intracranial oxygenation. In another study of severe TBI patients, dynamic changes in Pbto₂ were reflected by changes in Stco₂. Sjco₂ and SjvO₂ have also been noted to change with the occurrence of cerebral events (hypoxemia, increased ICP, decreased CPP, and cerebral hyperemia). The above literature and study findings suggest that Stco₂ values reflect mixed arteriovenous intracranial oxygenation in severe TBI.

CPP does not represent all of the factors that affect tissue oxygenation after brain injury. Regional flow patterns, blood oxygen tension level, hemoglobin content, and brain cellular metabolism all impact the cellular oxidative process. A decrease in cerebral blood flow has been associated with decreasing cerebral oxygen levels. Several studies have shown an association of SjvO₂ with neurologic outcome. Cruz et al. showed a significant improved outcome in patients with severe TBI when treatment was based on SjvO₂ as well as CPP rather than on CPP alone. Clinical studies have shown a relationship between Pbto₂ and regional cerebral blood flow. Pbto₂ has been shown to correlate with mortality and Glasgow Outcome Scale score results. Investigators have described not uncommon technical limitations with the invasive cerebral oxygen devices, SjvO₂ and Pbto₂.

Stco₂ is a noninvasive method using near-infrared technology to measure cerebral oxyhemoglobin saturation. Near-infrared spectroscopy is a continuous method that has been used to monitor cerebral oxygenation in severe TBI. In our pilot study, we hypothesized that Stco₂ may detect cerebral tissue hypoxia and may be a useful noninvasive adjunct to CPP. Four patients with severe TBI, GCS score ≤ 8, were studied in which 1,037 observations of Stco₂ were...
recorded. There was a statistically significant correlation of SteO₂ with CPP and other clinically important variables. Kiening et al. reported a close correlation of CPP with both SjvO₂ and PftO₂ that we found to be similar to the SteO₂ versus CPP relationship identified in our pilot study. This suggests that the association of SteO₂ with CPP is similar to that of SjvO₂ and PftO₂.

The current study includes 18 patients (4 from the pilot study) with severe TBI. The brain AIS score was 4.6 ± 0.5, and craniotomies were performed on more than one half of the patients. Bilateral forehead sensors provided for 36 attempts (18 patients) at reading of the transcranial oxygen saturation over a 6-day period for a total of 3,722 observations. The sensors were effective in detecting cerebral oxygenation in 92% of the applications. A cable problem was detected in one patient. Two other patients had a unilateral forehead hematoma that impaired proper detection by the sensor, and no readings were displayed. This suggests that the sensors effectively detect a transcranial signal in the absence of barriers such as forehead hematoma or edema. Gopinath et al. made a similar observation when they detected the development of a frontal subdural hematoma when the transcranial oxygenation sensor signal was lost. We also had a recent similar experience in a patient not included in this study in which an extensive forehead scalp edema and a bilateral, large, frontal subdural hematoma prevented signal detection (Fig. 6).

An SteO₂ < 60 was mathematically derived from our pilot study to represent clinically discriminate cerebral hypoxia. In the current study, the incidence of SteO₂ < 60 increased as the admission GCS score decreased (Table 2). Zeuner et al. also demonstrated that cerebral hypoxia increased as the GCS score decreased. As expected, the lower GCS score correlates with a higher ICP and lower CPP in our study group, which was similarly observed by Cruz et al. The admission GCS score in our group was independently associated with SteO₂ < 60 and CPP. This observation is supportive of the conclusion made by Cruz et al. that brain oxygenation monitoring is an adjunct to CPP and not simply a confirmatory measurement.

We found that brain hypoxia (SteO₂ < 60) was greater in the patients with higher CT scores (Table 3). Our data also indicate that the CT score is related to intracranial hypertension and cerebral hypoperfusion. Other investigators have also shown that intracranial hypertension is associated with midline shift and abnormal cisterns. Furthermore, the CT score was associated with Glasgow Outcome Scale results. These findings suggest that our CT score may be a method of delineating severe brain injury patients at increased risk for intracranial hypertension, cerebral hypoperfusion, cerebral hypoxia, and poor neurologic outcome.

The data in this study clearly relate SteO₂ to survival (Table 4). Cerebral hypoxia has also been demonstrated to be associated with an increased risk for death in studies monitoring SjvO₂ and PftO₂. We also found that survival was independently associated with SteO₂ and CPP. This suggests that CPP and SteO₂ monitoring are complementary.

The current investigation showed that brain hypoxia (SteO₂ < 60) was associated with cerebral hypoperfusion (Table 5). Other studies have shown an association of brain hypoxia with increased ICP and decreased CPP. Cerebral hypoperfusion (CPP < 70) and cerebral hypoxia (SteO₂ < 60) were independently associated with decreased admission GCS score, CT score 2/3, and death. Accordingly, cerebral hypoxia is associated with cerebral hypoperfusion; however, brain hypoxia has a relationship with patient outcomes that is independent of cerebral hypoperfusion. This implies that cerebral oxygen and perfusion assessment may provide a more comprehensive data profile to optimize patient care.

SteO₂ increases with frontal lobe injury. This is in contradistinction to CPP < 70, CT score 2/3, and death, which are associated with a decrease in SteO₂. Other investigators have also described cerebral hyperoxia in severe TBI patients. Cerebral hyperoxia may be secondary to an increase in cerebral oxygen delivery or an impairment in cerebral oxygen extraction. Poor outcome has been related to cerebral hyperoxia, particularly when oxygen extraction and CMRO₂ are impaired. SteO₂ was found to be independently related to CPP < 70, CT score 2/3, death, and frontal lobe injury. These findings suggest that multisite cerebral oxygen monitoring may provide complementary data.

The patients with CPP ≥ 70 had an SteO₂ < 60 incidence of 16%. Oertel et al. and Diringer et al. also documented cerebral hypoxia in patients with CPP ≥ 70. Meixensberger concluded that cerebral blood flow may be insufficient despite CPP ≥ 70 in TBI patients. These observations suggest that the CPP does not account for all factors that determine whether the oxygen needs of the brain tissue are being met. On further review of the group of patients with hypoxia and acceptable CPP (SteO₂ < 60, and CPP ≥ 70), there was a higher incidence of intracranial hypertension (ICP ≥ 20, and ICP ≥ 25) (Table 7). Also, more therapeutic interventions were required to manage the intracranial hypertension in these patients. Intensivists and neurosurgeons ordered therapeutic interventions on the basis of ICP and CPP values. The hourly SteO₂ readings did not influence treatment strategies. These findings suggest that cerebral ischemia may exist when intracranial hypertension is present and aggressive measures are required to maintain CPP ≥ 70.

At the present time, the optimal anatomic site for cerebral oxygen sensor placement is uncertain. The frequent asymmetry between left and right SteO₂ in our study and similar findings with SjvO₂ by others imply that there are differences in regional blood flow or oxygen extraction. More specifically, other investigators have demonstrated regional variance in cerebral blood flow in patients with severe TBI. Regional diversity in cerebral oxygenation is likely related to the presence or absence of injured brain. Our study
demonstrated that cerebral oxygen values varied according to whether the sensor was placed near an injured or noninjured frontal lobe. \(PbO_2\) has been found to be significantly associated with cerebral blood flow.\(^{30,43}\) Valadka et al. placed the probe in injured brain and found a linear relationship, whereas Menzel et al. placed the probe in noninjured brain and found a nonlinear relationship. These findings also suggest that cerebral oxygenation may vary in injured or noninjured brain. There are implications that \(SjvO_2\), \(PbO_2\), and \(StcO_2\) may provide complementary information. \(SjvO_2\) may better assess global brain oxygenation but can miss regional ischemia.\(^{11}\) In a study where \(SjvO_2\) and \(PbO_2\) were simultaneously monitored, the two sensors had a sensitivity well less than 100% for detecting cerebral hypoxia; however, they were complementary in the comprehensive detection of hypoxia.\(^{11}\) Valadka et al. made two important conclusions while studying \(PbO_2\) monitoring.\(^{17}\) \(PbO_2\) near injured brain may be decreased; however, the rest of the brain may have adequate oxygenation. \(PbO_2\) in noninjured brain may be adequate, yet the injured brain may be ischemic. The above current study and literature findings suggest that cerebral oxygenation may need to be assessed in multiple regions to detect hypoxia and hyperoxia and determine the impact of treatment interventions on the injured and noninjured brain.

**CONCLUSION**

The cerebral oximeter is noninvasive and offers multisite data acquisition. The system application success rate is high. Cerebral hypoxia was a frequent event and was related to decreased admission GCS score, CT score 2/3, cerebral hypoperfusion, and death. \(StcO_2\) increased with frontal lobe injury. The associations of \(StcO_2\) with these clinically important outcomes and the common variance between left and right frontal lobe \(StcO_2\) suggest that the oximeter parallels intracranial oxygenation. The independent relationship of \(StcO_2\) with CPP and frontal lobe injury supports the need for multisite monitoring. The independent association of CPP < 70 and \(StcO_2\) < 60 with the admission GCS score, CT score, and death indicate that CPP and cerebral oxygen monitoring provide complementary data. Despite a CPP \(\geq\) 70, cerebral hypoxia was relatively common. This observation also suggests that cerebral oxygenation monitoring may be important. The association of the CT score with intracranial hypertension, cerebral hypoperfusion, cerebral hypoxia, and neurologic outcome implies that this score may be useful to risk-stratify severely brain-injured patients.

**REFERENCES**


Transcranial Oxygen Relationships in Severe Brain Injury


**DISCUSSION**

Dr. Alex B. Valadka (Houston, Texas): I'd like to thank Dr. Dunham for sending me a copy of his slides and his article well in advance of the meeting. I appreciate Dr. Dunham's conclusion that cerebral ischemia may occur even
when cerebral perfusion pressure seems to be adequate. I also strongly agree with the discussion of the importance of regional heterogeneity of cerebral metabolism. In other words, the brain is not a black box that behaves the same way throughout, and there may be important pockets of the brain that are in serious metabolic trouble when most of it appears to be normal.

However, even though I agree with some of these conclusions, remember that back in math class in school, we all learned that getting the right answer is not as important as the steps we use to arrive at that answer. So, along the same lines, I’d like to make a few suggestions about some of the assumptions and methodologies used in this study.

The first is that a CPP of 70 may be excessive for most patients with brain injury. It’s true that a CPP of 70 was recommended by the Brain Trauma Foundation, both in the original guidelines and in their first update, but this recommendation was only an option. The initial studies supporting it were only case series. Subsequently, studies that were conducted in a more scientific manner, including one authored by my colleague, Claudia Robertson, suggested that these management strategies seem to be associated with risks that outweigh any benefits. I’m told that the next update of the CPP chapter of the guidelines will recommend that CPP be maintained above 60 mm Hg, not 70, and that this recommendation will increase in strength from an option to a guideline.

My second suggestion about methodology is to use endpoints that are truly independent of each other. Because lower GCS scores, lower CPP values, and worse-looking CT scans often coexist in severely injured patients, it’s logical to expect lower cerebral oxygenation to be associated with each of these findings. Demonstrating a significant association between hypoxia and each of these parameters is like repeating the same analysis several times over.

Also, in terms of endpoints of studies of head-injured patients, the best studies use functional outcomes like Glasgow Outcome Scale scores, extended Glasgow Outcome Scale scores, Disability Rating Scale scores, or similar tools. These assessments are all done at a fixed time point long after injury, such as 6 months. Many published studies use GCS scores at hospital discharge, which is a far inferior method and which simply reflects the weaknesses of our trauma databases because these databases don’t generally include long-term outcome data.

My third suggestion about methodology is to consider using a more widely used scale to grade CT scans. The scheme that has been published by Larry Marshall and the other Traumatic Coma Data Bank investigators may not be perfect, but it is quite valuable and it has the advantage of already being in widespread use.

My fourth and final comment concerns validation of the authors’ threshold value of 60% as a critical level for transcutaneous cerebral oximetry. Their pilot study, which enrolled only four patients, suggested that a range of 55% to 75% might be appropriate, and they called for further study. It might be interesting for them to repeat some of the data analyses that they just presented, but using different critical values. They might also want to consider correlating their measurements with some of the more invasive measures of brain tissue oxygenation.

Finally, I would like to thank the American Association for the Surgery of Trauma for the invitation to discuss this article, and I’d like to congratulate the authors for a fine presentation of a very interesting study.

Dr. Frederick A. Moore (Houston, Texas): We’ve had interest in near-infrared spectroscopy, and I question your assumption that a low SteO2 reflects tissue hypoxia. Do you have any correlation with mixed venous hemoglobin oxygen saturation in the jugular bulb? When the SteO2 is low, can you increase it by increasing oxygenation by increasing the FiO2? Thank you.

Dr. Stephen M. Cohn (Miami, Florida): I also found the article very provocative. I thought it was somewhat unusual, as someone interested in near-infrared spectroscopy, that a probe that measures regional tissue oxygenation, and is therefore sampling frontal lobe data, would have such contrary findings. The values were lower in patients who had less frontal injury and were actually higher in patients with more severe frontal lobe injury. Can you explain these conflicting findings? Thank you.

Dr. C. Michael Dunham (closing) I would like to thank Dr. Valadka for his kind, insightful, and provocative comments. Certainly, I think it’s reasonable, and my understanding is the European neurosurgeons and intensivists have embraced a targeted CPP of greater than or equal to 60 for some period of time.

I think we do know that the ability to elevate the CPP to 70 is oftentimes attributable in part to hyperventilation, and we know that cerebral hypoxia is commonly associated with that, so I concur with you that we’re constantly redefining the clinically appropriate and valuable targets.

To some degree, there is duplication, I guess, of the relationships; however, the monitoring of individual patients could have variation for their GCS score, although patients with GCS scores of 3 to 4 will tend to do worse. However, some of them will actually do quite well, so I think the individual ICP/CPP monitoring and the SteO2 monitoring may very well be beneficial.

Of course, the next obvious lead point would be to take these data and to determine whether interventions could positively affect the outcome of the patients. Julio Cruz has suggested that in his randomized controlled trial of patients managed by CPP, in which one arm had jugular venous oxygen saturation monitoring as an endpoint in addition to CPP therapy. Those patients had significantly better outcomes, so that’s, at least, suggestive that there may be therapeutic and survival benefit.

We currently have begun using the Licox Monitor. In fact, we recently had a patient in whom we had both trans-
cranial oxygen data and brain tissue PO₂, and we will be very interested in determining the correlates.

A value less than 60 is critical. Certainly, it seemed to relate to other clinically important outcomes.

I think the question is really at what level below 60 is it most critical, because I think some patients who have a slight reduction, whether it's transcranial saturation, brain tissue PO₂, or jugular venous saturation, that modest decrement still may be associated with maintenance of the CMRO₂ and a good outcome. What it actually shows is the patient is actually extracting oxygen and has functional neuronal tissues.

Obviously, with further decrement in cerebral oxygen delivery and a greater degree of hypoxia, that would suggest injury (ischemia). The comment on why might we have seen increased cerebral oxygen levels in patients with greater frontal lobe injury, Dr. Valadka and colleagues have studied that extensively and have shown that certain subsets of patients with significant brain injury may have decreased extraction of oxygen and a decrement in cerebral metabolic rate of oxygen.

What this increase in cerebral oxygen level represents is either neuronal death or neuronal dysfunction or the ability to unload oxygen from the hemoglobin, so I think there's at least some paradigm precedence for the observation that we made where increased frontal lobe injury was associated with higher cerebral oxygen values. Thank you.