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REVIEW ARTICLE

Monitoring of Brain and Systemic Oxygenation in Neurocritical Care Patients

Mauro Oddo · Julian Bösel · and the Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring

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Abstract Maintenance of adequate oxygenation is a mainstay of intensive care, however, recommendations on the safety, accuracy, and the potential clinical utility of invasive and non-invasive tools to monitor brain and systemic oxygenation in neurocritical care are lacking. A literature search was conducted for English language articles describing bedside brain and systemic oxygen monitoring in neurocritical care patients from 1980 to August 2013. Imaging techniques e.g., PET are not considered. A total of 281 studies were included, the majority described patients with traumatic brain injury (TBI). All tools for oxygen monitoring are safe. Parenchymal brain oxygen ($PbtO_2$) monitoring is accurate to detect brain hypoxia, and it is recommended to titrate individual targets of cerebral perfusion pressure (CPP), ventilator parameters ($PaCO_2$, PaO_2), and transfusion, and to manage intracranial hypertension, in combination with ICP monitoring. $SjvO_2$ is less accurate than $PbtO_2$. Given limited data, NIRS is not recommended at present for adult patients who require neurocritical care. Systemic monitoring of oxygen (PaO_2, SaO_2, SpO_2) and CO_2 ($PaCO_2$, end-tidal CO_2) is recommended in patients who require neurocritical care.

Keywords Brain oxygen · Jugular oxygen saturation · Near-infrared spectroscopy · Carbon dioxide · Systemic oxygenation · Neurocritical care

Introduction

Maintenance of adequate oxygenation is a primary objective of critical care, and the assessment of tissue oxygenation is essential to patient management. Hypoxia is defined as the reduction of tissue oxygenation to levels insufficient to maintain cellular function and metabolism. Hypoxia may result from ischemia—either macro-vascular (reduced/absent cerebral blood flow [CBF] e.g., vascular thrombosis, vasospasm, reduced carbon dioxide [$PaCO_2$]) or micro-vascular (perivascular edema, blood–brain barrier disruption, endothelial dysfunction)—anemia, and hypoxemia. Cytopathic hypoxia is primarily from failure of the cell to extract oxygen (e.g., oxygen diffusion barriers and/or mitochondrial dysfunction).

Failure to maintain adequate oxygenation aggravates secondary brain damage, therefore, detection and treatment of brain and systemic hypoxia are important. Hyperoxia also can aggravate outcome. Brain oxygen can be measured by two invasive bedside techniques: brain tissue oxygen tension ($PbtO_2$) and jugular bulb oxygen saturation ($SjvO_2$); or a non-invasive bedside method: near-infrared spectroscopy (NIRS). Monitoring of systemic oxygenation and CO_2 can be achieved invasively with arterial blood gas analysis and non-invasively with pulse oximetry and end-tidal CO_2 devices.

The Participants in the International Multidisciplinary Consensus Conference on Multimodality Monitoring are listed in "Appendix" section

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The objective of this systematic review was to (1) examine the safety and accuracy of systemic and brain oxygen and CO_2 monitoring; (2) evaluate its utility to guide therapy; and (3) analyze whether oxygen or CO_2 monitoring-guided therapy improves patient outcome after acute brain injury (ABI) including traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), acute ischemic stroke (AIS), or post-cardiac arrest (CA) coma.

Methods

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [1].

Search Criteria

Studies were considered eligible based on the PICO approach, which includes: (a) Patient population, i.e., critically ill TBI, SAH, ICH, AIS, or comatose CA patients; (b) Intervention provided, i.e., $PbtO_2$, $SjvO_2$, NIRS for regional cerebral oxygen saturation (rSO_2), arterial blood gas analysis (ABG) monitoring of arterial oxygen saturation (SaO_2)/partial arterial oxygen pressure (PaO_2)/partial arterial carbon dioxide pressure ($PaCO_2$), pulse oximetry (SpO_2), capnometry for partial end-tidal pressure of carbon dioxide ($ETCO_2$); (c) Controls, i.e., ABI patients without monitoring or patients without ABI who underwent monitoring, or ABI patients monitored with more than one device or in whom correlations with relevant variables were analyzed; (d) Outcome endpoints, i.e., mortality, Glasgow Outcome Score (GOS), Glasgow Coma Scale (GCS), modified Rankin Scale (mRS), functional independence scores, neurological outcome, National Institute of Health Stroke Scale, intensive care unit (ICU), and hospital length of stay, duration of mechanical ventilation, complications, therapy modification, and changes in physiological variables. Imaging techniques are not part of this review. After selection, the evidence was classified and practical recommendations were developed according to the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) system [2, 3].

Using the PubMed database, a systematic review was performed (1980–August 2013) of the English language literature. We did not consider unpublished data or congress presentations/abstracts. The search strategy included the terms: brain injury, traumatic brain injury (and related terms: head trauma, neurotrauma, head injury), subarachnoid hemorrhage, intracerebral hemorrhage, acute ischemic stroke, large hemispheric infarction, malignant middle cerebral artery infarction, cardiac arrest, hypoxic encephalopathy, brain oxygen, brain tissue oxygen, brain tissue oxygen pressure, brain tissue oxygen tension, brain oxygenation, brain tissue oxygenation, near-infrared spectroscopy, cerebral oximetry, cerebral oxygenation, cerebral tissue oxygenation, jugular bulb saturation, jugular venous bulb oxygen saturation, jugular venous oxygen saturation, jugular oximetry, systemic oxygenation, arterial oxygen saturation, pulse oximetry, oximetry, central venous oxygenation, arterio-venous oxygen saturation difference, partial arterial oxygen pressure, partial arterial carbon dioxide pressure, blood gas analysis, ischemia, secondary ischemia, brain hypoxia, brain tissue hypoxia, hypoxia, cerebral ischemia, brain ischemia, delayed cerebral ischemia, vasospasm, cerebral perfusion imaging, mean arterial pressure, intracranial pressure, cerebral perfusion pressure, cerebral blood flow, hemoglobin, hematocrit, anemia, transfusion, positive end expiratory pressure, fraction of inspired oxygen, hypoxemia, mortality, Glasgow Outcome Score, Glasgow Coma Scale, modified Rankin Scale, functional independence scores, neurological outcome, National Institute of Health Stroke Scale, Intensive Care Unit length of stay, duration of ventilation, hospital length of stay, discharge to home, discharge to institutional care, and prognosis.

Study Selection and Data Collection

Articles were independently pre-selected according to their title to identify those describing invasive brain oxygen, non-invasive brain oxygen, and systemic oxygen monitoring. We excluded: (a) review articles; (b) case reports or case series with $\leq$5 patients; (c) animal studies; (d) pediatric studies ($<$18 years); (e) studies that were not conducted on ICU patients; and (f) studies performed on patients without our pre-defined diseases.

Review Endpoints

The endpoints of this review were to answer the following broad questions on oxygen monitoring: (1) is monitoring safe and accurate, (2) does monitoring help guide management, and (3) does monitoring help to improve outcome? Specific questions that were addressed include:

1. What are the indications for brain and systemic oxygenation in neurocritical care patients?
2. What are the principal methods of reliable and accurate brain oxygen monitoring?
3. What is the safety profile of brain oxygen monitoring?
4. What is the utility of brain oxygen monitoring to determine prognosis in the comatose patient?
5. What is the utility of brain oxygen monitoring to direct medical and surgical therapy?

6. What is the utility of brain oxygen monitoring to improve neurological outcome?

Grading of Evidence

The quality of available evidence was judged based on the GRADE system. Summaries of the literature are followed by recommendations. Additional findings and conclusions are given in an on-line supplementary tables.

Results

Summary of the Literature

The initial search yielded 7,762 articles and abstracts and 529 articles were reviewed. After exclusions, the reviewers identified 281 articles for inclusion; 161 for $PbtO_2$, 57 on $SjvO_2$, 29 on NIRS, and 34 on systemic oxygenation monitoring. More than two-thirds of the articles described TBI patients. We found 3 randomized controlled trials (RCT) for $PbtO_2$ monitoring, 1 for $SjvO_2$ monitoring, 1 for NIRS monitoring, and 3 for systemic oxygen monitoring. All other studies were non-RCT (case-controlled studies, prospective/observational, retrospective studies). A large majority were retrospective studies. The structure of this chapter is separated into four main parts: (1) $PbtO_2$, (2) $SjvO_2$, (3) NIRS, (4) ABG and $ETCO_2$.

$PbtO_2$ Monitoring

Regional brain tissue oxygen tension ($PbtO_2$) monitoring requires insertion of a catheter into the brain parenchyma (sub-cortical white matter), through a single or multiple lumen bolt or tunneled. Generally patients are selected for $PbtO_2$ monitoring when intracranial pressure (ICP) is monitored.

Is $PbtO_2$ Monitoring Safe and Accurate?

Eight studies tested safety and accuracy [4–11]: in summary, they found no catheter-related infections, 0–3 % local bleeding around the catheter (with no clinical consequence), 6–14 % technical complications (e.g., dislocation or defect). Catheters are MRI 1.5 Tesla compatible. For data accuracy, adaptation time was $\sim$2 h, display error $\sim$2–3 mmHg, zero-drift $\sim$2 mmHg: display errors and drift were greater during the first 4 days of monitoring.

The Licox® system from Integra Neurosciences and the Neurovent-PTO® system from Raumedic are currently commercially available, and provide stable monitoring for up to 7–10 days. In comparative studies, there are differences in absolute $PbtO_2$ values, $PbtO_2$ response to FiO_2 increase, and $PbtO_2$-derived indexes between the two devices [12–16]. Fever ($\sim$39 °C) may affect the Licox data.

CBF and CPP are important determinants of $PbtO_2$ [17–30], but a $PbtO_2$ monitor is not simply an "ischemia monitor" since several variables such as $PaCO_2$ [31–40], PaO_2 [23, 41, 42], systemic factors that modify $CMRO_2$ (e.g., fever, shivering [43, 44]) alter $PbtO_2$. $PbtO_2$ best reflects the product of CBF and arterio-venous oxygen tension difference [23] and is influenced by the oxygen diffusion gradient [45]. Hence, when local tissue extraction of O_2 is impaired (e.g., peri-vascular edema), $PbtO_2$ may be low despite normal CBF.

"Normal" $PbtO_2$ is 23-35 mmHg [5, 46, 47] but depends on probe depth, being less in deeper brain regions [5]. Values $<$20 mmHg are considered abnormal and have been associated with greater evidence for cerebral ischemia and energy dysfunction [48–50]. In many centers, treatment is initiated when $PbtO_2$ is $<$20 mmHg although other authors describe treatment when $PbtO_2$ is $<$15 mmHg [51].

Probe location can influence how $PbtO_2$ responds to therapeutic interventions and its association with outcome in TBI [52–56]. In general, $PbtO_2$ absolute values and the response of $PbtO_2$ to FiO_2 are less in peri-contusional areas compared to normal brain visualized on CT scan [52–54, 56]. In SAH, the ability of a $PbtO_2$ probe to detect ischemia associated with vasospasm depends on probe placement and is better when the MCA or ICA is involved [57]. It is important, therefore, that $PbtO_2$ data be interpreted once a post-insertion CT scan has verified probe position.

Does $PbtO_2$ Monitoring Help Guide Management?

Most studies include comatose TBI patients and less frequently SAH patients. $PbtO_2$ monitoring can guide several aspects of patient care. $PbtO_2$ monitoring helps target "optimal CPP levels" (i.e., a CPP level to prevent/treat brain tissue hypoxia, [$PbtO_2$ $<$ 20 mmHg]) in individual patients or a level at which ICP requires treatment in TBI [22, 29, 58–62] and SAH [30, 63, 64]. $PbtO_2$ data can be used to identify deleterious effects of drugs on CPP [65–67] and document the effect of interventions such as induced hypertension to increase CPP [20, 68–70]. Patient's autoregulation state can be identified using the online correlation between CPP and $PbtO_2$, or the oxygen pressure reactivity index (ORx), which helps target CPP in TBI [18, 21, 71–73], SAH [27, 74], and stroke [26]. The effect of osmotherapy to control ICP can be guided by $PbtO_2$ data [75–78]. Other ICP therapies (hypothermia [79–83], barbiturates [84, 85], or decompressive craniectomy [86–88]) can be guided by $PbtO_2$ data. In patients receiving

hypothermia $PbtO_2$ monitors may detect deleterious effects associated with a change in CO_2 affinity or with shivering [43, 83, 89, 90]. Anemia (hemoglobin < 9 g/dl) is associated with lower $PbtO_2$ after TBI [91] and SAH [92, 93] and $PbtO_2$ monitoring may help guide transfusion endpoints [91, 94–97]. The variable effects of sedation, anesthetic agents, and "wake-up tests" on individual patients can be examined using $PbtO_2$ data [98–105]. $PbtO_2$ levels may help guide ventilator management [106]. There is a well-described relationship between hyperventilation, reduced $PaCO_2$, and decreased $PbtO_2$ as well as between impaired lung function and low $PbtO_2$: recruitment maneuvers (PEEP of 30-40 cmH2O) may thus help improve $PbtO_2$ [107] but this effect may depend on hemodynamic stability [108]. Finally $PbtO_2$ monitor use and changes in ORx are described in SAH induced vasospasm management [27, 74, 109–117] both to provide insight about an intervention or to "predict" delayed cerebral ischemia [109, 110, 114].

Does $PbtO_2$-Guided Care Influence Outcome?

Twenty-four studies (21 TBI, 3 SAH) describe an association between reduced $PbtO_2$ (using thresholds of <20, <15 and <10 mmHg) and worse outcome. In TBI, reduced $PbtO_2$ is associated with mortality [118–123], lower GOS score [124–130], and increased neuropsychological deficits [131]. $PbtO_2$ values of 0 mmHg are consistent with brain death [132, 133]. The tissue oxygen response (TOR; i.e. $PbtO_2$ response to 100 % FiO_2) also is associated with TBI outcome [134–136]. In SAH there is a relationship between reduced $PbtO_2$ and mortality but the relationship with morbidity is less robust than in TBI [114, 137, 138].

Interventions such as ventilator manipulation (e.g. a change in FiO_2 or PEEP), CPP augmentation, sedation, or osmotherapy are most frequently used to treat low $PbtO_2$. Overall medical therapy can correct three quarters of the episodes of compromised $PbtO_2$ (<20 mmHg) but varies with the specific therapy or combination of therapies [139, 140]. Increased FiO_2 generally is the most effective therapy and both normobaric and hyperbaric oxygen can increase $PbtO_2$, although the exact response may depend on probe position [52, 141–149]. Whether this translates into improved cerebral metabolism and better tissue outcome is still controversial.

A physiologic response to therapy to correct $PbtO_2$ is associated with better outcomes in TBI and SAH [139, 150]. Nine observational studies have described the effect of $PbtO_2$-directed therapy used with ICP/CPP management in severe TBI [151–159], suggesting a tendency to better outcomes with combined $PbtO_2$ and ICP/CPP therapy compared to ICP/CPP therapy alone in the majority of them.

$SjvO_2$ Monitoring

Jugular bulb catheters sample the intracranial circulation. Measuring jugular bulb venous oxygen saturation ($SjvO_2$) or the difference between arterial and jugular venous oxygen content ($AJVDO_2$) provides information about global cerebral oxygenation. The catheter should be in the dominant internal jugular vein and proximal to the first extra-cranial tributary, the facial vein for best results [160–163]. A cervical spine x-ray is recommended to define correct position [164].

Is $SjvO_2$ Monitoring Safe and Accurate?

Jugular bulb blood can be sampled intermittently with a catheter or continuously using a fiberoptic catheter. Catheters need frequent calibration usually every 8–12 h [165, 166]. Poor quality signals from extra-cranial contamination associated with inaccurate placement, clot formation, catheter, and venous thrombosis or inadequate calibration are common [167–171]. Hence data accuracy ranges between 40 and 80 % [171–173] of total monitored time. Several studies have compared $SvjO_2$ and $PbtO_2$ monitoring [172, 174–179]. Overall these studies show $SjvO_2$ is less accurate than $PbtO_2$.

Normal $SjvO_2$ is between 55 and 75 %. Although various definitions have been used, $SjvO_2$ values <55 % are consistent with cerebral ischemia [180–185]. At least 13 % of the brain volume needs to be ischemic for the $SjvO_2$ to be abnormal and so its ability to detect regional ischemia is limited [186–191].

Can $SjvO_2$ Monitoring Help Guide Management?

The majority of studies have been in TBI patients, with only few data in SAH or AIS. Reduced CPP is a common cause of $SjvO_2$ desaturation [192–198] and optimization of CPP can reduce these episodes of low $SjvO_2$ [196, 197, 199, 200]. Increased ICP also is associated with reduced $SjvO_2$ [192, 201, 202] but the response of $SjvO_2$ to ICP treatment including hyperventilation, osmotherapy, surgery, or hypothermia is variable [202–206]. A decrease in $SjvO_2$ associated with hyperventilation can be used to de-escalate therapy i.e., guide hyperventilation during ICP treatment [195, 196, 207–212]. A failure of $AVDO_2$ to improve once ICP is normalized is associated with a greater likelihood of cerebral infarction [213]. Sedatives such as propofol or opiates have an uncertain effect on $SjvO_2$ [103, 214, 215]. There are limited studies in SAH but they suggest changes in $SjvO_2$ or $AVDO_2$ may precede neurologic symptoms associated with vasospasm and so can be used to titrate or institute induced hypervolemia or hypertension [196, 216].

Does $SjvO_2$-Guided Care Influence Outcome?

In TBI patients, reduced $SjvO_2$ [180–182, 184, 203, 217], increased $SjvO_2$ (>75 %) [180], and increased $AVDO_2$ [185, 213, 218] are associated with worse outcome. An $SjvO_2 < 50$ % for more than 10 min or failure of the $AVDO_2$ to respond to treatment are associated with worse outcome [182, 213].

In a randomized controlled study, Robertson et al. [200] examined whether a CBF-targeted protocol, using higher CPP and optimized volume management but without targeting a specific range $SjvO_2$ improved outcome compared to standard ICP-based care in severe TBI. Patients assigned to the CBF-targeted management had fewer episodes with low $SjvO_2 < 55$ % but 6-month outcome was similar because of a greater incidence of pulmonary complications in the CBF-targeted protocol group.

Near-Infrared Spectroscopy (NIRS)

Near-infrared spectroscopy (NIRS) is based on the principle that light (wavelength 700–950 nm) passing through biological tissue is absorbed by blood depending on its oxygenation status. The attenuation of light allows estimation of oxygen status in the tissue volume reached by the light. While NIRS use is better described in cardiothoracic surgery and in neonatal or pediatric critical care, we only reviewed studies in adult neurocritical care in which commercially available devices were used. Most of these studies are small, there are several methodological limitations, and results are conflicting. Furthermore, NIRS has several limitations in adult use [219–223].

Currently, four commercial NIRS systems are available: (1) FORE-SIGHT (CAS Medical Systems, Branford, Connecticut, USA; FDA-approved); (2) EQUANOX (Nonin Medical, Plymouth, Minnesota, USA; FDA-approved); (3) INVOS (Covidien, Boulder, Connecticut, USA; FDA-approved); and (4) NIRO (Hamamatsu Photonics, Hamamatsu City, Japan; CE-marked). The INVOS and the NIRO are the most widespread in clinical use. There is insufficient data to recommend one device over the other. For inter-monitor comparisons and technical aspects, the reader is referred elsewhere [220, 223–237].

Is NIRS Monitoring Safe and Accurate?

While only two studies specifically addressed safety and the application of NIRS [219, 238], no adverse effects were described in other studies. Seventeen studies examined how NIRS compared to other measures of brain oxygen and perfusion including changes in these variables. The results are very variable with good [222, 239–249], partial [219, 222, 238, 240–250], or poor correlation [251–254]. In large part, this variability results from factors such as ambient light, scalp, skull, and CSF conditions [223] or extra-cranial circulation that influence the NIRS signal [220, 224].

Can NIRS Monitoring Help Guide Management?

Nineteen studies, mostly small observational studies, describe how NIRS may be used to understand patient physiology or guide management in neurocritical care. This includes use in ICP waveform analysis [255]; cerebral autoregulation [248, 249, 256]; CPP and MAP assessment [60, 222, 251, 257–260]; vasospasm [221, 261, 262]; head positioning [263], hematoma assessment, and surgical decision making [264–266]. The results are mixed.

Does NIRS Monitoring Help to Improve Outcome?

There are very limited data on this question and no studies to show that NIRS use helps to improve outcome in adult neurocritical patients. Ideally, NIRS should be used with other monitors and most studies suggest it is easy to incorporate NIRS into multimodal monitoring. This is best exemplified in its use to assess cerebral autoregulation [248, 249].

NIRS: Conclusions

While NIRS is an attractive monitor since it is non-invasive, it has several limitations in adult use and at present has little if any role in adult neurocritical care. In particular, NIRS, alone, is currently not indicated for routine monitoring of adult patients who require neurocritical care. Instead if NIRS is to be used, it is best integrated with other monitors to answer research questions but at the moment not to guide management.

Systemic Oxygen Monitoring

Systemic oxygen can be measured invasively by arterial blood gas analysis (ABG) for PaO_2 and SaO_2 and non-invasively with pulse oximetry (for SpO_2). There are a variety of devices to assess systemic oxygenation but too few technology validation studies in neurocritical care patients to allow recommendation of one device over the other. Most data are from TBI and SAH, thus limiting generalizability. Most studies are small, non-controlled, and suffer methodological weaknesses. Furthermore, systemic oxygen monitoring usually is not the primary endpoint but reported as part of the methods or as a secondary endpoint. Consequently, many studies were not designed to answer the review questions directly and instead provide indirect evidence only.

Is Systemic Oxygen Monitoring Safe and Accurate?

No studies specifically address this question in neurocritical care patients, although these devices are used in virtually all these patients. Pulse oximetry has been validated in healthy volunteers [267]. ABG and SpO_2 use are well studied in the operating room and the general ICU where their use is safe and associated with fewer episodes of hypoxia. The impact on outcome is less certain. There is no plausible reason to assume that safety, applicability, methodological reliability, or accuracy would be any different in neurocritical care patients although limited precision has been identified in select circumstances [268–270].

Can Systemic Oxygen Monitoring Help Guide Management?

Systemic hypoxia and hyperoxia are known to exacerbate outcome. Ten studies, including two small RCTs, addressed how systemic oxygen monitoring can guide neurocritical care management. In summary, pulse oximetry or ABG analysis can reliably detect pulmonary and circulatory abnormalities [271], and guide correction of brain oxygen in select patients when using normobaric hyperoxia [147, 272], PEEP [105, 107, 108, 273], recruitment maneuvers [274, 275], or prone positioning [276].

Does Systemic Oxygen Monitoring Help to Improve Outcome?

There are no outcome studies in neurocritical care that compare patients managed with or without systemic oxygen monitoring. However, two small observational studies and one large retrospective registry provide indirect evidence for the value of systemic oxygen monitoring in TBI. In particular, desaturation on pulse oximetry or both low and very high PaO_2 are associated with worse outcome [277–279]. Since cost and risk of systemic oxygen monitoring are low and the value in understanding patient pathophysiology is high, there is no reason not to use systemic oxygen monitoring as part of multimodal monitoring.

Systemic Carbon Dioxide Monitoring

Systemic carbon dioxide is assessed invasively by arterial blood gas analysis for $PaCO_2$ and non-invasively with capnography, capnometry, and continuous assessment of end-tidal CO_2 ($ETCO_2$). There are several devices to assess systemic carbon dioxide but too few technology validation studies in neurocritical care to allow recommending one device over the other. The reader is referred elsewhere for details on technology [280–283].The vast majority of studies on carbon dioxide monitoring are in TBI or SAH and usually CO_2 is not a primary endpoint, i.e., most evidence is indirect.

Is Systemic Carbon Dioxide Monitoring Safe and Accurate?

There is extensive research on CO_2 analysis using ABG or $ETCO_2$ monitoring in general critical care and in anesthesia that demonstrate feasibility and safety. These questions have not been specifically addressed in neurocritical care but there is no reason to expect a difference.

ABG-analysis of $PaCO_2$ is routine and in widespread use in all ICUs. Similarly, $ETCO_2$ is used routinely in the operating room [284]. End-tidal CO_2 correlates with $PaCO_2$ in healthy ventilated patients but with impaired pulmonary gas exchange (e.g., increased anatomic or physiologic dead space, or low cardiac output) there can be a gradient between $ETCO_2$ and $PaCO_2$ that may change over time [257]. Hence $ETCO_2$ is not a one-for-one substitute for $PaCO_2$ and when $ETCO_2$ is used it should be validated against $PaCO_2$.

Does Systemic Carbon Dioxide Monitoring Help Guide Management?

Fifteen studies address this question; most are prospective observational studies or case series and use $ETCO_2$ or $PaCO_2$ monitoring [31, 186, 203, 285–292]. $PaCO_2$ monitoring and less reliably $ETCO_2$ can help to detect and guide hyperventilation. There is a reasonable relationship with CBF and brain oxygen but less robust relationship with $CMRO_2$ and oligemia.

Does Systemic Carbon Dioxide Monitoring Help to Improve Outcome?

There are no outcome studies in neurocritical care that compare patients managed with or without systemic CO_2 monitoring. Six studies, including one RCT provide indirect evidence in that they show hyper- or, more often, hypocapnia, to be associated with worse outcome or mortality in TBI [279, 281, 293–295] and SAH [296]. Similar to oxygen monitoring, it makes physiologic sense that CO_2 monitoring be incorporated into multimodal monitoring.

Disclosures Mauro Oddo has received speaker and consultant honoraria from Integra Neurosciences. Julian Bösel has received speaker honoraria and travel support from Covidien, Sedana Medical, and Orion Pharma.

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