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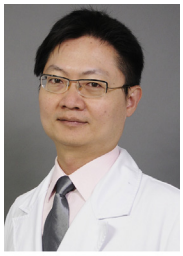
Review Article

Multimodal neurocritical monitoring



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ABSTRACT

Neurocritical monitoring is important in caring for patients in the neurological intensive care unit. Although clinical neurologic examination is standard for neurocritical monitoring, changes found during the examination are often late signs and insufficient to detect and prevent secondary brain injury. Therefore, various neuromonitoring tools have been developed to monitor different physiologic parameters, such as cerebral oxygenation, cerebral blood flow, cerebral pressure, cerebral autoregulation, cerebral electric activity, and cerebral metabolism. In this review, we have discussed current commonly used neurocritical monitoring tools. No single monitor is sufficient and perfect for neurocritical monitoring. Multimodal neurocritical monitoring is the current trend. However, the lack of common formatting standards and uncertainty of improvement in patients' outcomes warrant further studies of multimodal neurocritical monitoring. Nevertheless, multimodal neurocritical monitoring considers individual pathophysiological variations in patients or their injuries and allows clinicians to tailor individualized management decisions.

Neurocritical monitoring is important in caring for patients in the neurological intensive care unit. The main reasons for neurocritical monitoring are as the follows: (1) detect early neurological deterioration before irreversible brain damage occurs; (2) individualize patient care decisions; (3) guide patient management; (4) monitor therapeutic response to some interventions and avoid any consequent adverse effects; (5) allow clinicians to understand the pathophysiology of complex disorders; (6) design and implement management protocols; and (7) improve neurological outcome and quality of life in survivors of severe brain injuries [1]. Although clinical neurologic examination is standard for neurocritical monitoring, changes found during the clinical neurologic examination are often late signs and insufficient to detect and prevent secondary brain injury [2,3]. Serial neurologic examination was the main monitoring tool between 1960 and 1980, the so-called age of clinical neuromonitoring [4].

Between 1980 and 2000, intracranial pressure (ICP) monitoring became popular and was used to detect and treat increases in ICP before obvious clinical deterioration. This era was called the age of physiologic neuromonitoring [4]. Thereafter, various neuromonitoring tools have been developed to monitor different physiologic parameters, such as cerebral oxygenation, cerebral blood flow (CBF), cerebral autoregulation (CA), cerebral electric activity, and cerebral

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Table 1 Common neurocritical monitoring tools.

Physiologic events	Tools	Advantage	Disadvantage
Global neurological status	Glasgow coma scale	mostly commonly used	too late to prompt preventive strategies for potential secondary brain injury
	Full Outline of UnResponsiveness	manually	
	Nociception coma scale-revised	no need of expensive instruments	
	Intensive care delirium screening checklist		
Cerebral oxygenation	PET	Gold standard	usually unavailable in ICU Failure in continuous monitoring
	SjvO2	measure the global brain oxygenation	Invasive with complications
	Intraparenchymal oxygen sensors	measure the regional brain oxygenation	Invasive with complications. Variation by probe location
	NIRS	Noninvasive	Limited by depth of light penetration interference from other sources uniform distribution of infrared light in CSF
Cerebral blood flow	Thermal diffusion flowmetry Laser Doppler flowmetry	Gold standard measure regional CBF	sensitivity to ambient light and temperature sensitivity to positioning
	CT, MRI, PET	Noninvasive	Usually unavailable in ICU Failure in continuous monitoring
	TCD	Noninvasive Available in ICU	Limited by operator variability Usually failure in continuous monitoring
Cerebral pressure	Intracranial ICP sensors	Gold standard	Invasive with complications
	TCD	Noninvasive	less accurate;
	ONSD	Noninvasive	less accurate;
	TMD	Noninvasive	less accurate; large standard error and inter-subject variability not feasible in older people
Cerebral autoregulation	Intraparenchymal oxygen sensor and ICP monitoring	Gold standard	Invasive
	NIRS	Noninvasive	Less accurate
	TCD		
Cerebral electrical activity	EEG	measure brain electrical activity and detect epileptiform discharges	high expense need for technicians to place EEG leads and for experts to interpret the recordings (with variability between expert readers)
Cerebral metabolism	Microdialysis	measure common brain metabolites - markers of tissue injury, energy failure, cellular stress	timing consuming low temporal resolution volume limitation placement matters

Abbreviations: CBF: cerebral blood flow; CSF: cerebrospinal fluid; CT: computed tomography; EEG: electroencephalography; ICU: intensive care unit; MRI: magnetic resonance imaging; NIRS: near-infrared spectroscopy; ONSD: optic nerve sheath diameter; PET: positron emission tomography; SjvO2: jugular venous bulb oximetry; TCD: transcranial Doppler; TMD: tympanic membrane displacement.

metabolism in addition to cerebral pressure. However, no single monitoring modality is adequate and ideal for all patients at present [2].

In the 1990s, the concept of multimodal monitoring was introduced and integrated monitoring of CBF, brain tissue oxygenation, and intracerebral microdialysis [5]. We are presently in the so-called age of multimodality monitoring and neurophysiologic decision support [4]. Rather than simply reacting to harmful intracranial physiologic events, integrated multimodal monitoring with bioinformatics aims to identify useful trends, develop therapeutic strategies, predict clinical outcomes, and prevent secondary brain injury, such as delayed cerebral ischemia, cognitive impairment, and motor disability [3]. Here we reviewed the current commonly used neurocritical monitoring tools (Table 1).

Global neurologic status

In the assessment of consciousness level, the Glasgow Coma Scale (GCS, combined with assessment of pupils), or Full Outline of UnResponsiveness (FOUR) is recommended to be performed routinely in adult comatose patients with acute brain injury [6]. To assess pain, the Numeric Rating Scale, Behavioral Pain Scale, and Nociception Coma Scale-Revised are recommended in the intensive care unit according to the patient's cooperation level [6]. In the assessment of delirium, the Intensive Care Delirium Screening Checklist (ICDSC) is preferred to the Confusion Assessment Method for the ICU because it does not score changes in wakefulness and attention directly attributable to recent sedative medication as positive ICDSC points [6]. As mentioned above, clinical neurologic evaluation is often too late to prompt preventive strategies for potential secondary brain injury.

Cerebral oxygenation

Brain tissue oxygenation (PbtO2) is not equal to peripheral oxygen saturation and is actually a combination of cerebral arteriovenous oxygen tension difference, CBF, and tissue oxygen extraction [3]. Consequently, many factors affect PbtO2, including cerebral perfusion pressure (CPP), hemoglobin concentration, oxygen saturation, metabolic rate, and cerebral vasospasm [3]. PbtO2 can be measured by PET (considered the gold standard), intraparenchymal oxygen sensor, MR spectroscopy, jugular venous bulb oximetry (SjvO2), and near-infrared spectroscopy (NIRS) [7]. Intraparenchymal oxygen sensors, inserted in the subcortical white matter, are often used to monitor regional brain tissue oxygen tension. The probe location can influence how PbtO2 responds to therapeutic interventions and its association with outcome in traumatic brain injury (TBI) [8]. Intraparenchymal oxygen monitoring has potential complications, such as hemorrhage, migration and infection, although the complication rate is low [3]. NIRS is based on the mechanism by which living tissue absorbs infrared differently based on its oxygen saturation. Although noninvasive, NIRS has some limitations, such as depth of light penetration through the skull (2–3 mm, limited to the gray matter), contamination by extra- and intracranial sources, and uniform distribution of infrared light in the CSF layer [3,4]. The combination of PbtO2 and ICP monitoring showed better clinical outcomes, such as decreased disease duration and depth of brain tissue hypoxia, than ICP monitoring alone in patients with TBI [9], and a phase III trial of this combination is ongoing.

Global brain oxygenation can be measured using SjvO2. As an invasive procedure, SjvO2 is associated with several complications, such as catheter misplacement, infection, and jugular venous thrombosis [3]. The recognized threshold for ischemia requiring intervention is $\leq$ 55% of oxygen saturation [3]. If brain oxygenation monitoring is desired, the preferred choice is PbtO2, while the best application of SjvO2 is in patients with TBI and global injury [3].

Cerebral blood flow

Multiple mechanisms, such as autoregulation and metabolic, chemical, and neurogenic regulations, control CBF. Regional CBF can be measured by two types of invasive flowmetry: thermal diffusion flowmetry and laser Doppler flowmetry [3]. Thermal diffusion flowmetry estimates the blood flow by deducing heat loss through dissipation into the blood flow, while laser Doppler flowmetry directly measures the erythrocyte flux [3]. Both methods have limitations, such as sensitivity to ambient light and temperature, sensitivity to positioning, and uncertainty regarding their predictive values [3]. As to non-invasive methods of measuring CBF, several imaging modalities, such as CT, MRI, and PET, can be used. However, these require transferring the patient, and continuous imaging is impossible with these imaging modalities [10]. Transcranial Doppler (TCD), also a noninvasive tool, can be used to measure CBF and is easily available in the intensive care unit. TCD studies have shown high specificity for confirmation of intracranial circulatory arrest in brain death: brief systolic forward flow spikes with reversed or absent diastolic flow found bilaterally or in three different arteries are accepted TCD criteria supporting the diagnosis of brain death [4]. However, TCD is also limited by operator variability [10].

Cerebral pressure

Elevated ICP has been known to be deleterious to patients with TBI, associated with poor outcomes, and need further management [11]. ICP is recommended to be measured by ventriculostomy and intraparenchymal monitoring, while other monitoring tools are subject to daily drift and less accuracy [3]. In the presence of hydrocephalus, an external ventricular catheter is preferred for ICP monitoring [12]. However, the current methods of ICP monitoring cannot reliably define the limit of the brain's intrinsic compensatory capacity to manage increases in pressure [13]. Additionally, monitoring and maintaining ICP $\leq$20 mmHg in patients with severe TBI did not show superiority to care based solely on imaging and clinical examination as to functional and cognitive outcomes at 6 months [14]. As an invasive monitoring with risks for hemorrhage, brain tissue lesions and infection, ICP monitoring is recommended only in patients with a GCS score $\leq$8 and who have

abnormal head CT findings [3]. Moreover, ICP should not be used in isolation as a prognostic marker [12].

Noninvasive ICP monitoring includes TCD, optic nerve sheath diameter (ONSD), and tympanic membrane displacement (TMD). These noninvasive ICP monitoring tools are less accurate than invasive ICP monitoring [3]. Nevertheless, noninvasive ICP sensors have the potential to decrease the need for invasive interventions in a range of patients and thus warrant development [13]. TCD is commonly used to calculate the Gosling Pulsatility index, which correlates well with CPP and ICP [15]. Elevation in ICP can transmit through the CSF in the subarachnoid space, leading dilatation of the optic nerve sheath, which can be detected using transocular ultrasonography [13]. ONSD measurements may be a useful screening tool for ICP in settings where invasive monitoring is not promptly available [13,16]. A normal or low ICP produces an outward displacement (positive values) of the tympanic membrane while intracranial hypertension causes the tympanic membrane to move inward (negative values) [15]. However, the clinical feasibility of TMD has been questioned due to the difficulties in achieving an accurate TMD measurement, large standard error, and inter-subject variability [15]. Additionally, the use of TMD was precluded in older patients because the cochlear duct patency decreases significantly with age [15].

Cerebral autoregulation

The ability of the brain to maintain a constant CBF despite alterations in CPP is termed CA. The importance of CA monitoring is to delineate the optimal mean arterial pressure (MAP) or optimal CPP to prevent both hypoperfusion and hyperperfusion [3]. CA is obtained traditionally by invasive brain oxygen monitoring and ICP monitoring and can also be delineated by noninvasive NIRS-measured cerebral oximetry [17,18]. The most accurate CA indices to predict outcome in patients with acute TBI are pressure reactivity index (PRx), mean velocity index (Mx), and autoregulatory reactivity index. PRx relies on the correlation (-1 to $+1$) between arterial blood pressure and ICP, with negative values indicating intact CA and positive values indicating dysfunctional CA [19]. A positive PRx has been associated with a higher mortality rate in severe TBI [20]. PRx can determine optimal CPP; however, whether an optimal CPP may alter outcome is debated and needs further research [19]. The NIRS-derived cerebral oximetry index, derived from the correlation between PbtO2 and MAP, increases as CA is impaired and is correlated with decreased GCS scores [21].

Although the role of the autonomic nervous system in CA has been controversial, disturbed CA in patients with autonomic dysfunction has been confirmed [22]. Autonomic function can be measured by heart rate variability and baroreflex sensitivity, and autonomic dysfunction is significantly associated with increased mortality in patients with TBI [23].

Cerebral electrical activity

Cerebral electrical activity is commonly measured by electroencephalography (EEG). EEG both detects epileptiform activity and predicts clinical outcomes. The drawbacks to EEG include high cost, need for technicians to place EEG leads and for experts to interpret the recordings, and variability between expert readers [3]. Nevertheless, continuous and simultaneous EEG and ICP recordings showed a strong relationship, which could lead to the development of a medical device to measure ICP in a noninvasive way [24].

Cerebral metabolism

Cerebral metabolism is often measured by microdialysis, and the common metabolites monitored include glucose, lactate, pyruvate, glycerol and glutamate [3,7]. Low glucose levels correlate with increased tissue injury and poor outcome. An elevated lactate-to-pyruvate ratio is associated with energy failure and ischemia. Glycerol is a marker of cellular stress, low oxygen, or low glucose levels. Glutamate is an excitatory neurotransmitter and a marker of late injury [7]. Despite being a rather safe invasive procedure, cerebral microdialysis has some limitations such as time-demanding, low temporal resolution and question of placement, while the most severe limitation is unfinished work of defining markers of health and crisis in different clinical contexts [3]. Therefore, cerebral microdialysis is only recommended for use in combination with clinical indicators and other monitoring modalities for prognostication [12].

Summary

As mentioned above, no single monitoring tool is sufficient and perfect for neurocritical monitoring, so multimodal neurocritical monitoring is the trend. Multimodal neurocritical monitoring considers individual pathophysiological variations in patients or their injuries and allows clinicians to tailor individualized management decisions [25]. Integration of multimodal monitoring data and other clinical data such as laboratory values, imaging results and medical record documentation is nearly impossible manually and warrant informatics and a coordinated effort involving clinicians, engineers, computer scientists and experts in informatics and complex systems analysis [3,26]. However, the lack of common formatting standards is currently a barrier to true data integration [3]. Additionally, more monitoring and treatment may not necessarily translate to better outcomes [7]. Whether using multimodal neurocritical monitoring improves outcome warrants further clinical studies in the future. Nevertheless, multimodal neurocritical monitoring offers intensivists an opportunity to synthesize physiologic measures of brain function to deliver timely and individualized therapy in patients with acute brain injury [7].

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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