Chapter

Management of Patients with Brain Injury Using Noninvasive Methods

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Abstract

In the last decades, the development of new noninvasive technologies in critical care allowed physicians to continuously monitor clinical parameters, aggregating important information that has been previously inaccessible or restricted due to the invasiveness of the existing techniques. The aim of this chapter is to present noninvasive methods in use on intensive care units (ICU) for brain injured patients monitoring, collaborating to the diagnosis and follow-up, aiding medical teams to achieve better outcomes.

Keywords: noninvasive methods, brain injury, monitoring, ICP pulse waveform, ICPwf, US optic nerve sheath diameter, ONSD, CT scan optic nerve sheath diameter, MRI optic nerve sheath diameter, near-infrared spectroscopy, NIRS, transcranial Doppler, TCD

1. Introduction

The technological development achieved in recent decades has made possible to access previously unimaginable information. Sensors with greater sensitivity, more detailed imaging tools and accurate sound analyzers have brought to light patho-physiological parameters previously inaccessible. The new technologies also disclose a new trend to the medical area, the possibility of accessing patient information with noninvasive devices, minimizing risks, costs and opening new possibilities for better management.

This chapter addresses how the new tools can enlarge the therapeutic window, thereby bringing more patient safety and assertiveness to physicians. The following technologies will be presented in this chapter:

- Intracranial pressure pulse waveform monitoring
- Ultrasound optic nerve sheath diameter (ONSD)
- Computed tomography optic nerve sheath diameter
- Magnetic resonance imaging optic nerve sheath diameter

- Near-infrared spectroscopy - NIRS
- Transcranial Doppler - TCD

The objective of this chapter is to present these technologies and stimulate the search for more information to the application of these technologies in daily practice of health professionals.

2. ICP pulse waveform monitoring

Intracranial pressure (ICP) is an important clinical parameter, it is related to the volumes of the intracranial contents and the skull bone cavity. The ICP monitoring provides three distinct information:

- The average value of ICP
- The trend of ICP over time
- ICP pulse waveform (ICPwf)

The ICP mean value directly and punctually portrays the pressure value in the environment in which the sensor is inserted. Clinical experience has shown that as important as knowing ICP values, was to have information about the period of time in which the subject was submitted to hypertensive conditions, that is, the possibility of ICP trend following over time [1]. Studies initiated from the second half of the last century correlated the ICPwf with intracranial compliance, a new parameter introduced in medicine used to assist in the diagnosis and prognosis of patients [2].

The invasibility of methods that allowed obtaining ICP pulse morphology caused this parameter to be indicated only in high risk of herniation cases. Most ICP monitoring techniques do not present information on ICP pulse morphology. The absence of accurate ICP pulse morphological displaying and information on the waveform components relations in invasive methods make this analysis operator dependent.

The noninvasive detection of the morphology of ICP pulses became a reality in 2007, when Brazilian researchers began studies to monitor cranial elasticity over time. Cranial elasticity was initially analyzed by gluing strain-gauges to the cranial bone. This study was important to show that it is possible to capture pulses over the skull, and that these pulses are related to changes in intracranial volumes and pressure [3].

These results allowed the development of a noninvasive sensor (brain4care corp.), which touches the surface of the patient's scalp. This sensor mechanically captures the variations in the trend and morphology of the intracranial pressure pulse, without radiation, light or sound emissions for patients and operators [4].

ICP pulses are the result of blood pressure, breathing and cerebrospinal fluid (CSF) interaction. The cardiac-derived ICP pulse is formed by three components, P1 formed by the systolic wave, P2 originated by the scattering of fluids in this environment and p3, resulting from aortic valve closure [5] (**Figures 1** and **2**).

Subjects with ICP pulse morphology considered normal have the first component (P1), higher than the second (P2). When there is alteration of this order, ICPwf is considered abnormal [6].

This noninvasive sensor acquires beat by beat ICPwf spectrum and translates its peak relations to numbers. The algorithm calculates the amplitudes of pulses P1 and P2 and the ratio of these parameters (P2/P1 ratio = AmpP2/AmpP1). When the value of this ratio is greater than 1, morphology is considered abnormal as it indicates that peak P2 is greater than peak P1.

This method can be used to aid diagnosing and assisting patients with risk of intracranial hypertension (ICH), and consequently reduction of intracranial compliance (ICC) [4]. The latter is called with reference to the homeostasis among intracranial structures, such as the brain itself, vascular volume and CSF volume [7].

Figure 3 shows a monitoring sample with this technique, in a patient with neurological drawdown before and after the procedure to control ICH. The first waveform shows an altered morphology before the procedure, with 1.22 its P2/P1 ratio. Posterior to treatment, is presented his ICPwf pattern with a P2/P1 ratio of 0.87.

This technique is already in clinical use and has collaborated with the diagnosis and follow-up of patients who present suspicion, risk or confirmed conditions

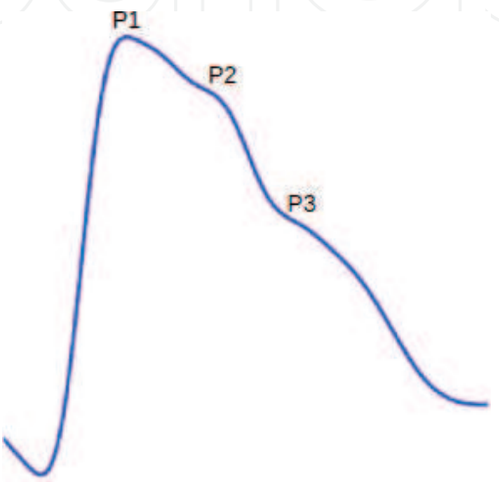

Figure 1.
Normal intracranial pressure pulse waveform.

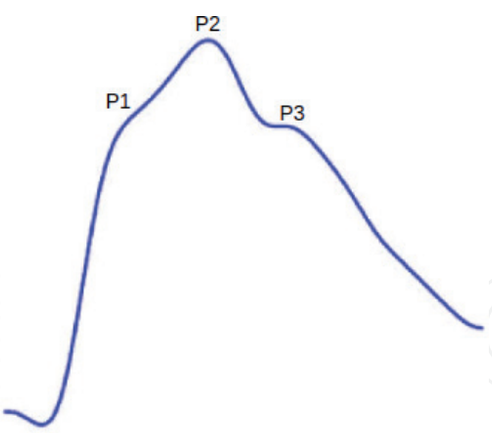

Figure 2.
Abnormal intracranial pressure pulse waveform.

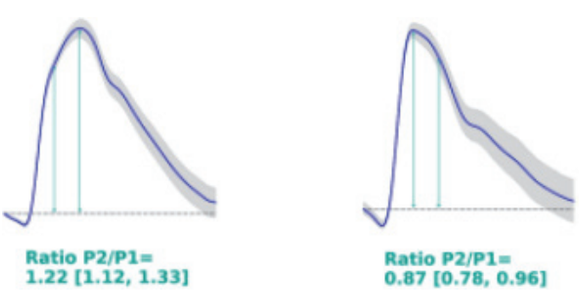

Figure 3.
Effect of a procedure to decrease the intracranial pressure monitored with the brain4care sensor.

of reduction of ICC, in situations as traumatic brain injury, stroke, intracranial tumors, hydrocephalus, central nervous system infections, reduction in cerebral flow, post cardiorespiratory arrest, liver diseases, kidney diseases and other conditions that may lead to ICH.

3. US optic nerve sheath diameter (ONSD)

The optic nerve can be anatomically subdivided into an intraocular, intraorbital, canalicular, and intracranial segment [8]. The optic nerve, as part of the central nervous system, is covered by a leptomeningeal sheath, which is expandable in the anterior segment, behind the globe.

Optic nerve sheath ultrasound is a simple, safe, inexpensive, bedside diagnostic test analogous to the measurement of BP and has the potential to replace invasive ICP monitoring in cases of raised ICH. Ophthalmic ultrasound typically uses a frequency between 5 and 10.5 MHz to evaluate the eye and orbit [9, 10].

Two measurements are made for optic nerve:

One in the transverse plane, with the probe in horizontal, and one in the sagittal plane, with the probe in the vertical.

The final ONSD is the average of these measurements. ONSD is measured 3 mm behind the optical disc [11, 12]. The optic nerve appears as a sagittal hypoechoic structure, 4.5 to 5 mm thick, with 25 mm in length that runs from the outer part of the eyeball to the apex of the orbit.

The optical disc is seen as a hyperechoic line at the posterior pole of the globe. With high interobserver agreement, with a median difference of 0.2–0.3 mm [11].

Ultrasonography of the optic nerve sheath is easy to perform. Despite this, in-depth knowledge of the anatomy of ultrasound and the scanning technique is mandatory for the proper use of the technique in the appropriate clinical setting [11, 12].

Most authors have suggested that the reasonable upper value of ONSD is 5 mm. However, further studies suggest that the cutoff value of the ONSD that provides the best precision for the prediction of intracranial hypertension (ICP = 20 mmHg) is 5.7–6.0 mm and that the ONSD values above this limit should alert the doctor for the presence of raised ICP [9–11].

According to Geeraerts et al., a strong relationship was found between the ONSD average and the ICP. When using 5.8 mm values as a cutoff point, a very low probability of having a high ICP was observed when the ONSD had smaller dilations [13–18].

Despite the advantages, ultrasound of the optic nerve sheath has some limitations. In patients with ocular trauma and other diseases of the optic nerve complex, the assessment of ONSD can be challenging. Traumatic optic neuropathy is seen in a significant number of patients with severe head trauma, and the effects of eye trauma on ONSD are unclear [3, 18–24].

4. CT scan optic nerve sheath diameter

Measurement of the optic nerve sheath by tomography is also a valid method. In a study with 41 patients, with a cut-off point of 6.35 mm, obtained a sensitivity of 0.93 (95% CI 0.84–1.00), specificity of 0.80 (95% CI 0.50–1.00), and AUC was 0.87 (95% CI 0.69–1.00). The values are different between several studies. Sekhon et al.

reported that ONSD measured 3 mm posterior to the retina by portable CT predict elevated ICP with a cutoff point of 6.0 mm, the sensitivity of 97% and specificity of 42% [15]. Vaiman et al. describe that ONSD could also predict elevated ICP when measured 10 mm posterior to the retina and with a cutoff point of 5.5 mm, the sensitivity of 83% and specificity of 94% [15, 16, 25–28].

Recently Liu et al. described that 4.99 mm was the ideal cutoff point to predict PIC>20 mmHg., with a sensitivity and specificity of 68.75% and 94.74%, respectively. Also, these authors developed a prognostic model with the admission GCS and Rotterdam tomographic scores. They observed that when the measurement of the optic nerve sheath was included, there was a higher discriminative power, sensitivity, and specificity for surgical indication. There are standard indications for surgical intervention described in the various guidelines (hematoma, compression of the cisterns at the base, deviation from the midline, and Glasgow coma scale). Complementary, the width of the sheath of the optic nerve, especially if higher than 5.09 mm (in this Liu et al. model) can be a predictor of surgical indication [15, 16, 22–30].

Despite this, we note that this analysis will help a lot in decision making. New studies with a more significant number of patients will be able to assess whether the sheath of the optic nerve will be included in flowcharts for surgical indication [16, 31, 32].

5. MRI optic nerve sheath diameter

The ONSD dimensions measured by MRI have been reliable in predicting ICP as reported by recent studies. Geeraerts et al. found that ONSD measured by conventional brain T2-weighted MRI correlates with invasive ICP [33]. They have demonstrated that an enlarged ONSD was a robust predictor of raised ICP with an area under Receiver Operating Statistic (ROC) curve equal to 0.94. An ONSD <5.30 mm was unlikely to be associated with raised ICP, whereas an ONSD above 5.82 mm was associated with a 90% probability of raised ICP.

The most significant limitation of its use in the acute phase of trauma is related to the examination duration and the need for care related to the magnetic field [30, 31].

6. Near-infrared spectroscopy - NIRS

Near infrared spectroscopy (NIRS) is an imaging technique used in both clinical and emergency medicine, as well as in research laboratories to quantify and measure the oxygenation status of human tissue non-invasively [34].

This is done by monitoring changes of the oxygen saturation of hemoglobin molecules in the body, based on the absorbance of near-infrared light by hemoglobin. The importance of such measures, especially in cerebral physiology, is that the human brain utilizes oxygen to continuously supply neurons with energy used for vital body functioning. In the absence of oxygen, as is the case during ischemic stroke or exsanguination, cognitive and functional impairment resulting in death often occurs.

Patients with raised ICP have alterations in the NIRS, mainly during the Lundberg B waves. Based on their observations in patients with TBI, spontaneous fluctuations in Hb and HbO2 changed their pattern with an increase in ICP [35–38].

The basis of NIRS relies upon two principles:

1. that tissue is relatively transparent to near-infrared light and

2. that there are compounds in tissue in which absorption of light is dependent on the oxygenation status of the tissue.

The propagation of light in tissue depends on the combination of absorption, scattering, and reflection properties of photons. Absorption and scatter in tissue is dependent on the wavelength. Scatter decreases with increasing wavelengths; thereby favoring the transmission of near-infrared light compared to visible light.

NIRS, like most technology, has various limitations. The most important of those limitations are as follows: interference from non-targeted chromophores; indefinite differential path-length; unknown scattering loss factor; and complicated signal interpretation.

Considering the pending technical challenges, the limited number of patients studied, and the conflicting results and opinions on this subject, we believe that this non-invasive method of predicting ICP should be restricted to research centers.

Cerebral injury due to hypoxic/ischemic and hyperperfusion are common issues associated with clinical and surgical practice. Monitoring of cerebral oxygenation during surgery, e.g.; cardiac and cerebral endarterectomy, has been shown to improve patient outcomes and reduce the risk of negative surgical outcomes. In addition to surgical monitoring, NIRS technology provides useful insight into cerebral hemodynamics when used in combination with other cerebral monitoring systems. NIRS monitoring and comparisons have been made with transcranial Doppler (TCD) and electroencephalography (EEG) in its ability to accurately predict cerebral ischemia and hyperperfusion. In addition to perioperative monitoring in clinical settings, many researchers utilize the various NIRS systems to reflect on the cerebral tissue oxygenation status during environmental and exercise interventions despite strong evidence and proper analytical techniques [36, 39].

7. Transcranial Doppler - TCD

Transcranial Doppler (TCD) was developed in Switzerland in 1982 by Aaslid et al. [28]. A low frequency transducer (≤2 MHz) emits and receives ultrasound waves able to pass through skull bone and allow hemodynamic brain evaluation noninvasively2, through the observation of arterial blood flow systolic and diastolic velocities (**Figure 4**). With the introduction of TCD in Neurology, Neurosurgery and Intensive Care, new frontiers were opened to the understanding of the physiopathology of the various diseases associated with the dynamics of brain blood flow. TCD is performed at the bedside, has low cost and can be repeated whenever necessary without the need for patient transport, allowing the diagnosis and evolutionary follow-up of cerebrovascular diseases.

The main applications of TCD for brain hemodynamic monitoring in adults and children are:

- functional evaluation of intracranial circulation by estimating cerebral perfusion pressure and reactivity tests at different stimuli (CO2, arterial pressure, etc.) [40, 41].

- subarachnoid hemorrhage (HSA)6, head trauma and other diseases that may occur with intracranial hypertension and segmental vessel stenosis [42]

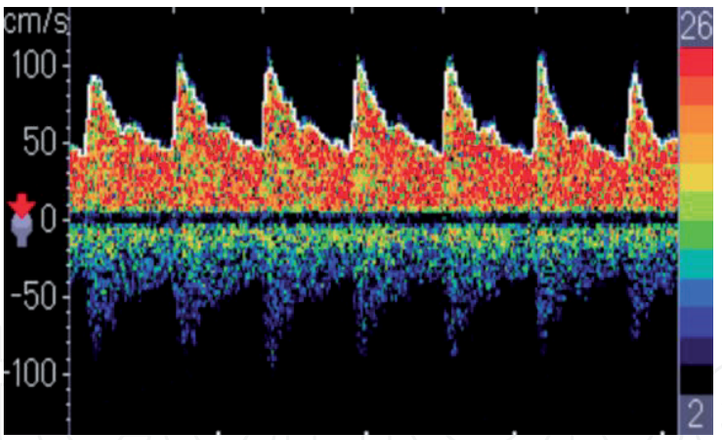

Figure 4.
Spectral wave graph that has a peak systolic velocity (A) and final diastolic velocity (B).

- evaluation in ischemic cerebrovascular disease with and without arterial diseases, of intra- and extracranial arteries [43, 44],
- ischemia mechanisms determination, whether arterial–arterial embolism, cardioembolic, arterial–venous shunting or hemodynamic [45, 46]
- measurement of hemodynamic repercussion in systemic diseases (sepsis and liver failure) [47, 48]
- risk of stroke evaluation and follow-up in sickle cell anemia16,
- complementary diagnosis of brain death [49, 50]

7.1 Hemodynamic indices of transcranial Doppler and functional evaluation

The indexes calculated from the spectra of blood flow velocities obtained by TCD allow the characterization of brain circulatory patterns (**Table 1**). Thus, the following variables are analyzed: mean velocity (Mv), systolic velocity (Sv), diastolic velocity (Dv), Gosling Pulsatility Index (PI), Pourcelot Resistance Index (RI), Lindegaard Index (LI), Soustiel Index (SI) and breath-holding index (BHI).

Mv is the central parameter of brain blood flow velocity spectrum analysis and is defined by the following formula: $Mv = Sv + (Dv \times 2)/3$ [51] .Mv is a variable influenced by different physiological factors and its interpretation cannot be performed in isolation. Changes in Mv are due to age, sex, temperature, partial CO_2 pressure ($PaCO_2$), mean arterial pressure (MAP), hematocrit, pregnancy, presence of hypermetabolic states, and administration of anesthetic/sedative drugs. In general, there is an increase of the Mv from 6 to 10 years of age, then, there is a lifetime reduction [52].

PI is the relationship between systole and diastole of the cerebral blood flow velocity spectrum. In situations where there are no cardiovascular pathologies and where there is no change in the diameter of the studied vessel, this index can be used to indirectly assess the integrity of the distal vascular bed and provide information on the microvascular brain resistance. It is calculated by the formula: Sv-Dv/Mv; its acceptable value ranges from 0.6 to 1.19 [53]. In stenosis or proximal occlusions, there may be a reduction in PI due to downstream arteriolar vasodilation. On the other hand, critical stenosis or distal occlusions, as well as microvascular vasoconstriction may be associated with PI elevation in proximal arterial segments. The PI below 0.5 may indicate the presence of intracranial arteriovenous malformation,

Index	Formula
Average speed (Mv)	Mv = Sv + (Dv × 2)/3
Pulsatility Index (PI)	IP = Sv - Dv / Mv
Resistance Index (RI)	IR = Sv – Dv / Sv
Lindegaard Index (LI)	IL = MCA Mv / extracranial ipsilateral ICA Mv
Soustiel Index (SI)	IS = BA Mv / VA Mv
Breath-holding index (BHI)	BHI = (Mv after apnea - Baseline Mv) / Baseline Mv) × 100/30

MCA - middle cerebral artery; BA - basilar artery; VA - vertebral artery; Mv – mean velocity; Sv - systolic velocity; Dv - diastolic velocity.

Table 1.
Brain hemodynamic indexes.

since the resistance in the proximal vessels is reduced due to the absence of brain tissue between arterioles and venules. PI can correlate positively with intracranial pressure (ICP); changes of 2.4% in PI may reflect a variation of 1 mmHg in PIC. The RI is calculated by the following formula: Sv-Dv/Sv. In practice, it has the same function of PI and values greater than 0.8 indicate an increase downstream of resistance to blood flow [54].

LI is defined as the relationship between the Mv of the middle cerebral artery and the Vm of the ipsilateral extracranial internal carotid artery. In the condition of significant increase of Mv in the middle cerebral arteries, this index allows the differentiation between hyperdynamic blood flow and vasospasm [55]. A LI lower than 3 may suggest hyperdynamic blood flow and an LI greater than 3 may suggest narrowing of an artery segment as occurs in vasospasm. SI consists of the relationship between the Mv of the basilar artery and the extracranial vertebral artery. This index is used for the diagnosis of vasospasm in the posterior brain circulation. These indices together with Mv in the studied arteries are also used to classify the degree/severity of vasospasm, as shown in **Table 2**.

7.1.1 Reactivity test

BHI or voluntary apnea Index evaluates CO2 reactivity and is given by the following formula: (Mv after apnea - baseline Mv) /baseline Mv) × 100/30, in which 30 represents time in seconds of voluntary apnea performed by the patient. This index evaluates brain circulatory reactivity to hypercapnia (CVR), that is, the vasodilator capacity of brain circulation during elevation of carbon dioxide induced by apnea. BHI > 0.6 indicates preserved CVR, between 0.21 and 0.60 indicates compromised reactivity, and ≤ 0.20 reserves significantly compromised. Impairment of CVR may be related to a higher risk of cerebral ischemia caused by hemodynamic mechanism [56].

7.1.2 Noninvasive estimation of cerebral perfusion pressure

Several studies have shown that the measurement of blood flow velocities in the middle cerebral arteries by TCD allows an alternative noninvasive method of estimating cerebral perfusion pressure (eCPP) with high positive predictive value and low negative predictive value. The estimation of eCPP by TCD uses a method that involves Fourier's analysis of the first harmonic of the waveforms of both systemic blood pressure and the velocity of blood flow in the middle cerebral artery [57].

Vasospasm severity (MCA)	**Mv (cm/s)**	**LI**
Take	120–130	3rd-3.9th
Moderate	131–180	4–6
Serious	>180	>6
Vasospasm Severity (AB)	**Mv (cm/s)**	**SI**
Take	70–85	2–2.49
Moderate	>85	2.5–2.99
Serious	>85	>3

MCA - middle cerebral artery; BA - basilar artery; Mv - mean velocity; LI - Lindegaard Index; SI - Soustiel Index.

Table 2.
Diagnostic criteria for vasospasm by CTD.

Several studies have demonstrated an adequate correlation between TCD to estimate eCPP and invasive measurement through the ICP catheter. Therefore, it has been proposed as a safe technique with the potential benefit of allowing intermittent or continuous analysis through monitoring. It can be used in situations where invasive measurement cannot be performed or when eCPP does not appear to be real or questionable. It is a robust, noninvasive method and allows qualitative analysis of CBF and tissue perfusion. Therefore, it can be used as an important guide for clinical management of patients who are victims of acute brain injury [58].

7.2 Subarachnoid hemorrhage (SAH)

Patients with SAH may experience cerebral blood flow and metabolic changes that may culminate in increased intracranial pressure and ischemia. Three hemodynamic stages can be identified in this context: hyperemia, oliguemia and vasospasm. With TCD recognition of hemodynamic stages, physicians can be guided for optimal patient treatment [59].

7.2.1 Oliguemia stage

In general, in the first 24 hours, there is an overall decrease in cerebral blood flow (CBF) which may be due to two mechanisms: increased intracranial pressure associated with reduced cerebral perfusion pressure and intense microvascular constriction associated with low concentrations of nitric oxide (NO). These phenomena can trigger tissue hypoperfusion, decreased supply of tissue O2 with consequent ischemia.

TCD in the hyper-acute phase of SAH may demonstrate cerebral oliguemia status. Thus, it helps decision-making in clinical conduct to be adopted, such as: 1) management of mean arterial pressure (MAP) more appropriate; 2) avoid hyperventilation, which in turn will cause hypocapnia and further reduction of CBF; and 3) avoid states that increase brain tissue metabolic demand (e.g. fever, seizure, etc.).

7.2.2 Hyperemia stage

Brain microcirculatory vasodilation causes overall elevation of CBF. States of brain hyperemia may signal neurovascular decoupling and autoregulation impairment due to brain or systemic tissue acidosis and, in general, occurs 24 hours after the state of oliguemia.

TCD is able to identify the state of cerebral circulatory hyperdynamia and, consequently, guide the management of the hemodynamic condition of patients in order to avoid brain swelling associated with this condition. At this stage, situations that worsen the condition of brain hyperemia, such as hypercapnia, systemic arterial hypertension, anemia, and hypermetabolic brain conditions (e.g., seizure) should be avoided. In the study of cerebral autoregulation (CAR) the ability of the brain to maintain constant blood flow dynamics regardless of variations in systemic blood pressure is evaluated. SAH is one of the pathologies in which ra is impaired, which requires adequate systemic blood pressure levels to prevent hyperemia or oliguemia. TCD can identify CAR impairment through the relationship between flow velocity oscillations in the face of MAP changes (spontaneous or provoked); and this analysis is performed through modeling used in signals analysis, requiring the use of specific software for this purpose. Thus, TCD can help identify the most appropriate blood pressure range in impaired states.

7.2.3 Vasospasm stage

Vasospasm in SAH is one of the main causes of late cerebral ischemia. Therefore, its early recognition is mandatory in the clinical management of neurocritical patients. Before symptoms arise, vasospasm can be detected by TCD. Thus, clinical treatment of vasospasm can be instituted early, before the installation of neurological deficits.

There are several reasons that determine late cerebral ischemia in SAH-related vasospasm: 1) vasospasm intensity; 2) occurrence in multiple arteries or sequential vasospasm in "Tanden"; 3) presence or absence of activated collateral circulation; 4) early onset of vasospasm; 5) fast vasospasm progress (elevation of >25 cm/s/day); 6) associated tissue hypermetabolism; 7) mitochondrial tissue dysfunction; 8) presence of intracranial hypertension; 9) associated circulatory oliguemia; 10) impaired brain microcirculatory reserve; 11) preexistence of intracranial stenosis [60].

TCD is capable of detecting vasospasm in the middle and basilar cerebral arteries with high sensitivity and specificity [60]. Classically, vasospasm can occur between 4 and 14 days after the day of bleeding, and in some cases (13% of patients) can be detected early in the first 48 hours or late after 17 days. The possibility of monitoring vasospasm intensity may allow the optimization of clinical management. In severe vasospasm, the conjunction of other hemodynamic factors also observed by TCD determines the indication of, in addition to clinical measures, such as the use of vasoactive drugs and/or endovascular interventional treatment. The opportunity for the evolutionary follow-up of the response obtained to the treatment adopted is also an important benefit of TCD at this stage. **Table 2** shows the diagnostic and classification criteria of vasospasm severity by TCD using Mv and LI.

7.3 Traumatic brain injury

Intracranial circulatory abnormalities occur frequently in patients with TBI. Ischemic brain lesions can be identified in about 90% of patients who die after severe TBI [61], suggesting that changes in systemic and/or brain blood flow dynamics are frequent causes of ischemia and unfavorable outcomes. Studies of blood flow and brain metabolism suggest that hyperemic brain phenomena are the most frequently found in comatose patients after severe TBI [62].

7.3.1 Brain hemodynamic phases after severe TBI

As in SAH, there is a definition of 3 hemodynamic stages after severe TBI. The oliguemia stage occurs on the day of TBI (day 0) and is characterized by a reduction

in CBF. The hyperemia stage usually occurs on days one through three and is characterized by increased CBF. The vasospasm stage usually occurs from days 2 to 6 after TBI and there may be a reduction in CBF.

7.3.1.1 Oliguemia stage

Cerebral changes in the acute stage of moderate or severe TBI, characterized by reduced blood flow velocity and increased PI in intracranial arteries, can be revealed by TCD, including during the first three hours after TBI occurrence. At this stage, TCD should be used early in order to guide therapeutic approaches. When oliguemia has been demonstrated, the possibilities of systemic blood pressure insufficiency of maintaining CBF dynamics (MAP below the autoregulation range), hyperventilation with reduction of partial arterial CO2 pressure, resulting in cerebral microvasculature vasoconstriction, posttraumatic thrombosis of the carotid arteries, and intracranial hypertension (especially if associated with increased PI) should be considered. The reduction in blood flow velocity in cerebral arteries may also be due to brain hypometabolism that may be associated with severe brain lesions. Presence of oliguemia may be associated with a higher risk of brain ischemia and an unfavorable prognosis [63].

7.3.1.2 Hyperemia phase

Cerebral hemodynamic patterns indicative of hyperemia can be detected by TCD in about 30% of patients during the first two weeks after severe TBI. The occurrence of this pattern is associated with worsening brain swelling and increased intracranial pressure. TCD can identify patients with posttraumatic brain hyperemia prior to the development of brain swelling, which allows the establishment of therapies aimed at minimizing neural tissue lesions secondary to ICH, such as the determination of the best mean arterial blood pressure range or the determination of the best PCO2 for a patient on mechanical ventilation. Persistence of hyperemia status may be associated with poor neurological prognosis [64].

7.3.1.3 Vasospasm phase

Studies with TCD in TBI estimate the occurrence of vasospasm in 50% of patients. There is an important association between vasospasm with severe hemodynamic repercussion and unfavorable neurological prognosis, although this repercussion is lower than in cases of spontaneous SAH. It is important to highlight that posttraumatic vasospasm of the basilar artery doubles the possibility of unfavorable prognosis, compared to patients without spasm of this artery. The duration of vasospasm in patients with TBI tends to be shorter due to the non-inflammatory nature as a cause, unlike subarachnoid hemorrhage. Possibly the origin of traumatic vasospasm is associated with stretching of the arteries during trauma and peak intensity, in many cases, occurs between the fifth and seventh day after trauma, although a duration similar to SAH is observed in some cases [65].

Among other applications of TCD in severe TBI, it is worth mentioning: 1) to detect brain circulatory changes resulting from ICH; 2) to evaluate the degree of autoregulation and cerebrovascular reactivity impairment, enabling the prediction of prognosis; 3) to provide evidence of posttraumatic dissection or thrombosis of the arteries that irrigate the brain, allowing early investigation and adoption of

measures to prevent brain infarctions; 4) to verify relative changes in the dynamics of brain blood flow in response to the treatments instituted.

7.4 Intracranial hypertension

TCD is important for assessing the effects of ICH on brain circulation. It is especially useful in patients where invasive ICP monitoring is absent because it allows the estimation of cerebral perfusion pressure (eCPP) (Section 1.1.2). In addition, changes in intracranial pressure may be associated with alterations in intracranial flow waveform. Thus, the increase in ICP can lead to PI elevation with progressive reduction of mean and diastolic blood flow velocities. In general, PI modifications occur when CPP is less than 70 mmHg2. At the moment when ICP is equal to diastolic systemic blood pressure, the blood velocity of diastolic flow reaches zero, characterizing the momentary absence of cerebral blood perfusion during the diastolic phase of the cardiac cycle [66].

In other situations, even with invasive ICP monitoring, TCD also plays a key role as a real-time evaluator of the efficacy of therapeutic measures used for the treatment of ICH; TCD can also be used as an alternative method to detect erroneous measurements of ICP monitors. Furthermore, TCD may reveal that increased ICP may be associated with hyperdynamic brain circulation due to impaired cerebrovascular autoregulation. In this condition, CPP formula cannot be used as a parameter to improve cerebral perfusion in the presence of ICH.

TCD also allows the evaluation of intracranial compliance by means of simultaneous compression maneuvers of the internal jugular veins and the increase of MAP. Under normal conditions, this maneuver causes a slight increase in brain blood volume and ICP augmentation. In patients with reduced intracranial compliance, venous compression would cause PI elevation and reduction of mean brain blood flow velocities [67] leptomeningeal arteries during acute arterial occlusion. Still in the acute phase, the detection of emboli by TCD in the region of the occluded artery may be indicative of recanalization of this arterial segment.

In the subacute stage of ischemic cerebrovascular disease, TCD assesses the hemodynamic repercussion of extracranial carotid disease through CO2 reactivity tests and the presence and hemodynamic repercussion of intracranial stenosis. Embolic activity in a single intracranial arterial system may suggest an embolic source that originates from the ipsilateral carotid artery (arterial embolism) and this finding is suggestive of an increased risk of recurrence of the ischemic event when embolic activity is detected in multiple intracranial arterial systems such as bilateral carotids and vertebrobasilar, it may be suspected that the emboli have cardiac, aorta and/or paradoxical origin. With the infusion of saline solution with microbubbles (small particles of gas) in peripheral vein, TCD can detect the passage of microbubbles in brain circulation, allowing diagnosis of communication between arterial and venous circulations, such as the oval foramen persistence or pulmonary fistula [68].

In summary, TCD in ischemic cerebrovascular disease allows: 1) to detect intracranial arterial stenosis and occlusions; 2) to study the hemodynamic brain effects resulting from extracranial occlusive carotid diseases; 3) to evaluate the pattern and effectiveness of brain collateral circulation; 4) quantify vascular reserve by means of reactivity tests to carbon dioxide; 5) detect the passage of microemboli, in real time, through intracranial circulation; 6) to monitor the reopening of obstructed intracranial arteries, either spontaneous or consequent to thrombolytic therapy, in the acute stage of the ischemic cerebrovascular event.

7.5 Transcranial Doppler in systemic conditions

7.5.1 Liver cirrhosis with encephalopathy and liver failure

Several studies show that CBF is compromised in patients with acute or chronic severe liver disease, especially in the presence of hepatic encephalopathy (HE). In this condition, there is impairment of brain autoregulation and, consequently, the variation of MAP may be associated with changes in CBF. Although hyperammonemia is the main cause of HE, recent evidence suggests that abnormalities in CBF may also have some relationship in its pathophysiology. There is a hypothesis that cirrhotic patients with encephalopathy present cerebral vasoconstriction more pronounced and, consequently, progressive PI elevation and BHI reduction as the disease progresses (score CTP ≥ 7 or MELD ≥14). The more severe encephalopathy, the more changes are observed in cerebral hemodynamics [69].

In mild HE, there is also an increase in brain microcirculatory resistance and, consequently, an increase in PI and RI, with a significant correlation with the increase in Child-Pugh score. Therefore, TCD may be an aid in the diagnosis of HE in cirrhotic patients. An important complication of severe HE is intracranial hypertension. This is due to three main mechanisms: 1) brain swelling secondary to the cytotoxic effect of hyperammonemia; 2) breakage of the blood brain barrier and 3) hyperemia secondary to CAR impairment. TCD can provide information regarding the dynamics of brain blood flow in patients with ICH and assess CAR [70].

7.5.2 Sepsis and sepsis-associated encephalopathy

Hemodynamic impairment is a fundamental feature of sepsis. Brain microcirculation can be gradually compromised and, consequently, cause significant changes in CBF. These factors play an important role in the etiology of sepsis-associated encephalopathy (SAE) [71]. SAE is a frequent brain dysfunction that occurs in 50% of patients admitted to intensive care units, being one of the most common causes of delirium in this population. In addition, SAE is associated with an increase in mortality.

In the early phase of sepsis, there are progressive increases in Mv and PI over time, which are evident 24 hours after onset; at this stage, CAR may remain unchanged. In contrast, in the posterior stage of sepsis (patients with severe sepsis or septic shock), there are progressive reductions in Mv and PI, as well as impairment of CAR. The increase in PI associated with increased cerebrovascular resistance has been correlated with a higher prevalence of delirium and coma. Many of the factors that lead to changes in CBF (such as changes in CVR and CAR) are often the result of a dysfunction of brain tissue microcirculation due to the release of inflammatory mediators.

The use of TCD to assess brain hemodynamic patterns has some clinical advantages: 1) TCD can be used to identify cerebral hemodynamic patterns in sepsis that may precede systemic hemodynamic signs; 2) increased PI in confused patients may be an early sign of sepsis and help decrease time to diagnosis [71]; and 3) the identification of real-time CBF changes with TCD, correlating with systemic hemodynamic changes, may improve the management of blood pressure and blood volume in septic patients.

7.6 Brain death

Brain death is defined as total and definitive cessation of all brain functions. TCD is valued in the medical literature as an examination of choice for this purpose

due to the advantages of being noninvasive, of being performed at the bedside and of allowing repetition, if necessary38. TCD sensitivity for brain death diagnosis reaches values greater than 95% and specificity of 100% [50].

TCD should show no bilateral blood flow in the arteries of the intracranial carotid system and the vertebro-basilar system under normal body temperature conditions for at least 30 minutes. The criteria are: 1) presence of oscillatory flow (systolic velocity equal to reverse diastolic velocity – final flow zero) or 2) systolic spikes or 3) disappearance of intracranial flow with typical signs observed in the extracranial circulation [72].

8. Conclusion

Cerebral circulatory changes are often found in ICU daily practice and can lead to secondary tissue damage. Hypoxia, ischemia, intracranial hypertension, traumatic brain injury, stroke, kidney or liver failure, and sepsis can impair CAR. Since CAR mechanisms have been impaired, CBF passively follows MAP changes, which in turn compromise CPP.

A number of factors can influence the CBF and its regulation, so the monitoring and control of these factors by TCD can help adjust CBF to brain metabolic demands.

TCD has the advantage of allowing bedside access to brain hemodynamic modifications, whether intermittent or serial and continuous monitoring. The disadvantage of the method is given by operator dependence and intensive training requirement, so that it can be applied in practice by physicians with clinical expertise in various primary or systemic diseases that affect the CNS.

9. Last words

Noninvasive methods represent an advance in patient management, and will be increasingly present in hospitals. Understanding and proper use of these methods are essential to ensure that the best results will be achieved.

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