Chapter

Intracranial Pressure Waveform: History, Fundamentals and Applications in Brain Injuries

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Abstract

Intracranial pressure (ICP) can be analyzed for its absolute value, usually in mmHg or cmH2O, its tendency over time and the waveform of its pulse. This chapter will focus on the waveform of the ICP pulse (ICPwf), already observed since 1881, and for a long time not understood. Studies conducted in recent decades show the correlation between the ICPwf and intracranial compliance (ICC), another important clinical parameter added to the practice in the second half of the last century. ICC allows physicians early analyzing patients' neurological conditions related to disorders resulting from variations in cerebrospinal fluid (CSF), blood and intracranial tissue volumes. This chapter is an invitation to dive into the history and development of ICPwf analysis, clinical uses already adopted and others still under study.

Keywords: intracranial pressure waveform, intracranial compliance, ICP

1. Introduction

Technological development has brought the opportunity for significant advances in the health area. As new sensors have been developed, tools for image acquisition and treatment are improved and analytical methods using modern algorithms and artificial intelligence are developing, the set of tools available to assist in the diagnosis and monitoring of patients has been expanded.

ICP is a good example of how technological advancement has led to clinical understanding. Initially, only the number corresponding to the mean ICP was used to guide clinical procedures. Until then, there was only one number, and the information was punctual, it was as if we looked at a photo.

Advancing in understanding disclosed the value of having available real time information on early stages of intracranial hypertension (ICH), thus, techniques that show the pressure trend curve proved to be remarkable for the follow-up of critically ill patients.

The information resulting from morphology will be treated in greater detail in this chapter, and today it is known that monitoring ICP is far over knowledge of a mean value, but also its trend over time, and the morphology of the pressure pulse recognition.

2. History

The history of ICPwf is centuries-old. For understanding, it is necessary to go back to the year 1783, after researcher Alexander Monro [1], who started studies of intracranial structures. His work was later completed by George Kellie [2], giving rise to the Monro-Kellie doctrine. This doctrine showed that the volume of intracranial components (blood, CSF and brain tissue) and the bone box that contains them is fixed. The volume of these components needs to be under balance, if there is an increase in one, the others need to compensate by reducing their volumes. Thus, intracranial hypertension (ICH) emerges when this compensation ceases to happen [3]. The stiffness of the skull was later challenged by the work of Sérgio Mascarenhas in 2012 [4].

Angelo Mosso, at the end of the 19th century, presented results showing the influence of brain activity on its blood flow. For the first time, it was possible to observe the brain pulses, through a system that captured these pulses and recorded them on paper. These figures can be seen in Zago's manuscript [5]. Many years later these pulses were related to ICP and CSF [6].

Langfitt [7] brought an important contribution showing the mathematical hypothesis for the relationship between ICP and intracranial volume, making it easier to understand the importance of intracranial compliance (ICC=ΔV/ΔP) in critical care. Marmarou [8] in 1975 added to the pressure-volume curve the information about the increase in the amplitude of ICPwf as the mean value of ICP increases, and demonstrated that ICPwf contains unique information on intracranial contents, this data has already proven useful in several diseases such as stroke, hydrocephalus, idiopathic intracranial hypertension and brain injuries. It is important for gathering information on cerebrovascular hemodynamics and also of the cerebrospinal compensatory system. In 1983, Cardoso [9] showed that with the increase in ICP, in addition to the increase in the amplitude of its pulse, there was also a change in its configuration, as morphology became pyramidal with an increase in amplitude in the middle region of the pulse. Cardoso also shows the ICPwf configuration: P1 - systolic peak, P2 - tidal wave and P3 - venous return (explained in detail below).

Hu [10], understanding the possibility of using ICPwf as information to aid in diagnosis, created an algorithm called MOCAIP (Morphological Clustering and Analysis of Continuous Intracranial Pressure). This software is able to turn the waveform into numbers to facilitate the interpretation of the medical team. Nucci [11], in 2016, presented results of a software to calculate ICPwf parameters and clusters of waveforms for different stages of pathology.

Ballestero [12] and Bollela [13], in 2017, presented studies with hydrocephalus and meningitis respectively, that showed the applicability of a new noninvasive sensor to monitor the ICPwf, in the Ballestero study the ICPwf was analyzed through the relationship between the amplitude of the P2 and P1 pulses.

ICPwf is an important information, increasingly disseminated among physicians. New methods and analyses facilitate the use of this parameter, which is useful and disseminating over clinical institutions. The next chapters will provide more details and clinical applications of ICPwf.

3. Intracranial pressure- waveform pathophysiology

3.1 Waveform components

ICP is determined by the intracranial components volumes, as the brain tissue, the vascular or cerebral blood flow (CBF) and cerebrospinal fluid (CSF) [14, 15], and relations between them in a semi-rigid skull box, the Monroe-Kellie doctrine. Each cardiac beat corresponds to an ICP waveform composed of three peaks; arterial pulsation- P1, cerebral venous flow, secondary to autoregulation-derived cyclic fluctuations of arterial blood volume, reflecting intracranial compliance- P2, and the aortic valve closure- P3 (**Figure 1a**).

These cardiac-derived pulsatile signals are overlapped in time domain with the respiratory cycle, with influence in the cerebral venous pulsation by means of intrathoracic pressure generated by breathing, disclosed as slow waves [16] (**Figure 1b**). Moreover, ventilation plays a direct and remarkable role over CBF [17]. Thus, ICP is influenced by many physiological factors from extra and intracranial compartments. Moreover, factors as age, body posture, time of day as well as the clinical condition also are considerable variables, although in absence of disturbances, mean ICP is kept mostly within a range between 7 and 15 mmHg for adults, 3 and 6 mmHg in children, and between 1.5 and 6 mmHg in term infants [18].

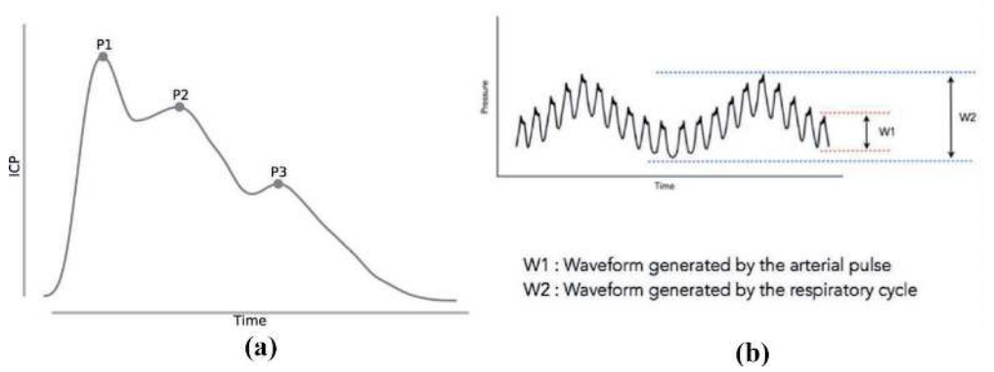

Figure 1.
(a) One single arterial pulse transmitted to the intracranial compartment, with three peaks observed; systolic peak (P1), tidal peak (P2) and aortic valve closure peak (P3). (b) Respiratory slow waves overlapping cardiac intracranial pulses spectrum (from Hall et al. [16]).

There is an existing volume of reserve in the brain which is around 60–80 mL in young persons and approximately 100–140 mL in geriatric population, because of ongoing cerebral atrophy with age. However, in normal conditions and for short time observations, the brain volume is typically static, with mean ICP varying mainly according to the CBF and the balance between production and absorption or outflow of the CSF. The relation observed between these intracranial components is named intracranial compliance (ICC). Compensatory mechanisms exist to maintain intracranial volume homeostasis by extrusion of the CSF or venous blood, in order to preserve ICC, otherwise, these efforts may be insufficient in pathological conditions (i.e. traumatic brain injury) with intracranial hypertension (ICH) and ICC impairment producing primary or secondary brain tissue damage [19, 20].

Langfitt et al. characterized the transmission of pressure across the intracranial compartments as the intracranial elastance curve, observing an exponential behavior between ICP and intracranial volume [21], from a stable ICP vs. volume relation until

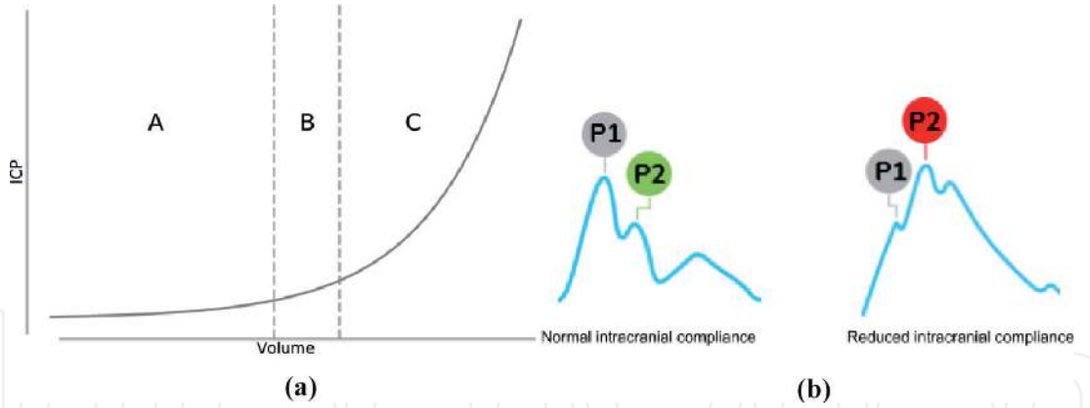

Figure 2.
(a) Langfitt curve representing volume x ICP exponential behavior with A- normal ICC, B- intracranial buffering capacity begins to exhaust and C- ICC impaired with rapid ICP elevation (from Canac et al. [18]) (b) representation of altered ICP curve with ICC impairment.

when a change in volume of any component will result in a commensurate change in ICP (**Figure 2a**). When ICP raises and compromises ICC, an inversion in ICP peaks relations may be observed [9], with ICH transmitted to the venous and ventricular compartments, affecting the buffering mechanisms (**Figure 2b**).

When mean ICP is elevated, the vascular (cardiac) waveform amplitude increases while the respiratory waveform amplitude decreases, associated with changes in the relationship between peaks P1, P2, and P3 [19, 22]. Different waves morphologies could reflect the residual compensatory capacity of the brain, since changes in the ICP wave shape are informative on an incoming or established alteration of the intracranial system (**Figure 3**) [11].

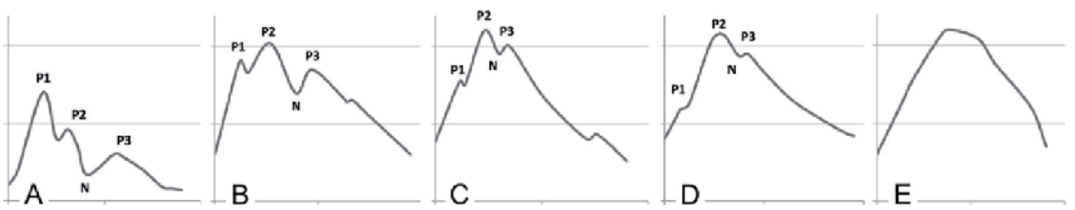

Figure 3.
A - Normal, if the first peak (P1) exceeds the other two; B - potentially pathological, if the tidal peak (P2) equals or slightly exceeds the systolic one (P1) and the dicrotic peak equals or is slightly inferior to P1; class C - likely pathological, if the tidal and the dicrotic peaks exceed the first one; D and E- pathological, if the tidal and the dicrotic peaks surmount the first one or if the shape of the curve is so rounded as not to permit the identification of the three peaks (from Nucci et al. [11]).

3.2 Slow waves

Additionally to all that was explained above, further phenomena in the observance of ICP waveforms may occur with high importance on alerting the neurophysician to initiate ICP control measures on an urgent basis. These phenomena were named slow waves by Lundberg et al., typically described as A, B and C waves (**Figure 4**). The A waves are denoted as plateau waves or vasogenic waves occurring during very high ICP (>50 mmHg), the B waves are short-duration elevations in ICP (1 to 2 per minute) with variable pressure levels up to 30–50 mmHg. C waves are more frequent (about 4–8 waves per minute) elevations of mean ICP (up to about 30 mmHg). A waves are clearly severe and with elevated risk of poor prognosis, whereas the clinical implication of the B waves is a research question that remains to be determined, since they are non-specific

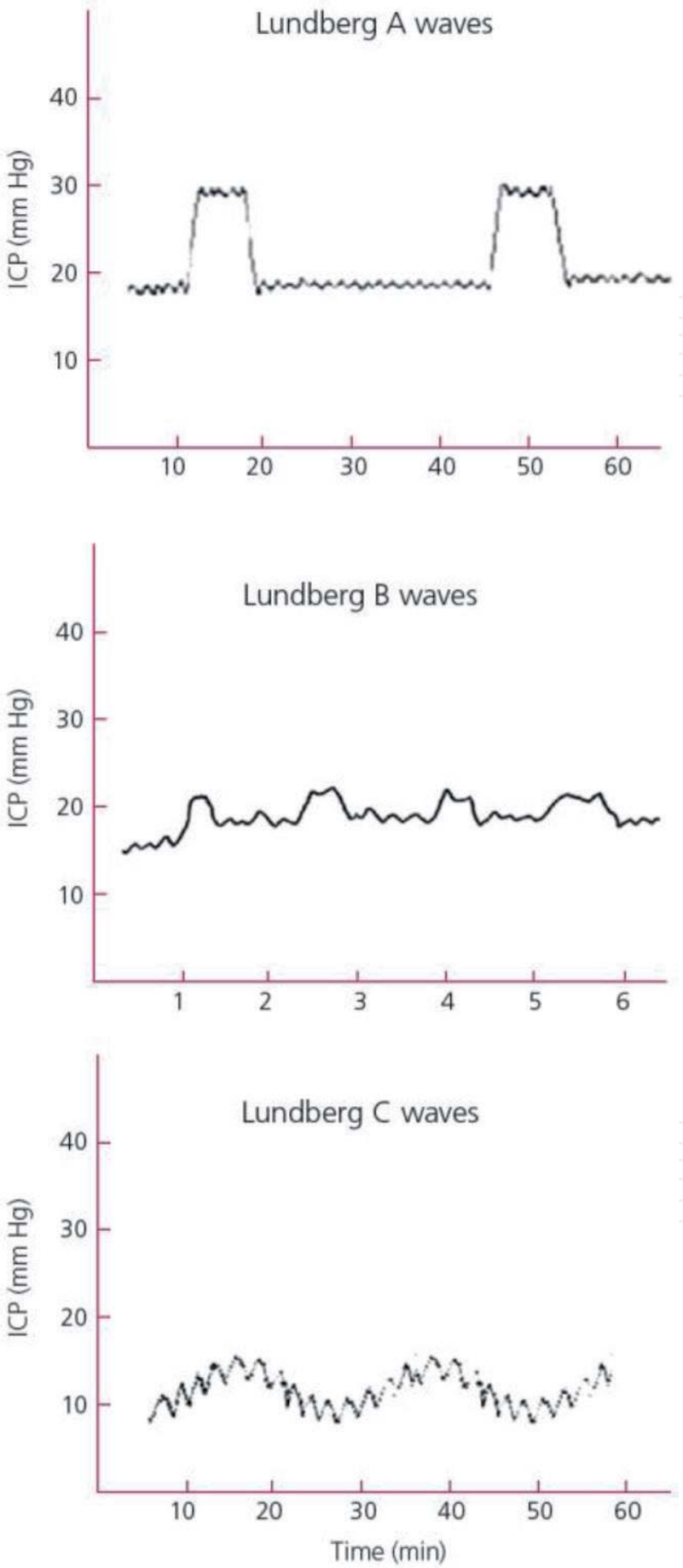

Figure 4.
Lundberg A, B and C waves (from Hirzallah et al. [23]).

indicators of diminished compliance and can also be present in patients with normal ICP [24]. Finally, C waves are products of cardiac and respiratory cycles interactions.

4. Intracranial compliance in real world

The next paragraphs will provide information on how to incorporate waveform information of ICP into clinical daily life, adding this information to the clinical set and adjunct with other diagnostic methods in different pathologies. It is worth mentioning that this information has been shown to be useful in situations where subjects present suspicion, risk or diagnosis of changes in ICC.

4.1 Aneurysm

Non-traumatic subarachnoid hemorrhage (SAH) is a situation that often results from the rupture of an intracerebral aneurysm [25]. SAH is associated with high morbidity and mortality and requires a multidisciplinary treatment, because of its high risk of complications [26].

Upon recognition, improved outcomes are dependent upon treatment by qualified high-volume centers with adequate neurovascular teams. Expeditiously determining the precipitating factor and subsequent mitigation of the cause(s) are the initial primary focus. Treatment involves early securing of a ruptured aneurysm, whether a surgical procedure or endovascular. Prior to securing the aneurysm, securing the airway, maintaining proper circulation, treating hydrocephalus, and managing blood pressure remain top priorities. After intervention, ICU observation and routine exams are compulsory.

Once patients presenting with aneurysmal SAH are acutely stabilized, they are evaluated for pathology-specific complications such as development of hydrocephalus and re-hemorrhage. Various grading scales are employed early in management to communicate the severity and prognosis of the pathology. Following stabilization and initial evaluation, patients should be transferred and admitted to intensive care units with a multidisciplinary team. Interim/short-term acute care strategies are employed to prevent rebleeding, assess hydrocephalus, maintain normotension, and reverse anticoagulant/antiplatelet agents. The risk of acute rebleed and long-term prevention of rebleed is not completely attenuated until aneurysm exclusion is performed.

Concurrent to the those risks above mentioned, in the extreme acute phase (first 48 hours) of SAH, the encephalic microvascular constriction promoted by hemoglobin degradation in the subarachnoid space may lead to a low cerebral blood flow (CBF) phenomena, with potential for brain swelling and ICC impairment. Techniques for monitoring ICC and CBF (such as transcranial Doppler) may play a crucial role in this phase.

Later, in the subsequent SAH phase, an inverse behavior is commonly seen in accordance with bleed severity, the so-called hyperemic phase. In this situation subjects present microvascular dilation, this time leading to ICC impairment for excess of CBF. An optimal therapy here is adapting CBF for satisfactory neuronal supply, under ICC adequate limits.

An additional threat for patients in this phase is the development of vasospasm, a complication which elevates risk of delayed cerebral ischemia, in opportunities needing endovascular management. The latter, associated with medical complications including fever, hyperglycemia, hyponatremia, cardiac and pulmonary complications, deep venous thrombosis and anemia may raise risk of ICC impairment. While scores classifications exist to determine an admission grade in order to provide prognostic information, outcomes are influenced by many additional

items, including a patient's values and preferences, comorbidities, social support, resilience, and time for recovery [27–31].

4.2 Tumor

The incidence and survival of patients with neuro-oncologic conditions have been increasing. Both primary central nervous and other types of cancer patients live longer due to early diagnosis and better treatment options. Global Burden Disease Study in 2016, there were 330,000 incident cases of CNS cancer and 227,000 deaths worldwide that year. It reflects the 17.3% increase in incidence between 1990 and 2016.

Extension of life expectancy and on the incidence of cancer itself predisposes to an increment in the occurrence of a variety of neurologic complications that can result in high morbidity and mortality [32, 33].

These conditions often result in hospital admissions, generally in an ICU bed, creating a heavy burden to the health care system since primary cancer patients' treatment costs 20-times more than age-matched controls without cancer [33].

The complications could occur due to a direct result of the tumor itself, to an indirect effect of cancer, or as a result of chemotherapy, radiotherapy, and other medical interventions. Recognizing the mechanism might help one early diagnosis and initiate treatment. As a mass effect directly, or even a compromise of CSF transit because of ventricle compression, intracranial neoplasm may lead to ICC impairment.

4.3 Traumatic brain injury

The World Health Organization considers traumatic brain injury (TBI) an important global health priority as it is a critical public health problem involving young adults worldwide. The leading causes of TBI are road traffic collisions, falls and interpersonal violence. This injury not only causes a large number of deaths, impairments and disabilities for individuals and their families, but also incurs great economic cost to healthcare systems due to required long-term care, rehabilitation, and loss of productivity [34].

TBI can be classified by clinical severity (mild, moderate, or severe) according to the Glasgow Coma Scale (GCS); pathoanatomic type (focal or diffuse) according to the extent of damaged area; and mechanism of injury (penetrating or blunt) according to the kinematics (**Table 1**) [35–38].

The TBI-related cellular injury involves two different processes. The primary damage occurs on the moment of trauma, immediately by the direct impact and/or structural lesion. It includes vascular and tissue tearing that causes various types of hemorrhage and nerve fibers disruption (axotomy). The secondary damage involves cellular reactive processes such as inflammation and biochemical cascades that gradually develop over the course of hours, days, even weeks after the trauma. It causes metabolic changes potentially leading to brain swelling or hydrocephalus but can also be caused by low blood pressure, hypoxia, seizures, or central nervous system infection [37, 38].

Both processes are intertwined and can contribute to complications, for instance, hemorrhagic progression of a contusion, a breakdown in the blood–brain barrier (BBB), and increased intracranial pressure (ICP). The expansion of an intracranial bleeding not only alters the dynamic shared space of encephalic parenchyma, vascular structures, and cerebral spinal fluid (CSF) inside cranial cavity – inferred intracranial compliance – but also triggers cytotoxic responses of brain cells. In addition, if there is a dysfunction of BBB its permeability changes letting plasma, proteins and proinflammatory mediators influx into the interstitial compartment causing edema, neurotransmitters imbalance, compressing all structures [38, 39].

Classification	Categories	Examples
Clinical severity	Mild	GCS: 13–15
	Moderate	GCS: 9–12
	Severe	GCS ≤ 8
Pathoanatomic type	Focal (one concise area)	Skull fracture Contusion Epidural hematomas Subdural hematomas Subarachnoid hemorrhage Intraparenchymal hemorrhage
	Diffuse (widespread area)	Diffuse axonal injury Concussion Chronic traumatic encephalopathy
Mechanism of injury	Penetrating	Gunshot wound/projectile Pierced object/weapons (knife, etc.)
	Blunt	Head rotation Jolt/blast Acceleration-deceleration

Table 1.
Different classifications of TBI.

As a result of this intricate association the ICP may rise if intrinsic compensatory mechanisms are not preserved and the sustained hypertension can prevent adequate perfusion depriving the brain of oxygen and nutrition. The combination of all situations related to TBI mentioned above need specific and adequate management through the whole trauma assistance from the pre-hospital setting to the critical care unit (CCU) and subsequent rehabilitation [36, 40].

The main method of assessment and management of severe TBI is monitoring and treatment of ICP. It is a level II-B of evidence recommended to reduce in-hospital and 2-week post-injury mortality [23, 41].

Neurocritical care specialists routinely base their clinical reasoning looking at the absolute value of ICP – measured in mmHg or cmH2O – combined with imaging exams – CT-scan or MRI. However, the numbers may not translate the entire complexity of intracranial dynamic. It is suggested that the ICP waves and the study of its morphology could bring differential evidence of altered intracranial compliance and changes of pressure regimen [14, 23, 42, 43].

A qualitative analysis of the ICP waveform [44] described the relationship between amplitude of ICP pulse wave, values of ICP, values of cerebral perfusion pressure (CPP), and the outcome of severe head-injured patients. Intracranial hypertension was evidenced by absolute values of ICP and CT-scan parameters. In those with fatal outcomes there was an increase in the ICP waveform amplitude along with an increase of ICP value up to 25 mmHg, however, above this value the amplitude began to decrease. This breakpoint trend in the amplitude-value relationship was not present in patients with good/moderate outcome. Thus, it is suggested that the physics involving ICP, CPP and parenchyma dynamics inside intracranial cavities was somehow translated into the waveforms, and its analysis and correlations could be a useful additional tool for outcome prediction.

Another study [45] involving TBI patients described the ICP plateau waves characteristics using multimodal brain monitoring as well as calculated indices of brain compensatory reserve and cerebrovascular reactivity. Plateau waves are associated with working cerebrovascular reactivity and occur in situations of

decreased volume-pressure compensatory reserve such as TBI and many other brain pathologies. It consists of sudden increases in ICP to peaks of 40-100 mmHg that persists for 5–20 minutes [14, 45, 46]. The study observed plateau waves in 44% of the patients and that abrupt increase of ICP above 40 mmHg was associated with an increase in amplitude of ICP pulse waveform and also with important decrease in CPP, cerebral blood flow and oxygenation, despite stable cardiovascular variables of arterial blood pressure and heart rate (**Figure 5**) [45].

When analyzing ICP pulse waveform during plateau waves, a statistically significant increase in amplitude and a change in its shape were noted. The ICP pulse components (P1 < P2 > P3) showed altered ICC [45] (**Figure 6**).

Although slight increases in ICP that last for short period are not usually associated with poor outcome, if plateau waves are sustained over 30 minutes it could have a negative impact on patient's recovery as intracranial hypertension compromises cerebral perfusion and implicates neuronal deterioration [14, 23, 42, 43, 46]. The analysis of ICP absolute values and waveform patterns over time could provide important information for early detection of ICH in TBI patients of the mentioned study [45].

The debate about how ICP waveform analysis could provide improved clinical benefit and a more actionable evidence to bedside addresses integrated metrics on brain's intrinsic compensatory capacity (autoregulation) and oxygenation, besides computational analysis of multiple continuous streams of neuro-monitoring data and equipment development to easily display this information [14, 23, 42–46].

In this way, non-invasive techniques are coming forward to give quick ICP information to neurocritical care team, including transcranial Doppler, optic nerve sheath diameter, near-infrared spectroscopy, tympanic membrane displacement, visual-evoked potentials, some other measurements of the optic nerve,

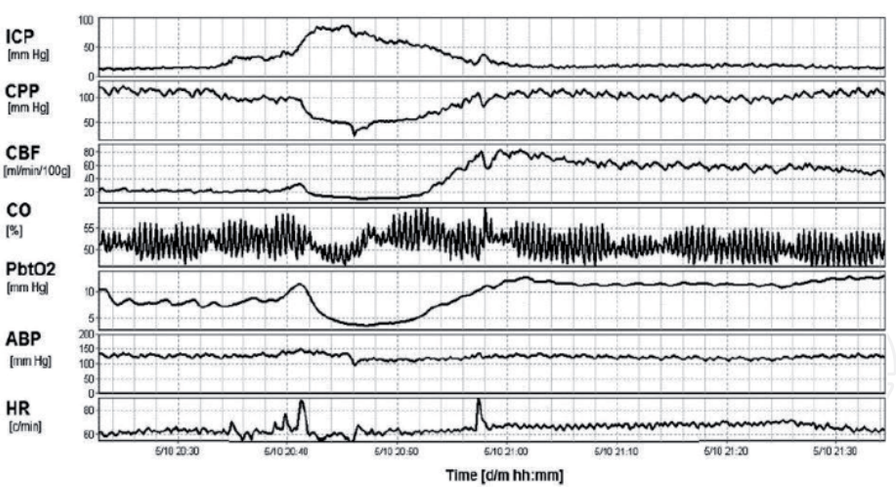

Figure 5.
Example of multimodal brain monitoring recording during plateau wave, extracted from Dias et al. [45].

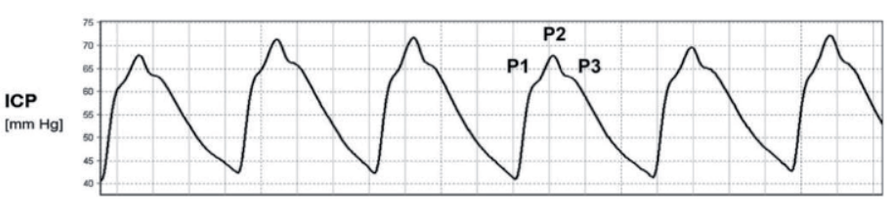

Figure 6.
Altered ICP pulse waveform indicating compromised intracranial compliance, extracted from Dias et al. [45].

retina, and pupil, besides the routinely used imaging exams of CT-scan and MRI [23, 42, 43, 45]. There is also a new non-invasive method of ICP monitoring that provides morphological data of ICP waves and intracranial compliance, adding celerity to this multimodal scenario [47, 48].

It is well established that ICH is an important issue after TBI because of its relationship to overall outcomes and all guidelines recommend a comprehensive ICP assessment – either invasively or non-invasively. Information about absolute values and waveform characteristics of ICP may together contribute to direct optimal management of TBI and good patient care [23, 42, 43, 45, 47, 48].

4.4 Increased ICP outside ICU environment

The brain constitutes approximately 80% of intracranial volume, and blood and CSF each account for 10% [49–51]. The first compensatory mechanism for maintenance of normal ICP involves displacement and reduction of the CSF compartment, reduction of CBF, and lastly, displacement of cerebral parenchyma causing herniation. The slower the increment in ICP, the more useful this regulatory system. Therefore, rapidly growing masses like malignant gliomas have a higher risk of causing brain herniation than slow-growing tumors like meningiomas or nerve sheath tumors [52].

Transient elevation in ICP, generally from 50 to 100 mmHg and 5 to 20 minutes, leads to plateau wave phenomena. It can occur spontaneously or start after coughing, sneezing, or changes in position. This transient intracranial hypertension period may be accompanied also by transient headache, transient alteration of the level of consciousness and focal deficits [49, 50].

Obesity and its relation with sleep apnea obstructive syndrome may show ICC impairment due to overnight hypercarbia leading to cerebral vasodilation. Also, this population is likely to develop chronic idiopathic intracranial hypertension. Moreover, hydrocephalus patients of any etiology, migraineurs, progressive neurological focal and/or gait disorders, all these situations mentioned here for outpatients practice raise the yellow sign on the need for ICC evaluation.

5. Conclusions

Advances on cerebral hemodynamics and intracranial compliance understanding brought to light by recent researches have made monitoring of these properties an essential practice in critical care. Likewise, advances in technology may convert intracranial compliance in a new vital sign present in daily practice in a near future.

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