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REVIEW

Intracranial pressure: current perspectives on physiology and monitoring

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Abstract

Intracranial pressure (ICP) monitoring is now viewed as integral to the clinical care of many life-threatening brain insults, such as severe traumatic brain injury, subarachnoid hemorrhage, and malignant stroke. It serves to warn of expanding intracranial mass lesions, to prevent or treat herniation events as well as pressure elevation which impedes nutrient delivery to the brain. It facilitates the calculation of cerebral perfusion pressure (CPP) and the estimation of cerebrovascular autoregulatory status. Despite advancements in our knowledge emanating from a half century of experience with this technology, important controversies remain related even to fundamental aspects of ICP measurements, including indications for monitoring, ICP treatment thresholds, and management of intracranial hypertension. Here, we review the history of ICP monitoring, the underlying pathophysiology as well as current perspectives on why, when and how ICP monitoring is best used. ICP is typically assessed invasively but a number of emerging, non-invasive technologies with inherently lower risk are showing promise. In selected cases, additional neuromonitoring can be used to assist in the interpretation of ICP monitoring information and adapt directed treatment accordingly. Additional efforts to expand the evidence base relevant to ICP monitoring, related technologies and management remain a high priority in neurosurgery and neurocritical care.

Keywords: Intracranial pressure, Traumatic brain injury, Critical care, Intracranial hypertension, Monitoring, Physiology, Non-invasive

Introduction

Injured tissue frequently exhibits hemorrhage and edema, increasing its volume. The injured brain is uniquely challenged by these processes because it resides within the fixed confines of the skull where a compartment syndrome readily develops. Focal pressure increases within the skull can precipitate herniation of brain tissue while generalized increases can impede the inflow of nutrients (Fig. 1). In this context, measurement of intracranial pressure (ICP) has played an important role in clinical care of the injured brain for the last half century. Although many fundamental questions await a resolution, progress is being made in understanding, measuring and treating intracranial hypertension. Here we share current perspectives on the physiology and monitoring of ICP.

The history of intracranial pressure monitoring

Although cerebral swelling and the consequences of opening the skull were understood by Galen, Hippocrates and early Egyptian physicians, the modern understanding can be traced to Kellie and Monro. The Monro-Kellie doctrine holds that because the brain is enclosed in a non-expandable skull, when the volume of an intracranial component increases compensatory displacement of blood and cerebrospinal fluid occurs [1]. When this

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compensation is exhausted, however, a linear increase in volume leads to an exponential increase in ICP (Fig. 2).

Measurement of cerebrospinal fluid (CSF) pressure in humans started in the late nineteenth century when Heinrich Quincke published his method of lumbar CSF pressure measurement in 1891 [2]. CSF pressure measurement was subsequently refined and considered to be a reliable indicator of ICP. However, even at that time, lumbar puncture was reported to precipitate the death of patients with intracranial pathology because of herniation events. This provided the rationale for measuring ICP directly within the cranium. Early descriptions of such intracranial measurements came from Guillaume and Janny in 1951[3] as well as by Nils Lundberg [4–10]. Lundberg described eponymous 'A', 'B', and 'C' waves of ICP [11] which remain fundamental aspects of brain pathophysiology[12]. 'A' waves are synonymous with plateau waves in which intracranial hypertension is sustained for 5–20 min, while 'C' waves reflect influence of the cardiac and respiratory cycles. 'B' waves are short repeating elevations in ICP with a frequency of 0.5–2 per minute that are of uncertain origin and relevance.

Take-home message

Intracranial pressure measurement and management continues to play a central role in traumatic brain injury and other severe brain insults. Here we review fundamental physiology as well as current views and technologies relevant to monitoring and managing intracranial pressure.

The notion that ICP elevation was harmful took longer to emerge. Douglas Miller associated marked ICP elevations with death and argued that values as low as 10 mmHg were harmful [13, 14]. In part because of Douglas Miller's efforts, ICP monitoring was implicit in the Brain Trauma Foundation's (BTF) subsequently published guidelines [15–18]. In fact, placement of an ICP monitor was used as a surrogate measure of guideline compliance in numerous studies [19, 20]. Of additional influence has been the American College of

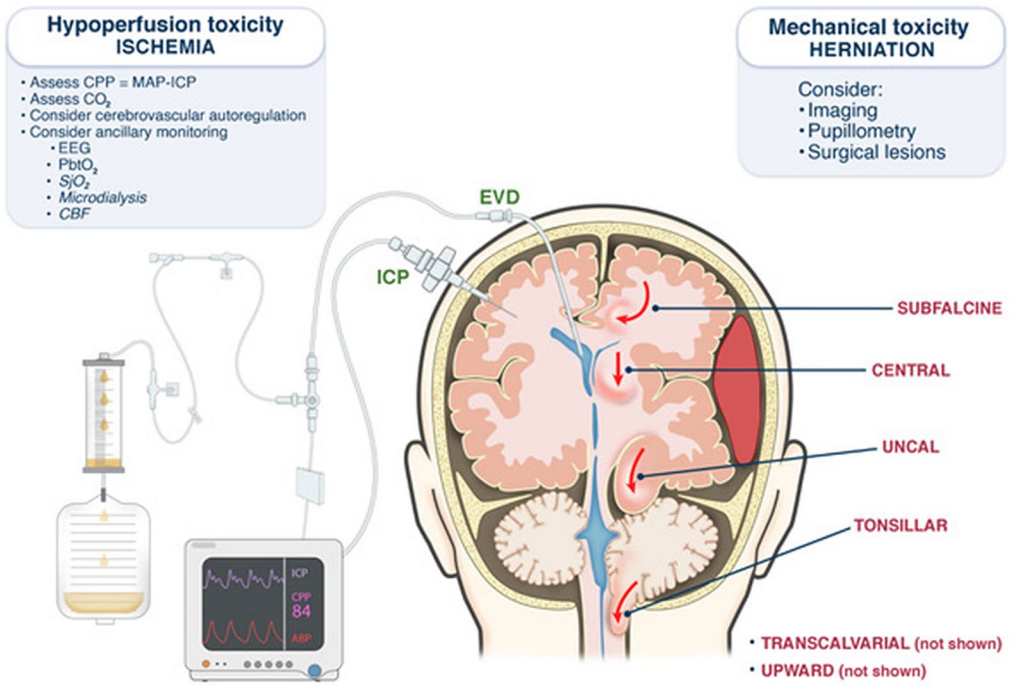

Fig. 1 Hypoperfusion and mechanical toxicities following traumatic brain injury. Following traumatic brain injury ICP monitoring can assist with the recognition of secondary insults. Mechanical toxicity can result from mass lesions and edema, potentially resulting in herniation of brain tissue. Herniation subtypes (shown in red text) are associated with elevated ICP in most cases and can cause injury through compression of brain tissue or cerebral vessels. Hypoperfusion toxicity is typically a more global cerebral insult characterized by insufficient cerebral perfusion. ICP monitoring can also allow this to be detected through the derivation of CPP and the recognition of insufficient values. Invasive ICP measurements can be made with a intraparenchymal transducer or an EVD. Ancillary monitoring can assist the detection and diagnosis of insults and can additionally suggest appropriate therapeutic maneuvers and assess response to therapy. CBF, cerebral blood flow; CPP, cerebral perfusion pressure; EEG, electroencephalogram; EVD, external ventricular drain; ICP, intracranial pressure, a parenchymal ICP monitor (green text) is in situ in the brain presented; MAP, mean arterial pressure; $PbtO_2$, partial pressure of brain tissue oxygen; SjO_2, jugulovenous oxygen saturation

Surgeons' decision to assess ICP monitor placement as part of trauma center accreditation [18, 21].

Harm from intracranial hypertension

A principal reason for ICP monitoring is the toxicity of intracranial hypertension. Indeed, ICP elevation is not merely a marker of injury severity. Without treatment, acute intracranial hypertension may be rapidly fatal: either because of trans-tentorial brain herniation and brainstem compression, and/or because of critical cerebral perfusion pressure (CPP) reductions leading to global brain ischemia (Fig. 1).

Patients may suffer different "doses" of high ICP. The impact of these ICP doses—which reflect both the magnitude and time of exposure to intracranial hypertension—on outcome has been studied in different series. A seminal analysis based on the Traumatic Coma Data Bank showed that prolonged ICP values higher than 20 mmHg were associated with unfavorable outcome [22]. ICP refractory to treatment has been shown to be associated with worse 6-month outcome in a multicenter study of 407 TBI patients [23]. These findings have been confirmed in subsequent multivariable models. For instance, the area under the curve (AUC) of the ICP recording calculated in 93 patients with traumatic brain injury (TBI) was a significant predictor of poor outcome (and specifically of death) at 6 months [24]. Across a wide range of ICP intensity/duration combinations, the ICP dose was found to be independently associated with mortality in a multicenter study, including 261 adults and 99 pediatric TBI victims [25]. Finally, the AUC of the ICP profile in the first 48 h of monitoring was an independent predictor of mortality in 499 patients [26]. This is additionally informed by studies on decompressive craniectomy (DC) performed for refractory intracranial hypertension. When DC is performed and ICP surgically controlled, mortality is reduced [27, 28], providing further evidence of the lethal potential of prolonged high ICP. The same concepts apply also to subarachnoid hemorrhage patients [29, 30].

While the association of high ICP with mortality seems consistent across observational [22–26] and interventional [27, 28] studies, the long-term effects of high ICP on survivors remains less clear. The dose of ICP has been associated with worse outcomes over the entire Glasgow Outcome Scale (GOS) range, not only mortality [14, 25]. After adjusting for predictors intracranial hypertension has not always, however, been associated with long-term outcome in multivariable analyses [24–26]. It does seem indisputable that ICP elevation is harmful when one considers the extreme scenario of brain death in which intracranial pressure exceeds arterial pressure, preventing the intracranial flow of blood [14]. Undoubtedly, less extreme ICP values not immediately resulting in brain death are associated with harm from impaired nutrient delivery to the brain, though the relevant ICP threshold remains uncertain.

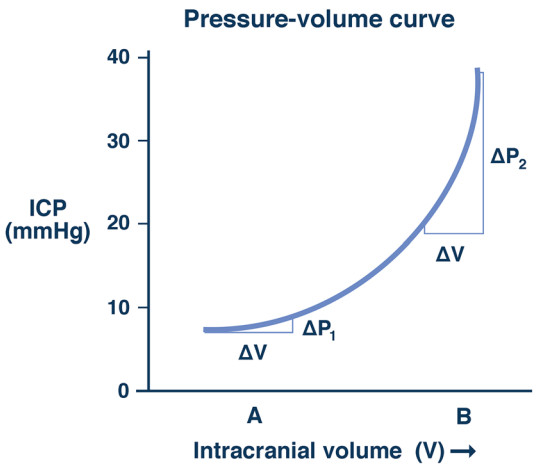

Fig. 2 Pressure volume curve. As intracranial pressure increases linearly, intracranial pressure (ICP) increases exponentially—a fundamental tenet of TBI physiology. The change in pressure in relation to the change in volume is referred to as compliance. Patient (B) who falls to the right side of this curve has reduced compliance as compared with patient (A). Patient (B) is at greater risk for intracranial hypertension and will likely require more aggressive treatment to maintain acceptable ICP values. Adapted from Tadevosyan & Kornbluth, 2021 [70]

Indications for invasive ICP monitoring in trauma and non-traumatic neuroemergencies

The indications for insertion of an ICP monitor have been long debated and have sought a point of equilibrium between benefits and risks. In a seminal retrospective study published in 1982, Narayan et al. [31] tried to identify, using first generation computed tomography (CT), TBI patients with greater risk of intracranial hypertension. Narayan's study recognized ICP elevation in some patients with normal cranial CT studies and has strongly influenced the indications for ICP monitoring in the BTF guidelines since their first edition [21]. The BTF guidelines thus stated that ICP "should be monitored in all salvageable patients with a severe TBI (Glasgow Coma Scale (GCS) score between 3-8 after resuscitation) and an abnormal CT scan. An abnormal CT scan of the head is one that reveals hematomas, contusions, swelling, herniation, or compressed basal cisterns" with the addition, inspired by Narayan's study, that "ICP monitoring is [also] indicated in patients with severe TBI with a normal CT scan if two or more of the following features are noted at admission: age over 40 years, unilateral or bilateral motor posturing, or systolic blood

pressure (BP) < 90 mm Hg". In recent decades, clinicians have tended to use the first part of this guideline, but ICP monitor insertion in the presence a negative CT scan has been less common. Notably, the most recent edition of the BTF guidelines [18], using more strict methodological criteria than in the past, judged there to be insufficient evidence to support a Level I or IIA recommendation for this topic.

An alternate perspective comes from the International Multidisciplinary Consensus Conference on Multimodality Monitoring whose recommendations are relevant to a broader neurocritical care patient population [32]. The consensus panel opined that ICP and CPP monitoring are recommended as a part of protocol-driven care in patients who are at risk of elevated ICP based on clinical and/or imaging features (*strong recommendation, moderate quality of evidence*) and that ICP and CPP monitoring be used to guide medical and surgical interventions and to detect life-threatening imminent herniation (*strong recommendation, high quality of evidence*). However, different centers interpret this information variably and substantial between-center variation in the use of ICP monitoring has been documented by the CENTER-TBI study [33].

Recently a prediction tool for intracranial hypertension has been developed by Alali et al. [34] with a sensitivity of 94% and specificity of 42%. Per this tool, high ICP would be suspected in the presence of 1 major or ≥ 2 minor criteria. Major criteria are: compressed cisterns (CT classification of Marshall diffuse injury III), midline shift > 5 mm (Marshall diffuse injury IV), or non-evacuated mass lesion. Minor criteria are GCS motor score ≤ 4, pupillary asymmetry, abnormal pupillary reactivity, or Marshall diffuse injury II. This tool may help to identify patients who require ICP monitoring in high-resource settings or who require ICP-lowering treatment in resource-limited environments.

In other acute severe brain pathologies such as subarachnoid hemorrhage (SAH) and intraparenchymal hemorrhage, indications for ICP monitoring are less formalized but the concepts discussed above apply [32]. Acute hydrocephalus in SAH patients should be managed by an external ventricular drain (EVD) as indicated by the American Heart Association (*Class I, Level of Evidence B*) [35]. Similar concepts apply also to spontaneous intracranial hemorrhage (ICH) where, in presence of coma and clinical evidence of transtentorial herniation or significant hydrocephalus, consideration should be given to ICP monitoring and treatment with an EVD [36]. ICP monitoring is more controversial in other conditions such as meningitis and hypoxic encephalopathy.

The SYNAPSE-ICU study is a large, international, multi-centre observational study intended to investigate the current status of ICP monitoring in TBI, SAH and ICH [37]. It included 2395 patients, 55% of whom had an ICP monitor. It documented large variability between centers and countries in the current use of ICP monitoring. This study also demonstrated that the use of ICP monitoring is more common in patients with severe acute brain injury with specific pre-injury characteristics (younger with lower prevalence of pre-injury comorbidities) and injury-related characteristics (pathological CT findings and normal pupil reactivity). In this study ICP monitoring and treatment was associated with significantly lower 6-month mortality in patients with at least one unreactive pupil.

Invasive ICP monitoring techniques

The optimal ICP monitoring device should be accurate, reliable, cost-effective, and cause minimal patient morbidity as first described by Lundberg in 1965 [9]. More recently it has been specified that an ICP measuring device should have a pressure range of 0–100 mmHg, accuracy ± 2 mmHg in the 0–20 mmHg range, and maximum error of 10% in the 20–100 mmHg range (https://www.aami.org). ICP monitoring devices differ in their accuracy, reliability, and cost (Table 1).

Ventricular catheters

Measurement of ventricular fluid pressure is the current gold standard for measuring ICP as it is the most accurate, low-cost, and reliable method of monitoring ICP [38]. This method permits periodic recalibration and—very importantly—therapeutic drainage of CSF. Major drawbacks of external ventricular drains are that obstruction of the catheter can occur, and that the external transducer must be maintained at a fixed reference point (the external auditory meatus). Changes in position of the transducer may lead to inaccurate assessment of ICP. Occlusion of the holes at the tip of the catheter can impede pressure transduction and result in underestimation of ICP. Moreover, this system allows accurate ICP measurements only when the ventricular drain is closed. If an attempt is made to record the ICP while the catheter is draining CSF, the recorded ICP is always equal to or lower than the drainage level because of hydrostatic laws. Some commercially available ventricular catheters have a pressure transducer within their lumen which do allow for simultaneous accurate ICP monitoring and CSF drainage. Placement of EVDs can also be challenging when the ventricles are compressed or shifted; frameless stereotaxy can assist accurate positioning.

Although placement of the external ventricular catheter is often seen as a minor procedure, it can be associated with serious haemorrhagic and infectious complications

Table 1 Summary of the main characteristics of invasive and non-invasive methods for intracranial pressure (ICP) estimation

	Availability	Accuracy	Risks of infection/hemorrhage	Operator dependency	Cost
External ventricular drain	Moderate/high	High	Moderate	Low (Level of external transducer)	Moderate (antibiotic impregnation approximately doubles cost)
ICP microtransducer	Moderate/high	High	Low	None	High (higher than both conventional and antibiotic impregnated EVDs)
Radiological findings (MRI/CT)	High	Low	None	Low	Low/moderate
ONSD	High	Low	None	High	Low
Transcranial Doppler	High	Low	None	High	Low
Automated pupillometry	High	Low	None	Low	Low

MRI, magnetic resonance imaging; CT, computed tomography; ONSD, optic nerve sheath diameter

as well as neurological deficits. Based on a meta-analysis, the overall haemorrhagic complication rate is approximately 7%, with a lower risk of significant haemorrhage (0.8%) [39]. Catheter-related ventriculitis and meningitis are potentially life-threatening complications. The quoted incidence of ventriculostomy related infection is wide, ranging from 0% to greater than 20% depending on the definition of infection used and the characteristics of the study population. Antibiotic or silver-impregnated catheters are associated with a significant decrease in infection risk [18].

Intraparenchymal transducers

The second most common device used for ICP monitoring is the intraparenchymal transducer. Such devices are of two types—solid-state devices based on pressure-sensitive resistors or those that incorporate a fibreoptic design. Fibre optic devices, such as the Camino ICP Monitor (Integra LifeSciences, Plainsboro Township, New Jersey, USA) transmit light via a fibreoptic cable towards a displaceable mirror at the tip. Changes in ICP distort the mirror and the differences in intensity of the reflected light are translated into an ICP value. Solid-state devices, such as the Codman MicroSensor (Codman & Shurtleff, Raynham, MA, USA), the Raumedic Neurovent-P ICP sensor (Raumedic, Helmbrechts, Germany) and the Pressio sensor (Sophysa, Orsay, France), belong to the group of piezoelectric strain gauge devices. When the transducer is deformed because of a change in ICP, resistance changes and this is converted into an ICP value. Intraparenchymal ICP probes are usually placed in the right frontal region at a depth of approximately 2 cm. The Codman and Raumedic sensors are compatible with magnetic resonance imaging but the Camino and Pressio sensors contain ferromagnetic components and are not.

All microtransducers share a common drawback—it is not possible to recalibrate them after placement. Although both types of systems are very accurate at the time of insertion, there is a degree of zero-drift over time which can result in a measurement error after several days. No clinical complications related to such drift have been reported as yet, however. The overall safety of microtransducer-based ICP monitoring devices is good with clinically significant complications, such as infection and hematoma occurring infrequently [38]. The cost of these microtransducers is, however, higher than both conventional and antibiotic impregnated ventricular systems. Of note, fracture of the transducer has been described in rare instances such as when patients are moved.

Subdural and epidural monitors are less accurate than intraparenchymal devices, and lower ICP values are measured in the subdural than epidural space. Such monitors are now rarely used in clinical practice.

Estimating intracranial pressure non-invasively

Although the gold standard for ICP monitoring is invasive devices, their placement risks complications as discussed [40]. In addition, sometimes ICP monitoring is desirable but not definitively indicated. As a result there have been recent efforts to develop tools which can inform ICP non-invasively. Some are based on morphological features (magnetic resonance, computed tomography, and fundoscopy), and some on physiological changes (transcranial and ophthalmic Doppler, tympanometry, near-infrared spectroscopy, electroencephalography, otoacoustic emissions assessment) [41]. Particularly important have been ultrasound based methods and automated pupillometry which have the advantage of being safe, easily repeatable and inexpensive.

Sonographic measurement of optic nerve sheath diameter (ONSD) is a convenient, rapidly performed bedside technique which holds promise for assessing the presence, absence and magnitude of increased ICP [42]. The optic nerve sheath (ONS) is continuous with the dura mater of the brain, and therefore surrounds the subarachnoid space containing CSF [42]. As the ONS is distensible, when there is an increase in CSF pressure the ONSD enlarges [42]. To date, different ONSD thresholds have been proposed ranging from 4.5 and 6 mm. In a prospective study, non-invasively measured ICP (nICP) based on ONSD demonstrated superior correlation with ICP as compared with other ultrasound-based techniques such as arterial and venous transcranial doppler ($R = 0.76$ for ONSD) [43]. In addition, in a recent meta-analysis, the area under the hierarchical summary receiver-operating characteristic curve of ONSD for predicting increased ICP was 0.938 [42].

Transcranial doppler (TCD) is another promising ultrasound-based technique for the non-invasive assessment of ICP and it also holds promise for non-invasive CPP measurements. Intracranial hypertension produces specific changes in cerebral blood flow velocity and waveform with diastolic flow velocity being particularly sensitive [44]. Gosling Pulsatility Index (gPI) is one of the first parameters derived from the TCD for ICP assessment, but its clinical utility is questionable due to its poor precision as it is importantly influenced by changes in arterial blood pressure and carbon dioxide [45]. Other formulas have been proposed for ICP and CPP estimation. Among these, one of the most promising is based on the diastolic flow velocity and has been shown in a pilot study to have a sensitivity of 100% for detecting increased ICP [46]. A larger multicenter study of TCD (IMPRESSIT) including 262 patients has been concluded and it confirmed a high negative predictive value for intracranial hypertension (ICP > 20 mmHg = 91.3%, > 22 mmHg = 95.6%, > 25 mmHg = 98.6%) [47].

In recent years, automated pupillometry has seen increased use in the ICU setting. Different parameters have been evaluated and among these the neurological pupillary index (NPi) has a suggested association with ICP. In a cohort of 134 patients Chen et al. [48] demonstrated that in patients with normal pupil reactivity the average ICP was 19.6 mmHg, whereas in patients with abnormal pupillary reactivity the average ICP was 30.5 mmHg. Interestingly, pupil abnormalities were detectable 15.9 h before important increases in ICP, suggesting that NPi may provide early warning of intracranial hypertension. Subsequent studies have also demonstrated an inverse correlation between NPi values and intracranial pressure, further supporting that pupillometry may help to estimate ICP non-invasively [49].

At present, methods of measuring ICP non-invasively are limited by high intra and inter-observer variability, the need for training, and a lack standardized methodology. Most importantly, they are not yet accurate enough to substitute for invasive methods. These methods will undoubtedly be used, however, when invasive ICP monitoring cannot be utilized or is undesirable.

Intracranial pressure thresholds and additional applications of ICP monitoring

The BTF guidelines have recommended ICP treatment thresholds of 20 mmHg [15], 20–25 mmHg [16, 50], 20 mmHg [17, 51] and most recently 22 mmHg [18] over the course of its four editions, although it is generally acknowledged that the ideal value is still not known with certainty. Indeed, values lower than 20 mmHg may be harmful [13, 14], although there is also evidence that suprathreshold values can be tolerated [52]. ICP monitoring can, though, facilitate more than the maintenance of ICP below a threshold value. ICP monitoring can facilitate early detection of an expanding intracranial hematoma. It can provide reassurance of normal values which can be valuable when imaging or non-cranial procedures are needed. It can also assure the safety of therapeutic maneuvers such as mean arterial pressure (MAP) augmentation or hypoventilation. Moreover, ICP is needed to calculate CPP. Current evidence more strongly supports CPP-directed care than ICP-directed care [18].

ICP is also integral to the determination of a patient's autoregulatory status. Cerebral autoregulation is the process by which arterioles in the cerebral vasculature dilate or constrict in order to maintain a constant nutrient supply to the brain (Fig. 3) [53]. In understanding ICP and autoregulatory principles it is helpful for the clinician to understand the important role that the cerebral blood volume plays in second-to-second ICP changes. As recognized by Risberg and Lundberg [10], engorgement of the brain from autoregulatory mechanisms seems to underlie plateau waves. Rosner described vasodilatory and vasoconstriction cascades relevant to this process (Fig. 4) [54]. Treatments which increase nutrient delivery to the injured brain can induce vasoconstriction which reduces intracranial blood volume and ICP [55, 56]. When cerebrovascular autoregulation is active, ICP elevations are tolerated for a longer duration [25].

Pressure autoregulation—which maintains a constant flow of blood to the brain despite changing systemic blood pressures—is a subtype of autoregulation which all physicians caring for TBI should be able to assess and incorporate into their plan of care [55, 56]. Following a

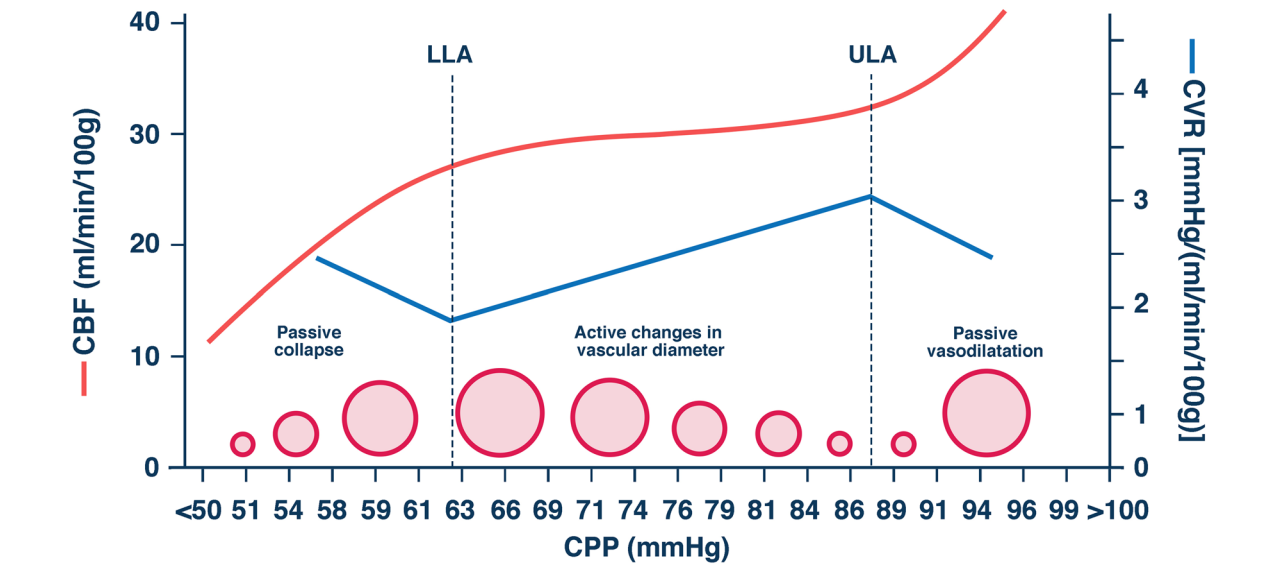

Fig. 3 Lassen Curve. Cerebrovascular autoregulation is the process by which the brain's arterioles alter their caliber to maintain a constant nutrient supply in relation to change in systemic blood pressure, blood viscosity, the concentration of nutrients and metabolites as well as other variables. Pressure autoregulation is the autoregulatory mechanism with highest familiarity and is depicted here in the Lassen curve. Between the upper and lower limits of pressure autoregulation cerebral blood flow remains relatively constant despite changes in systemic blood pressure because of changes in arteriole diameter. This mechanism can be lost as a result of brain injury and the brain becomes pressure passive as a result. It is now felt important for clinicians caring for severe TBI patients to be familiar with autoregulatory principles, to be able to measure the status of pressure autoregulation and to incorporate this knowledge into the care plan. Adapted from Budohoski et al., 2013 [71]

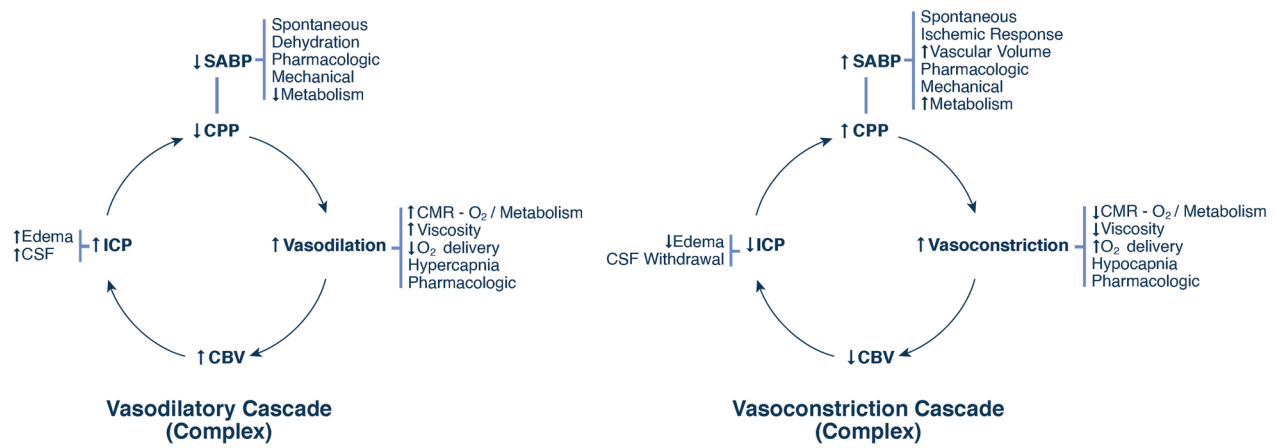

Fig. 4 Rosner's vasodilatory and vasoconstriction cascades. The vasodilatory and vasoconstriction cascades reflect broad autoregulatory processes which can influence the diameter of the cerebral vasculature and thus the cerebral blood volume and intracranial pressure despite injury to the brain. These cascades were described by Rosner based on clinical observations. These cascades are clinically relevant as they demonstrate a means by which ICP can be reduced by increasing nutrient delivery to the brain. Adapted from Rosner et al., 1995 [54]

TBI, pressure autoregulation can be disrupted making the brain pressure passive. The status of autoregulation changes the approach to patient care in important ways. For instance, a patient with deficient pressure autoregulation will do better with a lower CPP target (typically 60 mmHg, as long as perfusion needs are met), since higher values can elevate ICP [18]. Conversely patients with intact pressure autoregulation will do better with a higher CPP target (typically 70 mmHg) [18]. Different methods of assessing pressure autoregulation have been proposed, such as the pressure reactivity index (PRx) which is a running correlation coefficient between ICP and MAP values. There is, however, no consensus

on the accuracy, reproducibility or clinical validity of any such method at present [53].

An extension of autoregulatory principles has led to the notion of CPPopt, which has been defined as the CPP at which the PRx is most negative [57, 58]. The phase II COGiTATE study evaluated feasibility and safety of targeting CPPopt, calculated over a preceding 4 h period [59]. Currently, this approach is experimental with limited evidentiary support and can be laborious to implement. The notion of optimal CPP values has, though, also led to consideration that different patients could have distinct optimal ICP treatment thresholds. Experimental approaches are exploring the possibility that individualized ICP thresholds could be the ICP value at which PRx is consistently higher than + 0.20 [57, 60, 61].

In addition, important is the notion of compliance, another metric that can be derived when ICP values are known. Compliance refers to the amount the ICP increases related to a fixed increase in intracranial volume (Fig. 2). Patients with poor compliance have less reserve and likely require tighter ICP control. There are ongoing efforts to make compliance measurements available at the bedside given the value of these measurements in clinical care [62–64]. Analysis of the ICP waveform has long been known to reflect compliance, albeit with imprecision [12]. The RAP index, a correlation coefficient between mean ICP and the ICP pulse amplitude (defined as the difference between the highest and lowest ICP measured during one cardiac cycle), has shown promise for informing compensatory reserve and intracranial compliance [65]. Morphological Clustering Analysis of ICP Pulse (MOCAIP) is another computationally intense method being explored for similar purposes [66]. MOCAIP involves the analysis and measurement of various morphological characteristics of the ICP waveform [66].

Protocols for the treatment of intracranial hypertension

Early severe TBI management algorithms [15, 67] published by the BTF were widely used but were absent in later guidelines [17, 18] as they are not evidence-based. This left an unfilled gap between the evidence-report and bedside management. To address this, in 2019, a diverse group of over forty international and multidisciplinary severe TBI experts produced the Seattle International severe traumatic Brain Injury Consensus Conference (SIBICC) algorithms for the management of patients with ICP monitors (SIBICC I [56]) and with both ICP and $P_{bt}O_2$ monitors (SIBICC II [55]). Although they incorporate the fourth edition BTF evidence report [18] where applicable, these algorithms reflect expert opinion. They are meant to suggest a safe, modern, organized and comprehensive management protocol applicable to severe TBI patients that is available where expertise is limited. They are not a standard of care, legally binding, quality assurance tools, the right or only way, or a substitute for thoughtful care and clinical judgement. They may be adopted or adapted for use by a team or institution as felt indicated.

One method of dealing with the vagaries surrounding the existence of an absolute ICP threshold or patient-specific pathophysiology [68, 69] is to interpret the ICP in terms of its influence on two key insult categories. Over a patient's early course, marked variations in ICP often occur. By making use of ancillary monitoring, the presence and nature of "ICP toxicity" can be assessed (Fig. 1). When the ICP is elevated, in parallel with appropriate ICP-lowering treatment, observing the pupillary and motor exams, pupillometry readings, the ICP waveform, etc. provides insights into "herniation-related" toxicity of those elevated ICP values. Examining the concomitant values for the $PbtO_2$, $SjvO_2$, lactate/pyruvate ratio, electroencephalogram (EEG), CBF monitors, etc. provides similar insights into the "ischaemia-related" toxicity. These findings are also supplemented by the bedside nurse who may have observed trends not otherwise obvious. Considering careful modification of treatment thresholds under close clinical scrutiny may become reasonable when the patient seems to tolerate ICP values above 20–22 mm Hg. The advisability of performing a sedation-holiday-based "wake-up" test can also be influenced by such precision medicine approaches [56].

Conclusions

ICP measurement remains integral to the intensive care of severe brain pathologies and shows no sign of being supplanted by other monitoring techniques because of the utility of ICP measurements and derived values. Further development and proliferation of non-invasive techniques will improve safety and availability of ICP data. With many unresolved questions, however, every aspect of ICP monitoring should remain a high priority for further study.

Abbreviations

AUC: Area under the curve; BEST TRIP: Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure; BTF: Brain Trauma Foundation; CPP: Cerebral perfusion pressure; CSF: Cerebrospinal fluid; DC: Decompressive craniectomy; EVD: External ventricular drain; gPI: Gosling Pulsatility Index; ICH: Intracerebral hemorrhage; ICP: Intracranial pressure; ICU: Intensive care unit; MAP: Mean arterial blood pressure; MOR: Median odds ratio; nICP: Non-invasively measured ICP; NPi: Neurological pupillary index; ONS: Optic nerve sheath; ONSD: Optic nerve sheath diameter; PRx: Pressure reactivity index; SAH: Subarachnoid hemorrhage; SIBICC: Seattle International

severe traumatic Brain Injury Consensus Conference; TBI: Traumatic brain injury.

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Declarations

Conflict of interest
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