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Review Article

# The pressure reactivity index as a measure of cerebral autoregulation and its application in traumatic brain injury management

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ABSTRACT

Severe traumatic brain injury (TBI) is a major cause of morbidity and mortality globally. The Brain Trauma Foundation guidelines advocate for the maintenance of a cerebral perfusion pressure (CPP) between 60 and 70 mmHg following severe TBI. However, such a uniform goal does not account for changes in cerebral autoregulation (CA). CA refers to the complex homeostatic mechanisms by which cerebral blood flow is maintained, despite variations in mean arterial pressure and intracranial pressure. Disruption to CA has become increasingly recognised as a key mediator of secondary brain injury following severe TBI. The pressure reactivity index is calculated as the degree of statistical correlation between the slow wave components of mean arterial pressure and intracranial pressure signals and is a validated dynamic marker of CA status following brain injury. The widespread acceptance of pressure reactivity index has precipitated the consideration of individualised CPP targets or an optimal cerebral perfusion pressure (CPPopt). CPPopt represents an alternative target for cerebral haemodynamic optimisation following severe TBI, and early observational data suggest improved neurological outcomes in patients whose CPP is more proximate to CPPopt. The recent publication of a prospective randomised feasibility study of CPPopt guided therapy in TBI, suggests clinicians caring for such patients should be increasingly familiar with these concepts. In this paper, we present a narrative review of the key landmarks in the development of CPPopt and offer a summary of the evidence for CPPopt-based therapy in comparison to current standards of care.



## 1. Introduction

After many years of largely unchanged prognosis following severe traumatic brain injury (TBI), several therapies are emerging which hold promise to improve outcomes.[1,2] The Brain Trauma Foundation guidelines have seen some refinement over time, but the cardinal paradigm of treating an intracranial pressure (ICP) above a certain threshold (e.g., 22 mmHg) and maintaining a cerebral perfusion pressure (CPP) between 60 and 70 mmHg remain central and familiar to clinicians.[3] Observational data indicate that the targeted control of ICP and CPP are important components of management linked with improved outcomes.[4–8]

There is increasing recognition, however, that this approach in TBI fails to consider the unpredictably varied disruption of cerebral autoregulation (CA), which in health acts to stabilise cerebral blood flow (CBF). A growing body of evidence suggests that excessive ICP or insufficient CPP are most strongly associated with poor outcomes when they occur in the setting of impaired CA, a situation where the cerebral vasculature is unable to compensate for dynamic fluctuations in their relationship.[9,10] This body of research has led to the concept of an individualised optimal cerebral perfusion pressure (CPPopt), at which the injured brain and its vasculature are best able to regulate blood flow.

Prospective implementation of this index in clinical care requires clinicians to have greater familiarity with its derivation and inherent limitations. Hence, the primary aim of this review was to provide a narrative summary of the work underpinning the application of CPPopt in TBI. To achieve this, two separate electronic searches were conducted using Ovid MEDLINE, Embase, Scopus and

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PubMed (inception through September 2022). Initially, we focused on retrieving literature underpinning the development and assessment of the pressure-reactivity index (PRx) and CPPopt. Then, we sought to identify observational and interventional studies comparing outcomes associated with adherence to fixed CPP thresholds (i.e. 60-70 mmHg) compared with CPPopt-guided management of TBI. The results of these searches are presented in Table 1. Additional details of the search strategies employed and the relevant study selection flowcharts are provided in the Supplementary Materials section.

## 2. The development of the CPPopt

### 2.1. Cerebral autoregulation

CA refers to the homeostatic ability of the brain and cerebral vasculature to regulate both global and regional blood flow appropriate to its metabolic demands across a range of physiological conditions.[10] In the context of severe TBI and intracranial hypertension, blood flow into the cranial vault is of central concern, and here, CA refers narrowly to the phenomenon whereby the brain is able to regulate a stable and appropriate CBF in response to changes in mean arterial pressure (MAP) and ICP.[23,24] Lassen's eponymous triphasic curve describing this relationship has shaped clinicians' understanding for decades (Fig. 1).[25,26] In the context of the Monro-Kellie doctrine, CBF is a major determinant of ICP and is thus tightly regulated in health. TBI commonly alters the intrinsic myogenic, biochemical, and neuronal autoregulatory mechanisms responsible for CA, predisposing the brain to hyperaemic and/or ischaemic insults.[23,27] Blood flow may be dysregulated globally, regionally, or locally and when compliance of the cranial vault is also impaired (be it by a mass lesion, oedema, or obstructed CSF flow) this takes on further critical importance.[10] Impairment of CA in this setting is convincingly associated with increased mortality and poorer functional neurological outcomes.[11,28–31] The CPP below which CBF begins to constitute hypoperfusion is conceptualised as the lower limit of autoregulation and the CPP above which CBF becomes hyperperfused is conceptualised as the upper limit of autoregulation. The upper limit of autoregulation has itself recently seen refinement, and is now thought to have two upper points of inflection each with an anatomical basis.[32] Hypoperfusion is generally considered more harmful than hyperperfusion because of the potential for ischaemia, but concerns about the propensity of hyperperfusion to exacerbate cerebral oedema and injury of the blood brain barrier are also substantial.[29,33] Despite acknowledging the likely significance of impaired CA, the most recent Brain Trauma Foundation guidelines (2016) were unable to offer a recommendation about monitoring for, or appropriate treatment of this common pathophysiological phenomenon, due to a lack of high-quality evidence.[3]

### 2.2. The pressure reactivity index

The PRx described by Czosnyka et al. in 1997 is the most commonly employed measure of CA status following TBI.[11] It is defined as the Pearson correlation coefficient between thirty consecutive 10-s averages of MAP and ICP (i.e., 5 min of data), repeated every minute in an overlapping fashion to provide an updated value each minute.[34,35] Each PRx value therefore shares 4 min of data with each of its neighbours. PRx is therefore a measure of the linear association between the slow wave components of MAP and ICP.[36] In physiological terms, a positive correlation coefficient between MAP and ICP—*a positive PRx*— is seen when a rise in MAP leads to a rise in ICP—that is, CA is impaired (Fig. 2). An intact CA would normally prevent this rise. A negative PRx, indicates a compensatory cerebrovascular response, which leads to a lower ICP in response to an increased MAP.[37] It is important to note that the magnitude of the Pearson correlation coefficient is *not* a measure of the proportionality of the relationship between MAP and ICP but rather a measure of how closely (to perfect linearity) the two are associated. The sign of the coefficient denotes the direction of the relationship—that is, whether ICP rises or falls in response to rising MAP. This potential for interdependence between MAP and ICP is not apparent on first consideration of the Monroe-Kellie doctrine, the relationship indeed being more complex.[38] This was demonstrated by Kow et al. who showed that a MAP challenge resulted in a *lower* ICP in two thirds of patients with elevated ICP and TBI.[39]

The potential clinical utility of PRx has grown out of an increasing body of literature over the last 25 years.[8,11–14] This work was pioneered in Cambridge, UK, through a collaboration between engineers, neuroscientists, intensivists, and neurosurgeons. A large prospective cohort of patients and their outcomes has been collected over many years, and forms the 'derivation cohort' for many of the key developments in the study of CA following TBI.[40] However, despite generating invaluable insights into cerebrovascular pathophysiology, uptake into clinical practice and research has been slow outside of academic neuro-intensive care centres. In part, this is likely attributable to the pioneering nature of this work and what was, until recently, the mainly observational nature of the evidence underpinning it. Calculation of the derived parameters also relies on proprietary software (e.g., *Intensive Care Monitor Plus (ICM+)* by Cambridge University, or *CNS Envision* by Moberg ICU Solutions) the use of which is typically a novel step for clinicians, that requires both a high degree of understanding of and confidence in the underlying science.[41]

Further, implementation has been hindered by the requirement for additional computer hardware, data storage capacity, lack of standard data file formats, and the lack of interoperability between electronic medical records and these proprietary software systems.[41] Finally, the interpretation of PRx assumes a constant relationship between ICP and CBF. Interventions such as decompressive craniectomy, deep sedation, and physical manipulation may all alter ICP without parallel changes in CBF.[15,26] Decompressive craniectomy has been a common exclusion criterion for studies involving PRx and its impact upon CA is not well studied in this population.[42,43] There is, however, some evidence to suggest that the relationship between ICP and CBF may be preserved even after decompression and that this exclusion may be unwarranted.[44] For completeness, we note that several other measures of CA have been developed and although all are of academic interest, none enjoy the same level of development or association with prognosis as PRx, which has emerged as the most common measure of CA in the TBI setting.[35,45–49]

### 2.3. Optimal cerebral perfusion pressure

The development of the concept of CPPopt in 2002 represents the next key landmark in the study of CA and its potential application to neurotrauma management.[12] The hypothesis that a low PRx may be clinically desirable during intracranial hypertension leads logically to the question—at what CPP is the PRx the lowest? Collecting PRx and CPP values over several hours and then plotting these values against one another classically produces an 'U-shaped' curve, which spans the range of observed CPPs (Fig. 2D). The CPP which corresponds to the nadir of PRx on this curve was

**Table 1**
Summary of articles relevant to (i) the development of the PRx and CPPopt measurement protocols and (ii) the evidence comparing CPPopt-guided therapy against Brain Trauma Foundation derived CPP targets in severe TBI patients.

| Source | Design | Location | N | Key Developments/Results |
|---|---|---|---|---|
| **Development of the PRx and CPPopt measurement protocol** | | | | |
| Czosnyka et al., 1997[11] | PC | UK | 82 | • Development of the pressure reactivity index (PRx), originally defined as the moving Pearson correlation coefficient of 40 consecutive 5-s averages of ICP and ABP slow waveforms. |
| Steiner et al., 2002[12] | RC | UK | 114 | • Introduction of the concept of optimal CPP (CPPopt), the CPP value(s) at which PRx is most negative (i.e., CA most active).<br>• To determine CPPopt, minutely mean CPP and PRx are recorded over 4-min windows. The corresponding PRx values are then plotted against CPP bins spanning 5 mmHg, the nadir of the resultant 'U-shaped' curve designated as CPPopt.<br>• Determination of CPPopt (i.e., synthesis of the prerequisite 'U-shaped' curve) was only possible in 60% of analysed patients. |
| Smielewski et al., 2005[13] | TR | UK | 78 | • Development and commercialisation of the Intensive Care Monitor Plus (ICM+) software, which calculates in real-time PRx and CPPopt based on continuous measures of ABP and ICP.<br>• The Cambridge ICM + package serves as the successor to the ICM software initially developed in Poland in 1986. |
| Aries et al., 2012[4] | RC | UK | 327 | • Adapted the CPPopt derivation algorithm to facilitate continuous determination of CPPopt after just 2 h of ABP and ICP monitoring. |
| Depreitere et al., 2014[14] | RC | MULT | 180 | • Developed an automatic method to enhance the percentage (up to 95%) of monitoring time in which determination of CPPopt is possible. |
| Weersink et al., 2015[15] | RC | UK, NL | 48 | • Analysed patient characteristics and elements of neurotrauma care which may impede the detection of a 'U-shaped' PRx-CPP curve.<br>• Factors found to be associated with inability to produce such a curve include absence of slow ABP waves, higher PRx values, lower sedative-analgesic load, lack of neuromuscular blockers, higher vasoactive medication load and decompressive craniectomy. |
| Aries et al., 2016[16] | CS | NL | 4 | • Introduced a novel visualisation technique embedded in the ICM + system to retrospectively assess temporal changes in CPP, PRx, and CPPopt. |
| Liu et al., 2017[17] | RC | UK | 526 | • In a similar fashion to Depreitere et al. (2014), a multi-window method was employed to enhance the percentage (94%) of monitoring time in which determination of CPPopt was possible. |
| Cabeleira et al., 2018[18] | RC | UK | 280 | • Examined the prevalence of non-physiological fluctuations in ICP and ABP data producing "false positive" CPPopt curves.<br>• Found that 11.5% of generated CPPopt curves over total monitoring time are the result of chance alignment of data in ICP and ABP. |
| Kelly et al., 2018[19] | TR | UK | NA | • Using computational simulations, determined that there is a significant propensity for current algorithms to affix a 'U-shaped' curve to random ABP and ICP data.<br>• Authors suggest Fisher transformation of PRx data prior to CPPopt calculation to reduce this occurrence. |
| Lee et al., 2019[20] | RC | KOR | 309 | • Developed a deep learning technique to autonomously and reliably remove true signal artefacts from continuous ICP and ABP data. |
| Beqiri et al., 2021[8] | RC | UK | 813 | • Adapted the CPPopt multi-window algorithm to enhance suitability for prospective interventional research and clinical purposes.<br>• The resultant algorithm only considered U-shaped (not ascending/descending) curves for derivation of CPPopt. This improved the reliability (i.e., less 'false positives') of the CPPopt calculation at the expense of a lower overall yield (detectable 83% of monitoring time). |
| Tas et al., 2022[21] | PC | NL | 16 | • Demonstrated that application of ventilator cyclic PEEP oscillation slowed ABP waveform morphology, reducing the variability in calculated PRx. |
| **CPPopt-guided therapy - observational evidence** | | | | |
| Aries et al., 2012[4] | RC | UK | 327 | • Deviation below one's CPPopt (median CPP > CPPopt − 2 mmHg) served as a better discriminative threshold (chi-square = 45, $p < 0.001$) of dichotomous (alive vs. dead) outcomes at six months, compared to deviation below the BTF-advised thresholds of 60 and 70 mmHg. |
| Donnelly et al., 2017[5] | RC | UK | 729 | • Deviation of CPP below the PRx-derived LLR (PRx = +0.30) was a better predictor of mortality and poor outcome at six months compared to deviation below a fixed threshold of 60 mmHg. |
| Wettervik et al., 2019[6] | RC | SWE | 362 | • Both cumulative CPP within 10 mmHg of CPPopt and cumulative CPP within the BTF 60–70 mmHg range were associated with favourable outcomes (GOS-E = 5–8) at six months.<br>• Relative hyperperfusion in both contexts (i.e., >+10 mmHg above CPPopt and >70 mmHg) were associated with poor outcomes (GOS-E = 1–4) at six months. This was not observed with relative hypoperfusion (i.e. <-10 mmHg below CPPopt and <60 mmHg). |
| Wettervik et al., 2021[7] | RC | SWE | 98 | • Cumulative CPP within both the BTF range of 60–70 mmHg (OR = 1.05, $p = 0.02$) and CPPopt ± 10 mmHg (OR = 1.06, $p = 0.03$) were independent predictors of favourable clinical outcomes (GOS-E = 5–8) at six months. |
| Beqiri et al., 2021[8] | RC | UK | 813 | • Deviation from CPPopt was a better determinant of dichotomous (alive vs. dead) outcome at six months compared to deviation from a fixed BTF value of 60 mmHg but did not reach significance ($p = 0.014$). |
| **CPPopt-guided therapy – interventional evidence** | | | | |
| Tas et al., 2021[22] | RCT | NL, UK, BEL | 60 | • CPPopt-guided therapy resulted in almost half the rate of mortality (23% intervention vs. 44% control) and double the rate of patients having made a 'good recovery' (GOS = 5) at six months (30% intervention vs. 15% control). However, these findings did not achieve statistical significance. |

ABP: arterial blood pressure; BTF: Brain Trauma Foundation; CS: case series; GOS: Glasgow Outcome Scale; GOSE: Glasgow Outcome Scale – Extended; ICP: intracranial pressure; mCPPopt: mean CPPopt; NP: not provided; PC: prospective cohort; RC: retrospective cohort; RCT: randomised controlled trial; TR: technology report.

conceptualised as CPPopt.[12] This value represents the CPP at which ICP is least determined by the incident MAP and, inferentially, is most determined by intact CA. PRx has emerged as the lead contender among several candidate CA indices for the derivation of CPPopt, largely due to its strong (albeit retrospective) association with neurological outcome.[4,12] In addition, other clinically significant physiological parameters including cerebral oxygenation, glucose metabolism, and transcranial doppler flows also appear to be optimised by the achievement of CPPopt.[7,50,51] Consequently, PRx-derived CPPopt remains the best validated and most promising method for individualised patient management based on indices of CA in the severe TBI patient cohort.

## 3. Discussion

### 3.1. Outcomes associated with PRX and CPPOPT-guided therapy

The 2002 paper which introduced the concept of CPPopt reported an association between deviation from CPPopt and poorer neurological outcome.[12] In 2012, this study was repeated with the aid of the newly created ICM+. The group were able to demonstrate that a median CPP < CPPopt was more strongly associated with mortality than deviation from Brain Trauma Foundation guidelines of CPP 60–70 mmHg.[4] Additionally, median CPP > CPPopt was associated with increased rates of severe disability. Around this time, growing evidence began to suggest that while recommendations for a wide CPP range may be appropriate at a population level, the range of safe CPP for the individual patient is likely narrower.[4,32,52] Similarly, a high PRx had also been demonstrated in a compelling body of observational evidence to be associated with poor outcomes and death. A sustained PRx of $\geq$0.25–0.3 consistently appeared to be an important breakpoint (Fig. 2D) for increased morbidity and mortality. Conversely, maintenance of PRx below this threshold tends to be associated with favourable outcomes.[45,53–58]

The “CPPopt Guided Therapy: Assessment of Target Effectiveness” (COGiTATE) study was the first prospective, multicentre RCT comparing CPPopt-guided therapy against Brain Trauma Foundation guideline CPP targets of 60–70 mmHg.[22] There were fewer deaths and twice the number of patients who made a ‘good recovery’ (GOS = 5) in the CPPopt group than standard care. However, this pilot study was powered for feasibility and these differences did not reach statistical significance. In regard to these findings, the following should be noted. First, the use of a CPPopt-guided management strategy did not generate a signal of harm in terms of cardiac injury, fluid status, or ICP burden. Second, the two groups experienced mean CPPs that differed by 3 mmHg, the control, and intervention arms averaging CPPs of 69 mmHg and 72 mmHg, respectively. The majority of preceding observational studies demonstrate CPPopt is generally in the realm of 70–75 mmHg.[4,5,7] The control group's CPP exceeded 70 mmHg for 30.7% of the monitoring period, while in the intervention group, it did so 64.9% of the time. Whether the higher absolute average of CPP or the personalisation of the CPP target was responsible for the difference cannot be directly addressed by the study design. Third, it is worth noting the changes in “usual care” over time in one of the study centres demonstrated a trend towards higher CPPs from approximately 60 to 75 mmHg, with a concomitant fall in average ICP from 19 to 12 mmHg.[40] However, improved outcomes have not been contemporaneously reported, undermining the hypothesis that simply increasing the CPP target in guidelines might translate into improved outcomes. Further randomised controlled trials are awaited with great interest.

### 3.2. Challenges of implementation

Apart from the ongoing need for high-quality evidence to support its adoption into TBI guidelines, there are several practical obstacles impeding widespread clinical implementation of PRx/CPPopt TBI management. It is important to recognize that ICP and MAP data may contain random and aberrant elements, commonly referred to as ‘noise’ in the context of data analysis.[59] This data artifact may make the derivation of PRx less reliable and requires careful consideration when interpreting automated calculation of CPPopt.[60] CPPopt derivation is also limited by the range of CPPs that the patient experiences during the preceding hours. If a CPP proximate to CPPopt is never experienced by the patient nor observed by the software, inference by extrapolation may be necessary.[60] These twin problems of noise and data sampling have historically represented what is in many ways an engineering problem—applying and implementing a theoretical model to the real world based on imperfect data. The classic manifestation of this difficulty in determining CPPopt is a failure to obtain the classic U-shaped curve and instead half of the ‘U’ is seen in isolation. In this case, the PRx may continue to fall at the upper limit of observed CPP or fall at the lower limit of observed CPP. Moreover, these outer limits of CPP may greatly exceed what are clinically acceptable (i.e. outside ~40 mmHg < CPP < ~120 mmHg).[48] Likewise, in a challenge common to all neurocritical care literature, comparability between centres may be confounded by variability in ABP transducer placement. In the context of 30-degree head elevation, there is variable impact of hydrostatic pressure upon measured ABP when the transducer is calibrated at either of the external auditory meatus (representative of arterial pressure in the middle cranial fossa) or the level of the right atrium. Complicating standardisation of practice, clinical guideline recommendations on ABP calibration are conflicting. Indeed, while the 2016 Brain Trauma Foundation guidelines propose calibration at the level of the right atrium, the Neuroanaesthesia and Critical Care Society of Great Britain and Ireland and the Society of British Neurological Surgeons recommend routine calibration at the level of the external auditory meatus.[3,61] A national survey conducted across the United Kingdom demonstrated that while the vast majority of neurotrauma centres routinely nursed patients in the 30-degree head-up position, there was significant inter-centre variation in ABP transducer placement and subsequent derivation of CPPopt.[61]

The CPPopt algorithm has also historically suffered from an inability to consistently calculate CPPopt for all patients over the entire monitoring period. A key refinement was made to the CPPopt ICM + algorithm in 2017 when Lui et al. (building on earlier work by Depreitere et al. in 2014) published a description of a revised method to enhance CPPopt yield.[14,17] This update introduced temporal smoothing by including the preceding 8 h of data in the calculation, but by weighting this so that the most recent data were more heavily relied on. Measurements with large error associated with them were also less heavily weighted. These refinements improved the ability of the algorithm to calculate a CPPopt from 50-60% to 90–95% of the total monitoring time.[8] Most recently COGiTATE illustrated this ongoing challenge—patients in the intervention group were only able to have their CPPopt determined 74% of the time.[22]

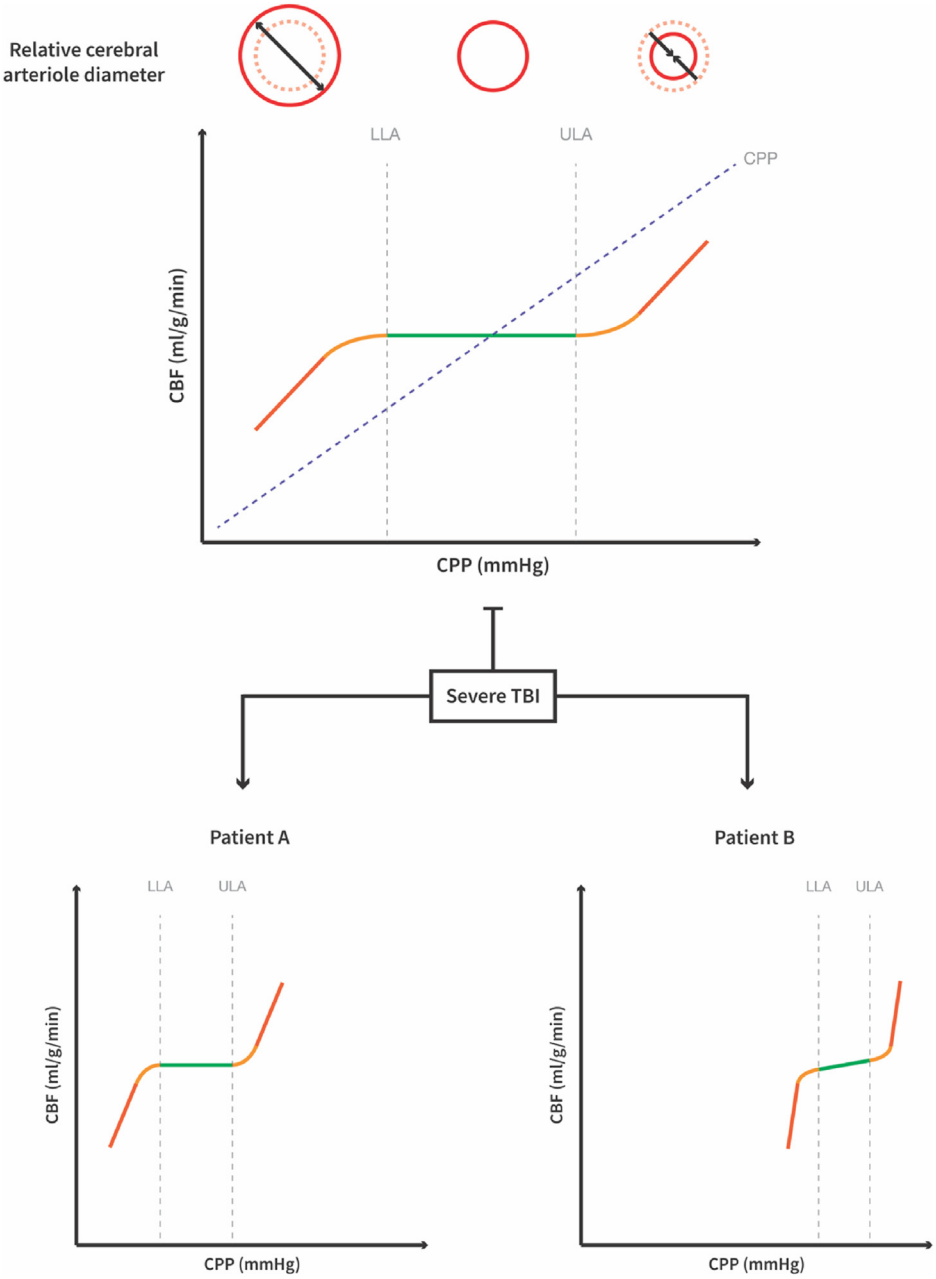


**Fig. 1. Lassen's original depiction of cerebral autoregulation.** In health, CA mechanisms function over a wide range of ABP to maintain appropriate CBF (green). To maintain CBF within this range, afferent cerebral arteries vasodilate as ABP decreases toward the LLA, and vasoconstrict as ABP increases towards the ULA. Following TBI, CA function may become disrupted and manifests as variable narrowing, unflattening, and displacement of the ABP range in which intrinsic mechanisms can stabilise CBF. This change to CA is patient specific (Patient A vs. Patient B) and evolves uniquely with time and the progression of secondary brain injury. ABP: arterial blood pressure; CA: cerebral autoregulation; CBF: cerebral blood flow; CPP: cerebral perfusion pressure; LLA: lower limit of autoregulation; TBI: traumatic brain injury; ULA: upper limit of autoregulation.

Several other refinements have been made to ICM+ and similar multimodal neuromonitoring software over the last 25 years, significantly improving their utility and reliability.[14,16–20] Further improvement in implementation may be achieved by other novel methods such as introducing a periodic undulation into the positive end expiratory pressure in ventilated patients in order to exaggerate changes in cardiac output and MAP and widen the range of MAP values sampled by the algorithm.[21] Despite all these challenges, authors of a single-centre study in which CPPopt-guided management was newly introduced as a therapy convey encouraging experiences in both medical and nursing staff. Clinicians exhibited strong agreement when detecting the presence of CPPopt and near-perfect agreement in designating a value of CPPopt in instances where it was agreed it was detectable.[62]

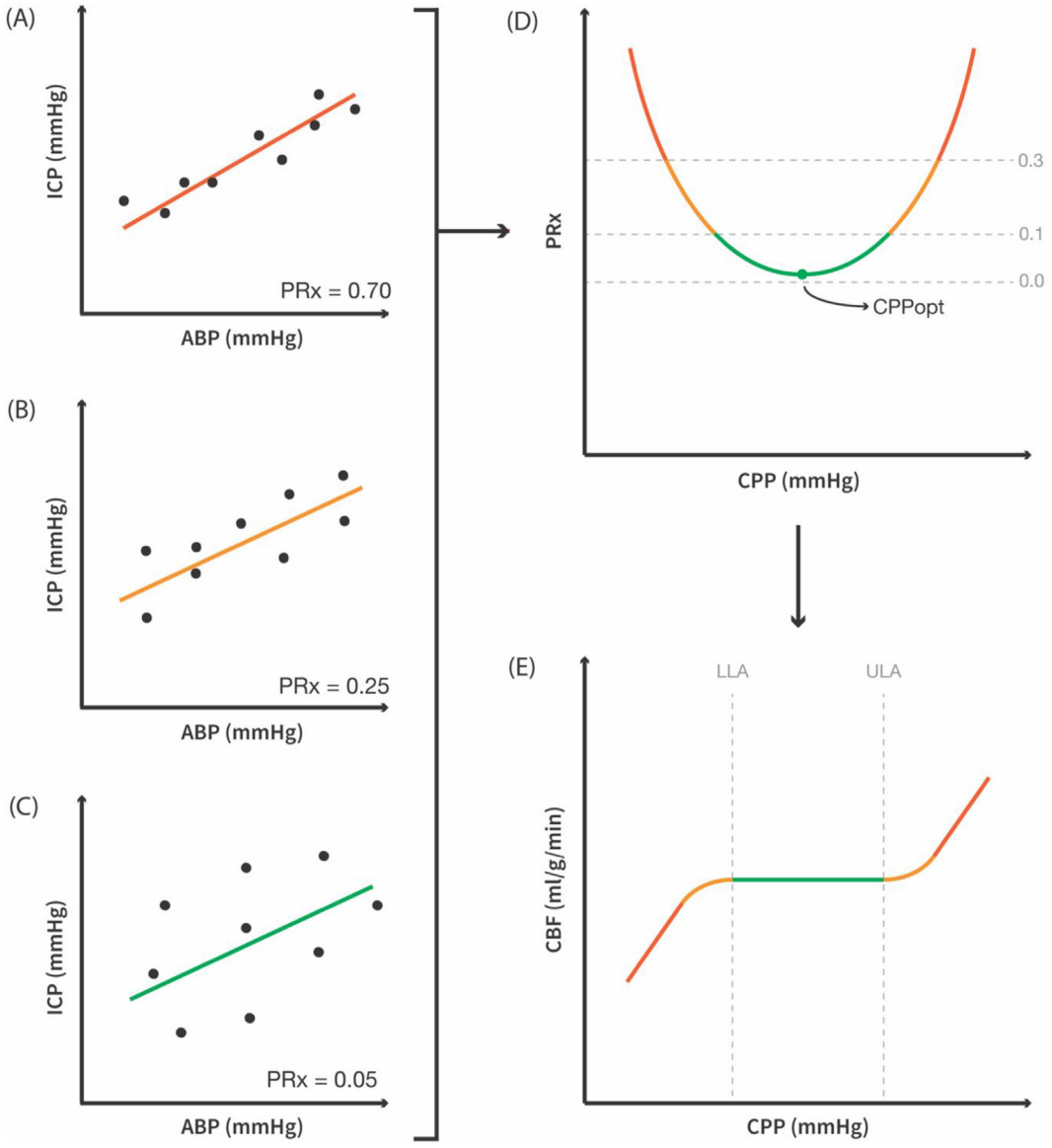


**Fig. 2. Principles of determination of CPPopt using the PRx.** Multimodal neuromonitoring software integrates ABP and ICP data to calculate PRx across the range of observed CPPs in a single patient over time (A–C). PRx <0 indicates well-functioning CA, while PRx>0.25–0.3 is associated with worse neurological outcomes and increased mortality. Curve fitting the CPP against PRx allows for determination of the CPP at which PRx is lowest (D). Note that derivation of this classically described curve is not possible in all patients, nor across all time points in any one patient. This dynamic depiction of CA can be conceptually related to the Lassen curve (E). ABP: arterial blood pressure; CA: cerebral autoregulation; CBF: cerebral blood flow; CPP: cerebral perfusion pressure; CPPopt: Optimal cerebral perfusion pressure; ICP: intracranial pressure; LLA: lower limit of autoregulation; PRx: pressure reactivity index.

## 4. Conclusion

The last 25 years of research has demonstrated that CA in severe TBI is an important physiological entity deserving of the attention of ICU clinicians. Indeed, the concept that impaired CA occurs post TBI has led to the development of CPPopt—the CPP at which autoregulation is maximally preserved. The CPPopt concept is supported by observational data, with a dose–response relationship—the closer a patient's CPP is to their CPPopt, the greater the likelihood of a favourable neurological outcome. Consequently, an alternative paradigm in CPP management is emerging, with the recent COGiTATE trial suggesting that larger phase III trials are warranted.

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## CRediT authorship contribution statement

Zac A. Tsigaras: conceptualization, methodology, investigation, writing - original draft, visualization. Mark Weeden: writing - original draft. Robert McNamara: writing - review and editing. Toby Jeffcote: writing - review and editing. Andrew A. Udy: conceptualization, writing - review and editing, supervision.

## Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Co-author Professor Andrew Udy holds the position of Associate Editor for Critical Care and Resuscitation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2023.10.009.

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