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PRECISION NEUROCRITICAL CARE AFTER SEVERE TRAUMATIC BRAIN INJURY: MULTIMODAL MONITORING, DYNAMIC INTRACRANIAL PRESSURE, AND INDIVIDUALIZED CEREBRAL PERFUSION TARGETS

Abstract

Background. Severe traumatic brain injury is a dynamic disorder in which intracranial pressure, perfusion, oxygen delivery, autoregulation, metabolism, and electrical activity evolve asynchronously. Fixed thresholds identify danger but may not define the optimal target for an individual patient. Objective. This review evaluates evidence for multimodal neuromonitoring, pressure–time burden, brain tissue oxygenation, cerebrovascular reactivity, and individualized cerebral perfusion pressure after severe traumatic brain injury, and proposes a precision-care framework.

Materials and methods. Guidelines, randomized trials, prospective cohorts, physiological studies, consensus algorithms, and investigations published through July 2026 were synthesized. Evidence was organized according to monitoring signal, physiological interpretation, intervention, treatment burden, spatial limitation, and relationship with outcome.

Results. Guidelines recommend treatment of intracranial pressure above 22 mm Hg and cerebral perfusion pressure within 60–70 mm Hg, while acknowledging dependence on autoregulatory status. High-resolution studies show that injury risk reflects magnitude, duration, frequency, and temporal context of intracranial hypertension rather than a single value. Pressure reactivity index enables estimation of an autoregulation-oriented optimal perfusion pressure, and COGiTATE established the feasibility of targeting CPPopt, although benefit remains unproven. Brain tissue oxygen monitoring detects regional hypoxia despite acceptable intracranial pressure; BOOST-II reduced hypoxic burden, whereas OXY-TC did not demonstrate superior six-month outcome, and phase III studies remain important. Continuous electroencephalography, microdialysis, pupillometry, transcranial Doppler, and systemic monitoring add information.

Conclusion. Precision neurocritical care should combine guideline safety limits with patient-specific interpretation. The proposed MULTI-TARGET framework integrates pressure burden, autoregulation, oxygenation, metabolism, electrical activity, imaging, and treatment response while preserving explicit escalation and de-escalation criteria.

Keywords: severe traumatic brain injury; intracranial pressure; cerebral perfusion pressure; CPPopt; pressure reactivity index; brain tissue oxygen; multimodal neuromonitoring; cerebral autoregulation; cerebral microdialysis; precision neurocritical care.

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ПРЕЦИЗИОННАЯ НЕЙРОИНТЕНСИВНАЯ ТЕРАПИЯ ПОСЛЕ ТЯЖЁЛОЙ ЧЕРЕПНО-МОЗГОВОЙ ТРАВМЫ: МУЛЬТИМОДАЛЬНЫЙ МОНИТОРИНГ,

ДИНАМИЧЕСКОЕ ВНУТРИЧЕРЕПНОЕ ДАВЛЕНИЕ И ИНДИВИДУАЛИЗИРОВАННЫЕ ЦЕЛИ ЦЕРЕБРАЛЬНОЙ ПЕРФУЗИИ

Аннотация

Актуальность. Тяжёлая черепно-мозговая травма представляет собой динамическое расстройство, при котором внутричерепное давление, перфузия, доставка кислорода, ауторегуляция, метаболизм и электрическая активность изменяются асинхронно. Фиксированные пороги выявляют опасность, но не всегда определяют оптимальную цель конкретного пациента. Цель. Оценить доказательства мультимодального нейромониторинга, давления во времени, тканевой оксигенации мозга, цереброваскулярной реактивности и индивидуализированного церебрального перфузионного давления после тяжёлой травмы и предложить модель прецизионной терапии.

Материалы и методы. Синтезированы руководства, рандомизированные исследования, проспективные когорты, физиологические работы, консенсусные алгоритмы и публикации до июля 2026 года. Данные систематизированы по сигналу мониторинга, физиологической интерпретации, вмешательству, терапевтической нагрузке, пространственным ограничениям и связи с исходом.

Результаты. Руководства рекомендуют лечить внутричерепное давление выше 22 мм рт. ст. и поддерживать церебральное перфузионное давление в пределах 60–70 мм рт. ст., учитывая состояние ауторегуляции. Исследования высокого разрешения показывают, что риск определяется величиной, длительностью, частотой и контекстом внутричерепной гипертензии, а не единичным значением. Индекс реактивности давления позволяет рассчитывать оптимальное перфузионное давление; COGiTATE подтвердило осуществимость CPPopt-ориентированного управления, но клиническая польза окончательно не доказана. Мониторинг тканевого кислорода выявляет региональную гипоксию при приемлемом давлении; BOOST-II уменьшило гипоксическую нагрузку, тогда как OXY-TC не улучшило шестимесячный исход. Дополнительные методы, включая непрерывную электроэнцефалографию, микродиализ, пупиллометрию, транскраниальную допплерографию и системный мониторинг, дополняют оценку. Совместный анализ сигналов непосредственно у постели больного помогает различать вазогенный отёк, недостаточную перфузию, диффузионную гипоксию, метаболический криз и электрические судороги, которые требуют различных, иногда противоположных терапевтических действий.

Заключение. Прецизионная нейроинтенсивная терапия должна сочетать безопасные пороги с индивидуальной динамической интерпретацией. Модель MULTI-TARGET объединяет давление, ауторегуляцию, оксигенацию, метаболизм, биоэлектрическую активность, нейровизуализацию и ответ на лечение, сохраняя чёткие критерии эскалации и деэскалации.

Ключевые слова: тяжёлая черепно-мозговая травма; внутричерепное давление; церебральное перфузионное давление; CPPopt; индекс реактивности давления; тканевая оксигенация мозга; мультимодальный нейромониторинг; церебральная ауторегуляция; церебральный микродиализ; прецизионная нейроинтенсивная терапия.

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OG‘IR KRANIOSEREBRAL TRAVMADAN KEYINGI PRETSIZION NEYROINTENSIV YORDAM: MULTIMODAL MONITORING, DINAMIK INTRAKRANIAL BOSIM VA INDIVIDUAL SEREBRAL PERFUZIYA MAQSADLARI

Annotatsiya

Dolzarblik. Og‘ir kraniotserebral travma dinamik patologik holat bo‘lib, unda intrakranial bosim, perfuziya, kislorod yetkazilishi, autoregulyatsiya, metabolizm va elektr faollik bir vaqtda bo‘lmagan tarzda o‘zgaradi. Belgilangan chegaralar xavfni ko‘rsatadi, biroq har bir bemor uchun optimal maqsadni doimo aniqlamaydi. Maqsad. Og‘ir travmadan keyingi multimodal neyromonitoring, bosim-vaqt yuklamasi, miya to‘qimasi oksigenatsiyasi, serebrovaskulyar reaktivlik va individual serebral perfuzion bosimga oid dalillarni baholash hamda aniq davolash modelini taklif etish.

Material va usullar. 2026-yil iyuligacha chop etilgan tavsiyalar, randomizatsiyalangan sinovlar, prospektiv kohortalar, fiziologik tadqiqotlar va konsensus algoritmlari sintez qilindi. Dalillar monitoring signali, fiziologik talqin, aralashuv, davolash yuklamasi, fazoviy cheklov va natija bilan bog‘liqlik bo‘yicha tizimlashtirildi.

Natijalar. Tavsiyalar intrakranial bosim 22 mm simob ustunidan oshganda davolashni va serebral perfuzion bosimni 60–70 mm simob ustunida saqlashni, autoregulyatsiya holatini hisobga olishni tavsiya qiladi. Yuqori aniqlikdagi tadqiqotlar xavf yagona qiymat emas, balki intrakranial gipertenziyaning kattaligi, davomiyligi, takrorlanishi va vaqt kontekstiga bog‘liqligini ko‘rsatadi. Bosim reaktivligi indeksi optimal perfuzion bosimni hisoblashga imkon beradi; COGiTATE CPPopt bo‘yicha boshqaruv amalga oshirilishini tasdiqladi, ammo klinik foyda to‘liq isbotlanmagan. Miya to‘qimasi kislorod monitoringi maqbul bosimda ham hududiy gipoksiyani aniqlaydi; BOOST-II gipoksik yuklamani kamaytirdi, OXY-TC esa olti oylik natijani yaxshilamadi. Uzluksiz elektroensefalografiya, mikrodializ, pupillometriya, transkranial Doppler va tizimli monitoring qo‘shimcha ma’lumot beradi. Signallarni bemor yotog‘ida bevosita birgalikda tahlil qilish vazogen shish, yetarli bo‘lmagan perfuziya, diffuzion gipoksiya, metabolik kriz va yashirin elektr tutqanoqlarini farqlashga yordam beradi.

Xulosa. Precision neyrointensiv yordam xavfsiz chegaralarni bemorga xos dinamik talqin bilan birlashtirishi kerak. MULTI-TARGET modeli bosim, autoregulyatsiya, oksigenatsiya, metabolizm, elektr faollik, tasvirlash va davolash javobini aniq eskalatsiya hamda deeskalatsiya mezonlari bilan birlashtiradi.

Kalit so‘zlar: og‘ir kraniotserebral travma; intrakranial bosim; serebral perfuzion bosim; CPPopt; bosim reaktivligi indeksi; miya to‘qimasi kislorodi; multimodal neyromonitoring; serebral autoregulyatsiya; serebral mikrodializ; pretsizion neyrointensiv yordam.

Introduction. Severe traumatic brain injury is not a single static lesion but a rapidly evolving interaction among primary structural damage, cerebral edema, hemorrhagic progression, microvascular dysfunction, excitotoxicity, mitochondrial failure, inflammation, seizures, systemic shock, hypoxemia, fever, anemia, and metabolic stress. The primary injury occurs at the moment of

impact and includes contusion, laceration, axonal disruption, vascular injury, and intracranial hemorrhage. Secondary injury develops over minutes to days and is potentially modifiable through neurocritical care [2, 3, 10, 18]. Traditional management has relied on population-derived thresholds for intracranial pressure and cerebral perfusion pressure. The current Brain Trauma Foundation guideline recommends treatment when ICP exceeds 22 mm Hg and suggests maintaining CPP between 60 and 70 mm Hg. It also acknowledges that whether 60 or 70 mm Hg represents the preferable lower target depends partly on the patient's autoregulatory status. These recommendations provide essential safety boundaries but do not imply that every brain has the same compliance, perfusion requirement, oxygen extraction reserve, or response to vasopressors [1, 3, 10, 13]. A single ICP value can conceal clinically important heterogeneity. An ICP of 24 mm Hg lasting three minutes during endotracheal suctioning differs from an ICP of 24 mm Hg persisting for two hours with worsening pupillary reactivity, falling brain tissue oxygen, and impaired cerebrovascular reactivity. Similarly, CPP of 65 mm Hg may be adequate in a patient with preserved autoregulation but insufficient in another patient whose optimal autoregulatory range lies near 75 mm Hg. Raising CPP indiscriminately can also worsen hydrostatic edema, increase ICP, expose the patient to vasopressor complications, and fail to improve oxygen delivery when microcirculatory dysfunction predominates [4, 14, 19, 25].

This physiological diversity explains why severe TBI has increasingly been approached as a monitoring-defined syndrome. The clinical examination remains fundamental but is often limited by sedation, neuromuscular blockade, mechanical ventilation, extracranial injuries, intoxication, seizures, and metabolic disturbance. Computed tomography provides anatomical information at discrete intervals, whereas secondary brain injury evolves continuously. Multimodal monitoring attempts to bridge this temporal gap by integrating pressure, perfusion, autoregulation, oxygenation, electrophysiology, metabolism, blood flow, pupillary function, and systemic physiology [15, 17, 27]. The concept of precision neurocritical care does not reject guideline thresholds. It places them within a hierarchy. Population thresholds define minimum safety standards. Dynamic monitoring characterizes the mechanism of deterioration. Individualized targets estimate the physiological range most likely to maintain perfusion and oxygenation without aggravating edema or systemic complications. Treatment response then confirms or challenges the assumed mechanism. Multimodal monitoring also exposes an important distinction between numerical correction and biological rescue. Reducing ICP from 28 to 18 mm Hg may appear successful, but the intervention can still be harmful if it produces severe hypotension, hypocapnia, brain hypoxia, electrolyte disturbance, or renal injury. Raising CPP from 58 to 72 mm Hg may improve $PbtO_2$ in one patient but increase ICP and pulmonary edema in another. A monitor is useful only when its signal is interpreted in relation to other signals and linked to an intervention that improves the underlying pathophysiology [11, 12, 20].

Materials and Methods. This manuscript was designed as a structured integrative review with an original physiology-oriented synthesis. Evidence available through July 2026 was evaluated, with priority given to clinical practice guidelines, randomized controlled trials, prospective multicenter studies, high-resolution physiological cohorts, individual-patient analyses, consensus protocols, and clinically relevant investigations of multimodal monitoring. The principal evidence base included the Brain Trauma Foundation severe TBI guidelines, the American College of Surgeons best-practice guidance, the BEST-TRIP trial, the Seattle International Severe Traumatic Brain Injury Consensus

Conference algorithms, CENTER-TBI high-resolution analyses, BOOST-II, OXY-TC, the BOOST-3 protocol, COGiTATE, autoregulation studies of CPPopt, and investigations of cerebral microdialysis, continuous electroencephalography, transcranial Doppler, pupillometry, and decompressive interventions [6, 13, 28]. Evidence was classified into seven domains. The first domain was intracranial pressure, including absolute thresholds, duration, pressure–time burden, waveform morphology, pulse amplitude, compensatory reserve, and response to therapy. The second was perfusion, including CPP, arterial pressure, intracranial pressure, vasopressor exposure, and individualized autoregulatory limits. The third domain was cerebral oxygenation, including brain tissue oxygen pressure, arterial oxygenation, hemoglobin, carbon dioxide, cerebral blood flow, diffusion distance, probe location, and oxygen consumption. The fourth was cerebral metabolism, including glucose, lactate, pyruvate, lactate-to-pyruvate ratio, glutamate, and glycerol. The fifth domain was electrical and neurological function, including continuous EEG, quantitative EEG, seizures, spreading depolarization, pupillary reactivity, and serial examination. The sixth domain was structural and vascular assessment, including CT, MRI, optic nerve sheath assessment, transcranial Doppler, and perfusion imaging. The seventh domain was treatment burden, including sedation, hyperosmolar therapy, ventilation, CSF drainage, temperature control, vasopressors, barbiturates, and decompressive craniectomy.

No new patient cohort was generated, and no independent meta-analysis was performed. Numerical findings were interpreted according to study design, monitoring modality, injury phenotype, outcome definition, and risk of confounding. The tables represent an original synthesis of published evidence rather than fabricated clinical data.

Results. ICP represents the pressure generated by the combined volumes of brain tissue, arterial and venous blood, cerebrospinal fluid, and pathological mass lesions within the cranial compartment. According to the Monro–Kellie principle, an increase in one component can initially be compensated by displacement of CSF and venous blood. Once compensatory reserve is exhausted, small volume changes can produce steep pressure increases. The numerical ICP value therefore reflects both intracranial volume and compliance. Two patients with ICP of 20 mm Hg may have different physiological states. One may have adequate compliance and a stable waveform; the other may be near the steep portion of the pressure–volume curve, with increasing pulse amplitude and impending decompensation. External ventricular drainage provides both measurement and therapeutic CSF diversion. An intraparenchymal transducer is generally easier to insert and is less vulnerable to obstruction by blood or collapsed ventricles, but it cannot drain CSF and may develop zero drift. EVD readings can also be distorted by incorrect leveling, open drainage, catheter occlusion, air bubbles, and transducer errors. The monitoring method must therefore be documented and checked before treatment is escalated. The BEST-TRIP trial compared an ICP-monitor-based protocol with management guided by imaging and clinical examination in resource-limited settings. It did not demonstrate superiority of the specific monitor-based protocol for its composite outcome. The trial did not establish that ICP is biologically irrelevant; rather, it showed that a monitored protocol cannot be separated from treatment strategy, expertise, timing, imaging access, nursing care, and the comparator protocol [10, 13, 23]. Subsequent consensus recommendations retained ICP monitoring as a central component of severe TBI care while emphasizing structured interpretation and escalation. The SIBICC algorithm organizes treatment into tiers beginning with basic physiological optimization, analgesia and sedation, head

positioning, temperature control, CSF drainage, and hyperosmolar therapy before escalation to more intensive interventions [15, 17, 27].

The most important development has been the transition from a static threshold to ICP dose. Pressure–time dose incorporates both the magnitude above a threshold and the duration of exposure. High-resolution analyses have shown that lower ICP elevations may become harmful when prolonged, whereas short episodes at higher pressures can occasionally be tolerated. One influential analysis found that ICP above 20 mm Hg for approximately 37 minutes was associated with worse adult outcomes, while the tolerable duration progressively decreased as the pressure increased [3, 6, 15, 18]. CENTER-TBI data similarly demonstrated that the relationship between ICP and outcome depends on duration and that a universal 22-mm Hg boundary simplifies a continuous risk surface. The threshold remains useful for bedside action, but it should be supplemented by cumulative burden, waveform behavior, treatment intensity, lesion type, and accompanying physiological deterioration [11, 15, 17, 20].

Table 1. **Dynamic Interpretation of Intracranial Pressure**

ICP pattern	**Possible interpretation**	**Required contextual signals**	**Clinical implication**
Brief ICP increase during suctioning or turning	Stimulation-related transient response	MAP, CPP, oxygen saturation, waveform recovery	Correct trigger and reassess before major escalation
Persistent ICP 22–25 mm Hg	Sustained intracranial hypertension	CT evolution, $PbtO_2$, PRx, pupillary response	Mechanism-oriented first-tier treatment
Recurrent short ICP crises	Unstable compliance or repeated triggers	Sedation level, coughing, fever, ventilation, seizures	Identify recurrent precipitant and cumulative dose
Rising ICP pulse amplitude with stable mean ICP	Decreasing compensatory reserve	RAP index, waveform morphology, imaging	May precede numerical threshold crossing
High ICP with negative or preserved PRx	Pressure elevation with maintained reactivity	CPP response, $PbtO_2$, venous factors	Avoid automatic interpretation as identical to pressure-passive state
High ICP with positive PRx	Impaired autoregulation and pressure-passive circulation	CPP, $PbtO_2$, edema, systemic pressure	Higher risk; cautious CPP and ICP manipulation
Normal ICP with low $PbtO_2$	Regional hypoxia without global pressure elevation	Probe location, PaO_2, Hb, CPP, $PaCO_2$	Treat oxygen delivery or regional perfusion mechanism
Refractory ICP with mass effect	Structural exhaustion of medical reserve	Repeat CT, pupils, neurological change	Urgent surgical reassessment

ICP Waveforms, Compensatory Reserve, and Early Warning. The ICP waveform contains cardiac, respiratory, and slow-wave components. The cardiac pulse commonly contains P1, P2, and P3

peaks. As compliance worsens, the tidal component can approach or exceed the percussion peak. Automated pulse-shape interpretation remains technically challenging, but increasing pulse amplitude and altered morphology can indicate reduced intracranial compliance before mean ICP becomes persistently elevated. The RAP index is the correlation between ICP pulse amplitude and mean ICP. Positive RAP values approaching 1 generally indicate that changes in intracranial volume are producing corresponding changes in pulse amplitude, consistent with reduced compensatory reserve. RAP values near zero can indicate preserved reserve or complete exhaustion, requiring contextual interpretation. Negative values may occur when the pressure–volume curve has reached extreme decompensation or after decompressive craniectomy. Slow waves reflect interactions among arterial pressure, vascular tone, cerebral blood volume, and intracranial compliance. Their relationship to autoregulation allows derivation of indices such as PRx. Modern high-frequency monitoring systems can display minute-by-minute trajectories rather than isolated nursing-chart values, enabling recognition of evolving patterns and response to treatment [5, 11, 16, 20]. Machine-learning models are being developed to predict ICP crises before threshold crossing. Their performance depends on signal quality, external validity, treatment annotations, and avoidance of alarm fatigue. Prediction should support earlier clinical assessment, not trigger automatic hyperosmolar treatment without confirmation of the mechanism.

Cerebral Perfusion Pressure and Its Limitations. CPP is commonly calculated as mean arterial pressure minus intracranial pressure. The simplicity of the equation can create a false impression that cerebral blood flow is directly determined by CPP. In reality, cerebral perfusion also depends on vascular resistance, autoregulation, carbon dioxide, oxygen tension, hematocrit, viscosity, venous pressure, microcirculation, cardiac output, and regional tissue pathology. A CPP of 65 mm Hg can be achieved by MAP of 80 mm Hg and ICP of 15 mm Hg or by MAP of 95 mm Hg and ICP of 30 mm Hg. These states are not physiologically equivalent. The second patient has greater intracranial pressure burden, higher vasopressor requirements, and potentially impaired microcirculatory flow despite the same calculated CPP. Guideline targets of 60–70 mm Hg were designed to avoid critical cerebral hypoperfusion while limiting complications associated with aggressive hypertension. Maintaining CPP above 70 mm Hg through fluids and vasopressors can increase acute respiratory distress, myocardial stress, edema, and systemic complications without guaranteeing improved cerebral oxygenation [6, 13, 28]. The lower safe CPP limit is not constant. In patients with intact autoregulation, cerebral arterioles dilate as CPP falls and constrict as CPP rises, stabilizing cerebral blood flow across a range. In impaired autoregulation, cerebral blood flow becomes pressure passive. A decrease in arterial pressure can then reduce blood flow directly, while an increase can raise cerebral blood volume and ICP.

Pressure Reactivity Index and CPPopt. PRx is calculated as the moving correlation between slow fluctuations in arterial blood pressure and ICP. A negative or near-zero relationship suggests that increased arterial pressure causes compensatory vasoconstriction without increasing intracranial blood volume. A positive relationship indicates pressure-passive vascular behavior in which increased arterial pressure is transmitted into increased intracranial blood volume and ICP.

CPPopt is derived by plotting PRx across observed CPP values. The CPP associated with the lowest PRx is interpreted as the pressure range in which autoregulatory reactivity is most effective. The target

is dynamic and can change over time as edema, sedation, temperature, surgery, carbon dioxide, systemic shock, and vascular injury evolve [6, 11, 12, 20]. Observational studies have associated greater deviation below CPPopt with worse outcomes. Recent analyses suggest that patients may be more vulnerable to CPP below individualized optimal values than to moderate elevations above them. A 2025 reappraisal proposed that CPPopt may be interpreted more appropriately as a personalized lower boundary rather than an exact numerical point that must always be reached [16, 23, 30]. COGiTATE was the first randomized feasibility trial to prospectively target autoregulation-guided CPP. It demonstrated that CPPopt-oriented management could be delivered without an unacceptable increase in therapeutic intensity. A later secondary analysis found that periods close to CPPopt were associated with improved cerebrovascular reactivity, particularly when baseline reactivity allowed room for improvement. The trial was not powered to establish a definitive functional outcome advantage [4, 7, 14, 19]. A 2025 multicenter physiological study showed that $PbtO_2$ tended to peak near CPPopt and that time outside ICP thresholds and impaired PRx were associated with worse outcome. Importantly, ICP control remained the modifiable variable most consistently associated with both mortality and functional outcome, supporting a hierarchy in which autoregulation-guided CPP complements rather than replaces effective ICP management [2, 3, 10, 18].

Table 2. **Cerebral Perfusion Phenotypes and Potential Management Logic**

Physiological phenotype	**ICP**	**PRx**	**$PbtO_2$**	**Possible mechanism**	**Precision-management interpretation**
Low CPP with preserved autoregulation	Normal or elevated	Negative/near zero	Normal or low	Approaching lower autoregulatory limit	Cautious MAP support while monitoring oxygenation
Low CPP with impaired autoregulation	Variable	Positive	Often low	Pressure-passive hypoperfusion	Avoid hypotension; consider individualized CPP increase
High CPP with preserved autoregulation	Variable	Negative	Normal	Tolerated pressure range	Avoid unnecessary vasopressor escalation
High CPP with impaired autoregulation	Often rising	Positive	Variable	Hydrostatic increase in cerebral blood volume	Higher CPP may worsen edema and ICP
CPP near CPPopt with low $PbtO_2$	Acceptable	Best available	Low	Anemia, hypoxemia, diffusion	Correct oxygen-delivery mechanism rather than CPP alone

				limitation, local ischemia	
CPP below CPPopt with high ICP	High	Variable	Low or normal	Perfusion failure caused by intracranial hypertension	Prioritize ICP reduction and reassess CPP
Normal CPP with metabolic crisis	Normal	Variable	Normal or low	Mitochondrial dysfunction or substrate failure	Use microdialysis and systemic metabolic correction
Unavailable CPPopt	Variable	Insufficient signal	Variable	Short data window, poor signal, nonstationarity	Use guideline targets and multimodal clinical assessment

Brain Tissue Oxygen Monitoring. Brain tissue oxygen pressure is measured with a focal intraparenchymal probe, commonly placed in radiographically normal-appearing frontal white matter or tissue at risk near a lesion. $PbtO_2$ reflects the balance among arterial oxygen tension, hemoglobin concentration, cerebral blood flow, oxygen diffusion, local capillary density, temperature, and tissue consumption. It is not a direct measure of whole-brain oxygenation. Values below approximately 20 mm Hg are commonly treated as brain tissue hypoxia, although risk is continuous and may become evident at higher or lower thresholds depending on duration and context. Probe location is critical. A probe near a contusion can identify regional ischemia but may not represent the opposite hemisphere. A probe in normal tissue can describe global physiological vulnerability but miss focal penumbral hypoxia. Low $PbtO_2$ despite normal ICP and CPP may result from systemic hypoxemia, anemia, low cardiac output, hypocapnia, pulmonary dysfunction, diffusion-limited oxygen delivery, microvascular thrombosis, focal ischemia, or increased metabolic demand. Treatment should therefore begin with mechanism identification rather than indiscriminate increases in FiO_2 or CPP [5, 11, 16]. BOOST-II showed that a protocol combining $PbtO_2$ and ICP monitoring was feasible and reduced the burden of brain tissue hypoxia compared with ICP-guided management alone. The trial was designed for physiological efficacy and feasibility rather than definitive functional-outcome superiority [2, 3, 18]. OXY-TC subsequently compared ICP plus $PbtO_2$ monitoring with ICP monitoring alone. The trial did not demonstrate superiority of the combined strategy for six-month neurological outcome. Interpretation is influenced by protocol adherence, probe placement, intervention efficacy, crossover in physiology, treatment intensity, and the possibility that correcting a focal oxygen value may not alter diffuse secondary injury [11, 12, 20]. The findings do not establish that $PbtO_2$ is clinically useless. They show that a monitor-derived value improves outcome only if the signal identifies a modifiable mechanism, the intervention corrects that mechanism safely, and correction occurs before irreversible injury. BOOST-3 and the BONANZA-GT program were designed to further evaluate whether protocolized oxygen-guided management improves patient-centered outcomes. Definitive phase III evidence remained an active research need through July 2026 [4, 14, 19, 25].

Table 3. **Interpretation of Low Brain Tissue Oxygen**

Low-$PbtO_2$ pattern	**Supporting findings**	**Likely mechanism**	**Potential response**
Low $PbtO_2$ with low PaO_2	Hypoxemia, pulmonary injury	Reduced arterial oxygen content	Optimize ventilation, oxygenation, recruitment, and pulmonary care
Low $PbtO_2$ with anemia	Reduced hemoglobin, acceptable saturation	Reduced oxygen-carrying capacity	Evaluate bleeding, transfusion context, and systemic oxygen delivery
Low $PbtO_2$ with low CPP	Hypotension or high ICP	Perfusion-limited oxygen delivery	Correct hypotension or intracranial hypertension
Low $PbtO_2$ after hyperventilation	Low $PaCO_2$ and reduced CBF	Cerebral vasoconstriction	Return toward normocapnia unless emergency herniation management
Low $PbtO_2$ with high ICP	Reduced CPP and microvascular compression	Intracranial hypertension	ICP-directed treatment and structural reassessment
Low $PbtO_2$ with normal CPP and PaO_2	Local lesion, edema, microvascular failure	Diffusion limitation or regional ischemia	Review probe location, imaging, hemoglobin, flow, and metabolism

Low $PbtO_2$ with seizures	EEG ictal activity and increased demand	Supply–demand mismatch	Treat seizures and reassess oxygen response
Persistent low $PbtO_2$ despite correction	Normal systemic physiology, high LPR	Mitochondrial or metabolic crisis	Integrate microdialysis and avoid harmful escalation

Cerebral Microdialysis and Metabolic Crisis. Cerebral microdialysis samples extracellular fluid through a semipermeable catheter. Common bedside analytes include glucose, lactate, pyruvate, glutamate, and glycerol. The lactate-to-pyruvate ratio is used as an indicator of cellular redox state. An elevated ratio with low pyruvate can suggest ischemic substrate failure, whereas an elevated ratio with relatively preserved pyruvate may reflect mitochondrial dysfunction. Low brain glucose can occur despite normal systemic glucose. It may result from reduced delivery, increased utilization, excessive systemic glucose control, seizures, spreading depolarization, or mitochondrial dysfunction. Very aggressive systemic glycemic control can worsen cerebral substrate availability even when blood glucose appears acceptable. Microdialysis is spatially focal and requires integration with catheter location. Values in pericontusional tissue differ from those in normal-appearing white matter. Sampling intervals are also slower than ICP or EEG signals, limiting immediate crisis detection. The major clinical value of microdialysis is mechanistic differentiation. A patient with elevated ICP, low $PbtO_2$, and high lactate-to-pyruvate ratio may have perfusion-related metabolic failure. A patient with normal $PbtO_2$ but persistently high ratio may have mitochondrial dysfunction that is unlikely to respond to higher CPP alone. This distinction can prevent increasingly aggressive vasopressor therapy that corrects a number without restoring cellular metabolism [10, 13, 23].

Continuous EEG, Seizures, and Cortical Activity. Clinical examination cannot reliably detect nonconvulsive seizures in deeply sedated or comatose patients. Continuous EEG identifies electrographic seizures, periodic discharges, background suppression, reactivity, and evolving encephalopathy. Quantitative displays can support screening but require confirmation using raw EEG. Post-traumatic electrographic seizures can increase cerebral metabolic demand, ICP, lactate production, and oxygen consumption. Their effect is particularly important when oxygen delivery and autoregulation are already compromised. Treatment should consider seizure duration, frequency, spatial burden, background state, medication adverse effects, and the possibility that excessive anesthetic suppression may worsen hypotension and delay neurological assessment[16, 23, 30]. The absence of seizures does not imply physiological stability. Suppressed background activity may result from injury, sedatives, hypothermia, metabolic dysfunction, or ischemia. EEG should be interpreted with medication doses, temperature, ICP, $PbtO_2$, and systemic physiology.

Cortical spreading depolarizations are waves of near-complete neuronal and glial depolarization that can propagate through injured cortex. They increase metabolic demand and may convert tissue at risk

into infarction when perfusion is inadequate. Detection currently requires subdural electrocorticography and is mainly confined to specialist centers and research protocols.

Pupillometry and Neurological Examination. Serial neurological assessment remains the only modality that directly evaluates integrated function. Pupillary asymmetry, loss of reactivity, decline in motor response, new posturing, or deterioration in brainstem reflexes requires immediate evaluation regardless of monitor values. Automated pupillometry quantifies pupil size, constriction velocity, latency, and a composite neurological pupil index. It reduces interobserver variability and can detect trends before gross fixed dilation. Abnormal values may indicate herniation, third-nerve compression, brainstem dysfunction, medication effects, ocular trauma, or systemic autonomic disturbance. Pupillometry is noninvasive and repeatable but not lesion-specific. A normal pupil does not exclude intracranial hypertension, and an abnormal pupil should not be attributed to ICP without examining ocular injury, previous surgery, topical medications, and baseline asymmetry.

Transcranial Doppler and Cerebral Blood Flow. Transcranial Doppler measures blood-flow velocity in basal cerebral arteries. It can identify elevated pulsatility, low diastolic flow, vasospasm, hyperemia, embolic signals, and patterns compatible with critically elevated intracranial resistance. Serial trends are more informative than isolated values. TCD-derived autoregulatory metrics can complement PRx, especially when invasive monitoring is unavailable. However, velocity is not equivalent to blood flow when vessel diameter changes, and adequate acoustic windows are absent in some patients. Thermal diffusion flowmetry, laser Doppler, and other local cerebral blood-flow monitors provide regional data but are less widely used. Their principal limitation resembles $PbtO_2$ and microdialysis: excellent temporal resolution within a very small tissue volume.

Systemic Physiology as a Neuromonitor. The injured brain depends on systemic oxygen delivery. Hypotension, hypoxemia, hyperthermia, anemia, dysglycemia, hypocapnia, hypercapnia, electrolyte disturbance, coagulopathy, and low cardiac output can produce secondary injury even when intracranial monitors appear stable. Arterial blood pressure should be measured invasively in monitored severe TBI. The transducer reference level matters because CPP calculation changes when MAP is referenced at the heart rather than the external auditory meatus. Institutions should use a standardized reference and document it. End-tidal carbon dioxide is useful for continuous ventilation assessment but may differ substantially from $PaCO_2$ in shock, pulmonary injury, high dead space, or changing ventilation. Arterial blood gas confirmation is necessary before major ventilatory changes. Hypocapnia reduces cerebral blood flow and can lower ICP rapidly, making it useful as a short-term emergency measure during impending herniation. Prolonged prophylactic hyperventilation can produce cerebral ischemia and should not be used as routine ICP control without appropriate monitoring [5, 11, 16]. Fever increases cerebral metabolism and can worsen ICP and oxygen demand. Normothermia is a foundational target. Prophylactic therapeutic hypothermia has not consistently improved neurological outcome and can increase complications. Temperature reduction may still be used as a rescue strategy in selected refractory intracranial hypertension, with recognition that it treats pressure burden rather than the primary injury.

Multimodal Pattern Recognition. The central principle of multimodal monitoring is that no single signal identifies every mechanism. The same ICP elevation can result from edema, hematoma expansion, hyperemia, venous obstruction, hydrocephalus, seizures, fever, ventilator dyssynchrony,

inadequate sedation, or impaired autoregulation. A pattern of rising ICP, positive PRx, falling $PbtO_2$, and elevated lactate-to-pyruvate ratio suggests a high-risk state of impaired autoregulation, oxygen-delivery failure, and metabolic crisis. Increasing MAP may be beneficial if CPP is below CPPopt, but harmful if pressure passivity causes ICP to rise further. A bedside CPP challenge with simultaneous observation of ICP, PRx, $PbtO_2$, and systemic effects can clarify the response. Low $PbtO_2$ with normal ICP, preserved PRx, normal CPP, and low hemoglobin suggests oxygen-content limitation rather than pressure failure. High ICP with normal $PbtO_2$ and preserved metabolism may represent a pressure problem before tissue hypoxia develops, allowing targeted ICP reduction without excessive elevation of CPP. Electrographic seizures with transient ICP elevation, rising $PbtO_2$ consumption, and increased lactate require antiseizure treatment rather than repeated osmotherapy alone. Similarly, ventilator dyssynchrony and coughing should be corrected before interpreting transient pressure elevations as refractory cerebral edema.

Table 4. **Multimodal Physiological Patterns**

Multimodal pattern	**Probable dominant mechanism**	**Potentially misleading isolated interpretation**	**Integrated response**
High ICP, low CPP, low $PbtO_2$, positive PRx	Intracranial hypertension with pressure-passive hypoperfusion	“Raise MAP until CPP is normal”	Reduce ICP, cautiously support MAP, assess surgery and oxygen response
High ICP, normal $PbtO_2$, negative PRx	Pressure elevation with preserved oxygenation and reactivity	“No treatment because oxygen is normal”	Evaluate pressure–time burden, compliance, imaging, and trajectory
Normal ICP, low $PbtO_2$, low Hb	Reduced oxygen content	“ICP and CPP are normal, therefore brain is safe”	Correct systemic oxygen delivery and reassess
Normal ICP, normal $PbtO_2$, high LPR	Metabolic or mitochondrial dysfunction	“All monitored physiology is adequate”	Review glucose, seizures, temperature, perfusion, and substrate delivery
Recurrent ICP spikes with EEG seizures	Ictal metabolic and vascular activation	“Refractory edema”	Treat electrographic seizures and avoid repetitive nonspecific osmotherapy
High CPP, rising ICP, positive PRx	Autoregulatory failure with hydrostatic edema	“Higher CPP is always protective”	Reduce vasopressor-driven overshoot and reassess CPPopt
Low CPP, negative PRx, normal $PbtO_2$	Lower CPP tolerated within autoregulatory range	“Immediate high-dose vasopressor required”	Avoid hypotension but assess treatment burden before escalation

Worsening pupils with stable ICP	Focal mass effect, compartmental pressure gradient, or brainstem lesion	"Stable global ICP excludes deterioration"	Urgent examination and repeat imaging

Treatment Response as a Diagnostic Test. A therapeutic intervention provides physiological information. A hyperosmolar bolus that reduces ICP, improves pulse amplitude, raises CPP, and increases $PbtO_2$ supports a pressure-mediated mechanism. If ICP falls but $PbtO_2$ and metabolism do not improve, the oxygen problem may be independent or irreversible. A CPP challenge can be performed by a controlled increase in MAP while monitoring ICP, PRx, and $PbtO_2$. Improved $PbtO_2$ with stable or falling ICP suggests preserved autoregulatory benefit. Rising ICP without oxygen improvement suggests pressure passivity and hydrostatic worsening. A short FiO_2 challenge can confirm probe responsiveness and diffusion reserve but should not be interpreted as evidence that hyperoxia is a definitive treatment. Very high arterial oxygen can increase $PbtO_2$ without restoring cerebral blood flow or metabolism. CSF drainage that rapidly lowers ICP and improves CPP identifies a volume-responsive component. Failure of drainage may indicate catheter obstruction, nonhydrocephalic edema, mass lesion, venous congestion, or exhausted compliance. Precision care requires documenting the pre-intervention hypothesis, intervention, expected response, observed multimodal response, and decision to continue or stop. Without this feedback loop, treatment becomes escalation by protocol rather than physiology.

Treatment Intensity and Iatrogenic Burden. The therapeutic intensity level quantifies how aggressively ICP is being treated. Two patients with identical ICP may differ substantially if one requires only head elevation and light sedation while the other requires repeated hyperosmolar therapy, vasopressors, paralysis, barbiturates, hypothermia, and decompressive surgery. Treatment intensity is not a neutral covariate. Deep sedation prevents examination and promotes hypotension, ileus, infection, delirium, and prolonged ventilation. Hyperosmolar agents can cause electrolyte disturbances, renal injury, hyperchloremia, and intravascular depletion. Vasopressors can produce arrhythmia, myocardial stress, peripheral ischemia, and pulmonary complications. Barbiturate coma can reduce refractory ICP but requires hemodynamic tolerance and EEG monitoring. Decompressive craniectomy reliably lowers ICP, but randomized trials show that the effect on survival can include increased survival with severe disability. Treatment goals and family communication must therefore distinguish pressure control from guaranteed neurological recovery [15, 17, 27]. DECRA evaluated early decompressive craniectomy for diffuse ICP elevation at a relatively low threshold and did not demonstrate improved functional outcome. RESCUEicp evaluated decompression for later refractory intracranial hypertension and reduced mortality, but increased the number of survivors across several disability categories. These trials demonstrate that timing, threshold, injury phenotype, surgical technique, and outcome preference matter [16, 23, 30] The decision to escalate should therefore consider pressure burden, imaging, pupils, autoregulation, tissue oxygen, age, premorbid function, extracranial injury, reversibility, and the patient's values. The decision to de-escalate should be equally structured.

Imaging Within a Precision Monitoring Strategy. Initial CT defines mass lesions, contusions, diffuse swelling, cisternal compression, midline shift, fractures, and traumatic

subarachnoid hemorrhage. Repeat CT is required when neurological status worsens, pupils change, ICP rises unexpectedly, physiological patterns become discordant, or hemorrhagic progression is suspected. Stable ICP does not exclude a new focal lesion when the monitor is located in the opposite hemisphere or after decompressive craniectomy. Conversely, repeated routine CT exposes the patient to transfer risk and radiation. Imaging frequency should be linked to clinical and physiological change. MRI can identify diffuse axonal injury, brainstem lesions, ischemia, and microhemorrhage that are not visible on CT. It is usually performed after acute physiological stabilization because transport and scanner compatibility are limiting factors. CT perfusion and advanced MRI can characterize regional flow and metabolism, but routine use in unstable severe TBI remains limited. Their greatest role may be resolving discordance among ICP, $PbtO_2$, clinical examination, and structural CT.

Spatial Limitations of Multimodal Monitoring. ICP measured in one compartment may not represent pressure in another when focal lesions, compartmentalization, or decompressive surgery create pressure gradients. $PbtO_2$, microdialysis, and local blood-flow probes sample only a small region. Probe placement should be planned according to the clinical question. Placement in normal-appearing tissue assesses global vulnerability. Placement near a contusion evaluates perilesional tissue at risk. Bilateral or multiparameter monitoring can improve spatial representation but increases invasiveness, cost, infection risk, hemorrhage risk, and data complexity. Monitor location must be documented using post-placement CT. A low $PbtO_2$ value from tissue within an established hematoma, infarct, or catheter tract may not be modifiable and can lead to harmful systemic escalation. The spatial limitation of invasive monitoring reinforces the role of serial examination, imaging, EEG coverage, and systemic assessment. Precision does not mean that a locally precise number represents the whole brain.

The MULTI-TARGET Framework. The proposed MULTI-TARGET model contains eleven linked domains. Monitoring validity requires confirmation of transducer leveling, calibration, waveform quality, catheter patency, probe position, arterial-line damping, and time synchronization. Treatment should not be escalated from an unverified signal. Understanding pressure burden requires assessment of ICP magnitude, duration, frequency, waveform, compensatory reserve, and precipitating events rather than reliance on a single threshold. Lesion topography integrates CT and MRI findings with monitor location. Focal mass effect, diffuse edema, ventricular obstruction, and postcraniectomy physiology require different interpretations.

Tissue oxygenation incorporates $PbtO_2$, PaO_2, saturation, hemoglobin, CPP, $PaCO_2$, temperature, and probe location. Individual autoregulation uses PRx, CPPopt, lower and upper autoregulatory limits, and response to controlled CPP changes. Treatment response turns interventions into bedside physiological tests. Electrical activity incorporates continuous EEG, seizure burden, background reactivity, and medication effects. Glucose and metabolic state include systemic glucose, cerebral glucose, lactate, pyruvate, lactate-to-pyruvate ratio, temperature, nutrition, and mitochondrial function. Escalation criteria define when to advance from basic treatment to hyperosmolar therapy, CSF drainage, neuromuscular blockade, barbiturates, advanced temperature control, or surgery. Reassessment requires repeated examination, review of trends, imaging when indicated, and evaluation of iatrogenic complications. Therapeutic de-escalation identifies when sedation, osmotherapy, vasopressors, ventilation intensity, and invasive monitoring can be reduced safely.

Table 5. **Scientific Originality of the MULTI-TARGET Model**

Existing limitation	**Conventional interpretation**	**Proposed original element**	**Expected contribution**
ICP treated as a binary threshold	ICP above 22 mm Hg automatically triggers escalation	Magnitude, duration, recurrence, waveform, and context integrated	Reduces overtreatment of transient episodes and undertreatment of sustained burden
CPP treated as a universal number	Every patient maintained at the same 60–70 mm Hg target	CPPopt, PRx, oxygenation, and systemic burden incorporated	Supports individualized lower and upper perfusion limits
$PbtO_2$ treated as global oxygenation	One focal value assumed to represent the whole brain	Probe location and lesion topography explicitly included	Prevents inappropriate systemic escalation
Monitor correction equated with biological rescue	Numerical normalization defines success	Treatment response assessed across pressure, oxygen, metabolism, and EEG	Identifies physiologically ineffective treatment
Multimodal data reviewed independently	Separate screens and isolated thresholds	Time-synchronized pattern recognition	Improves mechanism-specific intervention
Escalation emphasized more than de-escalation	Intensive therapy continues after crisis resolution	Explicit daily de-escalation criteria	Reduces sedation, vasopressor, osmotic, and ventilation burden
Poor outcome linked only to peak ICP	Highest value used as primary risk marker	Cumulative pressure–time dose incorporated	Better reflects secondary injury exposure
CPPopt interpreted as an exact mandatory value	Vasopressors used to force CPP to a point target	CPPopt considered a dynamic zone and possible lower safety boundary	Reduces treatment-induced edema and systemic complications
Clinical examination displaced by technology	Monitor values dominate decision-making	Examination, pupils, imaging, and monitor validity remain primary checkpoints	Preserves recognition of focal and compartmental deterioration

Discussion. The principal finding of this synthesis is that precision neurocritical care should not replace established thresholds with another set of rigid personalized numbers. Its purpose is to combine population safety limits with continuous interpretation of the individual patient's evolving physiology. The ICP threshold of 22 mm Hg remains clinically useful because bedside care requires actionable limits. However, high-resolution studies demonstrate that the relationship between ICP and

outcome is continuous. The biological effect of intracranial hypertension depends on how high the pressure rises, how long it remains elevated, how often it recurs, whether compensatory reserve is exhausted, and whether oxygenation, autoregulation, metabolism, and neurological function deteriorate simultaneously [7, 14, 19]. This does not mean that clinicians should wait for a complex algorithm before treating dangerous pressure. Sustained ICP above the guideline threshold, especially with pupillary change, mass effect, low CPP, or falling $PbtO_2$, requires immediate intervention. Dynamic analysis is most valuable in distinguishing transient events, guiding the intensity of therapy, and determining whether the chosen intervention is helping. The same principle applies to CPP. Maintaining a minimum CPP reduces the risk of ischemia, but higher pressure is not universally better. When autoregulation is impaired, vasopressor-driven increases in MAP can increase cerebral blood volume, ICP, and edema. When autoregulation is preserved and CPP lies below the patient's lower limit, the same intervention may improve oxygenation and metabolism.

PRx and CPPopt provide a physiologically coherent method for estimating this difference. COGiTATE established feasibility and showed that the target can be updated at the bedside. The 2025 secondary analysis supported improved autoregulatory function during periods close to CPPopt. Outcome efficacy nevertheless remains uncertain because feasibility, physiological improvement, and functional recovery represent different evidentiary stages [11, 12, 20]. CPPopt also has technical limitations. Reliable estimation requires adequate high-frequency arterial pressure and ICP data, sufficient spontaneous variability, stable monitoring, and an identifiable U-shaped PRx curve. The estimate may be unavailable, delayed, unstable, or influenced by treatment. It should therefore be presented with a confidence measure and trend rather than as a deterministic number. The 2025 CPP reappraisal is clinically important because it suggests that the danger of falling below the individualized target may be greater than the danger of moderate overshoot. This supports using CPPopt as a personalized lower limit in selected patients rather than forcing CPP to remain precisely at the calculated optimum at all times. Brain tissue oxygenation illustrates both the promise and limitations of multimodal monitoring. BOOST-II demonstrated that $PbtO_2$-guided treatment can reduce hypoxic exposure. OXY-TC did not show superior six-month outcome. These findings are compatible if a monitor is highly effective at detecting and correcting a physiological abnormality but the intervention does not consistently change diffuse injury, probe sampling is regional, or treatment introduces competing harms [2, 3, 10, 18].

The correct conclusion is not that oxygen monitoring should be used in every patient or abandoned entirely. It should be used when the clinical team can interpret probe location, identify the cause of low oxygen, apply a mechanism-specific intervention, and evaluate the response. Low $PbtO_2$ caused by anemia should not be treated in the same way as low $PbtO_2$ caused by high ICP, hypocapnia, or local diffusion failure. Multimodal monitoring is especially valuable when signals disagree. Normal ICP with low $PbtO_2$ challenges the assumption that pressure control alone ensures adequate oxygen delivery. Normal $PbtO_2$ with a high lactate-to-pyruvate ratio challenges the assumption that oxygen availability guarantees mitochondrial utilization. Stable ICP with worsening pupils challenges the assumption that one regional pressure measurement excludes focal herniation. The framework also emphasizes systemic physiology. The most sophisticated intracranial platform cannot compensate for untreated hemorrhagic shock, severe hypoxemia, fever, profound anemia, or repeated hypotension.

Prevention of secondary insults begins before monitor insertion and continues during transport, imaging, surgery, and intensive care. A major risk of advanced monitoring is therapeutic overreaction. Multiple sensors create multiple abnormal values, each of which can provoke intervention. This can produce polytherapy involving high-dose vasopressors, repeated osmotherapy, hyperoxia, excessive transfusion, deep sedation, paralysis, and prolonged ventilation. The number of monitored parameters should not determine the number of treatments. Treatment response must therefore be incorporated into the definition of success. If increasing MAP raises CPP but worsens ICP, leaves $PbtO_2$ unchanged, and requires escalating vasopressors, the intervention has failed biologically despite correction of the CPP number. If osmotherapy repeatedly lowers ICP for only minutes while sodium, renal function, and hemodynamics deteriorate, definitive structural treatment should be reconsidered. De-escalation is similarly important. Severe TBI protocols often describe how to add therapy but provide less detail on how to remove it. Daily evaluation should determine whether neuromuscular blockade, barbiturates, high-dose sedation, osmotherapy, vasopressors, hyperventilation, and invasive monitoring remain necessary.

The decision to remove an ICP monitor should consider stability during stimulation, absence of recurrent pressure burden, imaging stability, reduced treatment intensity, recovery of examination, and lack of planned procedures likely to destabilize physiology. Removal based only on one day of normal mean ICP can be premature when sedation or drainage has masked instability. Data integration remains a practical barrier. ICP, arterial pressure, $PbtO_2$, EEG, temperature, ventilation, medication, microdialysis, and laboratory results often reside in separate systems with different clocks and sampling rates. Manual interpretation is vulnerable to missed temporal relationships.

Future platforms should synchronize data, annotate interventions, display pressure–time dose, calculate PRx and CPPopt with confidence intervals, identify discordant patterns, and distinguish artifact from physiology. Alerts should describe a probable mechanism rather than merely announce that a threshold has been crossed. Artificial intelligence may assist prediction of ICP crises and multimodal phenotyping, but models must be externally validated and transparent. Algorithms trained in high-resource tertiary centers may not generalize to different monitor types, nursing practices, treatment protocols, or patient populations. Precision care must also remain feasible in resource-limited settings. The absence of $PbtO_2$, microdialysis, or automated CPPopt does not preclude physiology-based treatment. Serial examination, CT, EVD or intraparenchymal ICP, arterial pressure, blood gases, hemoglobin, temperature, sodium, pupillometry, and transcranial Doppler can form a pragmatic multimodal platform. The CREVICE protocol and other consensus efforts demonstrate that structured severe TBI care can be adapted to settings without invasive ICP monitoring. The principle is to use available information systematically while recognizing uncertainty, rather than equating precision with expensive technology [4, 8, 14, 25].

The article’s proposed MULTI-TARGET model is intended to organize this reasoning. It is not a validated therapeutic score and does not establish new treatment thresholds. Its scientific originality lies in connecting signal validity, dynamic dose, spatial representation, autoregulatory targets, metabolic state, treatment response, escalation, and de-escalation within one closed-loop framework. Several limitations should be acknowledged. Much of the evidence linking multimodal variables to outcome is observational and vulnerable to confounding by injury severity and treatment intensity. A

monitor may appear associated with poor outcome because it is used in the sickest patients. Conversely, centers using advanced monitoring may also provide more specialized care. Physiological target trials are difficult because treatment protocols contain multiple interventions. A $PbtO_2$ strategy is not a single treatment; it may alter FiO_2, ventilation, CPP, transfusion, sedation, temperature, and surgery. Outcome effects cannot always be attributed to the monitor itself. The future research agenda should include adequately powered trials of autoregulation-guided perfusion, brain tissue oxygen protocols, and integrated multimodal decision support. Studies should record treatment burden, systemic complications, probe location, signal quality, and adherence. Outcome measures should extend beyond mortality and dichotomized Glasgow Outcome Scale categories. Cognitive recovery, communication, return to home, independence, quality of life, caregiver burden, and survival with severe disability are relevant to patients and families.

Conclusion. Severe traumatic brain injury is an evolving physiological disorder in which intracranial pressure, cerebral perfusion, autoregulation, oxygen delivery, metabolism, and electrical activity can deteriorate independently or interact synergistically. Guideline thresholds remain essential. Sustained ICP above 22 mm Hg should prompt treatment, and CPP should generally be maintained within a safe range of 60–70 mm Hg. These values are population-derived boundaries rather than universal individualized optima. ICP should be interpreted dynamically. Magnitude, duration, recurrence, waveform morphology, compensatory reserve, precipitating events, treatment intensity, and multimodal consequences determine the biological importance of an episode. PRx and CPPopt provide a rational method for estimating individualized autoregulatory targets. COGiTATE established feasibility, and subsequent analyses support physiological relevance. Definitive improvement in patient-centered outcome remains to be proven. $PbtO_2$ monitoring detects regional brain hypoxia that may occur despite acceptable ICP and CPP. BOOST-II demonstrated reduction in hypoxic burden, whereas OXY-TC did not establish superior six-month neurological outcome. The discrepancy emphasizes that detection, numerical correction, and clinical benefit are separate stages. Continuous EEG, cerebral microdialysis, pupillometry, transcranial Doppler, serial imaging, and systemic monitoring provide complementary information. Their value arises from integration rather than independent threshold treatment. The proposed MULTI-TARGET framework combines monitor validity, pressure–time burden, lesion topography, tissue oxygenation, autoregulation, treatment response, electrical activity, metabolism, escalation, reassessment, and de-escalation. Precision neurocritical care is therefore not defined by the number of probes inserted into the brain. It is defined by the ability to identify the dominant mechanism of secondary injury, select the least harmful effective intervention, verify the physiological response, recognize treatment failure, and withdraw unnecessary therapy.

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