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Brain Tissue Oxygenation in Critically Ill Patients with Spontaneous Intracerebral Hemorrhage: A Prospective Observational Study

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Abstract

Background

Brain tissue oxygen pressure ($PbtO_2$) monitoring is increasingly used in neurocritical care, but whether $PbtO_2$ provides complementary information beyond conventional parameters such as intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in spontaneous intracerebral hemorrhage (ICH) is unclear.

Methods

We conducted a prospective, single-centre observational cohort study in a dedicated Neurocritical Care Unit between January 2021 and March 2023. Adult patients with spontaneous ICH requiring invasive multimodal brain monitoring were consecutively enrolled. Continuous monitoring included ICP, CPP, pressure reactivity index (PRx), bedside optimal CPP (CPPopt) and $PbtO_2$. Neuromonitoring data were analyzed during the first 48 hours and between days 3–7. Paired comparisons were used to assess temporal changes. Linear regression models were used to explore the relationship between $PbtO_2$, CPP, and PRx.

Results

Thirty-one patients were included, of whom 18 underwent $PbtO_2$ monitoring. ICP remained within normal ranges, while CPP increased significantly from the first 48 hours to days 3–7. PRx improved over time, suggesting better cerebrovascular autoregulation. In contrast, $PbtO_2$ values remained close to hypoxic thresholds and did not significantly differ between periods. During the first 48 hours, median $PbtO_2$ was 21.72 mmHg (IQR 18.67–27.04) despite preserved systemic oxygenation. No significant correlation was found between $PbtO_2$ and paO_2/FiO_2 ratio. In linear regression models the association between $PbtO_2$ and cerebral perfusion was more evident during the first 48 hours although visual inspection suggested a non-linear relationship, with higher $PbtO_2$ values clustering around a relatively narrow CPP range.

Conclusions

In critically ill patients with spontaneous ICH, brain tissue oxygenation, evaluated with $PbtO_2$, remains suboptimal despite controlled ICP, elevated CPP, and adequate systemic oxygenation. However, $PbtO_2$ may be closely related to cerebral perfusion dynamics, supporting its potential role as a complementary tool for individualized neurocritical care management.

Introduction

Spontaneous intracerebral hemorrhage (ICH) is a severe form of stroke with persistently high mortality and morbidity, often resulting in long-term disability, cognitive decline, and increased risk of recurrent vascular events.[1,2] Up to one quarter of initially awake patients experience early neurological deterioration, reflecting the dynamic nature of the disease.[3] Despite rising hospital admissions, outcomes remain poor, though it is believed that coordinated primary and specialized care with structured critical care pathways may improve prognosis.[4]

In recent years, patient-centered management after acute neurological injury has emphasized optimizing cerebral physiology while minimizing secondary brain injury, with invasive neuromonitoring playing a central role.[5] While intracranial pressure (ICP) monitoring remains foundational, elevated ICP alone provides limited insight into cerebral perfusion and autoregulation.[6,7] Derived variables such as Cerebral Perfusion Pressure (CPP), optimal CPP (CPPopt), Pressure Reactivity Index (PRx), and Brain Tissue Oxygen Tension ($PbtO_2$) are increasingly integrated in multimodal monitoring to guide bedside interventions.[5,8–10] PRx is the continuous correlation between arterial blood pressure and ICP, with negative values indicating more adequate autoregulation. CPPopt, corresponding to the lowest PRx, identifies the CPP value at which autoregulation is best preserved, which may differ from conventional guideline ranges (60-80mmHg).[9,11,12]

Brain tissue oxygen pressure ($PbtO_2$) is a focal measure of oxygen partial pressure within the brain parenchyma, allowing direct detection of cerebral hypoxemic hypoxia in acute brain injury.[13,14] $PbtO_2$ may be influenced by cerebral blood flow, systemic oxygenation, carbon dioxide levels, hemoglobin concentration, metabolic demand, and microvascular integrity[15,16], with normal values ranging from 25 to 50 mmHg and lower values associated with worse outcomes in a dose–response manner.[17]

$PbtO_2$-targeted therapeutic strategies are applied in traumatic brain injury.[14,18–22] In spontaneous ICH, PbtO2 monitoring remains insufficiently underexplored, and its potential contribution to individualized management not defined.[23,24]

Moreover, the clinical diagnosis of spontaneous ICH may not fully capture the underlying vascular pathology, which, in approximately 80% of the cases, reflects chronic microangiopathic processes such as hypertensive vasculopathy or cerebral amyloid angiopathy, that may precede the acute event silently by years.[1,25] These chronic vascular alterations may influence baseline cerebral oxygenation and autoregulatory capacity[26], further supporting the need for physiological monitoring in critically ill ICH patients.

The aim of this prospective observational study was to characterize brain tissue oxygenation profile of critically ill patients with spontaneous ICH during the first 48 hours and in the period of days 3–7, and to describe its association with cerebral perfusion pressure, and cerebrovascular autoregulation in a setting of optimized, individualized neurocritical care.

Methods

Study design and setting

We conducted a prospective, single-centre observational cohort study in the Neurocritical Care Unit (NCCU) of ULS São João, Porto, a tertiary referral centre with a dedicated neurocritical care team and established multimodal neuromonitoring protocols. Patient recruitment occurred consecutively between January 2021 and March 2023. Data collection was performed prospectively from the time of NCCU admission until the end of the neuromonitoring period.

The study was approved by the Ethics Committee of ULS São João (approval number 286/19) and conducted in accordance with the Declaration of Helsinki.[27] Written informed consent was obtained from each patient's legally authorized representative prior to inclusion, as all patients were unable to provide consent at admission due to the severity of their neurological condition and the need for sedation.

Patient Selection

Adult patients (> 18 years) admitted to the NCCU with a diagnosis of spontaneous intracerebral hemorrhage (ICH), confirmed by admission brain computed tomography (CT), were eligible for inclusion. Only patients requiring invasive multimodal brain monitoring and managed under deep sedation and mechanical ventilation were considered for the study.

Inclusion criteria comprised spontaneous ICH of any location and indication for invasive multimodal neuromonitoring according to institutional neurocritical care practice. Additionally, availability of valid neuromonitoring data for a minimum of 48 consecutive hours was a requisite for inclusion.

Patients with hemorrhage secondary to structural or vascular lesions (including aneurysms, arteriovenous malformations, tumors, or hemorrhagic transformation of ischemic stroke), with clinical or neuromonitoring data inadequate for analysis or pregnant were excluded.

Neurocritical care management

All patients were managed according to neurocritical care institutional protocols. Patients were deeply sedated, targeting a Richmond Agitation–Sedation Scale (RASS) score of -4 to -5 and mechanically ventilated. Normocapnia was controlled, with arterial carbon dioxide partial pressure kept within the normal physiological range, and oxygenation was optimized according to arterial blood gas analysis, with daily monitoring of the paO_2/fiO_2 ratio. Normothermia (< 38ºC) was actively maintained throughout the monitoring period.

Intracranial pressure, cerebral perfusion pressure and autoregulation

All patients underwent continuous invasive multimodal brain monitoring, including intracranial pressure (ICP), cerebral perfusion pressure (CPP), and cerebrovascular autoregulation assessment.

ICP was monitored using a parenchymal Codman® probe, which was systematically placed in the cerebral hemisphere contralateral to the dominant hemorrhagic lesion. Probe positioning and the absence of procedure-related complications were confirmed by post- insertion CT scan.

CPP was calculated as the difference between mean arterial pressure and ICP.

Cerebrovascular autoregulation was assessed continuously using the pressure reactivity index (PRx), calculated as the moving correlation between slow waves of ICP and arterial blood pressure. We established 0.2 as the PRx cut-off value, with values > 0.20 indicating impaired autoregulation and values ≤ 0.20 indicating preserved autoregulation.[28,29] Individualized optimal CPP (CPPopt) was derived from PRx analysis using established algorithms implemented in the ICM+® software (Cambridge Enterprise, UK). CPPopt-guided management was preferentially applied in all patients whenever reliable PRx data were available. In situations where CPPopt could not be reliably determined, CPP targets were guided by the most recently identified optimal CPP value for the individual patient or, when unavailable, by guideline-recommended CPP ranges.

Brain tissue oxygenation monitoring

Continuous brain tissue oxygen pressure ($PbtO_2$) monitoring was performed using a Licox® probe. Due to equipment availability, $PbtO_2$ monitoring could not be applied to all eligible patients. The decision to place a $PbtO_2$ probe was exclusively logistical and not based on patient characteristics or disease severity.

The $PbtO_2$ probe was inserted into the hemisphere contralateral to the main hemorrhagic lesion, and correct positioning was confirmed by CT imaging. Normal $PbtO_2$ values were defined as 25–50 mmHg.[17]

Data collection and variables

Physiological data, including ICP, CPP, PRx, CPPopt, and $PbtO_2$, were continuously recorded and integrated using the ICM+® software.

Admission clinical variables included age, sex, previous comorbidities, medication and neuroimaging characteristics. Neuroimaging data were obtained from admission brain CT scans and included hemorrhage location, hematoma volume, presence of intraventricular hemorrhage and hydrocephalus. Therapeutic interventions, including surgical procedures (hematoma evacuation, decompressive craniectomy or both) and the presence of an external ventricular drain, were also recorded.

Neuromonitoring data were analyzed during two predefined periods: first 48 hours after NCCU admission and days 3 to 7. For $PbtO_2$, the primary metric was the mean $PbtO_2$ value per patient within each period. Aggregate values across patients are reported as medians with interquartile ranges.

Bias and study size

To minimize potential sources of bias, patients were prospectively enrolled and managed exclusively within a single NCCU, using uniform treatment protocols and standardized neuromonitoring techniques. All measurements were obtained using the same equipment and software platforms.

Unavailability of $PbtO_2$ monitoring for all patients represents a potential source of selection bias; however, probe placement was determined solely by equipment availability and not by clinical or radiological characteristics.

An a priori sample size estimation indicated that at least 25 patients would provide 80% statistical power for exploratory analyses. During the study period, 31 consecutive patients fulfilling inclusion criteria were enrolled, of whom 18 underwent $PbtO_2$ monitoring.

Statistical analysis

Continuous variables are presented as medians with interquartile ranges, and categorical variables as counts with percentages. Baseline demographic and clinical characteristics were summarized descriptively

For patients undergoing $PbtO_2$ monitoring, neuromonitoring parameters were compared between 0–48 h and 3–7 days periods using paired Wilcoxon signed-rank tests, including only patients with complete data in both periods. Similar intra-patient comparisons were performed for ICP, CPP, and PRx in the full cohort.

The association between $PbtO_2$ and systemic oxygenation, assessed by the paO_2/FiO_2 ratio, was explored using Spearman's rank correlation coefficient during the first 48 hours and during days 3–7.

Linear regression models were fitted to explore the association between mean $PbtO_2$, CPP and PRx during each monitoring period. Separate models were built for the first 48 hours and for days 3–7, including CPP and PRx as covariates. Results are reported as beta coefficients with 95% confidence intervals.

Statistical analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria). The statistical significance cutoff was set at 0.05.

Results

Study participants

During the study period, 34 patients were admitted to the Neurocritical Care Unit with a diagnosis of intracerebral hemorrhage. Three patients were excluded according to predefined exclusion criteria (one due to secondary ICH caused by an underlying tumor and two due to insufficient neuromonitoring data caused by signal loss), resulting in a final study cohort of 31 patients.

All included patients had complete clinical and neuromonitoring data available for analysis. ICP, CPP and PRx were monitored in all 31 patients, with $PbtO_2$ monitoring in 18 patients (FIGURE 1).

Baseline demographic and clinical characteristics

Baseline demographic, clinical, and radiological characteristics of the study population are summarized in **TABLE 1**. The median age was 66 years (interquartile range [IQR] 51–74), and most patients were male (71%). The median Glasgow Coma Scale score at admission was 8 (IQR 7–9), reflecting the severity of neurological injury.

Table 1
Baseline demographic and clinical characteristics

	N = 31*
Age, years	66 (51–74)
Sex	
Female	9 (29%)
Male	22 (71%)
GCS at admission	8 (7–9)
Arterial hypertension	23 (74%)
Current smoker	5 (16%)
Coagulopathy	6 (19%)
Antiplatelet therapy	13 (42%)
Chronic kidney disease	5 (16%)
ICH location	
Basal Ganglia	16 (43%)
Lobar	6 (19%)
Thalamus	9 (29%)
ICH volume, mL	48 (21–74)
Intraventricular hemorrhage	19 (61%)
External ventricular drain	14 (45%)
Surgical evacuation	10 (32%)
6-month outcome	
Good outcome (mRS 1–2)	0 (0%)
Acceptable outcome (mRS 3–4)	10 (32%)
Poor outcome (mRS 5–6)	21 (68%)
ICH, Intracerebral Hemorrhage; mRS, Modified Rankin Scale	

Arterial hypertension was the most prevalent comorbidity (74%), and 42% of patients were on antiplatelet therapy prior to admission. Hemorrhages were exclusively supratentorial, involving the basal ganglia (43%) and thalamic (29%) regions. The median hematoma volume was 48 mL (IQR 21–74), and intraventricular hemorrhage was present in 61% of cases. External ventricular drainage was required in

45% of patients, and 32% underwent surgical hematoma evacuation, with no decompressive craniectomy.

At 6 months, ten patients (32%) had moderate disability (modified Rankin Scale (mRS) score 3–4) and 68% experienced poor outcomes (mRS 5–6), including 11 deaths. No patient achieved a mRS score of 1–2.

Table 2. Multimodal neuromonitoring: first 48 h vs days 3–7

Variable	First 48 h	Days 3–7	*p*-value
$PbtO_2$, mmHg	21.72 (18.67–27.04)	23.57 (17.44–26.72)	1.00
ICP, mmHg	7.75 (4.68–11.86)	7.91 (5.07–11.16)	0.50
CPP, mmHg	83.84 (79.98–88.37)	88.53 (85.15–90.91)	<0.001
CPPopt, mmHg	84.34 (80.05–97.22)	90.40 (82.83–101.00)	0.10
PRx	0.21 (0.04–0.32)	-0.001 (-0.06–0.17)	<0.001

CPP, Cerebral Perfusion Pressure; CPPopt, Optimal Cerebral Perfusion Pressure; ICP, Intracranial Pressure; $PbtO_2$, Brain Tissue Oxygen Tension ($PbtO_2$); PRx, Pressure Reactivity Index (PRx).

Multimodal Brain Monitoring

Continuous multimodal brain monitoring was successfully performed in all included patients, yielding approximately 3024 hours of high-resolution physiological data. Neuromonitoring parameters were analyzed over two predefined time periods

Median values of ICP, CPP, CPPopt, PRx, $PbtO_2$ and systemic oxygenation parameters are presented in Table 2.

Intracranial pressure, cerebral perfusion pressure and autoregulation

Median ICP values remained consistently below 20 mmHg during both analyzed periods, with no statistically significant difference between the two periods (median 8 mmHg [IQR 4.68–11.86] vs. 7.91 mmHg [IQR 5.07–11.16], $p = 0.50$).

In contrast, CPP increased significantly from the period 48h and the period days 3–7, with median values rising from 84 mmHg (IQR 79.98–88.37) to 89 mmHg (IQR 85.15–90.91; $p < 0.001$). CPPopt values showed a similar upward trend, although the difference did not reach statistical significance.

Cerebrovascular autoregulation, assessed by PRx, improved significantly over time. Median PRx decreased from 0.21 (IQR 0.04–0.32) during the first 48 hours to -0.001 (IQR – 0.06–0.17) during days 3 to 7 ($p < 0.001$), indicating a possible gain in autoregulation as time goes on.

Distribution of CPP, CPPopt, PRx, and $PbtO_2$ values across both time periods is illustrated in FIGURE 2, highlighting inter-individual variability despite relatively stable group-level medians.

Brain tissue oxygenation

Among the 18 patients undergoing $PbtO_2$ monitoring, median values during the first 48 hours were 22mmHg (IQR 19–27). During days 3–7, median $PbtO_2$ values were 24 mmHg (IQR 17–27), with no statistically significant difference between periods (p = 1.00).

Despite stable systemic oxygenation, as reflected by a median paO_2/fiO_2 ratio of 319 (IQR 288–407) during the first 48 hours, half of the patients exhibited $PbtO_2$ values below 22 mmHg. No significant correlation was found between $PbtO_2$ and paO_2/FiO_2 ratio during the first 48 hours (Spearman's rho = 0.01, p = 0.958) or during days 3–7 (Spearman's rho = 0.01, p = 0.984). These findings support the absence of a measurable association between systemic oxygenation and brain tissue oxygenation in this cohort.

Relationship between $PbtO_2$, CPP and PRx

The relationship between $PbtO_2$ and CPP, stratified by cerebrovascular autoregulation status (PRx ≤ 0.2 vs. PRx > 0.2), is depicted in FIGURE 3A (first 48 hours) and FIGURE 3B (days 3–7).

During the first 48 hours, $PbtO_2$ values did not increase linearly with CPP. Instead, higher $PbtO_2$ values tended to cluster within a relatively narrow CPP range, centred around 85 mmHg. This pattern was more apparent in patients with preserved autoregulation.

During days 3 to 7, the relationship between $PbtO_2$ and CPP was less distinct. Nevertheless, higher $PbtO_2$ values continued to be observed predominantly within a similar CPP range, despite overall improvement in autoregulatory function.

A multivariable linear regression model was fitted to explore the association between CPP and PRx with mean $PbtO_2$ during the first 48 hours and 3 to 7 days (Table 3). The association between $PbtO_2$ and cerebral perfusion was more evident during the first 48 hours than during days 3–7. During the first 48 hours, CPP was significantly associated with $PbtO_2$ after adjustment for PRx (β = -0.95, 95% CI -1.69 to -0.20, p = 0.016), while PRx showed a non-significant trend towards association (β = -19.89, 95% CI -42.15 to 2.37, p = 0.076). During days 3–7, neither CPP nor PRx reached statistical significance, although PRx maintained a borderline association with $PbtO_2$ (β = -21.52, 95% CI -44.00 to 0.97, p = 0.059). Although the direction and magnitude of the association suggest a relationship between

perfusion pressure dynamics and brain tissue oxygenation, the observed pattern in FIGURE 3 supports a non-linear physiological interaction rather than a simple linear dependency.

Table 3
Multivariable linear regression models for $PbtO_2$ during the first 48 hours and days 3–7

Predictor	Beta (95% CI)	p-value
CPP, first 48 h (mmHg)	-0.95 (-1.69 to -0.2)	0.016
PRx, first 48 h	-19.89 (-42.15 to 2.37)	0.076
CPP, 3–7 days	-0.49 (-1.24 to 0.26)	0.181
PRx, 3–7 days	-21.52 (-44 to 0.97)	0.059

CPP, Cerebral Perfusion Pressure; CPPopt, Optimal Cerebral Perfusion Pressure; $PbtO_2$, Brain Tissue Oxygen Tension ($PbtO_2$); PRx, Pressure Reactivity Index (PRx).

Discussion

Literature on $PbtO_2$ monitoring in ICH remains scarce, particularly compared with traumatic brain injury, where its clinical relevance has been more widely investigated.[14,18,20–22,30] Our study contributes with prospective data, integrating information from $PbtO_2$ with bedside continuous individualized cerebral perfusion pressure management and cerebrovascular autoregulation assessment.

In this prospective observational cohort study of critically ill ICH patients, we explored the profile of brain tissue oxygenation in 18 patients across two time periods and its relationship with established multimodal neuromonitoring variables.

The availability of continuous neuromonitoring data over the first seven days of admission allowed us to focus on two clinically meaningful time windows: the first 48 hours, when secondary brain injury risk is highest[10,31–33], and the subsequent 3 to 7 days. This temporal approach enabled the evaluation of physiological evolution under optimized neurocritical care conditions rather than isolated point measurements.

Intracranial pressure remained consistently below pathological thresholds in both periods, with no significant differences. This likely reflects the active management of intracranial hypertension in NCCU, including medical and surgical interventions when indicated. These findings support previous observations suggesting that, under contemporary neurocritical care, ICP alone may not fully capture the complexity of secondary brain injury mechanisms in ICH, and that derived indices may provide more informative insights.[5,9,10]

Cerebral perfusion pressure was maintained above conventional guideline thresholds throughout the monitoring period and further increased in days 3 to 7.

Regarding brain tissue oxygenation, values were near or below critical thresholds, even under conditions of normal ICP, adequate CPP and systemic oxygenation. Median $PbtO_2$ values did not differ significantly between the two analyzed periods, indicating a possible absence of brain oxygenation improvement over time, despite neurocritical care management.

By protocol, $PbtO_2$ probes were placed in the contralateral hemisphere to the main hemorrhagic lesion. This methodological choice provides information regarding cerebral oxygenation in non-lesion brain parenchyma rather than in perilesional area.[5,34] This may reflect baseline microvascular vulnerability in a population with high prevalence of chronic hypertension.[35,36] In this context, the observation that nearly half of patients exhibited $PbtO_2$ values below 22 mmHg during the first 48 hours, despite normal paO_2/fiO_2 ratios, highlights the possible dissociation between systemic oxygenation and cerebral tissue oxygenation in ICH. These results corroborate previous evidence, such as the study by Jung et al, which reported in an experimental model that, although paO_2 may have a statistically significant linear relationship with $PbtO_2$, it accounted for only a small proportion of the variance.[37]

Also, in our cohort, no association was observed between paO_2/fiO_2 ratio and $PbtO_2$ values. While the limited sample size may have reduced statistical power, this finding is also likely influenced by the relatively narrow range of systemic oxygenation values in a well-controlled intensive care environment. These results raise the hypothesis that cerebral hypoxia in ICH patients may not be primarily driven by arterial oxygenation but also by local and regional factors affecting oxygen delivery and utilization at the tissue level.

In this cohort, $PbtO_2$ was associated with cerebral perfusion dynamics rather than with measures of systemic oxygenation. Although the multivariable regression model suggests an association between CPP and $PbtO_2$ during the first 48 hours, visual inspection of the data indicates that this relationship is unlikely to be linear. Instead, higher $PbtO_2$ values clustered within a relatively specific CPP range, approximately centred around 85 mmHg. This pattern appeared more evident during the first 48 hours, particularly among patients with preserved autoregulation. During days 3–7, despite an overall improvement in PRx, the relationship between CPP and $PbtO_2$ became less distinct. According to this finding, there have been studies reporting a non-linear association between $PbtO_2$ and CPP, whereby $PbtO_2$ remained stable when CPP was at or above CPPopt, but declined when CPP dropped below CPPopt in aneurysmal subarachnoid hemorrhage and traumatic brain injury.[38,39]

The overall burden of poor functional outcomes in this cohort underscores the severity of illness and the unmet need for improved physiological targeting strategies. The persistence of suboptimal $PbtO_2$ despite optimal perfusion management suggests that perfusion-based strategies alone may not fully address the mechanisms underlying cerebral hypoxia in ICH.

Integrating $PbtO_2$ into a multimodal framework that includes cerebral perfusion pressure and cerebrovascular autoregulation may help identify patients in whom conventional targets fail to ensure

adequate tissue oxygenation and may guide more nuanced, patient-specific management strategies. Studies in this topic with larger cohorts should be pursued.

Limitations

The first limitation is that the $PbtO_2$ analysis relied on summary metrics representing extended time periods, which may obscure short-lived but clinically relevant episodes of hypoxemic hypoxia. Also, $PbtO_2$ monitoring was available in only a subset of patients due to limitation of devices availability, limiting statistical power and external validity.

Despite these limitations, the prospective design, standardized neurocritical care protocols, high-quality neuromonitoring data and the scarcity of existing literature in this specific patient population sustain the relevance of our findings.

Conclusion

In critically ill patients with spontaneous intracerebral hemorrhage managed under individualized neurocritical care protocols, brain tissue oxygenation frequently remains suboptimal despite controlled intracranial pressure, adequate cerebral perfusion pressure and normal systemic oxygenation. $PbtO_2$ values appeared to be more closely linked to cerebral perfusion dynamics than to systemic oxygenation, although this relationship was not linear and was most evident during the first 48 hours.

Declarations

All authors contributed to the design and methodology of the present work; Authors AF and MD collected all clinical data, Authors AF and MD performed the statistical analysis; Author PAS, EM and CD reviewed statistical analysis for adequacy; Authors AF and MD produced the first draft; All authors reviewed subsequent drafts and approved the final manuscript for submission.

This manuscript has not been published elsewhere and is not under consideration by another journal.

The study protocol was approved by the Institutional Ethics Committee (no. 286/19).

The authors declare no conflict of interest.

The study is reported according to the STROBE Cohort guidelines.

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References

1. Cordonnier C, Demchuk A, Ziai W, Anderson CS. Intracerebral haemorrhage: current approaches to acute management. Lancet. 2018;392:1257–68. https://doi.org/10.1016/S0140-6736(18)31878-6.
2. Sheth KN. Spontaneous Intracerebral Hemorrhage. N Engl J Med. 2022;387:1589–96. https://doi.org/10.1056/NEJMra2201449.
3. Balami JS, Buchan AM. Complications of intracerebral haemorrhage. Lancet Neurol. 2012;11:101–18. https://doi.org/10.1016/S1474-4422(11)70264-2.
4. Qureshi AI, Tuhrim S, Broderick JP, et al. Spontaneous intracerebral hemorrhage. N Engl J Med. 2001;344:1450–60. https://doi.org/10.1056/NEJM200105103441907.
5. Zhao JL, Holste KG, Pandey AS, Hu J, Wu G. Intracranial Pressure Monitoring: an Effective Technique to Balance Cerebral Perfusion and Blood Pressure Reduction in ICH Patients. Transl Stroke Res. 2024;15:409–10. https://doi.org/10.1007/s12975-023-01129-5. 10.1007/s12975-023-01129-5.
6. Brain Trauma Foundation; American Association of Neurological Surgeons. Congress of Neurological Surgeons; Guidelines for the management of severe traumatic brain injury. VIII. Intracranial pressure thresholds. J Neurotrauma. 2007;24(Suppl 1). https://doi.org/10.1089/neu.2007.9988. :S55-S58.
7. Svedung Wettervik TM, Lewén A, Enblad P. Fine Tuning of Traumatic Brain Injury Management in Neurointensive Care-Indicative Observations and Future Perspectives. Front Neurol. 2021;12:638132. https://doi.org/10.3389/fneur.2021.638132.
8. Donnelly J, Aries MJ, Czosnyka M. Further understanding of cerebral autoregulation at the bedside: possible implications for future therapy. Expert Rev Neurother. 2015;15:169–85. https://doi.org/10.1586/14737175.2015.996552. 10.1586/14737175.2015.996552.
9. Le Roux P, Menon DK, Citerio G et al. The International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a list of recommendations and additional conclusions: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. *Neurocrit Care* 2014;21 Suppl 2:S282-S296 https://doi.org/10.1007/s12028-014-0077-6. 10.1007/s12028-014-0077-6
10. Greenberg SM, Ziai WC, Cordonnier C et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke* 2022;53:e282-e361 https://doi.org/10.1161/STR.0000000000000407. 10.1161/STR.0000000000000407
11. Steiner LA, Czosnyka M, Piechnik SK, et al. Continuous monitoring of cerebrovascular pressure reactivity allows determination of optimal cerebral perfusion pressure in patients with traumatic brain injury. Crit Care Med. 2002;30:733–8. https://doi.org/10.1097/00003246-200204000-00002.
12. Aries MJ, Czosnyka M, Budohoski KP, et al. Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury. Crit Care Med. 2012;40:2456–63. https://doi.org/10.1097/CCM.0b013e3182514eb6.
13. Maloney-Wilensky E, Le Roux P. The physiology behind direct brain oxygen monitors and practical aspects of their use. Childs Nerv Syst. 2010;26:419–30. https://doi.org/10.1007/s00381-009-1037-

x. 10.1007/s00381-009-1037-x.

14. Svedung Wettervik T, Beqiri E, Hånell A, et al. Brain tissue oxygen monitoring in traumatic brain injury-part II: isolated and combined insults in relation to outcome. Crit Care. 2023;27:370. https://doi.org/10.1186/s13054-023-04659-4.
15. Grinberg OY, Hou H, Roche MA, et al. Modeling of the response of ptO2 in rat brain to changes in physiological parameters. Adv Exp Med Biol. 2005;566:111–8. https://doi.org/10.1007/0-387-26206-7_16.
16. Gouvea Bogossian E, Battaglini D, Fratino S, et al. The Role of Brain Tissue Oxygenation Monitoring in the Management of Subarachnoid Hemorrhage: A Scoping Review. Neurocrit Care. 2023;39:229–40. https://doi.org/10.1007/s12028-023-01680-x. 10.1007/s12028-023-01680-x.
17. Brain Trauma Foundation. American Association of Neurological Surgeons, Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. X. Brain oxygen monitoring and thresholds. J Neurotrauma. 2007;24(Suppl 1):S65–70. https://doi.org/10.1089/neu.2007.9986.
18. Lin CM, Lin MC, Huang SJ, et al. A Prospective Randomized Study of Brain Tissue Oxygen Pressure-Guided Management in Moderate and Severe Traumatic Brain Injury Patients. Biomed Res Int. 2015;2015:529580. https://doi.org/10.1155/2015/529580. 10.1155/2015/529580.
19. Tas J, Czosnyka M, van der Horst ICC, et al. Cerebral multimodality monitoring in adult neurocritical care patients with acute brain injury: A narrative review. Front Physiol. 2022;13:1071161. https://doi.org/10.3389/fphys.2022.1071161.
20. Godoy DA, Lubillo S, Rabinstein AA. Pathophysiology and Management of Intracranial Hypertension and Tissular Brain Hypoxia After Severe Traumatic Brain Injury: An Integrative Approach. Neurosurg Clin N Am. 2018;29:195–212. https://doi.org/10.1016/j.nec.2017.12.001.
21. Stiefel MF, Spiotta A, Gracias VH, et al. Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg. 2005;103:805–11. https://doi.org/10.3171/jns.2005.103.5.0805. 10.3171/jns.2005.103.5.0805.
22. Shen Y, Wen D, Liang Z, et al. Brain tissue oxygen partial pressure monitoring and prognosis of patients with traumatic brain injury: a meta-analysis. Neurosurg Rev. 2024;47:222. https://doi.org/10.1007/s10143-024-02439-4.
23. Rass V, Solari D, Ianosi B, et al. Protocolized Brain Oxygen Optimization in Subarachnoid Hemorrhage. Neurocrit Care. 2019;31:263–72. https://doi.org/10.1007/s12028-019-00753-0. 10.1007/s12028-019-00753-0.
24. Hemphill JC 3rd, Morabito D, Farrant M, Manley GT. Brain tissue oxygen monitoring in intracerebral hemorrhage. Neurocrit Care. 2005;3:260–70. https://doi.org/10.1385/NCC:3:3:260.
25. Lin WM, Yang TY, Weng HH, et al. Brain microbleeds: distribution and influence on hematoma and perihematomal edema in patients with primary intracerebral hemorrhage. Neuroradiol J. 2013;26:184–90. https://doi.org/10.1177/197140091302600208.

26. Brown R, Benveniste H, Black SE, et al. Understanding the role of the perivascular space in cerebral small vessel disease. Cardiovasc Res. 2018;114:1462–73. https://doi.org/10.1093/cvr/cvy113.
27. World Medical Association. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Participants. JAMA. 2025;333:71–4. https://doi.org/10.1001/jama.2024.21972.
28. Santos E, Diedler J, Sykora M, et al. Low-frequency sampling for PRx calculation does not reduce prognostication and produces similar CPPopt in intracerebral haemorrhage patients. Acta Neurochir (Wien). 2011;153:2189–95. https://doi.org/10.1007/s00701-011-1148-5. 10.1007/s00701-011-1148-5.
29. Diedler J, Santos E, Poli S, Sykora M. Optimal cerebral perfusion pressure in patients with intracerebral hemorrhage: an observational case series. Crit Care. 2014;18:R51. https://doi.org/10.1186/cc13796.
30. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2015;46:2032–60. https://doi.org/10.1161/STR.0000000000000069. 10.1161/STR.0000000000000069.
31. Mittal MK, LacKamp A. Intracerebral Hemorrhage: Perihemorrhagic Edema and Secondary Hematoma Expansion: From Bench Work to Ongoing Controversies. Front Neurol. 2016;7:210. https://doi.org/10.3389/fneur.2016.00210.
32. Shah VA, Bhende B, Biyani S, et al. Acute care of spontaneous intracerebral hemorrhage. Neurol Res Pract. 2025;7:96. https://doi.org/10.1186/s42466-025-00454-4.
33. Lim-Hing K, Rincon F. Secondary Hematoma Expansion and Perihemorrhagic Edema after Intracerebral Hemorrhage: From Bench Work to Practical Aspects. Front Neurol. 2017;8:74. https://doi.org/10.3389/fneur.2017.00074. 10.3389/fneur.2017.00074.
34. Gerloff C, Bushara K, Sailer A, et al. Multimodal imaging of brain reorganization in motor areas of the contralesional hemisphere of well recovered patients after capsular stroke. Brain. 2006;129:791–808. https://doi.org/10.1093/brain/awh713.
35. Lioutas VA, Beiser AS, Aparicio HJ, et al. Assessment of Incidence and Risk Factors of Intracerebral Hemorrhage Among Participants in the Framingham Heart Study Between 1948 and 2016. JAMA Neurol. 2020;77:1252–60. https://doi.org/10.1001/jamaneurol.2020.1512.
36. Hosking A, Samarasekera N, Moullaali TJ et al. Predisposing Factors, Pathologies, and Precipitating Factors Causing Intracerebral Hemorrhage. *Stroke* https://doi.org/10.1161/STROKEAHA.125.051831. 10.1161/STROKEAHA.125.051831.
37. Jung YH, Shamsiev K, Mamadjonov N, et al. Relationship of common hemodynamic and respiratory target parameters with brain tissue oxygen tension in the absence of hypoxemia or hypotension after cardiac arrest: A post-hoc analysis of an experimental study using a pig model. PLoS ONE. 2021;16:e0245931. https://doi.org/10.1371/journal.pone.0245931.

38. Lang EW, Czosnyka M, Mehdorn HM. Tissue oxygen reactivity and cerebral autoregulation after severe traumatic brain injury. Crit Care Med. 2003;31:267–71. https://doi.org/10.1097/00003246-200301000-00042.
39. Megjhani M, Weiss M, Ford J, et al. Optimal Cerebral Perfusion Pressure and Brain Tissue Oxygen in Aneurysmal Subarachnoid Hemorrhage. Stroke. 2023;54:189–97. https://doi.org/10.1161/STROKEAHA.122.040339.

Figures

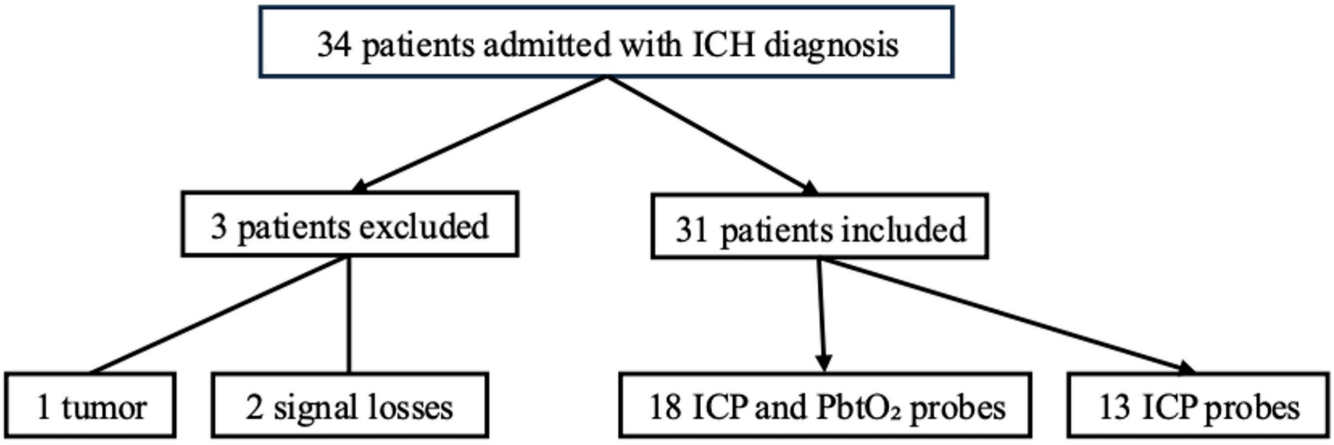


Figure 1. Flow diagram of patient inclusion and neuromonitoring allocation.

Figure 1

Flow diagram of patient inclusion and neuromonitoring allocation.

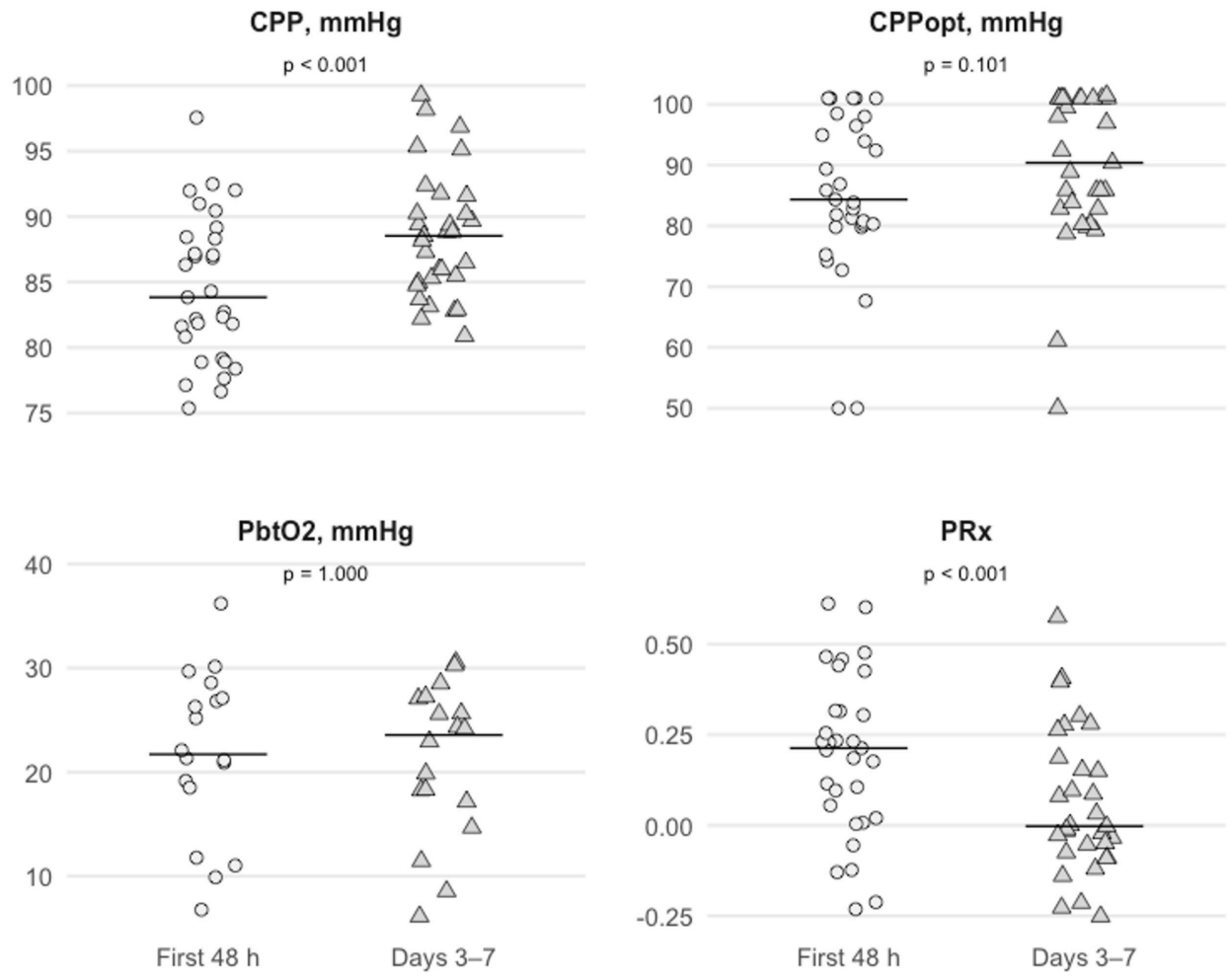


Figure 2. Distribution of CPP, CPPopt, PRx and $PbtO_2$ from the first 48 hours and 3 to 7 days.

Figure 2

Distribution of CPP, CPPopt, PRx and $PbtO_2$ from the first 48 hours and 3 to 7 days.

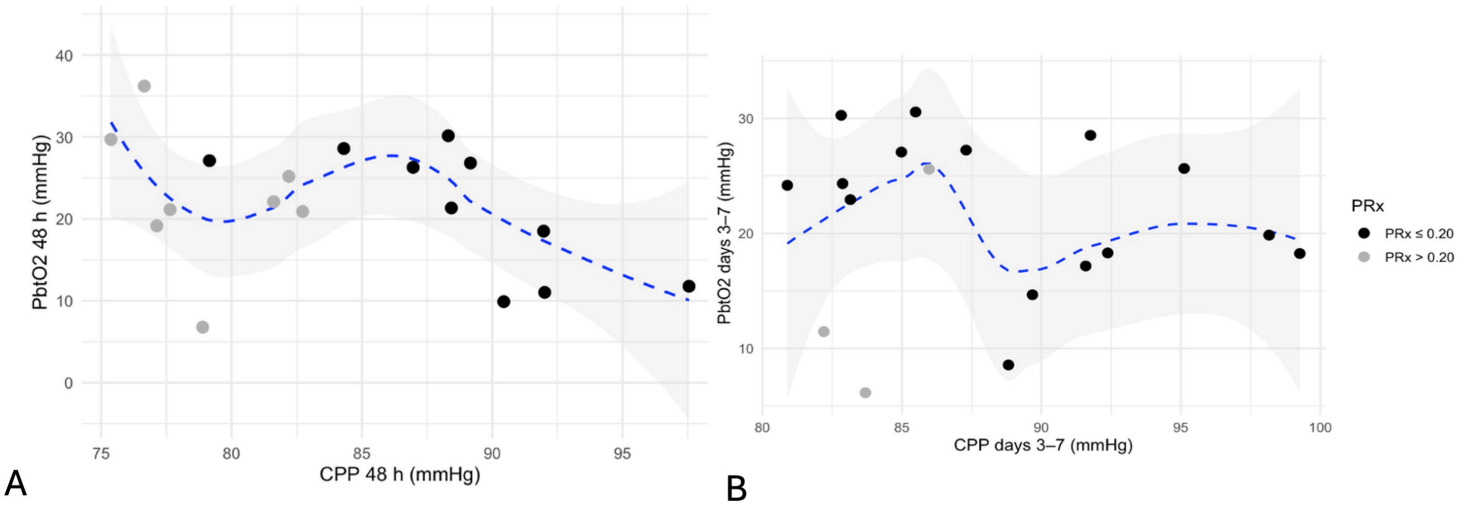


Figure 3. Relationship between brain tissue oxygen pressure ($PbtO_2$) and cerebral perfusion pressure (CPP) stratified by cerebrovascular autoregulation status (PRx ≤0.2 vs. PRx >0.2), during the first 48 hours (A) and during days 3 to 7 (B).

Figure 3

Relationship between brain tissue oxygen pressure ($PbtO_2$) and cerebral perfusion pressure (CPP) stratified by cerebrovascular autoregulation status (PRx ≤0.2 vs. PRx >0.2), during the first 48 hours (A) and during days 3 to 7 (B).

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