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REVIEW

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Bridging brain and lung: optimizing mechanical ventilation in acute brain injury

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Abstract

Optimizing mechanical ventilation in patients with acute brain injury (ABI) presents a complex clinical challenge, requiring a delicate balance between minimizing secondary cerebral injury and preventing ventilator-induced lung injury (VILI). The intricate interplay between respiratory and cerebral physiology mandates an individualized approach to ventilatory management. Core goals include maintaining normoxia and normocapnia to avert cerebral ischemia from hypoxia or hypocapnia while avoiding intracranial hypertension associated with hypercapnia. However, evidence guiding the ideal tidal volume and positive end-expiratory pressure (PEEP) settings in this population remains limited, particularly regarding their impact on cerebral perfusion pressure and oxygen delivery. Advanced neuromonitoring modalities—such as transcranial Doppler ultrasound and brain tissue oxygen tension ($PbtO_2$) monitoring—offer critical real-time data to inform ventilation strategies. Additionally, emerging technologies, including automated and adaptive modes of ventilation, show promise in enhancing patient–ventilator synchrony and gas exchange. This narrative review synthesizes current physiological principles, discusses the challenges inherent in protecting both the brain and lungs, and explores the evolving role of precision ventilation strategies supported by multimodal monitoring. Integrating these approaches may improve neurological and respiratory outcomes and help close the evidence gaps in ABI management.

Keywords Acute brain injury, Mechanical ventilation, Intracranial pressure, Cerebral perfusion pressure, Multimodal monitoring

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Introduction

Mechanical ventilation (MV) is a cornerstone of intensive care, essential for ensuring adequate gas exchange in critically ill patients [1]. While lifesaving, MV can contribute to ventilator-induced lung injury (VILI), and, more recently, ventilator-associated brain injury has been recognized as a potential contributor to neurological damage via systemic inflammation, impaired cerebral perfusion, and hemodynamic instability [2].

MV is commonly employed in acute respiratory distress syndrome (ARDS), postoperative respiratory failure, and acute brain injury (ABI), a heterogeneous group of disorders encompassing traumatic brain injury (TBI), ischemic and hemorrhagic stroke, and subarachnoid hemorrhage. In ABI, ventilatory management poses unique challenges, requiring a careful balance between lung-protective ventilation (LPV) strategies and cerebral protection [3].

Maintaining normoxia and normocapnia is critical to preventing secondary brain injury. Hypoxemia and hypercapnia can elevate intracranial pressure (ICP) and impair cerebral perfusion, whereas excessive hyperventilation, although effective in transiently lowering ICP via cerebral vasoconstriction, risks reducing cerebral blood flow (CBF) if prolonged. Thus, precise control of arterial oxygen and carbon dioxide levels is essential [4].

Key ventilatory parameters, including tidal volume (VT), positive end-expiratory pressure (PEEP), driving pressure (ΔP), and mechanical power (MP), must be finely adjusted to minimize lung injury while preserving systemic and cerebral oxygen delivery. Recent advances in neuromonitoring techniques such as transcranial Doppler ultrasound and brain tissue oxygen tension ($PbtO_2$) monitoring have enhanced understanding of brain–lung interactions, providing real-time feedback on the cerebral effects of ventilation [5, 6].

Despite these technological advancements, the optimal ventilatory strategy for patients with ABI remains elusive, with limited evidence to guide individualized care [7]. This narrative review synthesizes current evidence on mechanical ventilation in ABI, emphasizing physiological principles, key ventilatory targets, and the role of multimodal monitoring in achieving the dual goals of brain and lung protection.

Pathophysiology of acute brain injury and ventilation challenges

Acute brain injury profoundly disrupts the brain's control of respiration, primarily due to damage in the brainstem respiratory centers, particularly the medulla oblongata and its neural pathways [8]. Figure 1 illustrates the complex, bidirectional interactions between ABI and respiratory physiology. Injury to these centers often impairs ventilatory drive, resulting in hypoventilation and consequent hypercapnia—characterized by elevated arterial carbon dioxide tension ($PaCO_2$).

Hypercapnia typically causes cerebral vasodilation by inducing cerebrospinal fluid (CSF) acidosis and pial

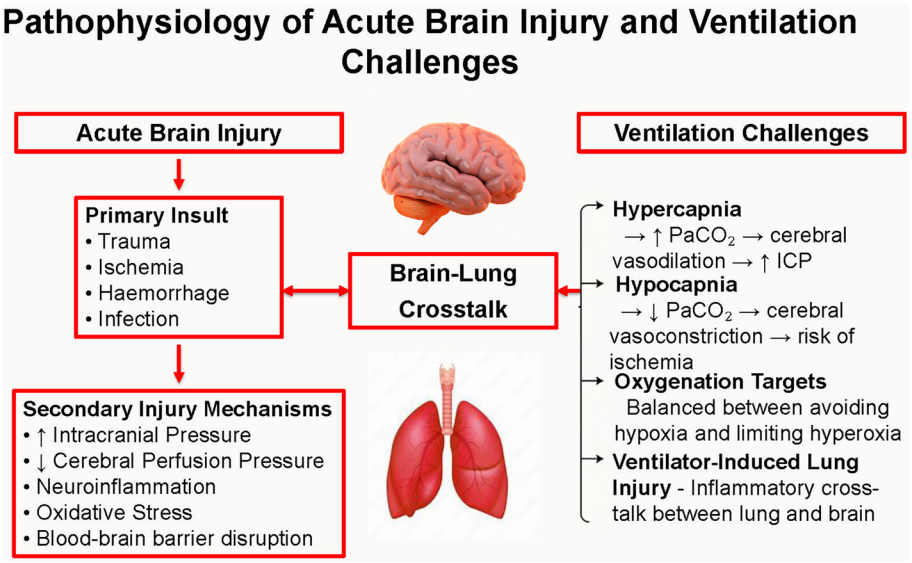

Fig. 1 This diagram shows the bidirectional brain–lung crosstalk in acute brain injury. Primary insults cause secondary damage such as increased intracranial pressure, reduced cerebral perfusion, and inflammation. Ventilation challenges—including hypercapnia, hypocapnia, and ventilator-induced lung injury—can worsen brain injury, emphasizing the importance of targeted respiratory management. ICP, intracranial pressure; $PaCO_2$, arterial partial pressure of carbon dioxide; VILI, ventilator-induced lung injury

arteriole relaxation, thereby increasing CBF. However, in the context of impaired cerebral autoregulation, which frequently occurs after ABI, this vasodilatory response can be dysfunctional, potentially reducing effective cerebral perfusion pressure [9]. Conversely, hypocapnia ($PaCO_2 < 35$ mmHg) leads to cerebral vasoconstriction via CSF alkalosis, decreasing CBF and increasing the risk of ischemia if sustained. These opposing effects highlight the critical need for individualized $PaCO_2$ targets, guided by advanced neuromonitoring modalities such as $PbtO_2$ and jugular venous oxygen saturation ($SjvO_2$) [10]. Permissive hypercapnia—accepting elevated $PaCO_2$ levels to mitigate VILI—is generally contraindicated in ABI due to its potential to increase ICP through cerebral vasodilation. Exceptions may apply in carefully selected patients, where continuous neuromonitoring confirms adequate cerebral oxygenation and perfusion [11]. Importantly, $PaCO_2$ autoregulation is usually preserved within a range of 30–40 mmHg but deteriorates progressively at levels ≥ 45 mmHg, raising concerns about permissive hypercapnia increasing the risk of complications such as intraventricular hemorrhage [12]. The Society of Neurocritical Care's SIBICC guidelines recommend maintaining $PaCO_2$ between 32 and 35 mmHg, advising caution with levels below 32 mmHg unless neuromonitoring data support safe oxygen delivery [13]. Therefore, precise titration of $PaCO_2$ is essential to balance ICP control and cerebral perfusion.

Advanced neuromonitoring techniques, including transcranial Doppler ultrasound and $PbtO_2$ monitoring, offer invaluable real-time insights into cerebral hemodynamics and the impact of ventilatory changes on brain physiology [14]. These tools facilitate the dynamic adjustment of ventilation to maintain optimal cerebral oxygenation and blood flow.

Arterial oxygen tension (PaO_2) influences CBF primarily through its role in determining arterial oxygen content (CaO_2), defined as $CaO_2 = [1.34 \times \text{hemoglobin} \times \text{arterial oxygen saturation } (SaO_2)] + [0.003 \times PaO_2]$. Cerebral oxygen delivery (CDO_2) is the product of CBF and CaO_2. $PaO_2 < 60$ mmHg induces compensatory cerebral vasodilation to preserve oxygen delivery, but when PaO_2 falls below 50 mmHg, these mechanisms may be insufficient, increasing the risk of cerebral ischemia. Conversely, $PaO_2 > 300$ mmHg can reduce CBF by 10–15%, largely due to nitric oxide depletion and consequent vasoconstriction, potentially compromising perfusion in vulnerable watershed areas [15, 16]. PaO_2 100–200 mmHg generally has minimal impact on CBF. While hyperoxia has been investigated as a neuroprotective strategy in ischemic stroke and traumatic brain injury, prolonged exposure may exacerbate oxidative stress and impair blood flow to sensitive brain regions [17]. Thus, careful optimization of PaO_2 is essential to avoid both hypoxemia and excessive hyperoxemia, ensuring adequate cerebral oxygen delivery and minimizing secondary injury [18].

Mechanical ventilation in acute brain injury

The primary goals of MV in ABI are to ensure adequate oxygenation and ventilation while minimizing secondary brain injury caused by hypoxemia, hypercapnia, or VILI [19]. The complex interplay between respiratory and cerebral physiology makes ventilatory management particularly challenging [20]. Ventilatory settings such as VT and PEEP have significant and sometimes opposing effects on cerebral dynamics. Elevated PEEP increases intrathoracic pressure, which can reduce venous outflow and raise ICP, especially in patients with impaired intracranial compliance. Furthermore, when applied above a critical threshold, high PEEP can cause overdistension of relatively preserved lung regions, leading to increased physiological dead space and impaired CO_2 elimination [21]. Conversely, low VT, while contributing to LPV, may lead to permissive hypercapnia, potentially exacerbating ICP. Achieving an optimal balance between cerebral perfusion and lung protection is therefore critical [19]. Figure 2 illustrates a stepwise approach to intubation, ventilator initiation, and monitoring strategies for patients with ABI.

Elevated ICP, a frequent complication in ABI, can be influenced by positive-pressure ventilation, particularly at high PEEP levels [22]. The effect of PEEP on ICP depends on lung recruitability: in patients with high recruitability, such as those with ARDS, PEEP may improve oxygenation and reduce atelectrauma without significantly increasing ICP [23]. In contrast, patients with low recruitability—such as those with neurogenic pulmonary edema—may experience impaired venous return and elevated ICP with increased PEEP. Consequently, individualized bedside assessment, including PEEP trials with ICP monitoring or transpulmonary pressure measurements, is essential to optimize ventilator settings [2]. Electrical impedance tomography (EIT) provides a real-time, noninvasive assessment of regional lung ventilation and can guide individualized PEEP titration according to recruitability. By identifying the level of PEEP that minimizes both alveolar collapse and overdistension, EIT may help balance oxygenation goals with the risk of increased ICP in patients with ABI. However, its clinical utility in this population remains to be fully established [24]. Figure 3 provides a conceptual overview of the interactions between VT, PEEP, hypoxia, and ICP regulation in mechanically ventilated patients with ABI.

Positive-pressure ventilation increases intrathoracic pressure, potentially reducing venous return, cardiac output, and cerebral perfusion pressure, especially in hypovolemic

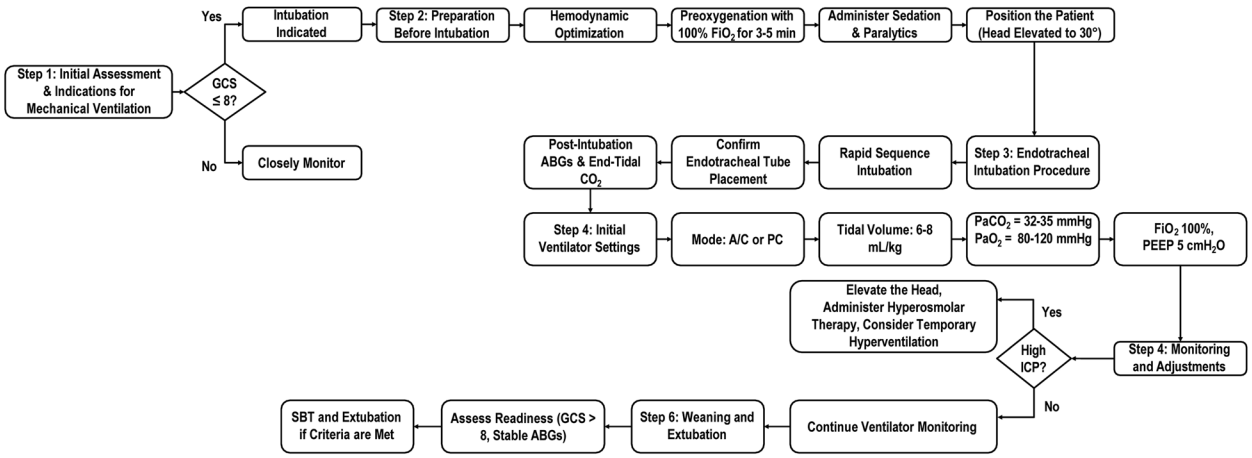

Fig. 2 Stepwise approach to mechanical ventilation in acute brain injury patients. Decision points are represented by diamonds (♦), while clinical actions are indicated by rectangles (▭). GCS, Glasgow Coma Scale; FiO_2, fraction of inspired oxygen; ABG, arterial blood gas; $PaCO_2$, partial pressure of carbon dioxide; PEEP, positive end-expiratory pressure; A/C mode, assist-control ventilation mode; PC mode, pressure-controlled ventilation; SBT, spontaneous breathing trial; ICP, intracranial pressure

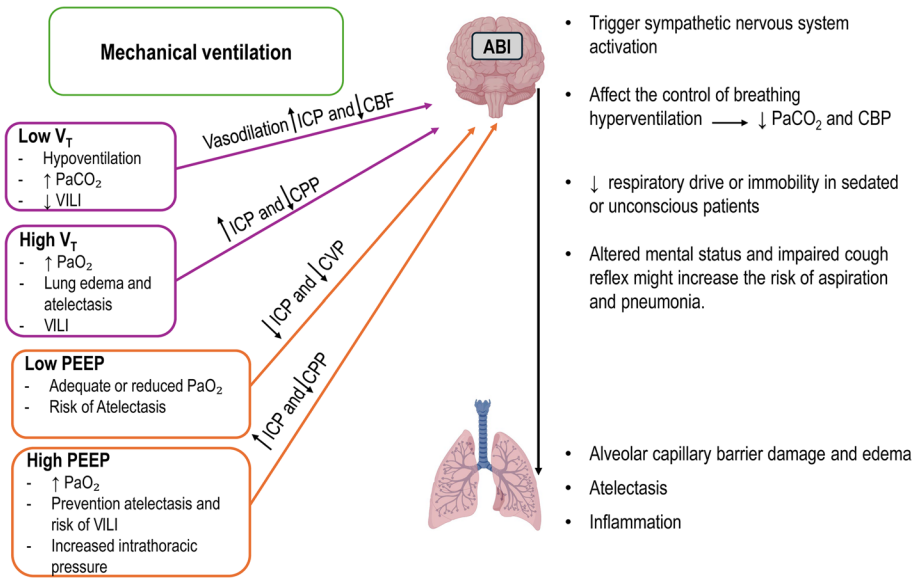

Fig. 3 Interactions between mechanical ventilation parameters and cerebral physiology in acute brain injury. ABI, acute brain injury; VT, tidal volume; PEEP, positive end-expiratory pressure; PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; ICP, intracranial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; CVP, central venous pressure; VILI, ventilator-induced lung injury; VALI, ventilation-associated lung injury

patients [25]. Hemodynamic monitoring tools, such as stroke volume variation and pulse pressure variation, are vital to guide fluid resuscitation and vasopressor use during PEEP escalation [26, 27]. In ABI patients, hypovolemia should be avoided, and a mean arterial pressure (MAP) ≥ 80 mmHg should be targeted, particularly when cerebral autoregulation is impaired [16, 28].

Ventilatory strategies in ABI must balance optimal oxygenation and carbon dioxide regulation with cerebral protection [5]. Maintaining normocapnia ($PaCO_2$ 35–45 mmHg) avoids hypercapnia-induced cerebral vasodilation that can increase ICP, as well as hypocapnia-induced vasoconstriction that may reduce CBF [29].

Hypoxemia was defined as $PaO_2 < 80$ mmHg, normoxemia as PaO_2 80–120 mmHg, mild to moderate hyperoxemia as PaO_2 121–299 mmHg, and severe hyperoxemia as $PaO_2 \geq 300$ mmHg [30]. Recent evidence suggests that PaO_2 values outside the approximate range of 92–156

mmHg are associated with increased inhospital mortality, underscoring the need to refine optimal oxygenation targets as additional clinical data become available [31].

Clinical scenarios and practical ventilation strategies

The VENTIBRAIN study, a large-scale, multicenter, prospective observational investigation, evaluated the impact of ventilation strategies on outcomes in patients with ABI across 74 ICUs in 26 countries [32]. The study included 2095 invasively ventilated patients with various forms of ABI, including TBI, intracranial hemorrhage (ICH), subarachnoid hemorrhage (SAH), and acute ischemic stroke (AIS). While LPV ventilation strategies were commonly employed, their implementation varied considerably among countries. Median ventilatory parameters included a VT of 6.5 mL/kg predicted body weight (PBW), PEEP of 5 cmH_2O, plateau pressure (Pplat) of 15 cmH_2O, and ΔP of 9 cmH_2O.

Interestingly, despite the presence of intracranial hypertension ($ICP > 20$ mmHg) in some patients, ventilator settings were not consistently adjusted in response to elevated ICP. The study found that higher Pplat, peak inspiratory pressure (PIP), and ΔP were significantly associated with increased ICU and 6-month mortality (e.g., ICU mortality hazard ratio for Pplat: 1.50; 95% *CI*: 1.27–1.78). In contrast, higher VT was paradoxically associated with reduced mortality [33]. This paradoxical association may, in part, reflect confounding, as higher VTs could indicate greater respiratory system compliance and thus less severe lung injury. Notably, the study did not stratify outcomes by compliance (Crs), limiting the ability to assess whether unfavorable outcomes were more frequent in patients with lower compliance and greater difficulty achieving adequate gas exchange. These findings highlight the critical influence of ventilatory parameters on survival in ABI patients and underscore the need for evidence-based, standardized ventilation protocols [33].

The observed association between higher ΔP and mortality in VENTIBRAIN may be confounded by the underlying severity of lung injury, rather than reflecting a causal relationship [32]. This confounding is plausible, as patients with reduced compliance (higher driving pressure) are more likely to encounter difficulties in achieving gas exchange targets, leading to hypoxemia or hypercapnia that may worsen outcomes independently of driving pressure. Likewise, the unfavorable results of the PROLABI (Protect Lung in Acute Brain Injury) trial may have been influenced by excessive sedation, which can impair CO_2 clearance and exacerbate cerebral derangements [34]. This emphasizes the necessity of individualized approaches over uniform LPV protocols in ABI.

Emerging data suggest that the benefit of LPV is context-dependent, particularly on the basis of respiratory system compliance. In patients with low compliance, such as in ARDS, lower VT combined with higher respiratory rates may be protective. However, in patients with high compliance, such as those with isolated brain injury, these strategies may be harmful. The PROLABI [34] trial randomized ABI patients to LPV ($VT = 6$ mL/kg PBW, $PEEP = 8$ cmH_2O) or conventional ventilation ($VT > 8$ mL/kg PBW, $PEEP = 4$ cmH_2O). Surprisingly, LPV was associated with worse clinical outcomes, including higher 28-day mortality, ventilator dependence, and ARDS incidence (61.5% vs. 45.3%, relative risk [RR] = 1.35, $p = 0.025$), as well as increased rates of death or persistent vegetative state ($RR = 1.55$, $p = 0.044$). Although these findings challenge the universal application of LPV in ABI, limitations such as sample size, missing data, and confounding variables warrant cautious interpretation.

Collectively, these results highlight the complexity of lung–brain interactions and raise concerns about ventilator-induced brain injury. Insights from ARMA, PReVENT, RELAx, and PROLABI demonstrate how low VT ventilation must be tailored to specific patient populations. For example, ARMA showed benefits in deeply sedated, low-compliance ARDS patients [35], while PROLABI suggested potential harm from LPV in high-compliance ABI patients under deep sedation [34]. These findings reinforce that strategies beneficial in ARDS may not translate to ABI and should be applied with caution in non-ARDS populations.

Prone positioning, a cornerstone of ARDS management, remains controversial in ABI due to potential adverse effects on cerebral hemodynamics [36].

Nevertheless, the lifesaving potential of prone positioning in severe ARDS may warrant its use even in patients with ABI. The main cerebral hemodynamic concern is impaired jugular venous drainage due to neck malposition, which can increase ICP. These risks can be reduced through a systematic approach: proning should be undertaken after optimization of intravascular volume and with deep sedation, often combined with neuromuscular blockade, to limit surges in intra-abdominal and intrathoracic pressures. Careful head positioning in a neutral, slightly elevated posture is essential to facilitate venous outflow. Continuous ICP and hemodynamic monitoring are mandatory. Although a transient rise in ICP during the turning maneuver is often clinically acceptable, a sustained elevation requires prompt reassessment and, if necessary, supination. In patients with refractory hypoxemia and stable ICP, the marked improvement in oxygenation and potential reduction in ventilator-induced lung injury may justify prone positioning as a high-risk,

high-reward intervention when performed in specialized neurocritical care settings [37, 38].

When ABI and ARDS coexist, a dual-protection approach is essential: preventing secondary brain injury while minimizing VILI. Carbon dioxide levels should be maintained within 30–40 mmHg, avoiding hyperventilation unless required to manage life-threatening intracranial hypertension. PEEP should be titrated to the lowest level that achieves adequate oxygenation (SpO_2 92–96%) without exacerbating ICP. Initial VT should be set at 6 mL/kg PBW but can be increased to 7–8 mL/kg if needed to control CO_2 and prevent ICP elevation. Prone positioning should generally be avoided when ICP exceeds 25 mmHg [39, 40].

Ventilation modes and their impact on ABI patients

Volume-controlled ventilation (VCV) delivers a fixed VT with each breath, ensuring stable alveolar ventilation. This stability is critical in patients with ABI, as $PaCO_2$ directly influences CBF and ICP through its vasoregulatory effects [41].

In contrast, pressure-controlled ventilation (PCV) delivers a set inspiratory pressure, allowing VT to vary depending on lung compliance and airway resistance [42]. By limiting inspiratory pressures, PCV reduces the risk of barotrauma. However, the inherent variability of VT with this mode can lead to fluctuations in $PaCO_2$ and minute ventilation, particularly in patients with evolving respiratory mechanics or reduced compliance and may occasionally result in the delivery of excessively high VTs. Because maintaining stable $PaCO_2$ is critical in ABI, clinicians may need to frequently adjust the pressure control level or, in some cases, increase the set respiratory rate to compensate for low VTs, as these adaptations are not automated within the mode [43, 44].

Although PCV is commonly used in patients with impaired compliance, close monitoring is essential in ABI to ensure effective ventilation and ICP stability [20]. Regardless of the ventilator mode selected, individualized management with frequent reassessment is required to optimize both cerebral and pulmonary outcomes [45].

Pressure-regulated volume control (PRVC) is widely available and delivers pressure-controlled breaths to achieve a set VT while continuously monitoring delivered volumes. This allows real-time assessment of respiratory system compliance and facilitates adjustment of ventilatory support to patient-specific mechanics [46].

Emerging modes of ventilation and their potential benefits in ABI patients

Neurally adjusted ventilatory assist (NAVA) improves patient–ventilator synchrony by delivering support in proportion to diaphragmatic electrical activity. While NAVA can reduce asynchrony and preserve CBF, it requires an intact central respiratory drive and functional phrenic nerve activity—both of which may be impaired in ABI, particularly with brainstem involvement [47]. Spontaneous breathing efforts during partial support modes, such as pressure support ventilation (PSV), can generate marked negative intrathoracic pressures that are transmitted to the cerebral venous system. The resulting fall in central venous pressure increases cerebral transmural pressure (intravascular minus extramural pressure), promoting venous engorgement, impairing CSF outflow, and raising intracranial blood volume. These changes may exacerbate cerebral edema and elevate ICP, a mechanism particularly relevant in patients with reduced intracranial compliance [48].

A study comparing NAVA with PSV in patients recovering from ABI [49] demonstrated that both modes preserved CBF velocity, while NAVA significantly improved ventilator synchrony. These results suggest that NAVA may offer a safe and effective alternative to PSV in the weaning phase, potentially reducing the risk of secondary cerebral insults from dysregulated breathing. Its efficacy, however, relies on an intact central respiratory drive and functional phrenic nerve activity—both of which may be impaired in ABI, particularly in cases involving the brainstem [50].

Separately, automated ventilation systems—such as proportional assist ventilation + (PAV+), adaptive support ventilation (ASV), SmartCare, and INTELLiVENT-ASV—are increasingly implemented in general critical care, though their use in ABI patients remains limited [51]. Among these, ASV, SmartCare, and INTELLiVENT-ASV are true closed-loop modes, while PAV+ and PRVC are patient-driven or hybrid but not fully closed-loop. INTELLiVENT-ASV, the most advanced of these systems, may be particularly beneficial in ABI. It automatically adjusts VT and respiratory rate to maintain normocapnia and modifies FiO_2 and PEEP based on continuous SpO_2 monitoring, thereby optimizing both oxygenation and ventilation while reducing the risk of dysoxia and abrupt CBF shifts [52].

In patients with severe TBI, INTELLiVENT-ASV was associated with more stable $PaCO_2$ regulation and fewer episodes of hypo- or hypercapnia compared to conventional pressure-controlled ventilation while requiring fewer manual adjustments [53]. The ongoing ACTiVE trial, a multicenter randomized controlled study that includes ABI patients, is expected to provide further insights into the efficacy of INTELLiVENT-ASV in this population [54]. Although the study's primary outcome was the percentage of time within the target $PaCO_2$ range, the resulting improvement in $PaCO_2$ stability—a critical determinant of cerebral vasomotor tone—likely

Table 1 Comparison of ventilation modes and their impact on acute brain injury patients

Ventilation mode	Mechanism	Benefits	Limitations
Volume-controlled ventilation (VCV)	Delivers a fixed tidal volume regardless of airway pressure	Ensures consistent $PaCO_2$ levels	May increase risk of barotrauma and volutrauma in patients with low lung compliance
Pressure-controlled ventilation (PCV)	Maintains set inspiratory pressure during each breath	Limits peak airway pressures and reduces barotrauma risk	Variable tidal volume may cause inconsistent $PaCO_2$ control and requires close VT monitoring to prevent hypo- or hyperventilation
Pressure-support ventilation (PSV)	Delivers pressure-limited, time-cycled breaths to support spontaneous effort. Breaths may be triggered by patient-generated pressure or flow changes	Improves comfort during weaning and enhances synchrony in cooperative patients	Excessive respiratory effort may raise intracranial pressure and requires intact respiratory drive, contraindicated in brainstem injury or severe agitation
Neurally adjusted ventilatory assist (NAVA)	Synchronizes ventilatory support with diaphragmatic electrical activity	Improves patient-ventilator synchrony and may reduce ICP fluctuations	Requires intact diaphragm function and specialized equipment needed
Proportional assist ventilation (PAV)	Adjusts support in proportion to the patient's inspiratory effort	Reduces work of breathing and enhances comfort	Limited applicability in sedated or paralyzed patients
Proportional assist ventilation plus (PAV+)	Advanced PAV mode with automated adjustments for changing mechanics	Optimizes synchrony and adapts support to dynamic respiratory needs	Requires specialized equipment and limited evidence in ABI
INTELLiVENT-ASV	Closed-loop mode that automatically adjusts ventilation and oxygenation parameters	Optimizes gas exchange and may reduce ventilator-induced lung injury	Limited direct evidence in acute brain injury and requires advanced monitoring capabilities

translates into more consistent CBF and a reduced risk of secondary insults from hypocapnia-induced vasoconstriction or hypercapnia-induced vasodilation with elevated ICP. Direct measurements of CBF or cerebral perfusion pressure during INTELLiVENT-ASV in patients with ABI, however, remain an important focus for future research [54].

Integration of advanced neuromonitoring

Advanced neuromonitoring tools—including brain tissue oxygen pressure ($PbtO_2$), ICP, and cerebral autoregulation indices—can guide real-time titration of ventilatory parameters. For example, a decrease in $PbtO_2$ despite adequate FiO_2 may prompt clinicians to increase PEEP to improve oxygenation, though this must be weighed against the risk of ICP elevation [10]. Similarly, end-tidal CO_2 and cerebral oximetry may help guide $PaCO_2$ management to ensure optimal CBF without inducing intracranial hypertension.

Limitations and challenges

Despite the promise of these advanced modes, several limitations exist. In particular, patients with severe ABI may experience myoclonus or erratic breathing patterns that are not linked to gas exchange needs, interfering with closed-loop algorithms. These disturbances may limit the applicability or reliability of automated systems and require algorithm overrides or temporary reversion to controlled ventilation modes.

In summary, emerging ventilation strategies such as NAVA and INTELLiVENT-ASV offer promising opportunities to optimize oxygenation, reduce ventilator-induced lung injury, and improve CO_2 regulation in ABI patients. However, direct evidence in this population remains limited. Further studies are essential to clarify their role in neurocritical care. Table 1 provides a comparative overview of conventional and advanced ventilation modes, outlining their mechanisms, advantages, and limitations in the management of ABI.

Monitoring techniques in mechanical ventilation for acute brain injury

Intracranial pressure monitoring

ICP monitoring remains a cornerstone in the management of ABI. Elevated ICP is a major contributor to secondary brain injury and is directly influenced by mechanical ventilation parameters [20]. Continuous ICP monitoring, using intraventricular catheters or intraparenchymal sensors, enables real-time guidance of ventilatory strategies, including the adjustment of PEEP, VT, and $PaCO_2$ levels.

Ventilator settings exert a significant influence on ICP. Elevated levels of PEEP increase intrathoracic pressure, which may impede cerebral venous return and elevate ICP—particularly in patients with reduced intracranial compliance [55]. Evidence from a meta-analysis suggests that $PEEP \geq 10$ cmH_2O is associated with increased ICP, whereas moderate levels (5–8 cmH_2O) achieve adequate

pulmonary support with minimal adverse effects on cerebral dynamics.

$PaCO_2$ control is equally critical. Hypocapnia induces cerebral vasoconstriction, decreasing CBF, while hypercapnia causes vasodilation, potentially elevating ICP [3].

Similarly, $PaCO_2$ control is crucial, as hypocapnia leads to cerebral vasoconstriction and reduced cerebral perfusion, while hypercapnia causes vasodilation and potential ICP elevation [3]. A retrospective study analyzing 28,644 paired PEEP and ICP data points from 341 ICU patients with severe ABI evaluated the effects of PEEP stratified by lung injury severity [56]. In most patients, PEEP exerted no clinically significant impact on ICP or cerebral perfusion pressure (CPP). However, in those with severe lung injury ($PaO_2/FiO_2 < 100$), each cmH_2O increase in PEEP was associated with a modest rise in ICP (0.31 mmHg; $p = 0.04$) and a decline in CPP (−0.85 mmHg; $p = 0.02$). Although statistically significant, these changes were minor and likely not clinically relevant.

Brain tissue oxygen monitoring

$PbtO_2$ monitoring provides direct, continuous measurement of regional cerebral oxygenation via a parenchymal probe [57]. This modality enables real-time titration of ventilatory and hemodynamic parameters to optimize cerebral oxygen delivery [57].

Ventilatory settings, particularly PEEP, influence $PbtO_2$ indirectly through their effects on CPP [10]. Elevated PEEP may reduce MAP, thereby lowering CPP and compromising oxygen delivery. As such, $PbtO_2$ values should always be interpreted in the context of concurrent MAP and ICP measurements to guide appropriate ventilatory adjustments.

In a study involving 425 patients with traumatic brain injury (TBI), $PbtO_2$ values below 20 mmHg occurred during 17% of the monitoring time, frequently without parallel alterations in ICP, CPP, or the pressure reactivity index (PRx). Notably, $PbtO_2$ declined sharply when CPP dropped below 30 mmHg or when deviations from optimal CPP (ΔCPPopt) exceeded 30 mmHg—suggesting that impairments in oxygen diffusion and microcirculatory function may independently affect cerebral oxygenation [58].

When titrating PEEP, trends in $PbtO_2$ must be carefully interpreted alongside ICP and MAP. A decrease in $PbtO_2$ despite stable ICP may indicate impaired cerebral perfusion due to compromised venous outflow from increased intrathoracic pressure [10]. In such scenarios, reducing PEEP or optimizing systemic hemodynamics with fluid resuscitation or vasopressors may help restore cerebral oxygenation. Conversely, a rise in ICP with preserved $PbtO_2$ may reflect compensatory cerebral vasodilation; in these cases, interventions such as controlled hyperventilation or sedation may be necessary to lower ICP and maintain cerebrovascular reserve.

Jugular venous oxygen saturation

$SjvO_2$ monitoring provides insights into global cerebral oxygen utilization by measuring oxygen saturation in the jugular bulb [59]. Declining $SjvO_2$ indicates increased cerebral oxygen extraction, often reflecting inadequate oxygen delivery [60].

Ventilatory parameters—particularly those affecting $PaCO_2$—significantly influence $SjvO_2$ [61]. Hypocapnia may reduce $SjvO_2$ due to vasoconstriction, while hypercapnia raises $SjvO_2$ through vasodilation, though excessive CO_2 retention can elevate ICP.

A study involving 63 patients with severe TBI assessed the relationship between $SjvO_2$ and the Full Outline of Unresponsiveness (FOUR) score. While a weak, nonsignificant positive correlation was observed at admission ($r = 0.246$, $p = 0.052$), significant negative correlations emerged at 48 and 72 h ($r = -0.751$, $p < 0.001$; $r = -0.49$, $p = 0.002$). Both lower FOUR scores and abnormal $SjvO_2$ values independently predicted mortality. These findings suggest that combining neurological assessments with $SjvO_2$ monitoring enhances prognostication in intubated TBI patients [62].

Brain ultrasonography

Brain ultrasonography offers a noninvasive method for assessing ICP, CPP, and cerebral hemodynamics, particularly in patients where invasive techniques pose risks or are impractical [63]. Two key modalities are optic nerve sheath diameter (ONSD) and transcranial Doppler (TCD) ultrasonography [64].

The optic nerve sheath communicates with the subarachnoid space, and its diameter increases in response to elevated CSF pressure [65]. As a result, ONSD measurement serves as a surrogate for estimating ICP, with values > 5.0 mm suggestive of elevated pressure [66].

TCD ultrasonography measures CBF velocities—primarily in the middle cerebral artery (MCA)—and can estimate ICP and CPP indirectly [67]. The pulsatility index (PI), calculated as (systolic-diastolic velocity)/mean flow velocity, correlates with ICP. A $PI > 1.2$ suggests elevated ICP (> 20 mmHg), while a $PI > 1.4$ may indicate dangerously high ICP (> 30 mmHg), potentially signaling impending herniation [67].

TCD is also useful in assessing the cerebral effects of ventilator changes. For instance, hyperventilation-induced hypocapnia reduces CBF, which can be dynamically observed as decreased flow velocities or increased PI [68]. This feedback enables clinicians to fine-tune ventilation strategies while monitoring cerebrovascular impact [69].

Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) is a noninvasive technique that measures regional cerebral oxygen saturation (rSO_2) using light in the near-infrared spectrum [70]. Although limited to superficial cortical regions, NIRS provides continuous cerebral oxygenation data, which can be particularly valuable during interventions or in settings where invasive monitoring is not feasible [70].

NIRS complements other neuromonitoring modalities by providing real-time feedback on oxygenation status. When used alongside ICP monitors, TCD, or $PbtO_2$, it enhances clinicians' ability to detect and respond to cerebral hypoxia [71]. For example, a decline in rSO_2 during mechanical ventilation adjustments may signal impaired perfusion, guiding changes in PEEP, FiO_2, or hemodynamic support.

Ventilation also impacts systemic hemodynamics, influencing CPP through changes in MAP and ICP. Neuromonitoring systems—including NIRS—detect these fluctuations, enabling early intervention to maintain cerebral homeostasis and reduce the risk of secondary brain injury [72].

Sedation and paralysis during mechanical ventilation in ABI patients

Sedation plays a critical role in the management of mechanically ventilated patients with ABI, exerting both direct and indirect effects on cerebral physiology and ventilatory synchrony. Commonly used agents, such as propofol and midazolam, differ substantially in their profiles. Propofol reduces the cerebral metabolic rate and facilitates ICP control but may impair CO_2 clearance—potentially worsening intracranial hypertension in patients with compromised autoregulation. Midazolam offers greater hemodynamic stability but is associated with prolonged sedation and delayed neurological evaluation [73].

Sedative selection and depth should be individualized based on multimodal neuromonitoring, particularly $PbtO_2$ and ICP, to optimize patient–ventilator interaction, CO_2 clearance, and cerebral perfusion. A multinational cohort study of 262 patients with severe TBI found that propofol was the most frequently administered sedative (35.4%), followed by midazolam (25.6%) [74]. Propofol use was more common in patients with lower illness severity, whereas midazolam was often co-administered with opioids. Sedative choice was not independently associated with 60-day mortality; rather, higher APACHE II and Injury Severity Scores were the main predictors of adverse outcomes.

Recent reviews have emphasized the importance of tailoring sedation strategies to the evolving needs of ABI patients. Propofol remains the agent of choice for ICP control but carries a risk of propofol infusion syndrome at high doses. Midazolam is preferred in hemodynamically unstable patients, although it may delay awakening and prolong mechanical ventilation. A stepwise, individualized approach—guided by ICP trends, cerebral compliance, and multimodal data—has been proposed to optimize sedation titration [75].

Recent reviews have emphasized the importance of tailoring sedation strategies to the evolving needs of ABI patients. Propofol remains the agent of choice for ICP control but carries a risk of propofol infusion syndrome at high doses. Midazolam is preferred in hemodynamically unstable patients, although it may delay awakening and prolong mechanical ventilation. A stepwise, individualized approach—guided by ICP trends, cerebral compliance, and multimodal data—has been proposed to optimize sedation titration [76]. Bolus NMBA administration is effective in reducing transient ICP elevations during tracheal suctioning or physiotherapy, but not during bronchoscopy. A systematic review of 34 studies on NMBA use in TBI reported that non-depolarizing agents such as atracurium variably reduced ICP, CPP, and MAP, with inconsistent effects across studies [77]. Continuous NMBA infusions were associated with adverse outcomes, including longer ICU stays, increased risk of ventilator-associated pneumonia, and sustained periods of $ICP > 20$ mmHg. While NMBAs may offer short-term ICP control, their long-term impact on functional and neurological outcomes remains uncertain, warranting careful risk–benefit assessment and intermittent reassessment.

Conclusions

Mechanical ventilation in patients with ABI demands a delicate balance between optimizing respiratory support and preserving cerebral physiology. Advances in ventilatory strategies and neuromonitoring have enhanced our capacity to individualize care, mitigate secondary brain injury, and improve clinical outcomes. Key parameters, including VT, airway pressures, and $PaCO_2$—must be meticulously adjusted to ensure lung protection while maintaining adequate cerebral perfusion and oxygenation.

Emerging approaches, such as multimodal brain monitoring and personalized ventilatory modes, offer promising avenues for refining management. Future research should focus on validating these strategies across diverse ABI phenotypes and integrating novel technologies that bridge the interface between respiratory and neurological care.

By embracing a multidisciplinary, physiology-driven, and evidence-based approach, clinicians can meaningfully influence the trajectory of recovery in ABI patients, transforming critical care into a platform for both protection and repair.

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SAS, CR, MS, PRMR wrote the main manuscript. SAS and PRMR prepared the Figs. 1–3. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

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