

Ventilator Weaning and Extubation in Acute Brain Injury: Challenges and Evidence-Based Approaches

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ABSTRACT

Weaning from invasive mechanical ventilation is a critical phase of intensive care management. While structured protocols, daily readiness assessments, and spontaneous breathing trials (SBTs) improve outcomes in general ICU populations, their application in patients with acute brain injury (ABI) is challenging. In these patients, respiratory mechanics are frequently preserved, whereas impaired consciousness, ineffective airway protective reflexes, and excessive secretions predominantly determine extubation readiness and success. This narrative review reframes Boles's Six Stages of Weaning within a neurocritical care perspective, incorporating ABI-specific considerations including stabilization and pre-weaning optimization; suspicion that weaning may be possible; readiness assessment; performance of SBTs; extubation decision-making; and recognition and management of extubation failure. Across these stages, evidence consistently demonstrates that neurological factors, especially cough strength, swallowing function, ability to follow commands, and level of consciousness, are the main determinants of extubation success in ABI patients. In contrast, traditional respiratory predictors, such as rapid shallow breathing index (RSBI) or maximal inspiratory pressure (MIP)/negative inspiratory force (NIF), show limited discriminatory value in this population. Emerging data suggest that integrated models combining neurological and respiratory variables provide a more accurate framework for extubation decision-making in ABI. By highlighting the limitations of conventional weaning and extubation criteria, this review proposes practical, physiology-driven

strategies to guide ventilator liberation in neurocritical care, with the goal of reducing extubation failure and minimizing secondary neurological injury.

Keywords: Invasive mechanical ventilation; ventilator weaning; extubation; brain injury; neurocritical care; spontaneous breathing trial; weaning predictors; extubation predictors.

INTRODUCTION

Weaning from invasive mechanical ventilation (IMV) is a major determinant of outcome in critically ill patients [1-3]. Prolonged ventilation increases the risk of ventilator-associated pneumonia, respiratory and peripheral muscle dysfunction, delirium, and extended intensive care unit (ICU) stay, whereas premature extubation raises the likelihood of reintubation, a complication consistently associated with worse prognosis [4, 5]. Accurate identification of weaning readiness and optimal timing of extubation are therefore central components of ICU care.

To structure this process, a multidisciplinary task force described weaning as a six-stage continuum, spanning from initiation of IMV to sustained spontaneous breathing after extubation [6]. This framework, subsequently incorporated into clinical practice and guidelines, emphasizes respiratory mechanics, gas exchange, and tolerance of spontaneous breathing trials (SBTs). However, delayed recognition of readiness unnecessarily prolongs exposure to mechanical ventilation, while overly aggressive liberation strategies increase the risk of extubation failure [7, 8].

Patients with acute brain injury (ABI), including ischemic or hemorrhagic stroke, subarachnoid hemorrhage, traumatic brain injury (TBI), and other acute neurological insults, represent a particularly vulnerable population during weaning and extubation. The interplay of primary and secondary brain injury, impaired consciousness, autonomic instability, and complex critical care needs requires individualized ventilatory and neurological management [9, 10]. In many of these patients, lung function is often relatively preserved or rapidly recovers, and intubation is performed primarily for airway protection rather than respiratory failure [11]. As a result,

conventional respiratory indices often fail to predict successful extubation. Extubation failure occurs more frequently in ABI patients (approximately 20–38%) than in general ICU populations (10–15%) [12, 13].

Extubation failure in ABI is not a benign event. Reintubation may precipitate hypoxemia, hypercapnia, hypotension, and sympathetic surges, all of which can impair cerebral perfusion and exacerbate secondary brain injury, particularly in the setting of altered cerebral autoregulation [11]. Beyond reintubation itself, the weaning process poses unique challenges in ABI: spontaneous breathing may increase intracranial pressure (ICP) through fluctuations in intrathoracic pressure, changes in arterial partial pressure of carbon dioxide (PaCO₂), agitation, or increased work of breathing. Consequently, neurological rather than respiratory constraints often determine the timing and trajectory of ventilator liberation in this population [6].

In this narrative review, we propose an adaptation of Boles’s Six Stages of Weaning tailored to patients with ABI. By integrating clinical evidence with physiological principles, we examine how neurological injury modifies each stage of the weaning process, highlight the limitations of standard respiratory criteria, and discuss practical strategies to optimize extubation readiness while minimizing the risk of secondary brain injury. This physiology-driven framework aims to support safer and more individualized ventilator liberation in neurocritical care.

REVIEW METHODS

This narrative review focused on adults (≥ 18 years) with ABI, including TBI, subarachnoid hemorrhage, intracerebral hemorrhage, ischemic stroke, who required IMV.

Eligibility Criteria

Eligible studies enrolled adult ABI patients receiving IMV and reported outcomes related to ventilator weaning, SBTs, airway protection, extubation readiness, extubation success or failure, or tracheostomy. We included prospective and retrospective cohort studies, randomized controlled trials, and systematic reviews published in peer-reviewed journals. Pediatric studies, case reports, conference abstracts, narrative opinions without original data, and studies not addressing weaning or extubation outcomes were excluded. Only articles published in English were considered.

Conceptual Framework

Boles's Six Stages of Weaning served as the conceptual framework for this review. Each stage was adapted to address ABI-specific physiological and clinical challenges. This framework guided synthesis of evidence related to weaning readiness, SBT performance, extubation decision-making, and extubation failure, with particular attention to interactions among neurological status, sedation, airway protection, respiratory drive, and ventilatory support. It was also used to illustrate why conventional ICU weaning protocols and respiratory indices frequently perform poorly in ABI patients.

Literature Search and Study Selection

A targeted, non-systematic search of PubMed, Scopus, and Google Scholar was conducted to identify clinically relevant and influential studies on ventilator weaning and extubation in ABI. Search terms included combinations of "acute brain injury," "neurocritical care," "mechanical ventilation," "weaning," "spontaneous breathing trial," "airway protection," and "extubation failure." The search included articles published up to the final search date (Month Year). Google Scholar was used to identify highly cited studies not captured in database searches.

Titles and abstracts were independently screened by two reviewers, followed by full-text review of selected articles. Disagreements were resolved by consensus. Study selection prioritized clinical relevance, methodological rigor, and contribution to understanding ABI-specific determinants of weaning and extubation outcomes rather than exhaustive coverage of the literature.

STAGE 1. FROM “TREATMENT OF ACUTE RESPIRATORY FAILURE” TO AN ABI-FOCUSED “PRE-WEANING OPTIMIZATION STAGE”

In Boles’s original framework, Stage 1 refers to the treatment and resolution of acute respiratory failure (ARF) before initiating the weaning process [14]. In ABI patients, however, IMV is most commonly required for airway protection, depressed level of consciousness, or perineurosurgical management rather than for primary ARF [15]. Consequently, resolution of ARF alone is insufficient to define readiness to enter the weaning process in this population. Instead, early progression toward ventilator liberation is predominantly constrained by neurological status rather than pulmonary recovery.

We therefore propose reframing Stage 1 as a Pre-Weaning Optimization Stage tailored to the specific physiological priorities of ABI patients. This stage encompasses the stabilization of respiratory, hemodynamic, and neurological parameters required to safely consider subsequent weaning steps.

Basic respiratory prerequisites remain necessary but, in ABI patients, should be interpreted conservatively, ensuring that ventilatory targets (e.g., slightly higher positive end-expiratory pressure or lower arterial partial pressure of oxygen) do not compromise intracranial dynamics. At this stage, the objective is not readiness for extubation, but transition from rescue ventilation

to a physiologically stable condition in which gas exchange is adequate and ventilatory settings are tolerated without inducing intracranial hypertension or reducing cerebral perfusion pressure (CPP). This includes absence of clinically significant hypoxemia or severe respiratory acidosis, use of airway pressures compatible with stable ICP and CPP, manageable airway secretions, and respiratory mechanics allowing progressive de-escalation of full ventilatory support. The presence of spontaneous breathing effort is not mandatory, as ventilatory drive may remain intentionally controlled for neurological indications. Hemodynamic stability should be ensured, defined by stable mean arterial pressure with minimal or no vasopressor support and absence of ongoing circulatory instability that could compromise cerebral perfusion during ventilatory transitions.

Neurological optimization is central to this stage. Progression toward active weaning should only be considered once ICP has been durably controlled (e.g., <22 mmHg for ≥ 24 hours) [16], Tier 3 therapies for refractory intracranial hypertension (such as barbiturate coma, decompressive craniectomy, or hypothermia) have been discontinued, and there is no evidence of evolving intracranial pathology on serial neuroimaging [16]. Although high-quality data directly linking these criteria to weaning outcomes are limited, they reflect contemporary neurocritical care standards aimed at minimizing secondary brain injury during ventilatory transitions.

Sedation management represents a critical and dynamic component of pre-weaning optimization. Sedatives should be minimized and carefully titrated using validated scales such as the Richmond Agitation–Sedation Scale (RASS) [17], balancing the need for neurological protection, control of intracranial hypertension, and patient–ventilator synchrony. When feasible, protocols favoring short-acting agents, adequate analgesia, and non-pharmacological measures should be employed.

In summary, Stage 1 in ABI is defined not by resolution of respiratory failure, but by completion of a comprehensive pre-weaning optimization process in which neurological stability is the dominant determinant.

STAGE 2. SUSPICION THAT WEANING MAY BE POSSIBLE

In ABI patients, controlled ventilation is often maintained despite preserved pulmonary mechanics because neurological rather than respiratory factors govern ventilatory management. Suppression of spontaneous breathing is frequently required to ensure tight control of ICP and PaCO₂, both key determinants of cerebral blood flow. Even modest PaCO₂ fluctuations associated with spontaneous effort may provoke clinically relevant ICP changes. In addition, spontaneous breathing may increase agitation, cerebral metabolic demand, and intrathoracic pressure swings that impair cerebral venous drainage [18].

As a result, many ABI patients remain on controlled ventilation beyond the point at which assisted modes would be acceptable in other ICU populations [15]. Progression to Stage 2 therefore reflects completion of pre-weaning optimization rather than recovery from the primary brain injury. Criteria include sustained ICP control, reduction of sedative requirements, manageable secretions, stable or improving neuroimaging, and discontinuation of Tier 3 therapies [19].

At this stage, the central clinical question is whether spontaneous breathing can be cautiously reintroduced without precipitating ICP elevation, ventilatory instability, or agitation. Suspicion that weaning may be possible arises when neurological and systemic stability suggest that limited respiratory effort may be tolerated. Given the dynamic and individualized nature of ABI, spontaneous breathing should be introduced gradually, with close physiological monitoring and

frequent reassessment before formal weaning readiness testing. Beyond traditional physiological criteria, recent evidence highlights the potential role of sensory and cognitive stimulation in supporting ventilator liberation. In a randomized trial of 45 patients receiving controlled mechanical ventilation for neurological disease, repeated exposure to audio recordings of patients' relatives during assisted ventilation significantly reduced the duration of controlled mechanical ventilation and increased measurable brain activity, particularly in right fronto-central regions, without adverse effects [20]. Although this intervention did not significantly reduce weaning failure, these findings underscore that engagement of cortical and cognitive networks may complement respiratory and neurological assessments, potentially facilitating earlier progression through the weaning stages.

STAGE 3. ASSESSING READINESS TO WEAN

Readiness to wean is generally assessed by evaluating clinical and physiological stability, including adequate oxygenation, hemodynamic stability, preserved respiratory mechanics, and sufficient neurological function to maintain ventilatory drive and airway protection. In patients with ABI, however, these general criteria are often insufficient, as ventilator dependence is more strongly influenced by neurological status and airway protective capacity rather than respiratory mechanics alone [21, 22].

Once pre-weaning optimization has been achieved and spontaneous breathing is considered physiologically tolerable (Stage 2), the limiting factor often shifts from ventilatory ability to airway competence and neurological integrity. Gas exchange and respiratory system mechanics are commonly preserved, allowing early tolerance of assisted ventilatory modes. Progression beyond this stage is nevertheless often constrained by uncertainty regarding airway protection rather than true respiratory failure [22].

This pattern should not be interpreted as failure of the weaning process. Rather, it reflects a distinct neurocritical care phenotype in which extubation is deferred because of anticipated neurological risk. Neurological severity and systemic inflammatory burden further modulate ventilator liberation in ABI. For example, in TBI, higher C-reactive protein to albumin ratios have been independently associated with weaning failure, whereas higher Glasgow Coma Scale (GCS) scores predict successful liberation. The combined assessment of inflammatory and neurological markers improves prognostic discrimination, underscoring that ventilator dependence in this population reflects a complex interaction between systemic physiology and brain injury severity [23].

In selected patients with borderline pulmonary reserve, adjunctive physiological indices may help refine the assessment of readiness to wean. Parameters reflecting respiratory drive and inspiratory muscle performance, such as airway occlusion pressure at 100 ms ($P_{0.1}$), maximal inspiratory pressure during airway occlusion (P_{occ}) in non-collaborative patients, or maximal inspiratory pressure/negative inspiratory force (MIP/NIF) in cooperative patients, can be integrated with composite measures such as the pressure–muscle index (PMI) to provide a bedside evaluation of the relationship between imposed respiratory load and neuromuscular capacity. Other objective tools such as diaphragm ultrasonography may guide supportive strategies, including respiratory physiotherapy, inspiratory muscle training, and gradual reduction of pressure support with respiratory muscle training [24, 25]. Although these variables sometimes change the decision to proceed with a SBT, markedly abnormal values may indicate limited physiological reserve and justify postponement in patients considered at elevated risk of weaning failure [26].

Building on the adjunctive assessment of respiratory drive and inspiratory effort described above, a similar rationale applies to patients who remain ventilator-dependent despite preserved pulmonary mechanics. In such cases, serial evaluation of inspiratory muscle performance may be considered to monitor physiological reserve over time rather than to determine immediate readiness for extubation. These interventions aim to preserve respiratory muscle integrity; however, the incremental value of advanced respiratory muscle assessments appears limited in ABI, where definitive progression beyond this stage depends primarily on neurological recovery and airway competence rather than respiratory mechanics alone. In a prospective study of mechanically ventilated patients undergoing a first SBT, ultrasonographic measurement of diaphragmatic excursion demonstrated poor discriminative ability for predicting weaning failure (AUC 0.65) and did not outperform the Medical Research Council score, highlighting the limited bedside utility of diaphragmatic ultrasound as a standalone predictor of weaning outcomes [27].

STAGE 4. SPONTANEOUS BREATHING TRIALS

As part of assessing readiness to wean (Stage 3), once basic physiological prerequisites are met, adequate oxygenation on minimal ventilatory support, hemodynamic stability without escalating vasoactive requirements, and preserved respiratory drive, patients may undergo an SBT to confirm the ability to sustain spontaneous breathing [28]. A successful SBT confirms the ability to maintain adequate ventilation, gas exchange, and cardiovascular stability under reduced support but does not guarantee extubation success in patients with ABI. In this population, the SBT primarily evaluates tolerance to decreased ventilatory assistance rather than definitive readiness for tube removal [29]. While this distinction also exists in the general ICU population; where extubation requires not only SBT success but also adequate consciousness and effective cough, the divergence between ventilatory tolerance and extubation suitability is

considerably more pronounced in ABI, where neurological status and airway protection are often the decisive factors.

In general, different modes of SBT produce modest differences in work of breathing and hemodynamic load [30]. Regardless of technique, excessive prolongation of the SBT should be avoided [31]. Typical trial durations range from 30 to 120 minutes [32]. This consideration is particularly relevant in patients with ABI, in whom fatigue, agitation, hyperventilation, or sustained physiological stress during a prolonged SBT may increase metabolic demand, alter carbon dioxide levels, and potentially precipitate secondary neurological injury. Criteria for SBT failure include tachypnea, hypoxemia, hemodynamic instability, respiratory distress, and acidosis. In ABI patients, agitation or delirium may also necessitate early termination of the trial. Such findings should prompt reassessment of both respiratory and neurological factors before further weaning attempts are pursued [33, 34]. In many patients with ABI, ventilatory support can be reduced early, yet extubation is often delayed due to impaired consciousness, ineffective airway protection, or excessive secretions [35, 36]. In this setting, repeated or prolonged SBTs add little information and may impose unnecessary physiological stress [18, 33, 37].

In patients with ABI, the GLOBAL WEAN study showed that an unassisted SBT (PSV0-PEEP0) most closely reproduced post-extubation inspiratory effort. However, the study did not evaluate extubation success as an outcome. Therefore, while PSV0-PEEP0 may better reflect true respiratory workload in ABI, there is no evidence that its use improves extubation rates or clinical outcomes in this population [38]. Recent evidence from the ENIO cohort indicates that neither the SBT modality (pressure support, T-piece, or continuous positive airway pressure) nor the duration of the trial significantly predicts extubation failure in ABI patients. Instead, airway

protective capacity, particularly the presence of a vigorous cough, remains the primary determinant of successful extubation [37].

In ABI patients, over-assistance during pressure support ventilation is common and may mask true respiratory capacity. The ENVISION study demonstrated that reducing ventilatory support during SBT is generally safe, improving regional ventilation distribution and respiratory effort without affecting brain oxygenation or electrical activity. Measures such as P0.1 and respiratory muscle pressure (P_{mus}) accurately identify under-assistance and can help guide titration of support during weaning [39]. Such findings support the use of physiologically informed monitoring to optimize SBTs and prevent both over- and under-assistance in ABI patients. Considering these new findings, in ABI patients the SBT modality selection should be guided by local practice, patient comfort, and careful monitoring of physiological responses.

While SBT remain a cornerstone of ventilator liberation, recent evidence highlights the benefits of prompt extubation immediately following a successful trial in patients with ABI. In a multicenter observational study of 1,406 adults with ABI, including TBI, ischemic or hemorrhagic stroke, seizures, and SAH, extubation on the same calendar day as the first successful SBT was associated with a significant increase in ventilator-free days up to 28, without reported safety concerns [36]. These findings support early extubation when neurological and airway criteria are met, while acknowledging that certain injury patterns, particularly brainstem lesions affecting swallowing or autonomic function, may still necessitate delayed extubation despite preserved consciousness and respiratory mechanics.

Respiratory complications may further confound interpretation. In large neurocritical care cohorts, ventilator-associated pneumonia and post-SBT tracheobronchitis have been associated with delayed extubation, higher tracheostomy rates, and prolonged ICU stay, underscoring that

failure to progress may reflect pulmonary complications rather than neurological impairment alone [40, 41]. Notably, acute respiratory distress syndrome (ARDS) occurs in a meaningful subset of ABI patients and is associated with increased ICU mortality, longer mechanical ventilation duration, and prolonged ICU stay, with a trend toward higher extubation failure, highlighting the impact of brain–lung interactions on ventilator liberation [42].

Finally, complex numerical respiratory indices, such as RSBI and vital capacity, may provide adjunctive information during ventilatory liberation. Vital capacity is typically assessed prior to SBT as a screening indicator of ventilatory reserve, whereas RSBI is usually measured during SBT to evaluate tolerance to reduced ventilatory support. However, in patients with ABI, these indices have limited incremental value for predicting extubation success and should be interpreted alongside neurological and airway protective assessments [11] (**Table 1**).

STAGE 5. EXTUBATION

Extubation success is defined as the ability to maintain adequate ventilation and effective airway protection after removal of the endotracheal tube without the need for reintubation. Unplanned extubation, including both self- and accidental, is a relatively frequent occurrence in ICUs, accounting for approximately 9% of all endotracheal removals. While accidental extubation is associated with higher ICU mortality, self-extubation does not increase mortality compared with planned extubation, though failure to maintain airway protection remains independently linked to poor outcomes [43].

Common definition for extubation failure in general ICU patients is the occurrence of reintubation within 48 hours (and up to 72 hours in some studies) [22, 44]. ABI-specific cohorts have adopted longer observation periods to account for delayed neurological and airway

complications. Notably, the ENIO study defined extubation failure as reintubation within 5 days, reflecting the unique pathophysiology and time course of deterioration in this population. Accordingly, extubation readiness in patients with ABI requires additional neurological and airway-focused assessment beyond standard respiratory criteria [45]. This emphasis on neurological assessment is consistent with contemporary ICU practice: in a recent national survey of French intensivists, impaired level of consciousness was the most frequently cited contraindication to extubation, reported by 69% of respondents, ranking above respiratory and airway-related factors such as weak cough, sputum retention, and swallowing disorders [46].

In addition to adequate gas exchange and respiratory mechanics, key elements for assessing extubation readiness in ABI patients include level of consciousness, integrity of airway reflexes, and the ability to manage secretions. The ability to follow simple motor commands; such as squeezing the examiner's hand or protruding the tongue on request, is particularly informative, as it reflects purposeful neurological engagement and correlates more closely with airway protection than eye opening alone [11, 41]. Failure to follow commands is consistently associated with a higher risk of extubation failure and often prompts delay of extubation or consideration of tracheostomy [41, 47]. Neurological status at the time of extubation remains a critical determinant of success in ABI patients. In a retrospective study of 641 adults with surgical ABI, including spontaneous intracerebral hemorrhage, aneurysmal SAH, and TBI-GCS scores at extubation independently predicted reintubation, while age and initial GCS were associated with prolonged intubation [48]. These findings underscore the importance of incorporating bedside neurological assessment, alongside airway protective reflexes, when evaluating extubation readiness in patients with ABI.

Effective cough, swallow, and gag reflexes are central to successful extubation. Tongue protrusion, reflecting hypoglossal nerve function, provides additional insight into airway integrity [49]. Secretions should be minimal and easily manageable, without the need for frequent suctioning. [50]. Patients who are obtunded or unable to clear secretions have a markedly increased risk of extubation failure, even when respiratory mechanics and gas exchange appear satisfactory [51, 52].

Predictors of Extubation Failure in ABI

In neurocritical care, extubation failure is driven predominantly by impaired airway protection rather than respiratory insufficiency. Prospective studies have developed clinical scores assessing eye, visual pursuit, swallowing attempts, GCS, cough, gag reflex, and deglutition, demonstrating strong predictive value for extubation success, reduced duration of mechanical ventilation, shorter ICU length of stay, and lower ICU mortality. In particular, Godet et al. proposed a pragmatic score for brain-injured patients incorporating cough, gag reflex, deglutition, and the Coma Recovery Scale–Revised visual subscale. Their study highlighted that the motor component of the GCS alone was not predictive of extubation tolerance and that patients with adequate airway protective function could be safely extubated even with low levels of consciousness [53, 54]. A meta-analysis including 928 patients demonstrated that neurological factors; such as low GCS scores (particularly 7–9), inability to follow commands, thick secretions, and absent cough or gag reflexes, were the strongest predictors of failure, whereas traditional weaning indices showed limited predictive value [41]. More recent multicenter data suggest that the sum of the eye and motor components of the GCS alone (GCS-EM) may not reliably predict extubation failure in ABI patients with predominantly moderate-to-high pre-extubation scores, highlighting the importance of integrating airway protective function and

command-following in extubation decision-making [55]. Additionally, neurocritical care practices; including ventilatory management and weaning strategies, are influenced by local resources and protocols. Survey data from the VENTILOMICS study, encompassing 204 respondents across 28 low- and middle-income countries, demonstrated that tidal volume selection, PEEP, and weaning approaches vary according to local practice and resource constraints, particularly in patients with intracranial hypertension [56]. These findings emphasize that extubation timing, tracheostomy decisions, and overall outcomes may differ depending on ICU setting and resource availability. A subsequent systematic review provided moderate-certainty evidence that intact cough and swallow reflexes are essential for extubation success in ABI [35].

Notably, many ABI patients exhibit preserved respiratory mechanics and gas exchange, frequently passing spontaneous breathing trials and demonstrating normal values for RSBI, negative inspiratory force, and vital capacity. **Extubation failure in ABI patients is primarily driven by impaired airway protection rather than respiratory mechanics. Structured clinical scores incorporating deglutition, gag reflex, cough, and visual tracking may help identify high-risk patients and guide extubation timing [57]. Similarly, ventilator parameters such as PEEP at initiation or at extubation have been associated with extubation failure and mortality, likely reflecting underlying disease severity rather than modifiable ventilatory targets [58]. Overall, mechanical ventilation strategies in ABI should balance brain, lung, and diaphragm protection using individualized ventilatory settings [59].** Conventional respiratory indices, including respiratory rate, tidal volume, minute ventilation, and PaO₂/FiO₂ ratio, often fail to distinguish between extubation success and failure in this population [41, 60, 61]. Moreover, effort-dependent measurements may be misleading: reduced alertness can underestimate true

respiratory capacity, while certain brainstem lesions may produce deceptively normal indices despite profound impairment of airway protection [62].

Accordingly, neurological and airway assessments are central to extubation decision-making in ABI and should be interpreted within the broader six-stage ventilator-liberation framework [63]. Both clinical assessment and objective measures, such as peak cough expiratory flow, consistently identify weak cough as an independent predictor of extubation failure in ABI patients [49]. Even with an endotracheal tube in place, evaluation of cranial nerve function such as asking patients to mouth words or move the lips or tongue can provide valuable information regarding airway protective capacity (**Figure 1**).

Integrated Scores and Models

Given the multifactorial nature of extubation failure in ABI, several composite tools have been proposed. In neurosurgical populations, the STAGE score [54], incorporating swallowing, tongue protrusion, airway protective reflexes (including cough), and motor response on the GCS, has been developed to support extubation readiness assessment. Another model combining command-following, preserved cough reflex, and adequate oxygenation demonstrated moderate sensitivity and specificity for predicting extubation success [64].

STAGE 6. EXTUBATION FAILURE

Extubation failure is generally defined as the need for reintubation, or death, within 5–7 days following endotracheal tube removal, a time window that captures the vast majority of failures and accommodates variability across studies [65]. In line with the CoVent Core Outcome Set, the isolated use of post-extubation noninvasive ventilation or high-flow nasal oxygen is not classified as extubation failure, although these modalities may delay reintubation and should be

interpreted cautiously [44, 66]. Despite meeting conventional readiness criteria and completing a successful spontaneous breathing trial, approximately 10–20% of general ICU patients require reintubation, an event consistently associated with prolonged mechanical ventilation, longer ICU stay, and mortality rates ranging from 25% to 50% [67-72] (**Table 2**).

In ABI patients, extubation failure most often reflects *neurological and airway-related mechanisms* rather than inadequate respiratory muscle performance or gas exchange. The predominant causes include ineffective airway protection due to absent or weak cough, impaired swallowing with aspiration, inability to clear secretions, and depressed consciousness leading to upper-airway obstruction, frequently related to posterior tongue displacement [73-75]. These mechanisms explain why extubation failure may occur despite preserved pulmonary mechanics and satisfactory performance during spontaneous breathing trials. Severity of neurological injury remains central: patients with markedly depressed consciousness or brainstem involvement are at particularly high risk, while advanced age and prolonged duration of mechanical ventilation further increase vulnerability, likely reflecting frailty and ICU-acquired weakness [73].

Importantly, extubation failure in ABI should not be interpreted as failure of the weaning process per se, but rather as a manifestation of unresolved neurological or airway-protection limitations. Recognition of these mechanisms is essential, as delayed reintubation after failed extubation may exacerbate secondary brain injury through hypoxemia, hypercapnia, agitation, or hemodynamic instability.

Tracheostomy

Against this background, tracheostomy frequently emerges as a management strategy following extubation failure or when extubation is deemed unsafe because of persistent neurological

impairment. Tracheostomy rates in ABI patients have increased over time, from approximately 17% in 2004 to over 20% in recent cohorts [76, 77]. reflecting both improved survival and ongoing challenges related to airway protection. ABI patients remain the ICU population most likely to undergo early tracheostomy, particularly when neurological recovery is uncertain and prolonged airway support is anticipated.

However, the optimal timing of tracheostomy remains controversial [78-83]. Contemporary multicenter trials have shown no significant differences in long-term functional or survival outcomes when tracheostomy is performed early (around day 5) versus later (approximately day 10) [84-86]. These findings support a more individualized approach, in which tracheostomy is deferred when there is a reasonable expectation of neurological improvement that may permit safe extubation. In routine practice, tracheostomy timing typically ranges between 9 and 12 days, although substantial inter-center variability persists (**Table 2**).

In ABI, the high prevalence of tracheostomy primarily reflects persistent deficits in consciousness, airway reflexes, and secretion management rather than failure to reduce ventilatory support. Many patients tolerate spontaneous or pressure-supported ventilation early but remain unsuitable for extubation because neurological recovery lags respiratory readiness. In this context, tracheostomy should be viewed not as an endpoint of failed weaning, but as a supportive strategy to facilitate airway clearance, neurological recovery, and rehabilitation while minimizing the risks associated with repeated extubation failure.

CONCLUSIONS

Weaning from invasive mechanical ventilation in patients with acute brain injury requires adaptation of conventional frameworks to account for neurological constraints not captured by

standard respiratory indices. By reframing Boles's Six Stages of Weaning for neurocritical care, this review emphasizes that ventilator liberation in ABI is driven primarily by cerebral physiology, airway protection, and neurological recovery rather than pulmonary mechanics alone.

In this population, successful completion of a spontaneous breathing trial does not equate to extubation readiness and must be interpreted alongside focused neurological and airway assessments. Extubation decisions are therefore guided predominantly by consciousness level, airway reflexes, and secretion management, while extubation failure most often reflects deficits in airway protection rather than inadequate gas exchange. Adoption of a physiology- and neurology-informed weaning framework may improve extubation safety, reduce preventable failures, and support more individualized decision-making in neurocritical care.

REFERENCES

- [1] Matić I, Majerić-Kogler V. Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. *Croatian medical journal* 2004;45(2):162-6.
- [2] Demling RH, Read T, Lind LJ, Flanagan HL. Incidence and morbidity of extubation failure in surgical intensive care patients. *Critical care medicine* 1988;16(6):573-7.
- [3] Esteban A, Alía I, Ibañez J, Benito S, Tobin MJ. Modes of mechanical ventilation and weaning. A national survey of Spanish hospitals. The Spanish Lung Failure Collaborative Group. *Chest* 1994;106(4):1188-93.
- [4] Romano AD, Paglia A, Bellanti F, Villani R, Sangineto M, Vendemiale G, et al. Molecular Aspects and Treatment of Iron Deficiency in the Elderly. *Int J Mol Sci* 2020;21(11).
- [5] Huang HY, Huang CY, Li LF. Prolonged Mechanical Ventilation: Outcomes and Management. *J Clin Med* 2022;11(9).
- [6] Boles J-M, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al. Weaning from mechanical ventilation. *29(5):1033-56*.
- [7] Roberts KJ, Goodfellow LT, Battey-Muse CM, Hoerr CA, Carreon ML, Sorg ME, et al. AARC Clinical Practice Guideline: Spontaneous Breathing Trials for Liberation From Adult Mechanical Ventilation. *Respir Care* 2024;69(7):891-901.
- [8] Zein H, Baratloo A, Negida A, Safari S. Ventilator Weaning and Spontaneous Breathing Trials; an Educational Review. *Emerg (Tehran)* 2016;4(2):65-71.
- [9] Robba C, Poole D, McNett M, Asehnoune K, Bösel J, Bruder N, et al. Mechanical ventilation in patients with acute brain injury: recommendations of the European Society of Intensive Care Medicine consensus. *Intensive Care Med* 2020;46(12):2397-410.
- [10] Taylor JD, Higgins AM, McArthur C, Quintard H, Shrestha GS, Udy A. Early management of adult severe traumatic brain injury: What researchers and clinicians must know. *Anaesth Crit Care Pain Med* 2025;44(6):101604.
- [11] Bösel J. Who Is Safe to Extubate in the Neuroscience Intensive Care Unit? *Semin Respir Crit Care Med* 2017;38(6):830-9.
- [12] Bösel J, Rabinstein AA. Extubation failure in patients with acute brain injury: a major problem still awaiting a solution. *Intensive Care Medicine* 2022;48(11):1611-3.
- [13] Namen AM, Ely EW, Tatter SB, Case LD, Lucia MA, Smith A, et al. Predictors of successful extubation in neurosurgical patients. *American journal of respiratory and critical care medicine* 2001;163(3 Pt 1):658-64.
- [14] Cinotti R, Bouras M, Roquilly A, Asehnoune K. Management and weaning from mechanical ventilation in neurologic patients. *Ann Transl Med* 2018;6(19):381.
- [15] Akella P, Voigt LP, Chawla S. To Wean or Not to Wean: A Practical Patient Focused Guide to Ventilator Weaning. *J Intensive Care Med* 2022;37(11):1417-25.
- [16] Robba C, Iannuzzi F, Taccone FS. Tier-three therapies for refractory intracranial hypertension in adult head trauma. *Minerva anesthesiologica* 2021;87(12):1359-66.

- [17] Tapia R, López-Herce J, Arias Á, Del Castillo J, Mencía S. Validity and Reliability of the Richmond Agitation-Sedation Scale in Pediatric Intensive Care Patients: A Multicenter Study. *Front Pediatr* 2021;9:795487.
- [18] Sharie SA, Almari R, Azzam S, Al-Husinat L, Araydah M, Battaglioni D, et al. Brain Protective Ventilation Strategies in Severe Acute Brain Injury. *Curr Neurol Neurosci Rep* 2025;25(1):68.
- [19] Bureau C, Demoule A. Weaning from mechanical ventilation in neurocritical care. *Revue Neurologique* 2022;178(1):111-20.
- [20] Sprügel MI, Isenberg ML, Sembill JA, Welte TM, Hopfengärtner R, Balk S, et al. Voices of patients' relatives to support weaning from mechanical ventilation: a randomized trial. *Brain Commun* 2025;7(3):fcf197.
- [21] Jeong BH, Lee KY, Nam J, Ko MG, Na SJ, Suh GY, et al. Validation of a new WIND classification compared to ICC classification for weaning outcome. *Annals of intensive care* 2018;8(1):115.
- [22] Pham T, Heunks L, Bellani G, Madotto F, Aragao I, Beduneau G, et al. Weaning from mechanical ventilation in intensive care units across 50 countries (WEAN SAFE): a multicentre, prospective, observational cohort study. *Lancet Respir Med* 2023;11(5):465-76.
- [23] Zeng J, Liu J, Lu Y, Fu J, Han D, Chen J, et al. C-reactive protein to albumin ratio and Glasgow Coma Scale score as the predictors for weaning outcomes in traumatic brain injury. *Ann Med* 2025;57(1):2472866.
- [24] Sclauser Pessoa IM, Franco Parreira V, Fregonezi GA, Sheel AW, Chung F, Reid WD. Reference values for maximal inspiratory pressure: a systematic review. *Canadian respiratory journal* 2014;21(1):43-50.
- [25] He Y, Zhao T. Ultrasound Evaluation of the Diaphragm in Clinical Anesthesia. *Journal of healthcare engineering* 2022;2022:2163225.
- [26] Sato R, Hasegawa D, Hamahata NT, Narala S, Nishida K, Takahashi K, et al. The predictive value of airway occlusion pressure at 100 msec (P0.1) on successful weaning from mechanical ventilation: A systematic review and meta-analysis. *Journal of critical care* 2021;63:124-32.
- [27] Carrie C, Gisbert-Mora C, Bonnardel E, Gauche B, Biais M, Vargas F, et al. Ultrasonographic diaphragmatic excursion is inaccurate and not better than the MRC score for predicting weaning-failure in mechanically ventilated patients. *Anaesth Crit Care Pain Med* 2017;36(1):9-14.
- [28] Roberts KJ, Goodfellow LT, Battey-Muse CM, Hoerr CA, Carreon ML, Sorg ME, et al. AARC Clinical Practice Guideline: Spontaneous Breathing Trials for Liberation From Adult Mechanical Ventilation. 2024;69(7):891-901.
- [29] Thille AW, Gacouin A, Coudroy R, Ehrmann S, Quenot J-P, Nay M-A, et al. Spontaneous-Breathing Trials with Pressure-Support Ventilation or a T-Piece. 2022;387(20):1843-54.
- [30] Figueroa-Casas JB, Montoya R, Arzabala A, Connery SM. Comparison between automatic tube compensation and continuous positive airway pressure during spontaneous breathing trials. *Respir Care* 2010;55(5):549-54.
- [31] Perren A, Brochard L. The importance of timing for the spontaneous breathing trial. *Ann Transl Med* 2019;7(Suppl 6):S210.
- [32] Frisvold S, Coppola S, Ehrmann S, Chiumello D, Guérin C. Respiratory challenges and ventilatory management in different types of acute brain-injured patients. *Crit Care* 2023;27(1):247.
- [33] Becker ER, Wetmore GC, Goodman MD, Rodriguez D, Jr., Branson RD. Review of Ventilation in Traumatic Brain Injury. *Respir Care* 2025;70(4):450-7.

- [34] Georgopoulos D, Taran S, Bolaki M, Akoumianaki E. Mechanical Ventilation in Patients with Acute Brain Injuries: A Pathophysiology-based Approach. *Am J Respir Crit Care Med* 2025;211(6):932-45.
- [35] Taran S, Angeloni N, Pinto R, Lee S, McCredie VA, Schultz MJ, et al. Prognostic Factors Associated With Extubation Failure in Acutely Brain-Injured Patients: A Systematic Review and Meta-Analysis. *Crit Care Med* 2023;51(3):401-12.
- [36] Angriman F, Amaral A, Fan E, Taran S, McCredie VA, Baker A, et al. Timing of Extubation in Adult Patients with Acute Brain Injury. *Am J Respir Crit Care Med* 2025;211(3):339-46.
- [37] Battaglini D, Taran S, Gualdi F, Cinotti R, Asehnoune K, Loggini A, et al. Spontaneous breathing trials as predictors of extubation outcomes in neurocritical care: insights from the ENIO study. *Intensive Care Med* 2026.
- [38] Capdevila M, De Jong A, Aarab Y, Vonarb A, Carr J, Molinari N, et al. Which spontaneous breathing trial to predict effort to breathe after extubation according to five critical illnesses: the cross-over GLOBAL WEAN study protocol. *BMJ Open* 2023;13(7):e070931.
- [39] Phoophiboon V, Rodrigues A, Ko M, Docci M, Madotto F, Schreiber A, et al. Pressure Support Ventilation in Neurosurgical Patients: Can We Safely Reduce Assistance? Evaluation of Neurosurgical Patients' Ventilation Distribution - The ENVISION Study. *Crit Care Explor* 2025;7(12):e1347.
- [40] Battaglini D, Parodi L, Cinotti R, Asehnoune K, Taccone FS, Orengo G, et al. Ventilator-associated pneumonia in neurocritically ill patients: insights from the ENIO international prospective observational study. *Respir Res* 2023;24(1):146.
- [41] Wang S, Zhang L, Huang K, Lin Z, Qiao W, Pan S. Predictors of extubation failure in neurocritical patients identified by a systematic review and meta-analysis. *PLoS One* 2014;9(12):e112198.
- [42] Taran S, Stevens RD, Perrot B, McCredie VA, Cinotti R, Asehnoune K, et al. Incidence and Outcomes of Acute Respiratory Distress Syndrome in Brain-Injured Patients Receiving Invasive Ventilation: A Secondary Analysis of the ENIO Study. *J Intensive Care Med* 2024;39(2):136-45.
- [43] Guillemin J, Rieu B, Huet O, Villeret L, Pons S, Bignon A, et al. Prospective multi-center evaluation of the incidence of unplanned extubation and its outcomes in French intensive care units. The Safe-ICU study. *Anaesth Crit Care Pain Med* 2024;43(5):101411.
- [44] Béduneau G, Pham T, Schortgen F, Piquilloud L, Zogheib E, Jonas M, et al. Epidemiology of Weaning Outcome according to a New Definition. The WIND Study. *Am J Respir Crit Care Med* 2017;195(6):772-83.
- [45] Patel S, Stollings JL, Casey JD, Wang L, Rice TW, Semler MW. Identifying Predictors of Extubation on the day of Passing an SBT in Critically ill Adults. *Journal of intensive care medicine* 2023;38(6):529-33.
- [46] Beuret P, Ennouari I, Tientcheu A, Giannoli A, Bonjean P, Capellier G, et al. National survey on practices of French intensivists in weaning from mechanical ventilation. *Anaesth Crit Care Pain Med* 2025:101658.
- [47] Wendell LC, Raser J, Kasner S, Park S. Predictors of extubation success in patients with middle cerebral artery acute ischemic stroke. *Stroke research and treatment* 2011;2011:248789.
- [48] Ho UC, Lu HY, Kuo LT. Risk Factors for Extubation Failure and Prolonged Intubation in Patients With Acute Brain Injury Following Surgery: A Retrospective Study. *World J Surg* 2025;49(10):2689-98.

- [49] Kutchak FM, Rieder MM, Victorino JA, Meneguzzi C, Poersch K, Forgiarini LAJ, et al. Simple motor tasks independently predict extubation failure in critically ill neurological patients. *Jornal brasileiro de pneumologia : publicacao oficial da Sociedade Brasileira de Pneumologia e Tisiologia* 2017;43(3):183-9.
- [50] Zeggwagh AA, Abouqal R, Madani N, Zekraoui A, Kerkeb O. Weaning from mechanical ventilation: a model for extubation. *Intensive Care Med* 1999;25(10):1077-83.
- [51] Bureau C, Demoule A. Weaning from mechanical ventilation in neurocritical care. *Revue neurologique* 2022;178(1-2):111-20.
- [52] Godoy DA, Rovegno M, Jibaja M. Extubation After Acute Brain Injury: An Unsolved Dilemma!! *Neurocritical care* 2024;40(2):385-90.
- [53] Asehnoune K, Seguin P, Lasocki S, Roquilly A, Delater A, Gros A, et al. Extubation Success Prediction in a Multicentric Cohort of Patients with Severe Brain Injury. *Anesthesiology* 2017;127(2):338-46.
- [54] Godet T, Chabanne R, Marin J, Kauffmann S, Futier E, Pereira B, et al. Extubation Failure in Brain-injured Patients: Risk Factors and Development of a Prediction Score in a Preliminary Prospective Cohort Study. *Anesthesiology* 2017;126(1):104-14.
- [55] Taran S, Perrot B, Angriman F, Cinotti R. Evaluating the Sum of Eye and Motor Components of the Glasgow Coma Score As a Predictor of Extubation Failure in Patients With Acute Brain Injury. *Crit Care Med* 2024;52(8):1258-63.
- [56] Prabhakar H, Mahajan C, Kapoor I, Shrestha GS, Picetti E, Robba C, et al. VENTilatory strategies for patients with severe traumatic brain injury in the LOW- and Middle-Income Countries. The VENTILOMICS survey. *Crit Care Sci* 2025;37:e20250062.
- [57] Chabanne R, Godet T, Andanson B, Borrel P, Astier L, Caumon E, et al. Prevention of extubation failure in neurocritical care patients with residual disorder of consciousness: the Brain-Injured Patients Extubation Readiness (BIPER) study protocol for a stepped-wedge cluster-randomised controlled trial. *BMJ Open* 2025;15(7):e104897.
- [58] Battaglini D, Cinotti R, Asehnoune K, Loggini A, Montagnani L, Ball L, et al. Associations of positive end-expiratory pressure (PEEP) with extubation failure and clinical outcomes in invasively ventilated patients with acute brain injury: A secondary analysis of the ENIO study. *J Crit Care* 2026;91:155274.
- [59] Battaglini D, Robba C, Patroniti NA. Mechanical ventilation in acute brain injured patients: balancing brain, lung, and diaphragm protection. *Curr Opin Crit Care* 2026;32(1):24-33.
- [60] Ko R, Ramos L, Chalela JA. Conventional Weaning Parameters do not Predict Extubation Failure in Neurocritical Care Patients. *Neurocritical Care* 2009;10(3):269-73.
- [61] Sterr F, Reintke M, Bauernfeind L, Senyol V, Rester C, Metzinger S, et al. Predictors of weaning failure in ventilated intensive care patients: a systematic evidence map. *Critical Care* 2024;28(1):366.
- [62] Caruso P, Albuquerque AL, Santana PV, Cardenas LZ, Ferreira JG, Prina E, et al. Diagnostic methods to assess inspiratory and expiratory muscle strength. *Jornal brasileiro de pneumologia : publicacao oficial da Sociedade Brasileira de Pneumologia e Tisiologia* 2015;41(2):110-23.
- [63] Ha TS, Oh DK, Lee HJ, Chang Y, Jeong IS, Sim YS, et al. Liberation from mechanical ventilation in critically ill patients: Korean Society of Critical Care Medicine Clinical Practice Guidelines. *Acute Crit Care* 2024;39(1):1-23.

- [64] Zhang X, Zheng S, Chen C, Wang S, Hu Y. Risk factors for failing endotracheal extubation in neurocritical patients: a retrospective cohort study. 2025;Volume 16 - 2025.
- [65] Miltiades AN, Gershengorn HB, Hua M, Kramer AA, Li G, Wunsch H. Cumulative Probability and Time to Reintubation in U.S. ICUs. *Crit Care Med* 2017;45(5):835-42.
- [66] Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 2013;187(12):1294-302.
- [67] Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients*. 2011;39(12):2612-8.
- [68] Frutos-Vivar F, Ferguson ND, Esteban A, Epstein SK, Arabi Y, Apezteguía C, et al. Risk Factors for Extubation Failure in Patients Following a Successful Spontaneous Breathing Trial. *Chest* 2006;130(6):1664-71.
- [69] Esteban A, Ferguson ND, Meade MO, Frutos-Vivar F, Apezteguia C, Brochard L, et al. Evolution of mechanical ventilation in response to clinical research. *American journal of respiratory and critical care medicine* 2008;177(2):170-7.
- [70] Frutos-Vivar F, Esteban A, Apezteguia C, González M, Arabi Y, Restrepo MI, et al. Outcome of reintubated patients after scheduled extubation. *Journal of critical care* 2011;26(5):502-9.
- [71] Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. *American journal of respiratory and critical care medicine* 1998;158(2):489-93.
- [72] Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. *Critical care medicine* 2011;39(12):2612-8.
- [73] Taran S, Angeloni N, Pinto R, Lee S, McCredie VA, Schultz MJ, et al. Prognostic Factors Associated With Extubation Failure in Acutely Brain-Injured Patients: A Systematic Review and Meta-Analysis*. 2023;51(3):401-12.
- [74] Zhang X, Zheng S, Chen C, Wang S, Hu Y. Risk factors for failing endotracheal extubation in neurocritical patients: a retrospective cohort study. *Frontiers in neurology* 2025;16:1562454.
- [75] da Silva AR, Novais MCM, Neto MG, Correia HF. Predictors of extubation failure in neurocritical patients: A systematic review. *Australian critical care : official journal of the Confederation of Australian Critical Care Nurses* 2023;36(2):285-91.
- [76] Tejerina E, Pelosi P, Muriel A, Peñuelas O, Sutherasan Y, Frutos-Vivar F, et al. Association between ventilatory settings and development of acute respiratory distress syndrome in mechanically ventilated patients due to brain injury. *Journal of critical care* 2017;38:341-5.
- [77] Cinotti R, Mijangos JC, Pelosi P, Haenggi M, Gurjar M, Schultz MJ, et al. Extubation in neurocritical care patients: the ENIO international prospective study. *Intensive Care Medicine* 2022;48(11):1539-50.
- [78] Kluge S, Baumann HJ, Maier C, Klose H, Meyer A, Nierhaus A, et al. Tracheostomy in the intensive care unit: a nationwide survey. *Anesthesia and analgesia* 2008;107(5):1639-43.
- [79] Veenith T, Ganeshamoorthy S, Standley T, Carter J, Young P. Intensive care unit tracheostomy: a snapshot of UK practice. *International archives of medicine* 2008;1(1):21.

- [80] Vargas M, Servillo G, Arditi E, Brunetti I, Pecunia L, Salami D, et al. Tracheostomy in Intensive Care Unit: a national survey in Italy. *Minerva anesthesiologica* 2013;79(2):156-64.
- [81] Añón JM, Escuela MP, Gómez V, García de Lorenzo A, Montejo JC, López J. Use of percutaneous tracheostomy in intensive care units in Spain. Results of a national survey. *Intensive Care Med* 2004;30(6):1212-5.
- [82] Fikkers BG, Fransen GA, van der Hoeven JG, Briedé IS, van den Hoogen FJ. Tracheostomy for long-term ventilated patients: a postal survey of ICU practice in The Netherlands. *Intensive Care Med* 2003;29(8):1390-3.
- [83] Vargas M, Sutherasan Y, Antonelli M, Brunetti I, Corcione A, Laffey JG, et al. Tracheostomy procedures in the intensive care unit: an international survey. *Critical care (London, England)* 2015;19(1):291.
- [84] Bösel J, Niesen WD, Salih F, Morris NA, Ragland JT, Gough B, et al. Effect of Early vs Standard Approach to Tracheostomy on Functional Outcome at 6 Months Among Patients With Severe Stroke Receiving Mechanical Ventilation: The SETPOINT2 Randomized Clinical Trial. *Jama* 2022;327(19):1899-909.
- [85] Camarda C, Premraj L, Pelosi P, Cho SM, Battaglini D. The stroke care puzzle: Does tracheostomy timing fit? *Critical care (London, England)* 2023;27(1):216.
- [86] Premraj L, Camarda C, White N, Godoy DA, Cuthbertson BH, Rocco PRM, et al. Tracheostomy timing and outcome in critically ill patients with stroke: a meta-analysis and meta-regression. *Critical care (London, England)* 2023;27(1):132.
- [87] Karthika M, Al Enezi FA, Pillai LV, Arabi YM. Rapid shallow breathing index. *Annals of thoracic medicine* 2016;11(3):167-76.
- [88] Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *The New England journal of medicine* 1991;324(21):1445-50.
- [89] Anderson CD, Bartscher JF, Scripko PD, Biffi A, Chase D, Guanci M, et al. Neurologic Examination and Extubation Outcome in the Neurocritical Care Unit. *Neurocritical Care* 2011;15(3):490-7.
- [90] Reis HFCd, Almeida MLO, Silva MFd, Moreira JO, Rocha MdS. Association between the rapid shallow breathing index and extubation success in patients with traumatic brain injury %J. 2013;25(3):212-7.
- [91] Casale R, Atzeni F, Bazzichi L, Beretta G, Costantini E, Sacerdote P, et al. Pain in Women: A Perspective Review on a Relevant Clinical Issue that Deserves Prioritization. *Pain and therapy* 2021;10(1):287-314.
- [92] Korupolu R, Uhlig-Reche H, Achilike EC, Reeh C, Pedroza C, Stampas A. Factors Associated With Ventilator Weaning Success and Failure in People With Spinal Cord Injury in an Acute Inpatient Rehabilitation Setting: A Retrospective Study. *Topics in spinal cord injury rehabilitation* 2022;28(2):129-38.
- [93] Xu SS, Tian Y, Ma YJ, Zhou YM, Tian Y, Gao R, et al. Development of a Prediction Score for Evaluation of Extubation Readiness in Neurosurgical Patients with Mechanical Ventilation. *Anesthesiology* 2023;139(5):614-27.
- [94] Bissett B, Leditschke IA, Green M, Marzano V, Collins S, Van Haren F. Inspiratory muscle training for intensive care patients: A multidisciplinary practical guide for clinicians. *Australian critical care : official journal of the Confederation of Australian Critical Care Nurses* 2019;32(3):249-55.
- [95] Chilakapati S, Rao JK, Paliwal B. Exploring the scope of inspiratory muscle training in difficult weaning: reflections on the multicentre RCT. *Journal of Intensive Care* 2025;13(1):13.

- [96] Parker MA, Sigmon SC, Villanti AC. Higher smoking prevalence among United States adults with co-occurring affective and drug use diagnoses. *Addictive behaviors* 2019;99:106112.
- [97] Bien Udós S, Souza GF, Campos ES, Farah de Carvalho E, Fernandes MG, Santoro I, et al. Maximum inspiratory pressure and rapid shallow breathing index as predictors of successful ventilator weaning. *Journal of physical therapy science* 2015;27(12):3723-7.
- [98] Videtta W, Vallejos J, Roda G, Collazos H, Naccarelli N, Tamayo A, et al. Predictors of Successful Extubation in Neurocritical Care Patients. *Acta neurochirurgica Supplement* 2021;131:91-3.
- [99] Major ME, Sommers J, Horrevorts E, Buist CM, Dettling-Ihnenfeldt DS, van der Schaaf M. Inspiratory muscle training for mechanically ventilated patients in the intensive care unit: Obstacles and facilitators for implementation. A mixed method quality improvement study. *Australian Critical Care* 2024;37(6):851-8.
- [100] Jo MR, Kim NS. The correlation of respiratory muscle strength and cough capacity in stroke patients. *Journal of physical therapy science* 2016;28(10):2803-5.
- [101] Kang SW, Shin JC, Park CI, Moon JH, Rha DW, Cho Dh. Relationship between inspiratory muscle strength and cough capacity in cervical spinal cord injured patients. *Spinal Cord* 2006;44(4):242-8.
- [102] Kang SW, Kang YS, Sohn HS, Park JH, Moon JH. Respiratory muscle strength and cough capacity in patients with Duchenne muscular dystrophy. *Yonsei medical journal* 2006;47(2):184-90.
- [103] Anderson CD, Bartscher JF, Scripko PD, Biffi A, Chase D, Guanci M, et al. Neurologic examination and extubation outcome in the neurocritical care unit. *Neurocrit Care* 2011;15(3):490-7.
- [104] He G, Han Y, Zhan Y, Yao Y, Zhou H, Zheng X. The combined use of parasternal intercostal muscle thickening fraction and P0.1 for prediction of weaning outcomes. *Heart & lung : the journal of critical care* 2023;62:122-8.
- [105] Flora D, Adel M, Pauline G, Quentin Q, Valentin C, Benoit P, et al. Automatic continuous P(0.1) measurements during weaning from mechanical ventilation: a clinical study. *Annals of intensive care* 2025;15(1):47.
- [106] Pérez J, Telias I. Airway Occlusion Pressure and Dyspnea during Mechanical Ventilation: Giving Words to the Pleas of the Respiratory Centers. 2024;210(2):139-41.
- [107] Telias I, Junhasavasdikul D, Rittayamai N, Piquilloud L, Chen L, Ferguson ND, et al. Airway Occlusion Pressure As an Estimate of Respiratory Drive and Inspiratory Effort during Assisted Ventilation. 2020;201(9):1086-98.
- [108] Muzette FM, Lima RBH, de Araújo Silva J, Comin TFB, Saraiva EF, Seki KLM, et al. Accuracy and Sensitivity of Clinical Parameters in Predicting Successful Extubation in Patients with Acute Brain Injury. *Neurology international* 2022;14(3):619-27.
- [109] Holm M, Tornvall P, Henareh L, Jensen U, Golster N, Alström P, et al. The MOVEMENT Trial. 2019;8(2):e010152.
- [110] Waljee JF, Cron DC, Steiger RM, Zhong L, Englesbe MJ, Brummett CM. Effect of Preoperative Opioid Exposure on Healthcare Utilization and Expenditures Following Elective Abdominal Surgery. *Annals of surgery* 2017;265(4):715-21.

- [111] van Oosten JP, Akoumianaki E, Jonkman AH. Monitoring respiratory muscles effort during mechanical ventilation. *Current opinion in critical care* 2025;31(1):12-20.
- [112] Bertoni M, Telias I, Urner M, Long M, Del Sorbo L, Fan E, et al. A novel non-invasive method to detect excessively high respiratory effort and dynamic transpulmonary driving pressure during mechanical ventilation. *Critical care (London, England)* 2019;23(1):346.
- [113] de Vries HJ, Tuinman PR, Jonkman AH, Liu L, Qiu H, Girbes ARJ, et al. Performance of Noninvasive Airway Occlusion Maneuvers to Assess Lung Stress and Diaphragm Effort in Mechanically Ventilated Critically Ill Patients. *Anesthesiology* 2023;138(3):274-88.
- [114] van Oosten JP, Akoumianaki E, Jonkman AH. Monitoring respiratory muscles effort during mechanical ventilation. 2025;31(1):12-20.
- [115] Pavez N, Damiani LF. Inspiratory and expiratory pause during pressure support ventilation: Maneuvers that we should incorporate into clinical practice. *Medicina Intensiva (English Edition)* 2022;46(4):213-6.
- [116] Carteaux G, Coudroy R. Monitoring effort and respiratory drive in patients with acute respiratory failure.10.1097/MCC.0000000000001271.

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Weaning Parameter	General ICU Patients (Thresholds & Predictive Value)	Brain-Injured Patients (Utility & Key Findings)
RSBI f/VT	RSBI < 105 breaths/min/L predicts weaning success with good sensitivity [87, 88]	Consistently shown to have poor predictive value in ABI [60, 89, 90].
VC	VC considered adequate when >10–15 mL/kg (~0.7–1.0 L), though specificity is limited [50, 91, 92]	Frequently unreliable due to reduced cooperation or cognitive impairment providing little predictive value for extubation readiness in ABI [93].
MIP	Thresholds ≤ –20 to –30 cmH ₂ O generally indicate sufficient inspiratory strength [62, 94-97].	Requires patient effort; measurements are often inaccurate or misleading and show no consistent association with extubation outcomes in ABI [98, 99]
MEP	Higher pressures reflect stronger expiratory muscle strength; values >28 cmH ₂ O have been associated with better outcomes in some	MEP is not a direct surrogate of cough strength. Cough strength is a critical determinant of success; weak or absent cough strongly predicts extubation failure in brain-injured patients [41, 47, 103].

	studies [50, 100-102].	
P0.1	Normal values ~3.5–4 cmH ₂ O; reflects respiratory drive with moderate predictive accuracy [26, 104-107]	Evidence is inconsistent; may contribute when combined with neurological assessments but has limited independent predictive value in ABI [26, 108-110]
Pocc	Helps assess effort reserve; <5 cmH ₂ O suggests weakness, >15 cmH ₂ O excessive effort [111-114].	Plays a limited and context-dependent role in ABI; extubation failure is more commonly driven by impaired airway protection and neurological dysfunction rather than respiratory mechanics [64, 75, 77, 98, 108].
PMI	Indicates balance between ventilatory support and patient effort; values >5–6 cmH ₂ O associated with risk of fatigue [115, 116].	May correlate with respiratory effort during weaning but adds limited value for extubation decision-making beyond neurological and airway protective assessments. [35, 98, 108, 109].

Comparison of commonly used respiratory weaning indices in general ICU populations and their applicability in patients with acute brain injury (ABI). ABI = acute brain injury; ICU = intensive care unit; MEP = maximal expiratory pressure; MIP = maximal inspiratory pressure; NIF = negative inspiratory force; P0.1 = airway occlusion pressure at 0.1 seconds; Pocc = maximal inspiratory occlusion pressure; PMI = pressure–muscle index; RSBI = rapid shallow breathing index; VC = vital capacity (maximal exhaled volume after deep breath).

Table 2: Comparison of Weaning and Extubation Outcomes in Patients With and Without Acute Brain Injury

Aspect	General ICU Patients	Neurocritical Care Patients
Extubation failure rate	Approximately 10–15% of planned extubations fail; rates may reach 30% in high-risk groups (COPD, heart failure, neuromuscular disease)	Higher failure rates (~20–25%), increasing to 30–38% in severe brain injury or neuromuscular respiratory failure
Primary causes of failure	Respiratory muscle fatigue, persistent pulmonary pathology, cardiac dysfunction, or upper airway obstruction	Predominantly impaired airway protection due to reduced consciousness, weak or absent cough/swallow, aspiration, or upper airway collapse; pulmonary factors may coexist but are seldom the primary cause
Tracheostomy	Considered after 7–10 days when prolonged ventilation is expected or repeated weaning attempts fail; performed in ~10–20% of ICU patients. Early tracheostomy may benefit selected subgroups	More common, especially in prolonged coma, severe stroke, or brainstem injury. Performed in ~30–50% of severe ABI cases. Timing is individualized; early tracheostomy has not demonstrated outcome benefits in major stroke trials
Outcome of extubation failure	Associated with increased ICU length of stay, morbidity, and mortality (25–50%); may delay rehabilitation. Post-extubation NIV can reduce failure risk in selected patients.	Similar morbidity and mortality risks, with additional concerns including delayed neurological assessment, sedation exposure, and potential cerebral hemodynamic consequences. Neuro ICUs typically defer extubation until maximal readiness is confirmed; if failure occurs, rapid reintubation and reassessment of reversible neurologic contributors are essential

Comparison of key determinants of weaning readiness, extubation success, and tracheostomy practices between general ICU and neurocritical care populations. ABI = acute brain injury; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; MIP = maximal

inspiratory pressure; RSBI = rapid shallow breathing index; SBT = spontaneous breathing trial;
VC = vital capacity.

Legend of the Figures

Figure 1. Neurological and Airway Readiness Markers for Extubation

This figure summarizes five key clinical indicators used to evaluate a patient's readiness for extubation. These include: (1) Spontaneous cough, reflecting the ability to clear airway secretions; (2) Neurological function, commonly assessed using the Glasgow Coma Scale (GCS) motor score; (3) Gag and swallow reflexes, which help determine adequacy of airway protection and secretion management; (4) Tongue protrusion, indicating preserved motor control and ability to follow commands; and (5) the VISAGE score, a structured assessment tool integrating these elements to support extubation decisions. Together, these markers assist clinicians in identifying patients who are neurologically and functionally prepared for safe liberation from mechanical ventilation [11, 41, 93].



Figure 2. Boles's six stages of weaning adapted for patients with acute brain injury.