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Review Article

Advances in mechanical ventilation for critically ill patients: strategies for respiratory support and complication management

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Abstract: Mechanical ventilation is essential for supporting critically ill patients with acute respiratory failure, especially those with acute respiratory distress syndrome (ARDS). In recent years, the focus of mechanical ventilation has shifted from simply improving gas exchange to implementing strategies that protect both the lungs and other organs. Lung-protective ventilation strategies - specifically low tidal volume ventilation and airway pressure limitation - have been shown to improve patient outcomes and are now considered standard care. More recent studies have emphasized the importance of driving pressure, individual positive end-expiratory pressure (PEEP) titration, and lung recruitability assessment in optimizing ventilation. Methods such as prone positioning, high-flow nasal cannula (HFNC) oxygen therapy, and noninvasive ventilation (NIV) have further expanded options for respiratory support. Simultaneously, emerging concepts such as patient self-inflicted lung injury (P-SILI), patient-ventilator asynchronies, and diaphragm dysfunction have enhanced our understanding of ventilator-related pathophysiology. Nonetheless, mechanical ventilation remains associated with various complications, including ventilator-induced lung injury (VILI), ventilator-associated pneumonia (VAP), intensive care unit-acquired weakness (ICUAW), and delirium. Effective prevention and management of these complications require an integrated approach, encompassing lung-protective ventilation, optimized sedation, early mobilization, and standardized weaning protocols. The potential of advanced monitoring and supportive technologies, such as electrical impedance tomography, esophageal pressure monitoring, closed-loop ventilation systems, and AI-assisted decision-making, continues to evolve. This review summarizes recent advances in clinical mechanical ventilation, including its underlying mechanisms, associated complications, and current prevention and treatment strategies, which may serve as references for the care of critically ill patients requiring respiratory support.

Keywords: Mechanical ventilation, ARDS, lung-protective ventilation, driving pressure, ventilator-induced lung injury, critical care medicine

Introduction

Respiratory failure is among the most common reasons for intensive care unit (ICU) admission and represents a major cause of mortality [1]. It imposes a substantial clinical burden due to its complex pathophysiology. Acute respiratory distress syndrome (ARDS) is a severe form of respiratory failure with high mortality rate and remains a major challenge in critical care medicine [2]. Many ICU patients require respiratory support for conditions such as ARDS, severe pneumonia, sepsis-induced respiratory failure, and acute exacerbation of chronic obstructive pulmonary disease (COPD). The rapid progression of these conditions often necessitates ventilatory support in addition to drug therapy. Mechanical ventilation is therefore a pivotal supportive therapy that stabilizes vital functions and allows time to treat the underlying disease.

Mechanical ventilation has evolved alongside modern critical care. The introduction of the "iron lung" during the poliomyelitis epidemic in the mid-century gradually replaced negative-pressure ventilation as the standard method for endotracheal intubation and positive-pressure

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ventilation. In the 21st century, the goals of respiratory support have changed fundamentally: correcting gas-exchange abnormalities is no longer the sole objective; greater emphasis is now placed on lung protection and preservation of organ function. In 2000, the ARDS Network published a randomized controlled trial demonstrating the clinical utility of low tidal volume ventilation, reducing 28-day mortality in ARDS patients from 39.8% to 31.0%, and ushering in an evidence-based era of mechanical ventilation [3]. Low tidal volume ventilation has since been established as an essential strategy in the management of ARDS. Noninvasive ventilation (NIV) and high-flow nasal cannula (HFNC) therapy have developed rapidly. Frat et al. [4] reported that these non-invasive modalities have become key first-line options in acute respiratory failure (ARF). Other studies have also shown that HFNC and NIV can improve oxygenation, reduce the need for endotracheal intubation and its associated complications [5]. Adjunctive techniques, including prone positioning and extracorporeal membrane oxygenation (ECMO), have also been integrated into the care of critically ill patients [6].

Evidence shows that mechanical ventilation itself can aggravate lung injury through inflammation and excessive lung stretch, a process known as ventilator-induced lung injury (VILI) [7]. Complications like ventilator-associated pneumonia (VAP), diaphragm dysfunction, ICU-acquired weakness (ICUAW), and delirium not only increase the duration of ventilation but may also adversely affect long-term quality of life and functional recovery. ICUAW has been associated with prolonged mechanical ventilation, longer hospital stays, and increased mortality [8], with nearly 50% of critically ill patients developing ICUAW, negatively impacting long-term functional outcomes [9].

Despite these risks, ventilatory parameters are still largely determined by clinical expertise, and individualized strategies remain underdeveloped. Pelosi et al. [10] suggested that ventilation tailored to lung physiology may represent a critical approach to optimizing outcomes. Therefore, a systematic review of recent advances in mechanical ventilation, along with a thorough examination of the mechanisms and prevention of associated complications, is both academically and clinically important. This review summarizes recent domestic and international studies, as well as key guidelines, to provide a reference for clinical practice.

Foundations of mechanical ventilation in respiratory support for critically ill patients

Core physiological mechanisms

Mechanical ventilation exerts multiple physiological effects. Increasing the fraction of inspired oxygen (FiO_2) enhances alveolar oxygenation. When combined with positive end-expiratory pressure (PEEP), additional benefits, including lung recruitment, improved ventilation-perfusion (V/Q) ratio, and increased functional residual capacity (FRC), contribute to correction of hypoxemia. HFNC may improve gas exchange by washing out anatomical dead space, reducing the work of breathing, and providing a low level of positive airway pressure [11]. Proper PEEP application also prevents shear stress caused by repetitive alveolar collapse and reopening, which is especially important in ARDS. Bos et al. [7] further emphasized that mechanical ventilation itself can contribute to lung injury, underscoring the need for lung-protective strategies.

Mechanical ventilation can also increase minute ventilation, facilitate carbon dioxide elimination, correct hypercapnia and respiratory acidosis, and help maintain internal homeostasis. Ventilatory support modifies respiratory mechanics, decreases the work of breathing, and improves ventilatory efficiency [12]. In cases of respiratory muscle fatigue or inadequate respiratory drive, mechanical ventilation can partially or completely substitute for the patient's spontaneous effort, thereby reducing oxygen consumption associated with breathing [13]. This support is essential for maintaining the balance between oxygen supply and demand. Moreover, careful control of arterial partial pressure of carbon dioxide ($PaCO_2$) along with renal metabolic compensation, helps maintain physiological pH and contributes to stable multi-organ function.

Clinical indications

Respiratory failure remains the primary indication for mechanical ventilation. Acute hypoxemic respiratory failure frequently occurs in severe pneumonia and ARDS. When standard oxygen therapy or noninvasive support fails to maintain adequate oxygenation, prompt esca-

lation to mechanical ventilation is critically warranted [11]. Progressive increase in $PaCO_2$ due to ventilatory failure frequently arises in acute exacerbation of COPD and in neuromuscular diseases. Previous study [14] demonstrated that pressure support modes such as bilevel positive airway pressure (BiPAP) can enhance carbon dioxide elimination and reduce respiratory muscle workload. Other important indications include impaired consciousness or loss of airway protective reflexes. For patients with acute hypoxemic respiratory failure, HFNC and NIV can serve as first-line therapies or as bridging support to prevent or delay endotracheal intubation [5, 15].

Selection of ventilatory support

Mechanical ventilation can be delivered in non-invasive or invasive approaches. NIV provides positive-pressure ventilation via a face mask or nasal mask. Strong evidence supports NIV in acute exacerbation of COPD and cardiogenic pulmonary edema. Rezoagli et al. demonstrated that continuous positive airway pressure (CPAP) and BiPAP increase end-expiratory lung volume, improve oxygenation, and reduce cardiac preload and afterload, thereby decreasing the need for intubation and mortality rates [14]. HFNC is increasingly recommended for patients with acute respiratory failure, as it washes out anatomical dead space, provides a low level of PEEP, and improves patient comfort [15, 16].

Patients with insufficient spontaneous ventilation or impaired airway protection require invasive mechanical ventilation. While invasive support provides a secure airway and more stable ventilatory assistance, it also carries risks such as ventilator-induced lung injury (VILI) [11]. Common modes include volume-controlled ventilation, pressure-controlled ventilation, and pressure support ventilation. These modes differ in how they regulate tidal volume, airway pressure, and the level of spontaneous breathing participation; therefore, selection should be individualized according to the patient's respiratory mechanics [17].

Recent advances in clinical strategies and technologies

Establishment and refinement of lung-protective ventilation

Over the past two decades, lung-protective ventilation strategies (LPVS) have become a mainstay of mechanical ventilation in critically ill patients. The 2000 ARDS Network trial introduced a low tidal volume strategy targeting 6 mL/kg predicted body weight and a plateau pressure <30 cmH_2O, designed for broad clinical application. This strategy significantly improved survival in ARDS patients compared with conventional higher tidal volume ventilation. Airway pressure-limited low tidal volume ventilation is now standard in ARDS management and has been shown to improve prognosis [18, 19]. Studies further recommended a tidal volume of 4-6 mL/kg and a plateau pressure below 30 cmH_2O to minimize VILI [20]. Some investigators have suggested that a fixed "6 mL/kg" target may need adjustment for individual patients to optimize lung protection [21].

Recently, driving pressure (ΔP) has gained increasing attention as a key safety indicator during mechanical ventilation. ΔP represents an integrated marker of lung stress and strain, and is specifically associated with mortality in ARDS [22]. Pelosi et al. [10] further emphasized that during individualized ventilation, driving pressure should be interpreted alongside PEEP and transpulmonary pressure. A 2015 analysis by Amato et al. demonstrated that driving pressure is a strong predictor of mortality in ARDS, indicating that clinicians should consider not only tidal volume and plateau pressure but also driving pressure when adjusting ventilator settings.

Individualized PEEP titration represents another key area of advancement. PEEP should be adjusted according to lung recruitability and hemodynamic status rather than applied as a fixed value [20, 23]. Metrics such as the recruitment-to-inflation (R/I) ratio can be used at the bedside to assess lung recruitability and guide PEEP selection [24]. Traditional fixed PEEP schemes (such as the ARDS Network FiO_2-PEEP table) are increasingly being supplemented by more precise approaches, including determination of the lower inflection point from pressure-volume curve, transpulmonary pressure-guided PEEP (with or without esophageal pressure monitoring), and bedside assessment of recruitability using ultrasound or electrical impedance tomography (EIT). Numerous studies have supported the utility of EIT in PEEP titration. For instance, findings from the ART and PHARLAP studies indicate that high PEEP combined with recruitment maneuvers is not superior to lower PEEP in all ARDS patients and may even be

harmful, further emphasizing the need for patient-specific PEEP titration [25, 26] (**Table 1**).

Permissive hypercapnia is widely accepted as an adjunct to low tidal volume ventilation. Evidence suggests that allowing moderate elevations in carbon dioxide, while closely monitoring acid-base status, may help preserve lung-protective effects. Intervention should be cautiously considered when pH falls below 7.20 (**Table 2**) [10].

Precision practice of individualized ventilation

With improved understanding of ARDS heterogeneity, ventilation strategies are moving away from a single-threshold model toward approaches based on phenotype recognition and lung recruitability. Pelosi et al. [10] suggest that ventilatory strategies customized according to lung physiology, morphology, and biological characteristics may better capture the true heterogeneity of ARDS than standardized approaches. Two broad inflammatory subphenotypes-hyperinflammatory and hypoinflammatory-have been consistently identified in ARDS populations using clinical and biomarker data. These subphenotypes differ substantially in their systemic inflammatory profiles, response to therapies such as PEEP and conservative fluid management, and overall prognosis. Although real-time bedside phenotyping is not yet widely implemented, recognizing these biological subtypes represents a major step toward truly individualized ventilation and may guide future therapeutic decisions [10].

Current management has transited from a focus solely on 'low tidal volume' toward a coordinated approach that simultaneously considers compliance, driving pressure, and recruitability [18]. Concurrently, bedside monitoring is increasingly integrated into precision ventilation. Optimizing PEEP should take into account both lung recruitability and hemodynamic response, and techniques such as EIT enable dynamic evaluation of regional ventilation. In summary, a key trend in the evolution of mechanical ventilation is the dynamic adjustment of ventilator settings guided by multiple indicators, including compliance, driving pressure, transpulmonary pressure, and bedside imaging (**Figure 1**).

Evidence-based progress in prone positioning

Prone positioning has evolved from an adjunctive measure into a core treatment for moderate-to-severe ARDS. Evidence indicates that prone positioning can improve oxygenation as part of lung-protective therapy by redistributing ventilation in the lungs [18]. Current guidelines recommend early implementation of prone positions in moderate-to-severe ARDS [27]. Prone ventilation enhances oxygenation by redistributing dorsal lung edema and exudate, recruiting collapsed alveoli (recruitment), and improving ventilation-perfusion (V/Q) matching through positional effects. The PROSEVA trial, published by Guérin et al. in 2013, demonstrated that among patients with moderate-to-severe ARDS (PaO_2/FiO_2 <150 mmHg), prone positioning for at least 16 hours per day significantly reduced 28-day mortality. Consequently, current recommendations generally favor early and prolonged prone positioning, usually at least 12-16 hours per session, for moderate-to-severe ARDS [27].

Awake prone positioning has gained significant attention during the COVID-19 pandemic. This strategy can enhance oxygenation and minimize or delay the need for intubation in non-intubated patients [5]. However, additional high-quality randomized controlled trials are needed to ascertain its impact on long-term outcomes, including mortality [18].

Expanded use of noninvasive ventilation and high-flow oxygen therapy

In recent years, HFNC has become one of the fastest-growing forms of noninvasive respiratory support. HFNC can deliver gas flow up to 60 L/min, allowing precise titration of FiO_2 from 21% to 100%. A PEEP-like effect may be achieved with the gas flow being delivered at 2-7 cmH_2O, and this maintains humidification of airway mucosa, thereby enhancing patient comfort. Evidence indicates that HFNC can reduce the need for escalation to invasive mechanical ventilation in ARF and has become an important first-line oxygen therapy [28]. By providing a stable high-flow of oxygen with a minor end-expiratory pressure effect, HFNC improves both oxygenation and patient comfort [29]. In the FLORALI trial, Frat et al. reported that HFNC was not inferior to NIV regarding intubation

Table 1. Framework for individualized ventilation strategies in ARDS

Dimension	Assessment Tool	Target Indicator	Applicable Population	Advantages	Limitations	Reference
Recruitability Assessment	R/I ratio	Recruitable vs non-recruitable	Moderate-to-severe ARDS	Guides individualized PEEP	Threshold variability	[24]
Regional Ventilation	EIT	Ventilation heterogeneity	All ARDS patients	Real-time monitoring	Limited availability	[25]
Transpulmonary Pressure	Esophageal pressure	Optimize lung stress	Selected complex cases	Physiological accuracy	Technically demanding	[10]
Driving Pressure Optimization	ΔP	<14 cmH_2O	All ARDS patients	Outcome-related	Affected by PEEP	[22]
Phenotype Stratification	Biomarkers/clinical data	Hyper- vs hypo-inflammatory	ARDS (research/ selected use)	Personalized therapy	Not widely implemented	[47]

Note: ARDS, acute respiratory distress syndrome; R/I ratio, recruitment-to-inflation ratio; EIT, electrical impedance tomography; ΔP, driving pressure; PEEP, positive end-expiratory pressure.

Table 2. Key parameters of lung-protective ventilation

Parameter	Recommended Range	Physiological Meaning	Potential Risk if Exceeded	Adjustment Strategy	Reference
Tidal Volume (VT)	4-6 ml/kg PBW	Reduce lung strain	Volutrauma	Adjust based on compliance	[48]
Plateau Pressure (Pplat)	<30 cmH_2O	Reflect lung stress	Barotrauma	Adjust VT or PEEP	[18]
Driving Pressure (ΔP)	<14 cmH_2O	Stress/strain indicator	Increased mortality	Optimize PEEP and VT	[22]
PEEP	Individualized	Prevent alveolar collapse	Hemodynamic compromise	Based on recruitability	[23]
$PaCO_2$	45-60 mmHg	Permissive hypercapnia	Acidosis if pH <7.20	Adjust respiratory rate	[10]

Note: VT, tidal volume; PBW, predicted body weight; Pplat, plateau pressure; ΔP, driving pressure; PEEP, positive end-expiratory pressure; $PaCO_2$, arterial partial pressure of carbon dioxide; FiO_2, fraction of inspired oxygen.

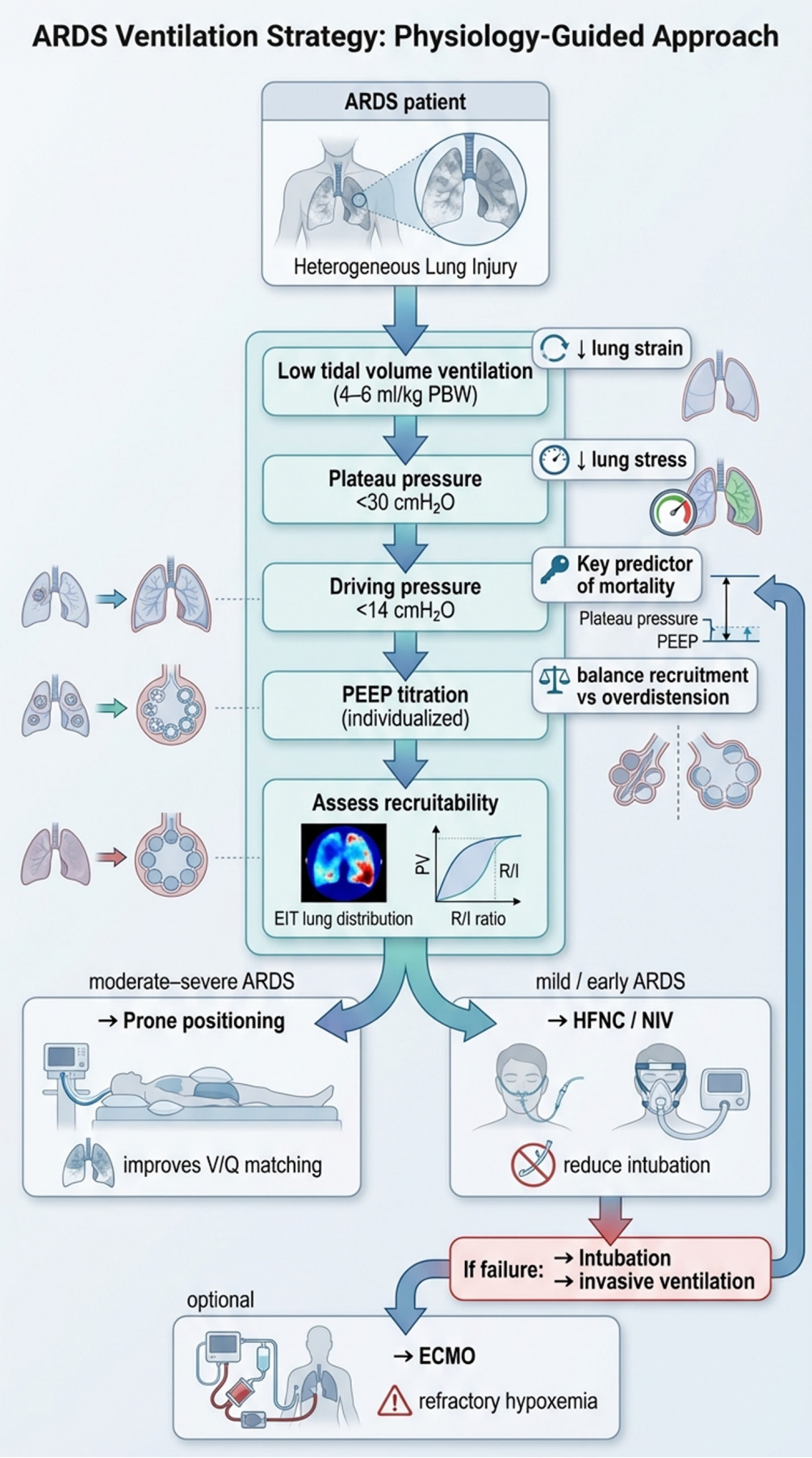
ARDS Ventilation Strategy: Physiology-Guided Approach
ARDS patient
Heterogeneous Lung Injury
Low tidal volume ventilation
(4–6 ml/kg PBW)
↓ lung strain
Plateau pressure
<30 cmH2O
↓ lung stress
Driving pressure
<14 cmH2O
Key predictor of mortality
Plateau pressure
PEEP
PEEP titration
(individualized)
balance recruitment vs overdistension
Assess recruitability
EIT lung distribution
PV
R/I
R/I ratio
moderate–severe ARDS
→ Prone positioning
improves V/Q matching
mild / early ARDS
→ HFNC / NIV
reduce intubation
If failure: → Intubation
→ invasive ventilation
optional
→ ECMO
refractory hypoxemia

Figure 1. Physiology-guided ventilation strategy for acute respiratory distress syndrome (ARDS). Mechanical ventilation in ARDS should be guided by respiratory mechanics and lung recruitability. Initial strategy includes low tidal volume ventilation (4-6 ml/kg predicted body weight), limitation of plateau pressure (<30 cmH_2O), and optimization of driving pressure (<14 cmH_2O) to reduce lung stress and strain. Positive end-expiratory pressure (PEEP) should be tailored to balance alveolar recruitment and overdistension. Assessment of lung recruitability using tools such as electrical impedance tomography (EIT) or recruitment-to-inflation (R/I) ratio may further refine ventilatory settings. In moderate-to-severe ARDS, early prone positioning improves ventilation-perfusion matching and oxygenation. In mild or early ARDS, noninvasive support such as high-flow nasal cannula (HFNC) or noninvasive ventilation (NIV) can be considered, with timely escalation to invasive ventilation if support fails. Extracorporeal membrane oxygenation (ECMO) may be used as rescue therapy in patients with refractory hypoxemia. Note: ARDS, acute respiratory distress syndrome; PBW, predicted body weight; PEEP, positive end-expiratory pressure; EIT, electrical impedance tomography; R/I ratio, recruitment-to-inflation ratio; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; ECMO, extracorporeal membrane oxygenation.

rates in acute hypoxemic respiratory failure and was associated with improved 90-day survival compared to standard face-mask oxygen therapy.

The ROX index, defined as the ratio of SpO_2/FiO_2 to respiratory rate, has been shown to be a reliable predictor of HFNC failure [30, 31]. It may therefore serve a useful tool for guiding sequential decisions regarding escalation of respiratory support.

The application of NIV has expanded in recent years. Current indications include ARF in immuno-compromised patients, prophylactic post-operative support, and sequential support following extubation. In certain populations, early extubation followed by NIV can reduce the duration of invasive mechanical ventilation and its associated complications [32]. HFNC and NIV may play complementary roles depending on the clinical scenario [28]. However, careful attention must be paid to the risk of patient self-inflicted lung injury (P-SILI) during noninvasive support, as discussed in Section 4.1. In cases of moderate-to-severe ARDS, timely escalation to invasive mechanical ventilation is essential in case of HFNC or NIV failure. Indicators of failure include persistent tachypnoea, pronounced use of accessory respiratory muscles, altered mental status, or worsening of oxygenation.

Frontiers in intelligent ventilation

Esophageal pressure monitoring enables estimation of transpulmonary pressure by assessing changes in intrathoracic pressure. This technique can be used to individualize PEEP settings based on physiological parameters. Currently, its application is mostly limited to research settings and complex clinical cases. Evidence suggests that ventilation guided by transpulmonary pressure may more accurately reflect lung tissue stress and help optimize PEEP [10].

Adaptive support ventilation (ASV) and INTELLiVENT-ASV are closed-loop ventilatory modes that can automatically adjust ventilator settings in real-time according to lung mechanics. Evidence indicates that ASV may reduce ventilation time and improve ventilatory efficiency compared to the conventional modes [33]. Closed-loop systems can also help maintain key respiratory parameters within target ranges, improve patient-ventilator interaction, and facilitate weaning [33].

Artificial intelligence (AI) and machine learning have shown potential in optimizing ventilator settings, predicting complications, and assessing readiness for weaning. Current research in AI-assisted mechanical ventilation is predominantly retrospective and may be subjected to bias and lack of external validation [34]. Other studies report that AI can perform effectively in ventilatory optimization and detection of effectively asynchrony, although broader clinical practice remains constrained by data quality and lack of standardization [35]. Large prospective studies are therefore required before these technologies can be reliably integrated into routine clinical decision-making.

In parallel with AI technologies, extracorporeal carbon dioxide removal ($ECCO_2R$) has attracted growing interest as a method to facilitate ultra-protective lung ventilation. By removing CO_2 through an extracorporeal circuit, $ECCO_2R$ allows further reduction of tidal volume (to below 4 mL/kg predicted body weight) and driving pressure, thereby potentially minimizing the mechanical forces that drive VILI. Although early clinical data demonstrate feasibility, evidence regarding safety, patient selection, and

impact on patient-centered outcomes remains limited. Current guidelines therefore restrict this strategy to carefully selected patients in experienced centers and highlight the need for additional randomized trials before wider implementation.

Nevertheless, even in their current form, these technologies offer incremental clinical value. ASV can serve as a safety net to prevent inadvertent delivery of injurious tidal volumes in patients with dynamic lung mechanics, while AI-assisted asynchrony detection may prompt earlier clinical review and ventilator adjustment. Their integration as decision-support adjuncts, rather than autonomous controllers, represents a pragmatic near-term translational goal.

Pathophysiology and integrated mechanism of ventilator-associated complications

The major mechanical ventilation-related implications, including VILI, VAP, VIDD, ICUAW, and delirium, together with their mechanisms, risk factors, early indicators, and prevention strategies, are summarized in **Table 3**.

Ventilator-induced lung injury and patient self-inflicted lung injury (VILI)

VILI represents the intrinsic risk of positive-pressure ventilation and involves several interrelated mechanisms. VILI primarily arises from excessive lung stress and strain and remains a major limitation of mechanical ventilation [36]. In addition, mechanical ventilation may affect distant organs via inflammatory and neural pathways [37]. Volutrauma, a form of VILI caused by overdistension, results from excessive tidal volume. Barotrauma occurs due to excessive transpulmonary pressure and may result in pneumothorax. Atelectrauma arises from repetitive alveolar collapse and reopening, particularly in heterogeneous lung injury, such as ARDS. These mechanical forces trigger an inflammatory response termed biotrauma. Evidence indicates that improper mechanical ventilation can exacerbate lung injury by eliciting inflammation and promoting patient-ventilator asynchrony, showing the interplay between mechanical and inflammatory processes in VILI [38]. The release of pro-inflammatory cytokines and infiltration of neutrophils may not only worsen lung injury but also damage distant organs, potentially leading to multi-organ failure. A vicious cycle between VILI and primary lung injury contributes to the high mortality observed in ARDS (**Figure 2**). The mechanical forces disrupt the alveolar-capillary barrier while upregulating pro-inflammatory mediators, perpetuating a feedback loop in which lung injury worsens systemic inflammation, which in turn renders the lung more susceptible to further mechanical stress [36, 37].

Parallel to VILI, patient self-inflicted lung injury (P-SILI) has emerged as an increasingly recognized entity. During periods of strong spontaneous respiratory drive, particularly under noninvasive support, vigorous inspiratory efforts can generate excessively high transpulmonary pressures and tidal volumes, thereby worsening lung injury [5]. Excessive inspiratory effort during noninvasive support may also increase the risk of lung injury in multiple studies [39]. The interplay between P-SILI and VILI highlights the importance of monitoring respiratory drive and promptly escalating to invasive ventilation when spontaneous efforts become injurious. Notably, P-SILI and VILI can coexist and exacerbate each other; persistent vigorous spontaneous efforts under insufficiently controlled ventilation increase transpulmonary pressure swings, increasing both atelectrauma and volutrauma, even when ventilator settings appear “protective” [5, 39].

P-SILI extends our understanding beyond ventilator-induced injury by showing that strong spontaneous respiratory effort alone can drive lung damage. Excessive respiratory drive generates large tidal volumes and strongly negative intrathoracic pressures, increasing global lung stress, causing pendelluft, and inducing regional overdistension, thereby worsening injury heterogeneity. This phenomenon is especially relevant during noninvasive support, where delayed recognition of excessive effort may lead to avoidable progression of lung injury. Management strategies for P-SILI therefore focus on early identification of high respiratory drive (using measures such as P0.1, esophageal pressure swings, or simple clinical signs) and timely escalation to controlled invasive ventilation with adequate sedation and analgesia to suppress injurious respiratory efforts [5, 39].

Ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is defined as pneumonia developing at least 48 hours after endotracheal intubation and initia-

Table 3. Mechanical ventilation-related complications

Complication	Mechanism	Risk Factors	Early Indicators	Prevention Strategies	Evidence Level	Reference
VILI	Excess lung stress/strain	High VT, high, high PEEP, patient-ventilator asynchrony	Reduced compliance	Lung-protective ventilation	Strong recommendation, high-quality evidence	[36]
VAP	Microaspiration and infection	Prolonged ventilation, antibiotic exposure, impaired airway humidification	Fever, secretions	VAP prevention bundle	Strong recommendation, moderate-quality evidence	[40]
VIDD	Diaphragm disuse or overload	Excessive or insufficient ventilatory support	Reduced diaphragm thickening fraction	Maintain spontaneous breathing; avoid over-assistance	Conditional recommendation, moderate-quality evidence	[42]
ICUAW	Inflammation and immobility	Deep sedation, immobility, systemic inflammation, malnutrition	Muscle weakness	Early mobilization	Conditional recommendation, moderate-quality evidence	[8]
Delirium	Sedation and inflammation	Benzodiazepines, deep sedation, immobility, sleep deprivation	Altered consciousness	ABCDEF bundle	Strong recommendation, moderate-quality evidence	[43]

Note: Evidence levels are graded according to current international guidelines. Strong recommendation indicates high confidence in the balance of benefits and harms; conditional recommendation indicates that the balance may depend on individual patient circumstances; VILI, ventilator-induced lung injury; VAP, ventilator-associated pneumonia; VIDD, ventilator-induced diaphragm dysfunction; ICUAW, intensive care unit-acquired weakness; VT, tidal volume; ΔP, driving pressure; PEEP, positive end-expiratory pressure.

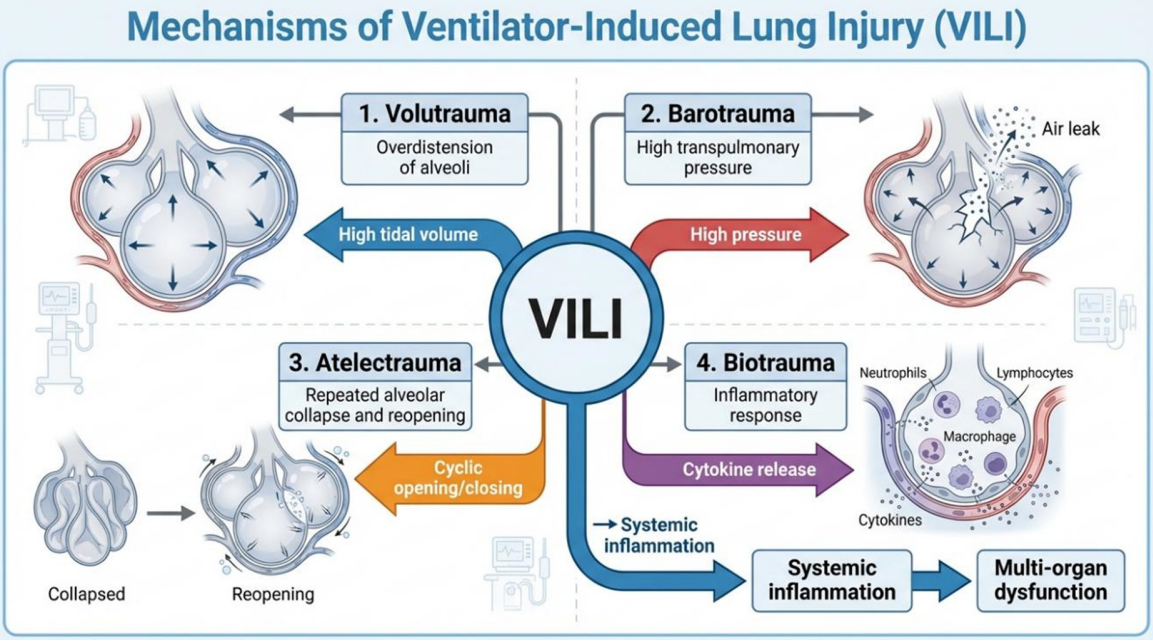

Figure 2. Pathophysiological mechanisms of ventilator-induced lung injury (VILI). VILI arises from the interaction of multiple mechanical and biological factors. Volutrauma results from alveolar overdistension caused by excessive tidal volume, while barotrauma is associated with elevated transpulmonary pressure, leading to structural disruption and air leakage. Atelectrauma is induced by repetitive alveolar collapse and reopening, generating shear stress in heterogeneous lung units. These mechanical insults activate biotrauma, triggering = inflammatory pathways, cytokine release, and immune cell recruitment. The resulting inflammatory cascade may extend beyond the lungs, contributing to systemic inflammation and multi-organ dysfunction. Note: VILI, ventilator-induced lung injury.

tion of mechanical ventilation. It is one of the most frequent hospital-acquired infections in the ICU. The risk of VAP is closely related to ventilation duration, ICU length of stay, and prior antibiotic exposure [40]. Impairment of airway humidification and impaired airway defense may further increase this risk [41]. VAP caused by multidrug-resistant organisms, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, is associated with particularly poor outcomes. The inflammatory milieu created by VILI and primary lung injury can also impair local innate immunity, rendering the lower respiratory tract more vulnerable to microbial invasion, thus establishing a bidirectional relationship between VILI and VAP [40, 41].

Diaphragm dysfunction and patient-ventilator asynchrony

Patient-ventilator asynchrony (PVA) is common in clinical practice but often underrecognized. Studies indicate that PVA can impair ventilatory efficiency, prolong ventilation duration, and worsen patient outcomes [35]. It has also been linked to lung injury and respiratory muscle injury [38], potentially worsening VILI and increasing sedation requirements. The incidence of PVA ranges from 10% to 40% of ventilated patients. Strategies to improve synchrony include optimizing trigger sensitivity, matching inspiratory flow to patient demand, and selecting an appropriate ventilation mode.

Diaphragm dysfunction is closely associated with PVA. Prolonged mechanical ventilation, especially in controlled modes, can cause diaphragmatic disuse atrophy. Diaphragm dysfunction may result not only from excessive ventilatory support but also from inadequate support or abnormal respiratory loading, such as that caused by PVA [38]. Recovery of diaphragm function is closely related to success weaning [42]. The diaphragm fiber cross-sectional area can decrease within hours of mechanical ventilation onset, a phenomenon termed ventilator-induced diaphragm dysfunction (VIDD). In addition to prolonging weaning, VIDD is also linked to long-term ventilator dependence. Excessive ventilatory assistance that almost completely replaces spontaneous effort is a major contributor, highlighting the

importance of maintaining some degree of safe spontaneous breathing. Critically, the interplay between PVA and diaphragm dysfunction forms a self-perpetuating loop: asynchrony promotes diaphragm injury and disuse, while a weakened diaphragm predisposes to eccentric contractions and further asynchrony during weaning, collectively increasing the duration of ventilation and the risk of VAP and VILI [35, 38].

These observations have led to the emerging concept of diaphragm-protective ventilation, which seeks to balance two opposing threats: disuse atrophy from excessive ventilator support and load-induced injury from insufficient support during high respiratory drive. Key elements of this strategy include maintaining inspiratory effort within a safe physiological range (often guided by P0.1, esophageal pressure-time product, or diaphragm electrical activity), monitoring diaphragm thickness and thickening fraction by ultrasound, and titrating pressure support to avoid both over-assistance and under-assistance [38, 42]. Integrating diaphragm-protective targets with conventional lung-protective ventilation remains a clinical challenge that requires further investigation. Current guidelines already caution against routine prolonged neuromuscular blockade and recommend early transition to assisted ventilation modes, implicitly reflecting diaphragm-protective principles [20, 27]. Formal incorporation of diaphragm-protective targets, including ultrasound-based thickening fraction monitoring and P0.1-guided pressure support titration, into future guideline revisions would represent a significant step toward operationalizing multiorgan protective ventilation at the bedside.

Hemodynamic effects

Positive intrathoracic pressure can significantly alter circulatory function. Evidence shows that alterations in respiratory mechanics during mechanical ventilation directly influence hemodynamic status, particularly at high PEEP [26]. Therefore, lung-protective ventilation must consider cardiopulmonary interactions. Increased intrathoracic pressure can compress the vena cava and reduce venous return and right ventricular preload, ultimately decreasing cardiac output. High PEEP may also elevate pulmonary vascular resistance and raise right ventricular afterload. Clinically, these changes may manifest as hypotension, narrow pulse pressure, and elevated central venous pressure. Accurate differentiation from hypovolemia is essential to guide appropriate fluid resuscitation and vasoactive therapy.

ICU delirium and weakness

Patients on mechanical ventilation frequently develop systemic complications, including ICU-acquired delirium and weakness. Studies have shown that sedation, immobility, and sleep disturbance are closely associated with delirium and can adversely affect prognosis [43]. Optimized sedation techniques may reduce these complications and improve ventilatory outcomes [44]. Delirium develops in about 60%-80% of ICU patients. Major contributing factors include deep sedation, immobility, sleep deprivation, pain, systemic inflammation, and benzodiazepine exposure. Delirium greatly increases the risk of long-term cognitive impairment and in-hospital mortality. ICUAW develops in up to 50% of patients undergoing prolonged mechanical ventilation, typically presenting as symmetric limb weakness and difficulty weaning from the ventilator. Persistent inflammation, immobility, malnutrition, hyperglycemia, and other metabolic disturbances contribute to its development and can adversely affect post-discharge quality of life. Delirium and ICUAW often interact in a vicious cycle: delirium-related agitation impedes early mobilization and exacerbates patient-ventilator asynchrony, while profound weakness prolongs ventilation and deepens sedation, further worsening cognitive dysfunction [43, 44].

Interplay and vicious cycles among ventilator-associated complications

The complications of mechanical ventilation are not isolated; rather, they are interconnected through shared pathophysiological pathways, creating multiple self-reinforcing vicious cycles with direct clinical implications. The core mechanical and biological drivers of these cycles are illustrated in **Figure 2**, and the concept can be conceptually extended to encompass systemic and neuromuscular dimensions. The first cycle links VILI, systemic inflammation, and VAP. VILI-induced release of pro-inflammatory cytokines and activation of neutrophil promotes systemic inflammation, which contributes to muscle catabolism and ICUAW [8, 36]. Simultaneously, the inflammatory milieu impairs

local innate immune defenses in the lower respiratory tract, increasing susceptibility to VAP caused by multidrug-resistant organisms [40]. VAP further prolongs mechanical ventilation, thereby amplifying cumulative exposure to VILI risk [40, 41].

The second cycle links diaphragm dysfunction, PVA, and prolonged ventilation. Excessive ventilatory support can causes disuse VIDD, while insufficient support or asynchrony causes load-induced injury [38]. A weakened diaphragm is more prone to eccentric contractions during weaning attempts, worsening asynchrony and increasing the need for sedation [35, 38]. Deeper sedation further suppresses respiratory drive and diaphragm activity, perpetuating VIDD and delaying liberation from the ventilator [42, 44]. The third cycle links delirium, immobility, and ICUAW. Delirium-related agitation interferes with early mobilization and physiotherapy, accelerating muscle wasting and ICUAW [43]. Profound weakness prolongs ventilation duration, increasing exposure to deep sedation, which further worsens cognitive dysfunction and delirium [43, 44]. This cycle significantly impacts long-term functional outcomes, as both delirium and ICUAW independently predict post-ICU cognitive impairment and reduced quality of life [8, 9].

Recognition of these interconnected cycles has direct clinical implications. Bundle-based interventions that simultaneously target multiple components are more effective than single-component strategies. For example, early mobilization interrupts both the immobility-ICUAW loop and the sedation-delirium loop; optimized pressure support titration addresses both VIDD and asynchrony; and shortened ventilation duration through daily weaning assessment reduces cumulative VAP and VILI risk. An integrated, multicomponent approach, coordinated through interdisciplinary rounds, daily checklists, and systematic audit, therefore represents the most clinically rational strategy for complication prevention [43, 45, 46].

Integrated bundles for weaning and prevention of complications

Standardized weaning protocols

Weaning is a critical step in mechanical ventilation management, accounting for approximately 40% of total ventilation time. Daily assessment of weaning readiness is essential. Eligible patients should undergo a spontaneous breathing trial (SBT) at the earliest opportunity. Evidence indicates that sequential NIV after extubation reduces ventilation time and related complications [32], and HFNC also plays an important role in preventing reintubation in high-risk patients [29]. Current clinical practice guidelines strongly recommend daily weaning readiness assessment and early SBT in eligible patients [32]. Diaphragm function is pivotal for successful liberation from the ventilator [42]. Weaning assessment should not rely solely on oxygenation and hemodynamic stability but also respiratory muscle function and general rehabilitation status.

Sedation, analgesia, and delirium prevention

The approach to sedation and analgesia has shifted from deep sedation toward analgesia-based light sedation. Comprehensive management according to the PADIS (Pain, Agitation, Delirium, Immobility, and Sleep) guidelines has been shown to reduce mechanical ventilation duration and length of ICU stay [43].

Daily sedation interruption has been shown to reduce ventilation duration and complication rates [44]. Deep sedation suppresses respiratory drive, and is also related to ICUAW, complicates weaning, and contributes to cognitive impairment. Current guidelines advocate maintaining the Richmond Agitation-Sedation Scale (RASS) between -1-0, with daily spontaneous awakening trials (SATs) and avoidance of benzodiazepines [43]. When sedation is required, propofol or dexmedetomidine are preferred over benzodiazepines due to a lower incidence of delirium [43]. Multimodal strategies combining daily SATs with SBTs significantly reduce mechanical ventilation duration in patients requiring prolonged support. Successful implementation of the ABCDEF bundle relies on consistent interdisciplinary rounds, validated assessment tools, and environmental modifications to promote sleep and early cognitive stimulation [43].

Early mobilization and diaphragm protection

Evidence supports that early rehabilitation can be safely performed once the patient is hemodynamically stable. Early mobilization may

enhance diaphragm function and shorten the duration of mechanical ventilation [45]. Recovery of diaphragm performance is closely correlated with successful weaning [42]. To maintain diaphragm activity, prolonged fully controlled ventilation should be avoided whenever possible, and assisted ventilation modes should be introduced early. Excessive ventilatory support may worsen diaphragm dysfunction [38]. As a result, routine use of neuromuscular blocking agents beyond 48 hours is not recommended due to the risk of VIDD [20, 27]. Randomized controlled trials indicate that early rehabilitation and timely transition to assisted ventilation modes can mitigate diaphragm dysfunction and reduce ventilation duration [38, 42, 46].

Maintenance of circulatory stability

Fluid resuscitation and vasoactive therapy adjustment should be guided by hemodynamic monitoring. Ventilator settings, particularly high PEEP and high-pressure ventilation, can significantly affect cardiac function and may overload the heart [26, 46]. In ARDS patients with acute cor pulmonale, limiting plateau pressure and driving pressure (≤14 cmH_2O), along with prone positioning, may lower pulmonary vascular resistance and right ventricular afterload [22, 26].

Prevention of VILI and VAP through bundle-based management

VILI prevention: Strict implementation of a lung-protective ventilation strategy (tidal volume of 4-6 mL/kg PBW, plateau pressure <30 cmH_2O, and driving pressure <14 cmH_2O) remains the cornerstone of VILI prevention [10, 20, 22]. Individualized PEEP titration, guided by lung recruitability rather than uniform high-PEEP application, is conditionally recommended [23, 24]. Emerging technologies such as EIT-guided PEEP optimization represents an emerging tool supported by systematic review evidence, though not yet incorporated into routine guideline recommendation [25]. In daily management, routine monitoring of respiratory mechanics, including airway resistance and compliance, is essential for early detection of lung stress and timely adjustment of ventilatory settings.

VAP prevention: Duration of ventilation and care-related factors are closely related to VAP [40], while airway humidification and quality of airway management directly affect VAP management outcomes [41]. Key interventions for VAP include: (1) Elevation of the head of the bed to 30°-45° to minimize aspiration risk; (2) Oral care to reduce bacterial colonization in oropharynx; (3) Use of endotracheal tubes with continuous subglottic suction when available; (4) Strict hand hygiene and aseptic technique by all healthcare personnel; (5) Daily assessment of weaning readiness to minimize the duration of mechanical ventilation [29]; (6) Appropriate antibiotic stewardship is also recommended to limit the emergence of resistant organisms [27, 40, 43]; (7) Maintenance of endotracheal cuff pressure between 20-30 cmH_2O, checked every 4-8 hours (with automatic regulation devices when available), to minimize microaspiration risk [40, 41]; (8) Proper airway humidification and regular suctioning to preserve mucosal function and reduce microaspiration risk [38, 41].

Evidence demonstrates that high compliance with these bundled interventions reduces VAP incidence and ICU length of stay [40, 41]. Effective implementation requires daily checklists, interdisciplinary rounds involving respiratory therapists and nurses, and ongoing audit with feedback to the clinical team [43].

Current problems and challenges

Despite consistent theoretical and technological advances in mechanical ventilation, several challenges remain in research and clinical practice. Achieving truly individualized ventilation remains difficult. Most ventilator settings still rely on population-based fixed targets. A lack of real-time feedback on physiological states limits precision. Optimal PEEP is primarily determined by individual lung recruitability and respiratory mechanics, not by a single parameter [23]. Bedside monitoring tools, such as EIT, can provide regional ventilation information; however, their broader applicability is limited by equipment availability and operational complexity [25]. Limited evidence and the absence of standardized implementation further restrict the practical application of individualized ventilation strategies [10].

Infectious complications remain difficult to prevent and manage. The incidence of VAP remains high in the ICU, often involving multidrug-resis-

tant organisms (MDROs). Risk factors include prolonged mechanical ventilation, antibiotic exposure, and suboptimal airway management such as airway humidification and aspiration prevention [41]. In daily practice, consistent adherence to preventive measures remains difficult.

Weaning difficulty and prolonged ventilator dependence are significant concerns. Each patient's health and specific condition strongly influence overall outcomes, including weaning success. Recovery of respiratory muscle function, particularly diaphragm performance, is essential for weaning success, and diaphragm dysfunction is common among patients with prolonged-ventilation [42]. Early extubation followed by NIV may improve outcomes in selected patients; however, evidence is limited and clinical decision-making remains uncertain [32].

Long-term outcome of ICU survivors represents another growing issue. Many patients are discharged with persistent cognitive impairment, muscle weakness, and psychological problems. Yet, most institutions lack fully established systems for systematic rehabilitation and long-term intervention.

Finally, the translation of intelligent ventilation technologies into clinical practice remains challenging. AI and machine learning have shown potential for optimizing ventilator settings, predicting complications, and assessing weaning readiness. However, most studies are retrospective, single-center, or both, and often lack external validation. For instance, Gallifant et al. [34] reported a lack of standardized reporting and a high risk of bias in many AI models. Interpretability and stability of AI systems in real-world clinical settings require further improvement [35]. Therefore, these technologies are not yet ready for routine clinical decision support.

Future perspectives

Mechanical ventilation is transitioning from experience-based practice to data- and physiology-driven precision management. Advances in respiratory mechanics monitoring and bedside imaging are enabling ventilation strategies tailored to lung recruitability, compliance, and transpulmonary pressure. Tools such as EIT allow dynamic assessment of regional ventilation and refinement of PEEP selection [23, 25].

AI and machine learning are paving the way for a new era of ventilatory management. Multidimensional data models have demonstrated potential for predicting patient-ventilator asynchrony and ventilation-related outcomes [35]; however, clinical application remains limited due to insufficient external validation and poor interpretability [34]. Advances in closed-loop ventilation may enable automatic adjustment of ventilator parameters based on the patient's condition. Abdelbaky et al. [33] proposed that adaptive ventilation modes might enhance ventilatory efficiency, but further studies are needed to establish their long-term clinical impact.

Future mechanical ventilation approaches are expected to adopt a broader organ-protective framework beyond the lungs. Mechanical ventilation may lead to ventilator-induced brain injury [37]. Furthermore, diaphragm protection and early rehabilitation are increasingly recognized as essential for improving prognosis [38]. Furthermore, extracorporeal support techniques, such as ECMO and extracorporeal carbon dioxide removal ($ECCO_2R$), have made ultra-protective ventilation feasible in patients with severe ARDS [18]. In summary, mechanical ventilation is likely to shift from isolated control of single parameters toward dynamic, multidimensional, and integrated decision support, emphasizing precision-driven and intelligent ventilatory management.

Translational perspective: from lung-protective to multi-organ protective, precision and intelligent closed-loop ventilation

Mechanical ventilation has evolved toward broader organ protection and increasingly precise decision-making, with direct implications for guidelines, clinical practice, and patient prognosis. Lung-protective ventilation established the principle of minimizing VILI via tidal volume restriction and plateau pressure limitation. However, accumulating evidence indicate that positive-pressure ventilation also affects hemodynamics, diaphragmatic integrity, and neurocognitive function, prompting a shift toward multi-organ protection. This broader framework has exposed the inadequacy of population-averaged parameters and catalyzed the development of precision ventilation guided by

individual respiratory mechanics. The complexity of individualized, real-time ventilation has created demand for intelligent closed-loop systems that integrate multidimensional physiological data to support automated decision-making.

From lung protection to multi-organ protection

Recognition that mechanical ventilation affects organs beyond the lungs has reshaped clinical targets and guideline recommendations. Regarding hemodynamic protection, limiting driving pressure to ≤14 cmH_2O and avoiding excessive PEEP reduces right ventricular afterload and prevent acute cor pulmonale, as increasingly reflected in expert consensus [22, 26]. Regarding diaphragmatic protection, the concept of diaphragm-protective ventilation - balancing disuse atrophy against load-induced injury by targeting a physiological range of inspiratory effort - has emerged as a clinical priority, supported by evidence linking preserved diaphragm thickening fraction to weaning success [38, 42]. Regarding neurocognitive protection, growing evidence demonstrates that both hypocapnia and hypercapnia may impair cerebrovascular autoregulation, highlighting the need for individualized $PaCO_2$ targets, particularly in patients with concomitant neurological injury [37]. Collectively, these developments have expanded ventilatory monitoring beyond airway pressures and oxygenation to include right ventricular function, diaphragm ultrasound assessment, and cerebral perfusion - a meaningful evolution in how ventilatory adequacy is defined in clinical guidelines [10, 20].

From standardized to precision ventilation

Precision ventilation translates population-level protective targets into individualized prescriptions tailored to patient respiratory mechanics and biological phenotype. Driving pressure has emerged as an outcome-relevant indicator, superior to tidal volume or plateau pressure alone: each 1 cmH_2O reduction in driving pressure is associated with a significant mortality risk reduction [22]. EIT-guided PEEP titration enables real-time detection of regional overdistension and collapse, achieving optimization beyond fixed FiO_2-PEEP tables [25]. The R/I ratio provides a bedside estimate of lung recruitability, identifying patients likely to benefit from higher PEEP while avoiding harm in others [24]. Recognition of hyperinflammatory and hypoinflammatory ARDS subphenotypes - which differ markedly in response to PEEP, fluid management, and anti-inflammatory therapies - further supports a phenotype-stratified approach to ventilation and adjunctive therapy [10, 47]. Although most of these precision tools are not yet strong guideline recommendations due to limited large-scale prospective evidence, their growing support in expert statements indicates they will likely inform future guideline revisions [10, 20, 27].

From manual adjustment to intelligent closed-loop ventilation

Closed-loop and AI-assisted ventilation systems represent the next translational frontier. These systems can continuously maintain ventilatory parameters within protective ranges and detect patient-ventilator asynchrony in real time. Meta-analyses show that adaptive support ventilation reduces ventilation duration and improves ventilatory efficiency compared with conventional modes [33], providing proof-of-concept that automated adjustment can deliver clinically meaningful benefits. AI-based algorithms have demonstrated promising sensitivity for asynchrony detection [35], which, if validated prospectively, could reduce the injurious effects of PVA on both the lungs and diaphragm. Nevertheless, clinical translation remains constrained by the predominantly retrospective, single-center design of existing studies [34], limited external validation, and insufficient model interpretability [35]. Before intelligent ventilation systems can be integrated into routine practice or guidelines, large multicenter randomized trials must evaluate their impact on patient-centered outcomes such as ventilation duration, complication rates, and long-term functional recovery.

Despite robust evidence underpinning current ventilation strategies, a considerable translational gap persists between research findings and routine bedside practice [10, 34, 47]. Bridging this gap requires not only technological innovation but also implementation science frameworks that promote interdisciplinary collaboration, standardized monitoring protocols, and systematic audit of guideline adherence. Integrating precision monitoring tools - such as EIT, esophageal pressure measurement, and

diaphragm ultrasound - into user-friendly clinical workflows represents a critical and immediately actionable step. Ultimately, the success of multi-organ protective, precision, and intelligent ventilation should be evaluated not only on physiological rationale but also on its ability to reduce complications, shorten ventilation duration, and improve long-term functional outcomes in critically ill patients.

The translational value of this conceptual transition can be understood in three dimensions. First, expanding the protective target from the lung alone to include the right ventricle, diaphragm, and brain gives clinicians a more comprehensive monitoring and intervention framework - a shift beginning to appear in updated international guidelines [10, 20]. Second, precision ventilation - guided by driving pressure, lung recruitability, transpulmonary pressure, and biological phenotyping - offers a pathway to individualize ventilatory prescriptions beyond fixed population targets, potentially improving survival and reducing complications in heterogeneous ARDS populations [22, 24, 25, 47]. Third, intelligent closed-loop systems and AI decision support - though not yet ready for routine implementation - offer a longer-term strategy to standardize adherence to evidence-based targets while preserving individualization, a combination that manual adjustment alone cannot reliably achieve [33-35]. Together, these advances outline a coherent, clinically actionable trajectory for mechanical ventilation, contingent upon future research prioritizing prospective validation, implementation science, and equitable access across diverse healthcare settings.

Conclusion

Mechanical ventilation remains an indispensable supportive therapy in modern critical care and is essential for the survival of patients with ARF. In recent decades, the field has evolved from establishing lung-protective ventilation to incorporating prone positioning, HFNC, and now toward individualized ventilation guided by physiological monitoring and emerging intelligent technologies. Accumulating high-quality evidence demonstrates that these advances have improved survival in critically ill patients.

Nevertheless, ventilator-associated complications, including VILI, VAP, diaphragm dysfunction, delirium, and hemodynamic suppression, continue to significantly impact outcomes. Prevention and management of these complications must be continuous throughout the entire ventilation course and requires close interdisciplinary collaboration and strict bundle-based management.

Key challenges persist, including limited individualization of ventilation, high complication burden, and difficulties in weaning. Optimized clinical practice should integrate bedside respiratory mechanics monitoring, ultrasound assessment, and biomarker-guided decision-making to dynamically modify ventilator settings. Coordinated implementation of early mobilization, rehabilitation, analgesia and light sedation, and standardized weaning protocols can mitigate iatrogenic harm, reduce ventilation duration, and improve long-term functional outcomes.

Looking forward, the integration of artificial intelligence for clinical decision support, closed-loop intelligent ventilation, and multi-organ protective strategies has the potential to usher critical care ventilation into a new era of precision, safety, and efficiency. The successful combination of standardized protocols with individualized care will continue to drive further development of mechanical ventilation.

Disclosure of conflict of interest

None.

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