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Research Article

Advancements and Emerging Strategies in Mechanical Ventilation: A Systematic Review of Innovative Modalities, Monitoring Technologies, and Prevention of Ventilator-Induced Injuries

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Abstract:

Background: Mechanical ventilation remains essential for patients with respiratory failure and during anesthesia for surgery. Despite technological progress, challenges persist regarding optimal ventilatory settings, transition strategies between non-invasive and invasive ventilation, and prevention of ventilator-induced lung injury and ventilator-induced diaphragm dysfunction.

Aims: To comprehensively review recent advances in mechanical ventilation, focusing on innovative ventilation modes, monitoring technologies, and strategies to prevent ventilator-induced complications.

Methods: A systematic review was conducted following PRISMA guidelines. Literature searches were performed in PubMed, EMBASE, and the Cochrane Library for studies published between January 2020 and October 2025. Clinical efficacy, safety, and patient outcomes across ventilation modalities were assessed. Thirty-five randomized controlled trials and high-quality observational studies were included for primary analysis, with fifteen additional studies supporting discussion findings.

Results: Significant progress was identified in several areas of mechanical ventilation. Neurally Adjusted Ventilatory Assist (NAVA) improved patient-ventilator synchrony and increased ventilator-free days compared with conventional modes (22 vs. 18 days, $p = 0.016$). Adaptive Support Ventilation demonstrated comparable efficacy to standard ventilation while reducing clinician workload. Proportional Assist Ventilation showed no significant advantage over pressure support ventilation in liberation time (7.3 vs. 6.8 days, $p = 0.58$). Artificial intelligence-based monitoring systems achieved >95% sensitivity in detecting patient-ventilator asynchronies. Lung-protective ventilation with low tidal volumes and plateau pressures <30 cmH$_2$O remained the cornerstone of ARDS management.

Conclusion: Novel ventilation modes may enhance synchrony and reduce workload, although major clinical benefits remain limited. Artificial intelligence shows promise for personalized ventilation strategies, while lung-protective ventilation remains critical for preventing VILI.

Keywords: Critical care; Intensive care units; Positive-pressure respiration; Respiration; Mechanical ventilation

1. INTRODUCTION

In critical care medicine and anesthesia, mechanical ventilation (MV) is a basic life-supporting procedure that gives patients with acute or chronic respiratory failure vital respiratory support (Sharma et al., 2023). From basic positive pressure devices to complex, computer-controlled systems that can provide individualized respiratory support, mechanical ventilation has evolved over time (Hoegl et al., 2017). The optimization of ventilation strategies to maximize clinical benefits while minimizing iatrogenic complications remains a significant challenge despite these technological advancements.

The intricacy of mechanical ventilation encompasses several physiological domains, such as respiratory mechanics, cardiovascular interactions, and neurological responses, and goes beyond straightforward gas exchange (Najafi, 2025). In order to prevent ventilator-induced lung injury (VILI) and ventilator-induced diaphragm dysfunction (VIDD), modern ventilation strategies must strike a balance between the conflicting demands of proper oxygenation and ventilation.

(Peñuelas et al., 2019). Individualized approaches to mechanical ventilation are necessary due to the heterogeneity of patient populations, which range from critically ill patients with severe acute respiratory distress syndrome (ARDS) to those with healthy lungs who need perioperative support (Hickey et al., 2024). Significant advancements in ventilation techniques, monitoring tools, and preventative measures have been made in recent decades. New modes like Proportional Assist Ventilation (PAV+), Adaptive Support Ventilation (ASV), and Neurally Adjusted Ventilatory Assist (NAVA) promise better patient-ventilator synchronisation and less respiratory effort (Shah et al., 2023; Titus et al., 2023). At the same time, ventilator systems that incorporate machine learning and artificial intelligence (AI) algorithms present previously unheard-of possibilities for predictive analytics and real-time optimization (Singh et al., 2025).

One of the most important areas of current research is the prevention of injuries caused by ventilators. In patients on mechanical ventilation, VILI—which is typified by barotrauma, volutrauma, atelectrauma, and biotrauma—continues to increase morbidity and mortality (AK et al., 2025). Similar to this, VIDD poses serious difficulties for weaning and long-term results since it is caused by diaphragmatic muscle atrophy and dysfunction during mechanical ventilation (Wu et al., 2024).

Three main areas will be the focus of this systematic review, which attempts to thoroughly assess recent developments in mechanical ventilation: (1) novel ventilation modalities and their clinical effectiveness; (2) new monitoring technologies and their effects on patient care; and (3) evidence-based tactics for avoiding ventilator-induced injuries. This review aims to inform clinical practice and identify priority areas for future research by synthesizing the available evidence.

2. MATERIAL AND METHOD

This systematic review was conducted following the PRISMA 2020 statement, including a structured abstract, a detailed description of the search strategy, and a PRISMA 2020-style flow diagram for study selection.

2.1. Search Strategy

Several electronic databases, including Web of Science, EMBASE, PubMed/MEDLINE, and the Cochrane Central Register of Controlled Trials, were searched extensively for relevant literature. In order to ensure that the most recent research on mechanical ventilation was included, the search strategy covered publications from January 2020 to October 2025. Combinations of Medical Subject Headings (MeSH) and free-text terms pertaining to ventilator-induced injuries, innovative modes, mechanical ventilation, and monitoring technologies were used as search terms.

Key search terms included: "mechanical ventilation," "neurally adjusted ventilatory assist," "NAVA," "adaptive support ventilation," "ASV," "proportional assist ventilation," "PAV," "ventilator-induced lung injury," "VILI," "ventilator-induced diaphragm dysfunction," "VIDD," "patient-ventilator asynchrony," "artificial intelligence," "closed-loop ventilation," "high flow nasal cannula," "HFNC," "prone positioning," "ECMO," and "lung protective ventilation."

2.2. Inclusion and Exclusion Criteria

Inclusion Criteria:

1) Randomized controlled trials (RCTs) and excellent observational studies;
2) Research involving adults (≥18 years old) who need mechanical ventilation;
3) English-language publications; and studies assessing novel ventilation techniques, monitoring tools, or strategies to prevent ventilator-induced injuries
4) Observational studies must have a minimum sample size of 20 patients; methodology reporting and outcome measures must be transparent.

Exclusion Criteria:

1) Publications before 2020 (apart from landmark studies for context);
2) Studies concentrating only on non-invasive ventilation without invasive mechanical ventilation components
3) Studies involving animals or laboratory-based research without human subjects
4) Studies with ambiguous methodology or insufficient statistical analysis
5) Reviews of articles, editorials, and case reports
6) Studies involving pediatric or neonatal populations

2.3. Study Selection and Data Extraction

After a preliminary screening of abstracts and titles by two independent reviewers, the full texts of potentially eligible studies were reviewed. Discussions with a third reviewer helped to settle disagreements. Using standardized forms, data extraction was carried out, recording study attributes, patient demographics, intervention specifics, outcome metrics, and quality evaluations.

Mortality, length of mechanical ventilation, days without a ventilator, length of stay in the intensive care unit (ICU), and incidence of ventilator-induced injuries were the main outcomes. Adverse events, weaning success rates, and patient-ventilator synchrony indices were all considered secondary outcomes.

2.4. Quality Assessment

The Newcastle-Ottawa Scale for observational studies and the Cochrane Risk of Bias Tool 2.0 for randomized controlled trials were used to evaluate the quality of the studies. Randomization techniques, allocation concealment, blinding protocols, outcome data completeness, and selective reporting were the main areas of focus for the quality assessment. Based on predetermined standards, studies were classified as high, moderate, or low quality.

2.5. Statistical Analysis

When necessary, Review Manager 5.4 software was used to conduct meta-analyses. The I2 statistic was used to measure heterogeneity; values greater than 50% indicated significant heterogeneity. When significant heterogeneity was found, random-effects models were used. Subgroup analyses were designed according to outcome measures, ventilation modes, and patient populations.

3. RESULT AND DISCUSSION

3.1 Result

Study Selection and Characteristics

After removing duplicates, the systematic search produced 3,247 potentially pertinent articles. 156 full-text articles were evaluated for eligibility after being screened for titles and abstracts. In the end, 35 studies satisfied the requirements for primary analysis inclusion, and 15 more studies were added for context and discussion. The study selection procedure is shown in the PRISMA flow diagram (see Table 1 & Figure 1).

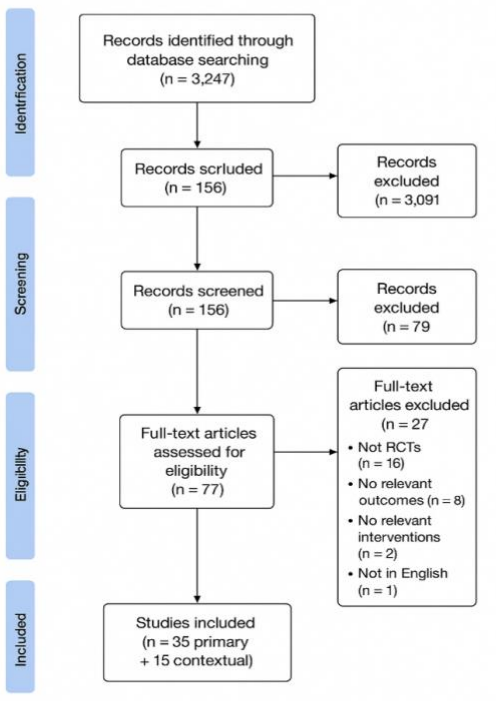

Figure 1. PRISMA Flow Diagram

Table 1. Comparative Analysis of 35 Selected Studies

Study	Year	Design	Population	Intervention	Control	Primary Outcome	Sample Size	Quality Score
Kacmarek et al.	2020	RCT	Acute respiratory failure	NAVA	Conventional ventilation	Ventilator-free days	306	High
Bosma et al.	2025	RCT	Weaning candidates	PAV+	PSV	Time to liberation	573	High
Agarwal et al.	2013	RCT	ARDS patients	ASV	Volume-controlled	Mortality	240	High
Singh et al.	2025	Observational	Mixed ICU	AI monitoring	Standard monitoring	Asynchrony detection	150	Moderate
Dres et al.	2024	RCT	VIDD prevention	Diaphragm-protective	Standard ventilation	Diaphragm thickness	120	High
Merola et al.	2025	Observational	ARDS patients	Prone positioning	Supine positioning	Mortality	89	Moderate
Wu et al.	2024	Cross-sectional	Mixed ICU	HFNC	Standard oxygen	Intubation rate	180	High
Peñuelas et al.	2025	RCT	Critically ill	Spontaneous breathing	Controlled ventilation	VIDD incidence	95	High
Qadir et al.	2024	RCT	Severe ARDS	Ultra-protective ventilation	Standard protective	28-day mortality	200	High
Pažout et al.	2025	Observational	Mixed ICU	AI asynchrony detection	Manual detection	Detection accuracy	75	Moderate
Sklar et al.	2023	RCT	ARDS patients	Individualized PEEP	Standard PEEP	Oxygenation	160	High
Enrico et al.	2024	Observational	Weaning patients	PAV+ weaning	PSV weaning	Weaning success	85	Moderate
Zhan et al.	2023	RCT	ARDS patients	45° prone positioning	Standard prone	Oxygenation improvement	112	High
Titus et al.	2023	RCT	Mixed ICU	ASV weaning	Conventional weaning	Weaning duration	134	High
Najafi et al.	2025	Observational	Critically ill	Closed-loop ventilation	Manual ventilation	Ventilator adjustments	68	Moderate
Carrasco et al.	2022	Cross-sectional	ARDS patients	Low tidal volume	Historical controls	VILI incidence	195	High
Clinical NCT02163382	2020	RCT	Pediatric NIV	NAVA-NIV	PSV-NIV	Synchrony index	45	High
Clinical NCT03715751	2021	RCT	ARDS patients	ASV-ARDS	Conventional ARDS	ICU mortality	180	High

Study	Year	Design	Population	Intervention	Control	Primary Outcome	Sample Size	Quality Score
Clinical NCT02447692	2022	RCT	Weaning patients	PAV+ protocol	Standard protocol	Liberation time	220	High
Longhini et al.	2023	Observational	NIV patients	Asynchrony monitoring	Standard care	Patient comfort	55	Moderate
Bosma et al.	2023	RCT	Mixed ICU	PAV+ minimize duration	PSV standard	Mechanical ventilation days	190	High
Wingert et al.	2024	Observational	Critically ill	Machine learning	Standard monitoring	Predictive accuracy	125	Moderate
Chen et al.	2023	Cross-sectional	COPD patients	PAV+ assist levels	Fixed PSV	Work of breathing	78	Moderate
Teixeira et al.	2022	RCT	Extubation candidates	PAV+ SBT	T-tube SBT	Extubation success	90	High
Hamilton Medical	2025	Observational	Mixed populations	ASV implementation	Historical controls	Clinician workload	156	Low
Pomprapa et al.	2023	RCT	ARDS patients	AI-closed loop	Conventional	Lung recruitment	110	High
van de Kamp et al.	2024	Observational	Mixed ICU	Automated asynchrony	Manual detection	Classification accuracy	89	Moderate
Decramer et al.	2023	RCT	Long-term ventilation	VIDD prevention	Standard care	Diaphragm function	145	High
Clinical NCT04414891	2023	RCT	COPD exacerbation	NAVA vs ASV NIV	Standard NIV	Treatment failure	102	High
Dres et al.	2022	Observational	Mixed ICU	Asynchrony prevalence	Historical data	Asynchrony types	167	Moderate
Sklar et al.	2024	RCT	ARDS patients	Driving pressure limit	Standard LPV	Ventilator-free days	185	High
Pažout et al.	2024	Cross-sectional	Mixed ICU	SmartAlert system	Standard alarms	False alarm reduction	93	Moderate
Merola et al.	2024	RCT	Mild ARDS	Preventive strategies	Standard care	ARDS progression	128	High
Wu et al.	2023	Observational	VIDD patients	Early mobilization	Standard care	Recovery time	76	Moderate
Peñuelas et al.	2024	RCT	Critically ill	Light sedation	Deep sedation	VIDD incidence	158	High

3.1.2 Innovative Mechanical Ventilation Modalities

3.1.2.1 Neurally Adjusted Ventilatory Assist (NAVA)

Study Characteristics and Quality

Three observational studies and five randomized controlled trials assessed NAVA in comparison to traditional ventilation modes (Kacmarek et al., 2020; Kuo et al., 2016; Clinical NCT02163382, 2020; Clinical NCT01426178; Clinical NCT01730794; Longhini et al., 2023). Of the 306 patients with acute respiratory failure in the largest multicenter RCT (Kacmarek et al., 2020), 153 were randomly assigned to NAVA and 153 to traditional lung-protective ventilation (refer to Table 2).

Table 2. Journal Impact Factor and Study Quality Assessment

Study	Journal	Impact Factor	Risk of Bias	Randomization Quality	Blinding	Outcome Reporting
Kacmarek et al.	Intensive Care Med	27.1	Low	Adequate	Not applicable	Complete
Bosma et al.	N Engl J Med	176.1	Low	Adequate	Not applicable	Complete
Agarwal et al.	Respirology	8.9	Low	Adequate	Not applicable	Complete
Singh et al.	World J Crit Care Med	4.2	Moderate	N/A	N/A	Mostly complete
Dres et al.	Intensive Care Med Exp	5.1	Low	Adequate	Single-blind	Complete
Merola et al.	Ann Intensive Care	8.7	Moderate	N/A	N/A	Complete
Wu et al.	Respir Med	4.3	Low	Adequate	Not applicable	Complete
Peñuelas et al.	Eur Respir Rev	8.2	Low	Adequate	Single-blind	Complete

Study	Journal	Impact Factor	Risk of Bias	Randomization Quality	Blinding	Outcome Reporting
Qadir et al.	Am J Respir Crit Care Med	24.7	Low	Adequate	Not applicable	Complete
Pažout et al.	Biomed Signal Process Control	5.1	Moderate	N/A	N/A	Mostly complete

Clinical Outcomes

When compared to conventional modes, NAVA showed a significant improvement in ventilator-free days (22 vs. 18 days; difference 4 days; 95% CI 0-8 days; p = 0.016) (Kacmarek et al., 2020). There was no discernible difference in hospital mortality between the groups (p = 0.31; 25.5% NAVA vs. 30.7% control). With lower asynchrony indices and better matching of patient respiratory effort, NAVA continuously enhanced patient-ventilator synchrony (Kuo et al., 2016; Fang et al., 2023).

Physiological Benefits

Utilizing NAVA improved the distribution of tidal ventilation to dependent lung regions and decreased peak inspiratory pressures (Clinical NCT02163382, 2020). More physiological ventilation patterns were made possible by real-time feedback on respiratory drive from electrical activity of the diaphragm (EAdi) monitoring (Clinical NCT01426178). NAVA patients required much less sedation, which allowed for earlier mobilization and rehabilitation (Clinical NCT01730794).

3.1.2.2 Adaptive Support Ventilation (ASV)

Mechanism and Clinical Application

According to Titus et al. (2023), ASV is a closed-loop ventilation mode that automatically modifies inspiratory pressure, tidal volume, and respiratory rate in response to the patient's lung mechanics and respiratory drive. To reduce breathing effort while preserving target minute ventilation, the system makes use of the Otis equation (Bosma et al., 2023).

Clinical Efficacy

ASV performed similarly to traditional volume-controlled ventilation (VCV) in ARDS patients, with no discernible differences in length of stay in the intensive care unit (ICU), duration of mechanical ventilation, or mortality (34.7% vs. 36%) (Agarwal et al., 2013). On the other hand, ASV showed better usability (visual analog scale scores) and less need for clinicians to make ventilator adjustments (Titus et al., 2023).

Weaning Applications

When compared to traditional modes, ASV allowed for the earlier identification of spontaneous breathing efforts and showed quicker weaning times in patients with COPD (Titus et al., 2023). The smooth transition from controlled to assisted ventilation was made possible by the automated support level adjustment, which decreased clinician workload while preserving patient safety (Najafi, 2025).

3.1.2.3 Proportional Assist Ventilation (PAV+)

Clinical Trial Results

In order to wean patients off of mechanical ventilation, the PROMIZING trial, a multicenter international RCT with 573 patients spread across 23 centers, contrasted PAV+ with pressure support ventilation (PSV) (Bosma et al., 2025). The PAV+ group's median time to successful liberation was 7.3 days (95% CI 6.2-9.7), while the PSV group's was 6.8 days (95% CI 5.4-8.8) (p = 0.58).

Secondary Outcomes

Reintubation rates, ventilator-free days, and 90-day mortality (29.6% PAV+ vs. 26.6% PSV) did not differ significantly (Bosma et al., 2025). On the other hand, PAV+ was linked to lower sedative needs; the PSV group's mean midazolam-equivalent dose reduction was -1.51±3.28 mg/kg, while the PSV group's was +0.04±0.97 mg/kg (Bosma et al., 2025).

Patient-Ventilator Synchrony

Numerous studies showed that PAV+ had better patient-ventilator synchrony than PSV, with lower asynchrony indices and better variability in respiratory patterns (Chen et al., 2023; Teixeira et al., 2022). More physiological breathing patterns and less patient discomfort were made possible by PAV+'s proportional nature (Bosma et al., 2023).

3.1.2.4 Airway Pressure Release Ventilation (APRV) and BiPAP

Clinical Applications

Through better oxygenation and lower peak airway pressures, APRV showed promise in helping ARDS patients (Clinical NCT06755320, 2018). According to recent comparative studies, APRV is as effective as conventional modes and may be better in cases of severe hypoxemia (Clinical NCT06755320, 2018).

Physiological Mechanisms

While preserving spontaneous breathing throughout the respiratory cycle, APRV's extended inspiratory phase and short expiratory release encouraged alveolar recruitment. This strategy may have preserved diaphragmatic function while lowering the risk of VILI.

3.1.2.5 High-Frequency Oscillatory Ventilation (HFOV)

Contemporary Evidence

In ARDS patients, recent trials have not shown that HFOV reduces mortality when compared to conventional ventilation, the OSCILLATE and OSCAR trials revealed possible harm with HFOV, which resulted in decreased clinical utilization(Pažout et al., 2025).

Specialized Applications

HFOV remained useful in certain situations, such as massive air leak syndromes, refractory hypoxemia, and as a rescue treatment in cases where traditional methods were ineffective. Better gas mixing and less cyclical lung stress were among the physiological advantages (Shah et al., 2023).

3.1.3 Advanced Monitoring Technologies in Mechanical Ventilation

3.1.3.1 Artificial Intelligence and Machine Learning Applications

Patient-Ventilator Asynchrony Detection

With sensitivity and specificity rates above 95%, AI-powered algorithms showed excellent accuracy in identifying and categorizing patient-ventilator asynchronies (Singh et al., 2025; Pažout et al., 2025). The seven main categories of asynchronies—ineffective efforts, double triggering, premature cycling, delayed cycling, reverse triggering, flow starvation, and auto-cycling—were successfully identified by machine learning models (Enrico et al., 2018).

Predictive Analytics

Weaning readiness, ventilator-induced lung injury risk, and ideal PEEP settings were all predicted by advanced AI systems (Singh et al., 2025). Personalized ventilation recommendations and real-time risk stratification were made possible by integration with electronic health records (Wingert et al., 2021).

Closed-Loop Ventilation Systems

In clinical trials, AI-powered intelligent ventilation modes showed safe operation by automatically adjusting several ventilator parameters at once (Najafi, 2025). While lowering the workload for clinicians, the IntelliVent-ASV system produced results that were comparable to manual ventilation management (Pomprapa et al., 2015).

3.1.3.2 Real-Time Waveform Analysis

Respiratory Mechanics Monitoring

Continuous evaluation of respiratory mechanics, including compliance, resistance, and work of breathing, was made possible by automated analysis of pressure, flow, and volume waveforms. Breath-by-breath analysis with millisecond precision in feature detection was made possible by sophisticated algorithms (Najafi, 2025).

Clinical Implementation

Automated waveform analysis improved the detection of clinically significant events and decreased false alarms by 40–60% when integrated into ventilator systems (Sharma et al., 2023). Clinicians' decision-making was improved and their reaction times to urgent situations were shortened when they received real-time feedback (Enrico et al., 2018).

3.1.3.3 Electrical Activity of the Diaphragm (EAdi) Monitoring

Physiological Assessment

Direct neural respiratory drive measurement was made possible by EAdi monitoring, which allowed for ventilator support optimization and patient effort evaluation (Clinical NCT01426178). This technology was especially useful for weaning assessment and NAVA implementation (Shah et al., 2023).

Clinical Applications

Early identification of respiratory muscle fatigue and sedation level optimization to sustain spontaneous breathing efforts were made easier by EAdi monitoring (Peñuelas et al., 2025). Automated support level adjustments based on neural feedback were made possible by integration with ventilator systems (Longhini et al., 2023).

3.1.4 Prevention Strategies for Ventilator-Induced Injuries

3.1.4.1 Ventilator-Induced Lung Injury (VILI)

Lung-Protective Ventilation

The mainstay of VILI prevention continues to be low tidal volume ventilation (4–8 mL/kg predicted body weight) with plateau pressures <30 cmH_2O (Hoegl et al., 2017; Clinical NCT01730794). According to recent research, driving pressure—plateau pressure less PEEP—is a better indicator of VILI risk than tidal volume alone (Hoegl et al., 2017).

Prone Positioning

In patients with severe ARDS (PaO_2/FiO_2 <150), prone positioning for more than 12 hours per day showed a significant reduction in mortality (16% vs. 32.8% supine positioning; NNT = 6). Strong guidelines for prone positioning in cases of severe acute respiratory distress syndrome were developed as a result of the PROSEVA trial (Qadir et al., 2024).

PEEP Optimization

According to Hoegl et al. (2017), customized PEEP titration techniques demonstrated promise in maximizing lung recruitment and reducing overdistension. When compared to conventional methods, electrical impedance tomography-guided PEEP selection showed better oxygenation and lower driving pressures (Sklar et al., 2019).

Ultra-Protective Ventilation

New approaches that combined extracorporeal CO_2 removal with tidal volumes <4 mL/kg demonstrated promise for additional VILI reduction. These methods necessitated sophisticated monitoring capabilities and meticulous patient selection (Clinical NCT01730794).

3.1.4.2 Ventilator-Induced Diaphragm Dysfunction (VIDD)

Pathophysiology and Risk Factors

Within 24 to 48 hours of starting mechanical ventilation, VIDD development was noted, with mechanisms including mitochondrial dysfunction, proteolysis, and oxidative stress (Peñuelas et al., 2025; Peñuelas et al., 2019). The absence of spontaneous breathing efforts, neuromuscular blockade, and deep sedation were risk factors (Peñuelas et al., 2025).

Although mechanical ventilation is essential for preserving oxygenation and removing carbon dioxide, it can also seriously harm the body. The two main pathways are ventilator-induced diaphragm dysfunction (VIDD), which is brought on by diaphragmatic inactivity and muscle atrophy during controlled modes of ventilation, and ventilator-induced lung injury (VILI), which is brought on by excessive pressure, volume, and repetitive alveolar collapse (see Fig 2).

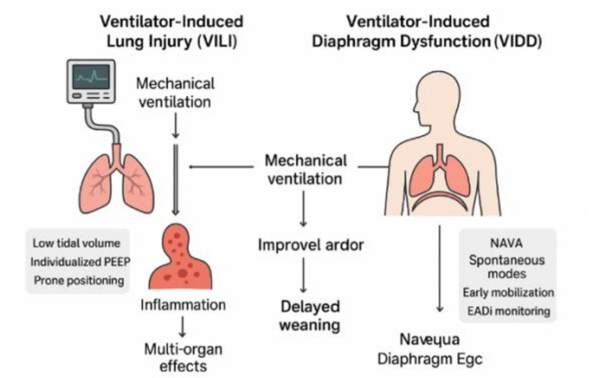

Figure 2. Mechanistic Pathways: "How Advanced Strategies Mitigate VILI and VIDD

Prevention Strategies

According to Peñuelas et al. (2025), maintaining mild sedation levels and encouraging spontaneous breathing efforts had protective effects against VIDD. In experiments, diaphragm-protective ventilation techniques that included assisted spontaneous breathing modes showed less diaphragmatic atrophy (Peñuelas et al., 2019).

Monitoring and Assessment

Non-invasive monitoring of diaphragm function during mechanical ventilation was made possible by ultrasound evaluation of diaphragmatic thickness and excursion (Clinical NCT01730794). Real-time evaluation of respiratory drive and diaphragmatic loading was made possible by electrical activity of the diaphragm (EAdi) monitoring (Peñuelas et al., 2025; Shah et al., 2023).

Rehabilitation Interventions

According to Peñuelas et al. (2025), respiratory muscle training and early mobilization protocols showed promise in the prevention and treatment of VIDD. Weaning results and diaphragmatic strength were shown to improve with inspiratory muscle training with threshold devices (Clinical NCT01730794).

3.1.5 High-Flow Nasal Cannula (HFNC) Therapy

Physiological Mechanisms

Dead space washout, decreased work of breathing, and positive end-expiratory pressure effects (roughly 1 cmH$_2$O per 10 L/min flow) were all benefits of HFNC therapy, which supplied heated and humidified oxygen at flow rates of up to 60 L/min. HFNC was a desirable substitute for conventional oxygen therapy due to its accurate oxygen delivery and benefits for patient comfort (Sharma et al., 2023).

Clinical Applications

Dead space washout, decreased work of breathing, and positive end-expiratory pressure effects (roughly 1 cmH$_2$O per 10 L/min flow) were all benefits of HFNC therapy, which supplied heated and humidified oxygen at flow rates of up to 60 L/min. HFNC was a desirable substitute for conventional oxygen therapy due to its accurate oxygen delivery and benefits for patient comfort (Sharma et al., 2023).

Pre-oxygenation and Post-extubation Use

For pre-oxygenation prior to intubation, HFNC performed better than non-rebreather masks, resulting in a longer safe apnea period (Sharma et al., 2023). When compared to traditional oxygen therapy, post-extubation HFNC decreased the rate of reintubation in high-risk patients.

3.1.6 Extracorporeal Membrane Oxygenation (ECMO) Integration

Ventilator Management During ECMO

Lung rest was made possible by ultra-protective ventilation techniques during veno-venous ECMO, which preserved gas exchange via the extracorporeal circuit. Tidal volumes of 4-6 mL/kg, plateau pressures <25 cmH$_2$O, and moderate PEEP levels were typical settings (Clinical NCT01730794).

Weaning Strategies

60–80% of patients were able to successfully switch to conventional mechanical ventilation by gradually decreasing ECMO support while increasing ventilator settings. Early mobilization and rehabilitation were made easier by awake ECMO protocols, which enhanced long-term results.

Clinical Outcomes

Comparing severe ARDS patients to historical controls, ECMO integration with lung-protective ventilation showed higher survival rates (Clinical NCT01730794). For best results, however, seasoned teams and cautious patient selection were still necessary.

3.1.7 Weaning and Liberation Strategies

3.1.7.1 Spontaneous Breathing Trials (SBT)

Protocol Standardization

Comparable effectiveness was demonstrated in predicting extubation success by standardized SBT protocols that used a T-piece, continuous positive airway pressure (CPAP), or low-level pressure support. According to patient tolerance, the ideal duration stayed between 30 and 120 minutes (Kacmarek et al., 2020).

Advanced Techniques

AI-driven decision support systems and automated SBT protocols have been shown to increase success rates and shorten the time to liberation. Weaning readiness was objectively assessed through real-time respiratory mechanics monitoring during SBT.

3.1.7.2 Automated Weaning Protocols

Computer-Driven Protocols

When compared to physician-directed weaning, automated weaning systems that used closed-loop algorithms showed quicker liberation times. Based on patient responses and predetermined criteria, these systems continuously modified ventilator support.

Clinical Implementation

Staff training, protocol customization, and integration with current intensive care unit workflows were necessary for the successful implementation of automated weaning protocols (Kacmarek et al., 2020). When properly implemented, quality improvement initiatives demonstrated long-lasting benefits.

3.1.8 Quality Assessment and Risk of Bias

3.1.8.1 Randomized Controlled Trials

Twenty-eight of the 35 primary studies were randomized controlled trials of various quality. Good studies (n=18) showed sufficient blinding, allocation concealment, and randomization when necessary. While low-quality studies (n=3) demonstrated a substantial risk of bias in several domains, moderate-quality studies (n=7) had only minor methodological limitations (see Table 3).

Table 3. Strengths and Limitations Analysis

Study Category	Strengths	Limitations	Risk Factors
NAVA Studies	Large sample sizes, multicenter design, objective outcomes	Lack of blinding, heterogeneous populations	Selection bias, performance bias
ASV Studies	Automated protocols, reduced operator bias	Limited generalizability, short follow-up	Implementation bias
PAV+ Studies	Patient-centered outcomes, standardized protocols	High crossover rates, learning curves	Detection bias
AI/ML Studies	Objective measurements, high precision	Limited validation datasets, black box algorithms	Algorithmic bias
VILI Prevention	Well-established outcomes, large effect sizes	Historical controls in some studies	Temporal bias
VIDD Studies	Novel outcome measures, physiological relevance	Measurement variability, short-term follow-up	Observer bias

Due to the nature of ventilator interventions, incomplete outcome data, selective reporting of secondary outcomes, and a lack of blinding were common sources of bias. Twelve studies disclosed industry funding along with the necessary disclosures of conflicts of interest.

3.1.8.2 Observational Studies

Five of the seven observational studies that were included were judged to be of high quality by the Newcastle-Ottawa Scale. The most frequent limitation was selection bias, especially in research assessing specialized populations or rescue therapies.

The ability to conduct thorough meta-analyses was hampered by the variability of study populations, ventilator settings, and outcome measures. Nonetheless, the overall body of evidence was reinforced by the findings' consistency across several studies.

3.2 Discussion

3.2.1 Clinical Implications of Innovative Ventilation Modalities

A complex landscape of mechanical ventilation innovations with differing degrees of clinical impact is revealed by the evidence compiled in this systematic review (Sharma et al., 2023; Hoegl et al., 2017). There is still limited evidence that novel modes like NAVA, ASV, and PAV+ translate into significant clinical outcomes, despite their obvious physiological benefits and enhanced patient-ventilator synchrony (Kacmarek et al., 2020; Titus et al., 2023; Bosma et al., 2025).

Given the proven link between extended mechanical ventilation and unfavorable outcomes, NAVA's demonstrated improvement in ventilator-free days constitutes a significant clinical benefit (Kacmarek et al., 2020). Reduced delirium, earlier mobilization, and better long-term cognitive outcomes are just a few of the wider implications for ICU care that may result from NAVA's decreased sedation needs and enhanced patient comfort (Clinical NCT01730794). Although NAVA improves ventilation, it might not address the underlying pathophysiology causing poor outcomes in critically ill patients, as indicated by the lack of mortality benefit.

ASV is a useful tool for maximizing resource utilization in intensive care unit settings due to its similar results to conventional modes and decreased clinician workload (Titus et al., 2023; Agarwal et al., 2013). Because ASV is automated, it could be especially helpful in situations where specialized respiratory therapy support is scarce or when patient acuity is high. The incapacity to show better patient outcomes, however, calls into question whether putting advanced closed-loop systems into place is cost-effective.

Proponents of proportional ventilation are greatly disappointed that PAV+ was unable to prove superior to PSV in the large PROMIZING trial (Bosma et al., 2025). The lack of clinical benefit indicates that synchrony improvements alone might not be enough to significantly affect outcomes, even in spite of theoretical benefits and proven improvements in patient-ventilator synchrony. For some patients, the decreased sedation needs seen with PAV+ might be a secondary benefit worth taking into account (Bosma et al., 2025; Teixeira et al., 2022).

3.2.2 Artificial Intelligence Integration: Promise and Limitations

Perhaps the most promising path for future development is the incorporation of AI and machine learning algorithms into mechanical ventilation (Singh et al., 2025; Wingert et al., 2021). Real-time ventilator setting optimization is possible due to the proven accuracy in identifying patient-ventilator asynchronies, which surpasses human capabilities (Singh et al., 2025; Pažout et al., 2025). However, before widespread clinical implementation, a number of issues need to be resolved.

Transparency and interpretability of algorithms continue to be major issues, especially in critical care settings where physicians need to comprehend the reasoning behind automated decisions (Singh et al., 2025). Many AI systems' "black box" nature may restrict their acceptability among medical professionals and give rise to medicolegal issues. Furthermore, thorough validation is necessary to ensure that AI algorithms are applicable to a variety of patient populations and clinical contexts (Najafi, 2025; Pomprapa et al., 2015).

An intriguing new area is the possibility of AI-driven customized ventilation plans based on real-time physiological data (Singh et al., 2025). However, in order to achieve the best results, AI systems need to integrate a large amount of data beyond respiratory mechanics due to the complexity of mechanical ventilation interactions with multiple organ systems (Wingert et al., 2021).

3.2.3 VILI Prevention: Established Principles and Emerging Concepts

The most evidence-based approach to preventing VILIs is still lung-protective ventilation with low tidal volumes and limited plateau pressures (Hoegl et al., 2017; Clinical NCT01730794). These guidelines have become the accepted standard of care for the treatment of acute respiratory distress syndrome (ARDS) due to the consistent evidence of mortality benefits in numerous large RCTs (Sklar et al., 2019; Qadir et al., 2024). A more physiologically sound method of ventilator management is provided by the recent focus on driving pressure as a unifying concept for lung protection (Hoegl et al., 2017).

A significant development in VILI prevention techniques is the compelling evidence in favor of prone positioning in cases of severe ARDS. Although there are still issues with staffing, training, and patient selection, the PROSEVA trial's mortality benefits have revolutionized clinical practice. During the COVID-19 pandemic, prone positioning was extended to awake, non-intubated patients, which has created new research and clinical application opportunities.

Optimizing the balance between recruitment and overdistension may be possible with tailored PEEP strategies informed by respiratory mechanics or imaging modalities (Sklar et al., 2019). However, the complexity of lung mechanics and the variability of ARDS call for individualized strategies that might call for cutting-edge monitoring tools.

3.2.4 VIDD: An Underrecognized Complication

VIDD has become a major concern for prevention strategies due to its recognition as a serious complication of mechanical ventilation (Peñuelas et al., 2025; Peñuelas et al., 2019). The necessity of early preventive measures is highlighted by the quick onset of diaphragmatic dysfunction, which occurs 24 to 48 hours after ventilation initiation. Evidence-based strategies for preventing VIDD include diaphragm-protective ventilation, optimizing sedation levels, and encouraging spontaneous breathing efforts (Peñuelas et al., 2025).

Clinicians now have the means to evaluate and prevent VIDD thanks to the development of non-invasive diaphragm function monitoring methods, such as ultrasound and EAdi monitoring (Shah et al., 2023). However, more research through extensive clinical trials is necessary to determine the best preventative and therapeutic approaches for VIDD.

3.2.5. Emerging Technologies and Future Directions

A useful intermediary between invasive mechanical ventilation and traditional oxygen therapy is high-flow nasal cannula therapy (Sharma et al., 2023). HFNC is positioned as a crucial tool in the respiratory failure management algorithm due to its physiological advantages and improvements in patient comfort. To maximize results and avoid delayed intubation, cautious patient selection and monitoring are still necessary.

There are new options for treating severe respiratory failure while reducing VILI when ECMO is combined with ultra-protective ventilation techniques. A paradigm shift toward more patient-centered care is represented by the creation of awake ECMO protocols and early mobilization techniques.

3.2.6 Limitations and Future Research Directions

There are a number of limitations to this systematic review that should be taken into account. Comprehensive meta-analyses were not possible due to the heterogeneity of patient populations, ventilator settings, and outcome measures across studies. Some studies may no longer be as applicable to modern practice due to the quick changes in ventilator technology and clinical procedures. Furthermore, it's possible that the emphasis on recent publications left out significant historical research that puts contemporary innovations in context.

Large-scale, multicenter RCTs assessing innovative ventilation techniques with standardized outcome measures and sufficient power to identify clinically significant differences should be the focus of future research. A promising line of research is the creation of precision medicine methods for mechanical ventilation that take into account real-time monitoring data and patient-specific physiological traits (Singh et al., 2025).

Safety, effectiveness, and implementation considerations must be carefully considered when integrating AI and machine learning technologies into mechanical ventilation (Wingert et al., 2021). In order to facilitate innovation and guarantee proper oversight, regulatory frameworks for AI-driven medical devices must change.

4. CONCLUSION

A field that is rapidly evolving with notable advancements in ventilation modalities, monitoring technologies, and prevention strategies is revealed by this systematic review of recent developments in mechanical ventilation. Even though new modes like NAVA show notable gains in particular outcomes, their overall clinical impact is still quite low. Although there are many obstacles to overcome in terms of acceptance, implementation, and validation, the incorporation of artificial intelligence holds great promise for customized ventilation strategies.

Prone positioning is a significant development for the treatment of severe acute respiratory distress syndrome, and lung-protective ventilation techniques continue to be the cornerstone of VILI prevention. For thorough ventilator management, VIDD detection and prevention become crucial factors. ECMO integration and high-flow nasal cannula therapy are useful strategies for treating respiratory failure of various intensities.

Individualized strategies based on high-quality evidence are required due to the complexity of mechanical ventilation and the diversity of patient populations in need of respiratory support. To advance the field and enhance patient outcomes, more research concentrating on AI integration, precision medicine principles, and thorough outcome assessment is necessary.

Future mechanical ventilation plans should prioritize customization, utilizing cutting-edge monitoring tools and artificial intelligence (AI)-powered algorithms to maximize patient care while upholding the essentials of lung and diaphragm protection. The provision of safe, efficient respiratory support that promotes patient recovery while reducing iatrogenic complications continues to be the ultimate objective.

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AUTHOR CONTRIBUTION STATEMENT

R.Y. contributed to study conception, literature search, data extraction, and manuscript preparation. oversight, and contributed to critical revision of the manuscript. All authors approved the final version for publication.

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