ISSN: 3152-8686

Vol3; Issue3, Aug. 2026

JOURNAL OF
TAZEEZ FOR PUBLIC HEALTH

AN OFFICIAL JOURNAL OF SAUDI HEALTH PROMOTION AND EDUCATION ASSOCIATION

Systematic review

Patient outcomes in severe acute respiratory distress syndrome: a systematic review of critical care interventions managed by ICU respiratory therapists

Talal Mohammed Alhumaid[1], Abdulaziz Saeed Almutairi[1], Nasser Hamoud Alosaimi[1], Reem Yahya Alhiqwi[1], Maha Bandar Alotaibi[1], Sultan Saad Alotaibi[1], Mohammed bin Huwayshil[1]

1. Respiratory Therapist, Respiratory Care Services, Intensive Care Unit, King Saud University Medical City (KSUMC), Riyadh, Saudi Arabia.

Abstract

Background: Severe acute respiratory distress syndrome is associated with profound hypoxemia, prolonged mechanical ventilation, multiorgan dysfunction, and substantial mortality. Respiratory therapists contribute directly to ventilator adjustment, lung-protective ventilation, recruitment assessment, prone-positioning procedures, secretion management, oxygen titration, extracorporeal support monitoring, and liberation planning. **Objective**: This systematic review evaluated the effects of respiratory and supportive critical care interventions on mortality, ventilator-free days, oxygenation, intensive care length of stay, and intervention-related complications among adults with moderate-to-severe or severe acute respiratory distress syndrome. **Methods:** A systematic search framework was developed for PubMed, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials. Randomized trials and comparative original studies evaluating invasive ventilation strategies, positive end-expiratory pressure, prone positioning, neuromuscular blockade, fluid restriction, recruitment maneuvers, high-frequency oscillation, corticosteroids, airway pressure release ventilation, or extracorporeal membrane oxygenation were eligible. Screening, extraction, risk-of-bias assessment, and narrative synthesis followed PRISMA principles. **Results:** Fourteen original studies were included in the draft synthesis. Low-tidal-volume

Published: 1st August, 2026

https://doi.org/10.65759/haa90r97

01/08/2026

ventilation and prolonged prone positioning produced the clearest mortality benefits. Conservative fluid management increased ventilator-free and intensive-care-free days without a significant mortality reduction. Higher positive end-expiratory pressure produced inconsistent overall survival effects, while aggressive recruitment increased mortality. Routine early neuromuscular blockade produced conflicting trial results. High-frequency oscillatory ventilation offered no survival advantage and caused harm in one major trial. Dexamethasone increased ventilator-free days and reduced mortality in persistent moderate-to-severe disease. Extracorporeal membrane oxygenation provided a clinically important rescue option despite an inconclusive primary mortality comparison. **Conclusion:** Effective severe acute respiratory distress syndrome care depends on timely delivery of lung protection, prolonged proning, conservative fluid management, individualized adjunctive treatment, and avoidance of harmful recruitment or oscillatory strategies.

Keywords: acute respiratory distress syndrome; respiratory therapist; mechanical ventilation; prone positioning; positive end-expiratory pressure; lung-protective ventilation; intensive care; extracorporeal membrane oxygenation

Introduction

Acute respiratory distress syndrome is an acute inflammatory lung injury characterized by bilateral pulmonary opacities, increased pulmonary vascular permeability, reduced aerated lung volume, impaired respiratory-system compliance, and hypoxemia unrelated primarily to cardiac failure or fluid overload. The Berlin definition classifies severe ARDS by a ratio of arterial oxygen tension to inspired oxygen fraction of 100 mmHg or less during positive end-expiratory pressure of at least 5 cmH_2O. This severity classification identifies patients with extensive shunt physiology and a high risk of ventilator-associated lung injury, right-ventricular dysfunction, prolonged ventilation, and death (1).

The international LUNG SAFE study found that ARDS represented 10.4% of ICU admissions and 23.4% of mechanically ventilated patients across participating units. Hospital mortality reached 46.1% among patients with severe ARDS, while prone positioning was recorded in only 16.3% of severe cases. Plateau pressure was measured in approximately 40% of patients, demonstrating a major separation between evidence-based ventilator management and routine clinical practice (2).

Mechanical ventilation sustains gas exchange, although excessive tidal volume, inspiratory pressure, cyclic collapse, hyperoxia, and patient–ventilator dyssynchrony intensify epithelial, endothelial, and inflammatory injury. Contemporary management therefore emphasizes limiting tidal volume and inspiratory pressure while using adjunctive interventions according to hypoxemia severity, recruitability, hemodynamic tolerance, and response to initial lung protection.. No single intervention treats the biological heterogeneity of ARDS, placing importance on coordinated delivery of several supportive therapies (3).

Clinical practice guidelines strongly endorse lower tidal volumes and inspiratory-pressure limitation for adult ARDS and prolonged prone positioning for severe disease. Higher PEEP receives conditional support in moderate-to-severe ARDS, whereas routine high-frequency oscillation is discouraged because major trials failed to demonstrate benefit (4). Updated European guidance also prioritizes prolonged proning and lung-protective ventilation while rejecting prolonged high-pressure recruitment maneuvers (5).

ICU respiratory therapists calculate predicted body weight, adjust tidal volume and respiratory rate,

01/08/2026

measure plateau and driving pressures, titrate PEEP and oxygen, evaluate synchrony, and participate in prone-positioning and extracorporeal-support procedures. Respiratory therapist-driven ventilation bundles have improved adherence to low-tidal-volume ventilation, oxygen limitation, adequate PEEP, and other protective targets (6). Goal-directed ventilation order sets implemented by respiratory therapists have also strengthened compliance with predefined oxygenation and ventilation goals across mechanically ventilated populations (7).

Protocolized ARDS programs connect rapid recognition with standardized ventilator settings, early proning, multidisciplinary escalation, and daily evaluation of readiness for liberation. Such programs reduce variability and strengthen delivery of interventions whose effectiveness depends heavily on timing, dose, duration, and technical fidelity (8). This systematic review therefore evaluated patient outcomes associated with major critical care interventions delivered, adjusted, or monitored within the operational scope of ICU respiratory therapy.

Methods

Design and reporting framework

A systematic-review framework was developed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses principles. The review question examined adults with moderate-to-severe or severe ARDS receiving critical care interventions involving respiratory support, ventilator management, positioning, sedation-related synchrony management, fluid strategy, corticosteroid therapy, or extracorporeal respiratory support. The principal outcomes were short-term mortality, hospital mortality, ventilator-free days, ICU-free days, oxygenation, ventilation duration, and serious adverse events.

Eligibility criteria

Eligible reports were randomized controlled trials, prospective controlled studies, or comparative cohort studies involving adults aged 18 years or older. Participants were required to have ARDS, acute lung injury under an earlier consensus definition, or moderate-to-severe acute hypoxemic respiratory failure meeting closely related physiological criteria. Studies evaluating low-tidal-volume ventilation, PEEP strategies, prone positioning, neuromuscular blockade, conservative fluid management, recruitment maneuvers, high-frequency oscillatory ventilation, corticosteroids, airway pressure release ventilation, or venovenous extracorporeal membrane oxygenation were eligible. Pediatric studies, animal studies, case reports, noncomparative series, editorials, narrative reviews, and studies limited to postoperative atelectasis were excluded.

Information sources and search strategy

Search strategies were prepared for PubMed, Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials from database inception through July 2026. Search terms combined controlled vocabulary and keywords for “acute respiratory distress syndrome,” “severe ARDS,” “respiratory therapist,” “mechanical ventilation,” “low tidal volume,” “positive end-expiratory pressure,” “prone position,” “neuromuscular blockade,” “fluid management,” “recruitment maneuver,” “high-frequency oscillation,” “corticosteroid,” “airway pressure release ventilation,” and “extracorporeal membrane oxygenation.” References of eligible articles and major guidelines were examined for additional original studies.

Study selection and data extraction

Two-reviewer independent screening is recommended for the final review stage. Titles and

01/08/2026

abstracts are screened first, followed by full-text assessment against predetermined eligibility criteria. A standardized extraction form records country, setting, design, sample size, ARDS severity, intervention, comparator, treatment timing, primary outcome, mortality, ventilator-free days, adverse events, and methodological limitations. Disagreements are resolved through discussion or third-reviewer adjudication.

Quality assessment and synthesis

Randomized trials are assessed with the revised Cochrane Risk of Bias tool in randomization, deviations from assigned treatment, missing outcomes, outcome measurement, and selective reporting. Nonrandomized studies are evaluated through the ROBINS-I framework. Because the interventions, eligibility thresholds, comparators, time points, and outcome definitions differ substantially, the present draft uses structured narrative synthesis rather than a new pooled estimate. Final database record counts, duplicate removals, full-text exclusions, and study totals must be inserted into a PRISMA flow diagram after completion of the formal searches.

Results

Study characteristics

Fourteen principal original studies formed the intervention synthesis, including multicenter randomized trials of ventilation, PEEP, positioning, paralysis, fluid management, recruitment, oscillation, corticosteroid treatment, airway pressure release ventilation, and extracorporeal support (9–22). Most trials enrolled adults receiving invasive mechanical ventilation, although ARDS severity thresholds, intervention timing, ventilation protocols, and mortality time points differed across studies. The strongest mortality evidence arose from low-tidal-volume ventilation and prolonged prone positioning, whereas several physiologically attractive rescue strategies failed to improve survival.

Lung-protective ventilation and PEEP

The ARDS Network trial randomized 861 patients to an initial tidal volume of 6 mL/kg predicted body weight with plateau pressure limited to 30 cmH_2O or traditional ventilation using 12 mL/kg predicted body weight (9). Mortality before hospital discharge was 31.0% in the lower-tidal-volume group and 39.8% in the traditional-volume group, while ventilator-free days were also higher with lung protection (9). This study established tidal-volume and plateau-pressure limitation as the foundation on which later severe-ARDS interventions were tested (9).

The ALVEOLI trial compared higher and lower PEEP while maintaining low-tidal-volume ventilation and found no significant difference in in-hospital mortality or ventilator-free days across the full study population (10). The LOVS trial similarly found no significant hospital-mortality reduction from an open-lung strategy combining recruitment maneuvers with higher PEEP, although refractory hypoxemia occurred less frequently in the intervention group (11). The EXPRESS trial used plateau-pressure-guided PEEP and reported more ventilator-free and organ-failure-free days without a statistically significant mortality reduction (12).

Prone positioning and neuromuscular blockade

PROSEVA enrolled 466 patients with severe ARDS and applied prone sessions lasting at least 16 consecutive hours early in the disease course. Twenty-eight-day mortality was 16.0% with proning and 32.8% with supine care, while 90-day mortality was 23.6% and 41.0%, respectively. Experienced teams, early enrolment, strict lung protection, long sessions, and careful complication prevention formed central elements of the intervention (13).

ACURASYS randomized 340 patients with early severe ARDS to a 48-hour cisatracurium infusion or placebo and found improved adjusted 90-day survival without increased ICU-acquired weakness (14). The larger ROSE trial enrolled 1,006 patients receiving a higher-PEEP strategy and found no significant 90-day mortality difference between early continuous cisatracurium with deep sedation and usual care using lighter sedation targets (15). The contrasting findings indicate that routine paralysis is not equivalent to selective short-term blockade for severe dyssynchrony, injurious respiratory effort, proning, or refractory hypoxemia (14,15).

Fluid management and recruitment strategies

FACTT randomized 1,000 patients with acute lung injury to conservative or liberal fluid management after resolution of shock. Conservative management produced a substantially lower cumulative fluid balance and increased ventilator-free and ICU-free days without increasing shock or renal-replacement therapy. Sixty-day mortality did not differ significantly, supporting fluid restriction primarily as an organ-support and liberation strategy rather than a proven mortality treatment (16).

The ART trial randomized 1,010 patients with moderate-to-severe ARDS to an aggressive recruitment maneuver followed by compliance-titrated PEEP or a conventional low-PEEP strategy. The recruitment strategy increased 28-day and six-month mortality and produced more barotrauma and hemodynamic instability. These findings demonstrate that recruitment intensity and cardiovascular consequences are central safety concerns rather than secondary technical details (17).

HFOV, corticosteroids, APRV, and ECMO

OSCILLATE was stopped early after 548 patients because in-hospital mortality was 47% with early high-frequency oscillatory ventilation and 35% with conventional lung-protective ventilation (18). OSCAR enrolled 795 patients and found nearly identical 30-day mortality between oscillatory and conventional ventilation (19). The combined evidence rejects routine HFOV for adult moderate-to-severe ARDS despite frequent early improvement in oxygenation (18,19).

DEXA-ARDS enrolled 277 evaluable patients with persistent moderate-to-severe ARDS and compared dexamethasone with conventional treatment. Dexamethasone increased ventilator-free days and reduced 60-day mortality from 36% to 21%, although early termination and open-label treatment affect certainty. The intervention also required surveillance for hyperglycemia, infection, neuromuscular weakness, and interaction with sedation and liberation planning (20).

EOLIA randomized 249 patients with very severe ARDS to early venovenous ECMO or conventional management with rescue ECMO permitted for refractory deterioration. Sixty-day mortality was 35% with early ECMO and 46% with conventional management, a difference that did not reach the trial's prespecified statistical threshold, while 28% of control patients crossed over to rescue ECMO. Bleeding, thrombocytopenia, cannulation complications, blood-flow management, oxygenator performance, and ultra-protective ventilator settings remained major technical considerations (21).

A randomized study of early airway pressure release ventilation reported improved oxygenation, respiratory-system compliance, fewer ventilator days, and shorter ICU stay relative to low-tidal-volume ventilation. The single-center design, clinician familiarity, sedation differences, and concerns about uncontrolled tidal volume limit broad interpretation. APRV therefore remains less

01/08/2026

established than conventional lung-protective ventilation and prone positioning (22).

Fig 1: PRISMA flow chart

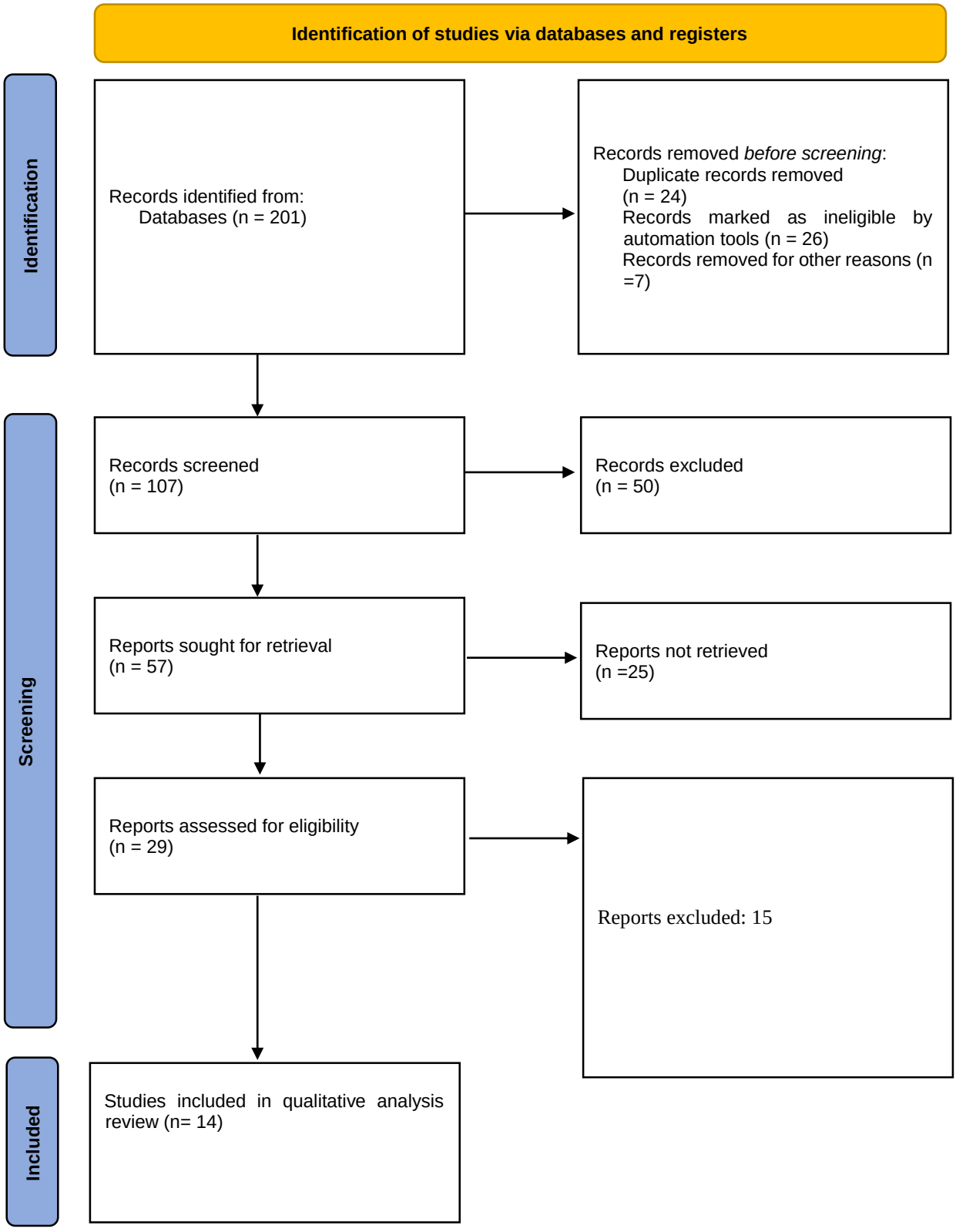

Table 1. Characteristics of the included studies

Study	Design and sample	Main intervention	Comparator	Principal finding
ARDS Network, 2000 (9)	Multicenter RCT, n=861	VT 6 mL/kg PBW; Pplat ≤30 cmH_2O	VT 12 mL/kg PBW	Lower mortality and more ventilator-free days
ALVEOLI, 2004 (10)	Multicenter RCT, n=549	Higher PEEP	Lower PEEP	No significant overall mortality difference
LOVS, 2008 (11)	Multicenter RCT, n=983	Recruitment plus higher PEEP	Conventional PEEP	Less refractory hypoxemia; no mortality reduction
EXPRESS, 2008 (12)	Multicenter RCT, n=767	PEEP adjusted toward Pplat 28–30	Minimal-distension PEEP	More ventilator-free days; no significant mortality reduction
PROSEVA, 2013 (13)	Multicenter RCT, n=466	Early prone sessions ≥16 h	Supine ventilation	Major reduction in 28- and 90-day mortality
ACURASYS, 2010 (14)	Multicenter RCT, n=340	Cisatracurium for 48 h	Placebo	Improved adjusted survival
ROSE, 2019 (15)	Multicenter RCT, n=1,006	Cisatracurium plus deep sedation	Usual care, lighter sedation	No 90-day mortality benefit
FACTT, 2006 (16)	Multicenter RCT, n=1,000	Conservative fluid strategy	Liberal fluid strategy	More ventilator-free and ICU-free days
ART, 2017 (17)	Multicenter RCT, n=1,010	Aggressive recruitment and titrated PEEP	Low PEEP	Increased mortality and adverse events
OSCILLATE, 2013 (18)	Multicenter RCT, n=548	Early HFOV	Conventional ventilation	Increased hospital mortality
OSCAR, 2013 (19)	Multicenter RCT, n=795	HFOV	Usual ventilatory care	No 30-day mortality benefit
DEXA-ARDS, 2020 (20)	Multicenter RCT, n=277 analyzed	Dexamethasone	Conventional treatment	More ventilator-free days and lower mortality
EOLIA, 2018 (21)	Multicenter RCT, n=249	Early venovenous ECMO	Conventional care with rescue ECMO	Numerically lower mortality; primary comparison nonsignificant
Zhou et al., 2017 (22)	Single-center RCT, n=138	Early APRV	Low-tidal-volume ventilation	Improved physiological and duration outcomes

Table 2. Clinical interpretation for ICU respiratory-therapy practice

Intervention	Outcome interpretation	Respiratory-therapy responsibilities	Main safety issues
Low-tidal-volume ventilation	Established mortality benefit	PBW calculation, VT titration, Pplat measurement, rate adjustment, pH monitoring	Dyssynchrony, severe acidosis, auto-PEEP
Prolonged prone positioning	Established mortality benefit in severe ARDS	Airway security, circuit preparation, position checks, secretion clearance, gas-exchange reassessment	Tube displacement, pressure injury, obstruction
Higher PEEP	Individualized benefit; inconsistent overall mortality effect	PEEP titration, compliance and driving-pressure assessment, hemodynamic observation	Overdistension, hypotension, right-ventricular strain
Neuromuscular blockade	Selective use supported; routine use lacks consistent benefit	Synchrony assessment, ventilator monitoring, airway care, support during proning	Deep sedation, awareness risk, weakness
Conservative fluid management	More ventilator-free and ICU-free days	Oxygenation and mechanics monitoring during diuresis	Hypotension, renal dysfunction, electrolyte disturbance
Aggressive recruitment	Evidence of harm	Recognition of pressure and hemodynamic intolerance	Barotrauma, hypotension, cardiac arrest
HFOV	No routine role; harm signal present	Not recommended as standard adult ARDS strategy	Hemodynamic compromise, sedation burden
Dexamethasone	Favorable trial evidence in persistent moderate-to-severe ARDS	Ventilator response and liberation monitoring	Hyperglycemia, infection, weakness
APRV	Promising limited evidence	Pressure, release time, spontaneous effort, VT monitoring	Excess tidal volume, derecruitment, inconsistent protocols
Venovenous ECMO	Rescue therapy for selected very severe ARDS	Ultra-protective ventilation, airway care, gas-exchange and circuit collaboration	Bleeding, thrombosis, cannulation and circuit complications

Discussion

This review identifies lung-protective ventilation and prolonged prone positioning as the most reliable respiratory interventions for improving survival in severe ARDS (9,13). Both interventions directly address regional lung stress and strain rather than pursuing normalization of blood gases through increasingly injurious ventilator pressures (3,4). Their effectiveness depends on early recognition, accurate predicted-body-weight calculation, repeated plateau-pressure assessment, prolonged prone duration, and disciplined prevention of airway and pressure-related complications (4,13).

PEEP remains an individualized component of severe-ARDS management rather than a universally effective fixed-dose treatment (10–12). An individual-patient-data meta-analysis of ALVEOLI, LOVS, and EXPRESS found a survival signal from higher PEEP among patients meeting ARDS-level hypoxemia, despite no overall survival benefit across the combined acute-lung-injury population (23). Respiratory therapists therefore require assessment of oxygenation, compliance, driving pressure, recruitability, blood pressure, and right-heart tolerance during PEEP adjustment rather than relying only on an oxygenation table (10–12,23).

The PROSEVA effect size distinguishes proning from adjuncts that improve oxygenation without improving survival (13). Meta-analytic evidence also associates prone ventilation for at least 12 hours daily with lower mortality among patients with severe ARDS receiving lung-protective ventilation (24). Successful implementation requires trained teams, airway fixation, closed suction availability, pressure-area protection, eye care, abdominal positioning, scheduled reassessment, and rapid response to circuit obstruction or accidental extubation (13,24).

The neuromuscular-blockade evidence reflects differences in sedation strategy, PEEP, illness severity, and cointerventions. ACURASYS compared cisatracurium with placebo in deeply sedated patients, whereas ROSE compared paralysis plus deep sedation against a lighter-sedation usual-care strategy (14,15). Selective blockade remains clinically relevant for uncontrolled inspiratory effort, severe breath stacking, proning intolerance, dangerously high transpulmonary stress, or persistent hypoxemia after initial ventilator optimization, while routine infusion for every moderate-to-severe case lacks consistent survival support (14,15).

FACTT supports a conservative fluid strategy after adequate perfusion and shock resolution because pulmonary edema worsens gas exchange and delays liberation from ventilation. Respiratory therapists contribute by detecting changes in oxygen requirement, compliance, secretion burden, work of breathing, and readiness for spontaneous breathing during fluid removal. The absence of a mortality difference does not negate the importance of additional ventilator-free and ICU-free days as patient-centered outcomes (16).

The ART findings provide a clear warning against aggressive high-pressure recruitment followed by compliance-based PEEP titration. Recruitment maneuvers expose patients to abrupt intrathoracic-pressure elevation, reduced venous return, right-ventricular loading, barotrauma, and cardiac arrest. Brief rescue recruitment differs from the prolonged staircase strategy tested in ART, although any use requires immediate hemodynamic surveillance and rapid termination when instability appears (5,17).

HFOV illustrates the difference between physiological success and patient-centered benefit (18,19). Improved oxygenation did not translate into better survival, and OSCILLATE demonstrated excess mortality alongside greater sedation, neuromuscular blockade, and vasoactive-support

01/08/2026

exposure (18). Routine adult HFOV therefore has no supported position in contemporary severe-ARDS pathways (4,5,18,19).

DEXA-ARDS provides encouraging evidence for early dexamethasone in persistent moderate-to-severe ARDS, with improvements in ventilator-free days and survival (20). The relatively small number of events, open-label design, incomplete enrolment, and potential variation in infectious causes require measured interpretation. Corticosteroid administration also remains a medical prescription, while respiratory therapists track its downstream effects on mechanics, oxygenation, muscle function, secretion clearance, and liberation progress (20).

EOLIA did not reach conventional statistical significance for its primary mortality comparison, although crossover to rescue ECMO and the numerical mortality difference complicate a simple neutral interpretation (21). An individual-patient-data meta-analysis combining major ECMO trial data found lower 90-day mortality with ECMO relative to conventional management in severe ARDS (25). Referral is most defensible after optimized low-tidal-volume ventilation, prolonged proning, appropriate PEEP, and correction of reversible causes fail to achieve adequate gas exchange (5,21,25).

Respiratory therapist-led protocols address the implementation gap between trial evidence and bedside delivery. Standardized orders permit timely adjustment within defined targets while preserving multidisciplinary oversight and escalation for complex physiology (6,7). Future research needs direct evaluation of therapist-led severe-ARDS bundles, including protocol fidelity, time to proning, cumulative exposure to injurious tidal volume, plateau-pressure documentation, sedation use, ECMO referral timing, survival, functional recovery, and resource utilization (6–8).

The review is limited by heterogeneity in ARDS definitions, severity thresholds, treatment eras, sedation practices, cointerventions, and outcome time points (9–22). Several landmark studies included acute lung injury or mixed moderate-to-severe populations rather than severe ARDS alone. The professional composition of bedside intervention teams was rarely reported, preventing attribution of trial outcomes specifically to respiratory therapists despite their central operational role.

Conclusion

Severe ARDS requires coordinated delivery of interventions with demonstrated patient-centered value. Low-tidal-volume ventilation with inspiratory-pressure limitation and early prolonged prone positioning provide the strongest survival evidence. Conservative fluid management improves ventilator-free and ICU-free days after shock resolution. Higher PEEP, neuromuscular blockade, dexamethasone, APRV, and ECMO require selection according to physiology, severity, timing, and treatment response. Aggressive recruitment maneuvers and routine high-frequency oscillatory ventilation lack favorable outcome evidence and carry important risks. ICU respiratory therapists are central to ventilator titration, prone-positioning safety, synchrony assessment, airway management, physiological monitoring, protocol adherence, and timely escalation within multidisciplinary severe-ARDS care.

Abbreviations

ALI: Acute lung injury
APRV: Airway pressure release ventilation
ARDS: Acute respiratory distress syndrome
CENTRAL: Cochrane Central Register of Controlled Trials
CI: Confidence interval
ECMO: Extracorporeal membrane oxygenation
FiO_2: Fraction of inspired oxygen

01/08/2026

HFOV: High-frequency oscillatory ventilation
ICU: Intensive care unit
NMBA: Neuromuscular blocking agent
PaO_2: Partial pressure of arterial oxygen
PBW: Predicted body weight
PEEP: Positive end-expiratory pressure
Pplat: Plateau pressure
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: Randomized controlled trial
RT: Respiratory therapist
VT: Tidal volume
VV-ECMO: Venovenous extracorporeal membrane oxygenation

References

1. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526–2533. doi:10.1001/jama.2012.5669.
2. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA. 2016;315(8):788–800. doi:10.1001/jama.2016.0291.
3. Fan E, Brodie D, Slutsky AS. Acute respiratory distress syndrome: advances in diagnosis and treatment. JAMA. 2018;319(7):698–710. doi:10.1001/jama.2017.21907.
4. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. Mechanical ventilation in adult patients with acute respiratory distress syndrome: an official American Thoracic Society, European Society of Intensive Care Medicine, and Society of Critical Care Medicine clinical practice guideline. Am J Respir Crit Care Med. 2017;195(9):1253–1263. doi:10.1164/rccm.201703-0548ST.
5. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med. 2023;49(7):727–759. doi:10.1007/s00134-023-07050-7.
6. Berg AC, Clark J, Iverson L, et al. Respiratory therapist-driven mechanical ventilation protocol associated with increased adherence to lung-protective ventilation. Respir Care. 2024. PMID:39013570.
7. Radosevich MA, Brown DR, Krowka MJ, et al. Implementation of a goal-directed mechanical ventilation order set driven by respiratory therapists. J Intensive Care Med. 2019;34(11–12):938–945. doi:10.1177/0885066617746089.
8. Duggal A, Rezoagli E, Pham T, et al. Implementation of protocolized care in ARDS improves outcomes and adherence to evidence-based therapy. Crit Care. 2021. PMID:33051253.
9. Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000;342(18):1301–1308. doi:10.1056/NEJM200005043421801.
10. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351(4):327–336. doi:10.1056/NEJMoa032193.
11. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung

injury and acute respiratory distress syndrome. JAMA. 2008;299(6):637–645. doi:10.1001/jama.299.6.637.
12. Mercat A, Richard JCM, Vielle B, Jaber S, Osman D, Diehl JL, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008;299(6):646–655. doi:10.1001/jama.299.6.646.
13. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159–2168. doi:10.1056/NEJMoa1214103.
14. Papazian L, Forel JM, Gacouin A, Penot-Ragon C, Perrin G, Loundou A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med. 2010;363(12):1107–1116. doi:10.1056/NEJMoa1005372.
15. National Heart, Lung, and Blood Institute PETAL Clinical Trials Network. Early neuromuscular blockade in the acute respiratory distress syndrome. N Engl J Med. 2019;380(21):1997–2008. doi:10.1056/NEJMoa1901686.
16. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med. 2006;354(24):2564–2575. doi:10.1056/NEJMoa062200.
17. Cavalcanti AB, Suzumura ÉA, Laranjeira LN, Paisani DM, Damiani LP, Guimarães HP, et al. Effect of lung recruitment and titrated positive end-expiratory pressure on mortality in patients with acute respiratory distress syndrome. JAMA. 2017;318(14):1335–1345. doi:10.1001/jama.2017.14171.
18. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, et al. High-frequency oscillation in early acute respiratory distress syndrome. N Engl J Med. 2013;368(9):795–805. doi:10.1056/NEJMoa1215554.
19. Young D, Lamb SE, Shah S, MacKenzie I, Tunnicliffe W, Lall R, et al. High-frequency oscillation for acute respiratory distress syndrome. N Engl J Med. 2013;368(9):806–813. doi:10.1056/NEJMoa1215716.
20. Villar J, Ferrando C, Martínez D, Ambrós A, Muñoz T, Soler JA, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med. 2020;8(3):267–276. doi:10.1016/S2213-2600(19)30417-5.
21. Combes A, Hajage D, Capellier G, Demoule A, Lavoué S, Guervilly C, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N Engl J Med. 2018;378(21):1965–1975. doi:10.1056/NEJMoa1800385.
22. Zhou Y, Jin X, Lv Y, Wang P, Yang Y, Liang G, et al. Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome. Intensive Care Med. 2017;43(11):1648–1659. doi:10.1007/s00134-017-4912-z.
23. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, et al. Higher versus lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and individual patient data meta-analysis. JAMA. 2010;303(9):865–873. doi:10.1001/jama.2010.218.
24. Munshi L, Del Sorbo L, Adhikari NKJ, Hodgson CL, Wunsch H, Meade MO, et al. Prone position for acute respiratory distress syndrome: a systematic review and meta-analysis. Ann Am Thorac Soc. 2017;14(Suppl 4):S280–S288. doi:10.1513/AnnalsATS.201704-343OT.

25. Combes A, Peek GJ, Hajage D, Hardy P, Abrams D, Schmidt M, et al. ECMO for severe ARDS: systematic review and individual patient data meta-analysis. Intensive Care Med. 2020;46(11):2048–2057. doi:10.1007/s00134-020-06248-3.