

**ACUTE RESPIRATORY DISTRESS SYNDROME: PATHOPHYSIOLOGY,
DIAGNOSIS, AND CONTEMPORARY MANAGEMENT**

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Abstract

Acute respiratory distress syndrome (ARDS) is a heterogeneous, life-threatening form of acute hypoxemic respiratory failure caused by diffuse inflammatory injury to the lungs. Increased permeability of the alveolar–capillary barrier allows protein-rich fluid to enter the interstitium and alveoli, impairing gas exchange and reducing functional lung volume. Common precipitating conditions include pneumonia, sepsis, aspiration, trauma, and pancreatitis. Diagnosis is clinical and depends on the acute time course, oxygenation impairment, bilateral pulmonary opacities, and assessment that respiratory failure is not primarily explained by cardiac failure or fluid overload. The 2023 global consensus definition broadened recognition by including selected patients receiving high-flow nasal oxygen, permitting lung ultrasound as an imaging option, and adapting oxygenation assessment for settings with limited resources. Management remains predominantly supportive: treat the underlying cause, use lung-protective ventilation, consider prolonged prone positioning in severe disease, individualize positive end-expiratory pressure, and avoid unnecessary fluid accumulation after shock has resolved. Outcomes vary with disease severity, comorbidities, and access to timely critical care. Survivors may experience physical, cognitive, and psychological sequelae, making rehabilitation and follow-up important. This narrative review summarizes core mechanisms, recognition, treatment principles, complications, and current research priorities.

Keywords: acute respiratory distress syndrome; ARDS; hypoxemic respiratory failure; lung-protective ventilation; prone positioning; critical care; pulmonary edema

1. Introduction

Acute respiratory distress syndrome is not a single disease but a clinical syndrome in which an acute insult produces widespread inflammation and impaired function of the lungs. It was first described in 1967, and definitions have since evolved as evidence and respiratory-support technologies have developed. ARDS can follow direct lung injury, such as pneumonia or aspiration, or indirect injury arising from systemic inflammation, including sepsis and major trauma. The resulting hypoxemia may progress quickly and often requires care in an intensive care unit (ICU) [1,2].

Its importance lies not only in the immediate risk of respiratory failure but also in the complexity of treatment. The injured lung is unevenly affected: some regions remain relatively aerated while others are fluid-filled or collapsed. Ventilation that is excessive for the remaining functional lung can worsen injury, so the goal is to support oxygenation while minimizing additional mechanical stress. Contemporary care therefore combines treatment of the trigger with carefully adjusted respiratory support, hemodynamic management, prevention of ICU complications, and rehabilitation [2,3].

This article is a narrative review of selected consensus statements, clinical practice guidelines, and influential clinical studies. It is intended for educational use rather than as a substitute for individualized clinical judgment.

2. Pathophysiology and Causes

The central biological event in ARDS is damage to the alveolar epithelium and pulmonary capillary endothelium. Inflammatory cells and mediators disrupt the normally selective barrier, allowing fluid and proteins to move into the lung tissue and air spaces. Surfactant function may be impaired, small airways and alveoli may collapse, and the lungs become less compliant. Blood continues to pass through poorly ventilated areas, producing ventilation–perfusion mismatch and intrapulmonary shunt. These processes explain why oxygen levels can remain low despite supplemental oxygen [1,2].

ARDS is commonly described as an early exudative phase, followed in some patients by proliferative repair and, in a subset, persistent fibrotic remodeling. These phases overlap rather than follow a fixed timetable. Recovery depends on resolution of inflammation, epithelial repair, clearance of alveolar fluid, and avoidance of secondary insults. Mechanical ventilation can be lifesaving, but high tidal volumes or excessive pressures may stretch vulnerable tissue and contribute to ventilator-induced lung injury; this is a key reason for lung-protective strategies [3].

Category	Examples	Mechanism / clinical relevance
Direct pulmonary injury	Pneumonia, aspiration of gastric contents, inhalational injury, pulmonary contusion	Initial damage occurs mainly in the airways and alveolar epithelium.
Indirect systemic injury	Sepsis, pancreatitis, major trauma, severe burns, transfusion-related injury	Systemic inflammation and endothelial dysfunction affect the pulmonary microvasculature.
Predisposing factors	Severe infection, shock, multiple injuries, major surgery, high-risk transfusion contexts	Risk varies with the insult, patient vulnerability, and speed of recognition.

3. Clinical Presentation and Diagnosis

Typical findings include rapidly worsening breathlessness, increased respiratory rate, low oxygen saturation, and increased work of breathing. Examination may reveal crackles, but no single physical sign confirms ARDS. In severe cases, patients may develop fatigue, altered mental status related to hypoxemia or systemic illness, and dysfunction of other organs. The underlying trigger can dominate the initial presentation; for example, fever and productive cough may accompany pneumonia, while hypotension may be prominent in sepsis.

Diagnosis integrates the timing of respiratory deterioration, oxygenation, chest imaging, and evaluation for alternative explanations. The Berlin definition describes onset within one week of a known clinical insult or new/worsening respiratory symptoms, bilateral opacities not fully explained by effusions or collapse, and respiratory failure not primarily caused by cardiac failure or fluid overload. Oxygenation severity is classified using the ratio of arterial oxygen partial pressure to inspired oxygen fraction ($\text{PaO}_2/\text{FiO}_2$) when appropriate respiratory support is in place [1].

A global consensus definition published in 2023 expanded the framework. It includes selected non-intubated patients receiving high-flow nasal oxygen at flows of at least 30 L/min, allows lung ultrasound when performed by trained operators, and permits an oxygen saturation-to-inspired oxygen ratio in specified circumstances. These changes

aim to improve recognition in different clinical settings, including facilities with limited access to arterial blood gases or advanced imaging. The definition supports recognition but does not replace clinical assessment [2].

Assessment	Purpose	Important limitation
Pulse oximetry and arterial blood gas	Assess oxygenation and acid–base status; calculate oxygenation indices when data allow.	Readings must be interpreted with oxygen delivery, perfusion, and clinical condition in mind.
Chest radiograph or CT	Identify bilateral opacities and evaluate alternative diagnoses.	Imaging patterns are not unique to ARDS.
Lung ultrasound	Identify bilateral loss of aeration or consolidations when expertise is available.	Operator training and the clinical context matter.
Cardiac assessment and fluid review	Consider cardiac dysfunction, fluid overload, and mixed causes of edema.	ARDS and cardiac disease can coexist.
Cultures and targeted investigations	Identify infection or another precipitating cause.	Tests should be guided by history and examination.

4. Severity and Clinical Monitoring

Severity is commonly grouped by the degree of oxygenation impairment, interpreted alongside respiratory support and the overall clinical picture. A low $\text{PaO}_2/\text{FiO}_2$ ratio indicates more severe oxygenation failure, but it should not be used in isolation to predict an individual outcome. Compliance, hemodynamics, renal function, mental status, infection control, and response over time also inform management. Repeated assessment is essential because ARDS can evolve over hours and because both the disease and its treatment may cause complications.

Severity category (Berlin framework)	$\text{PaO}_2/\text{FiO}_2$ ratio*	General interpretation
Mild	201–300 mm Hg	Oxygenation impairment; monitor trajectory and support needs.

Moderate	101–200 mm Hg	More substantial impairment; ventilatory support and careful monitoring are often required.
Severe	≤ 100 mm Hg	Marked impairment; consider evidence-based adjuncts such as prone positioning when clinically appropriate.

**The Berlin oxygenation categories are applied with the specified positive end-expiratory pressure condition. The expanded global definition includes additional pathways for selected non-intubated patients and resource-limited settings [1,2].*

5. Management

5.1 Treat the precipitating cause and provide supportive care

Management begins with identifying and treating the trigger. This may include appropriate antimicrobials and source control for infection, management of aspiration or trauma, and treatment of shock or other organ dysfunction. Supportive care includes oxygen delivery, monitoring, nutrition, prevention of venous thromboembolism and pressure injuries, delirium prevention, and early mobilization when feasible. Treatment should be individualized by an experienced critical-care team.

5.2 Lung-protective ventilation

For patients requiring invasive ventilation, guideline-supported practice is to use lower tidal volumes based on predicted body weight and limit plateau pressure. A common initial target is approximately 6 mL/kg predicted body weight, adjusted within a 4–8 mL/kg range according to clinical response, with plateau pressure generally kept below 30 cm H₂O. Predicted body weight is used rather than actual weight because lung size correlates more closely with height and sex than with body mass [3,4].

Positive end-expiratory pressure (PEEP) helps prevent repeated alveolar collapse, but the optimal level varies. Higher PEEP may be considered in moderate-to-severe ARDS without prolonged recruitment maneuvers, while excessive pressures can impair circulation or overdistend lung regions. Ventilator settings should therefore be titrated to oxygenation, mechanics, hemodynamics, and the patient's response rather than applied as a fixed recipe [4].

5.3 Prone positioning and fluid strategy

For appropriately selected patients with severe ARDS, prone positioning for more than 12 hours per day is recommended in established guidance. Turning the patient prone can improve the distribution of ventilation and reduce regional stress differences; it requires trained staff, a safety checklist, and careful protection of the airway and pressure points. It is not suitable for every patient and should be undertaken by a qualified team [3,4].

Fluid management must balance adequate organ perfusion against worsening pulmonary edema. During active shock, resuscitation and hemodynamic stabilization take priority. Once shock has resolved, a conservative fluid strategy may improve oxygenation and increase ventilator-free days, although it has not consistently shown a mortality benefit. Diuretics and fluid restriction require individualized decisions, particularly when kidney injury or ongoing circulatory instability is present [5].

5.4 Adjuncts and rescue options

Selected patients may require neuromuscular blockade, inhaled pulmonary vasodilators as temporary rescue measures, or referral for extracorporeal membrane oxygenation (ECMO) in specialized centers. These interventions are not universal treatments and their role depends on severity, contraindications, local expertise, and evidence of benefit. Routine use of high-frequency oscillatory ventilation is not recommended for moderate or severe ARDS in major guidelines. Supportive interventions should be reviewed frequently to avoid continuing therapies that are no longer needed [3,4].

6. Evidence Snapshot: Tables and Graph

Table 3 summarizes several widely accepted management principles. These recommendations represent a framework for clinician-led care; they are not a patient-specific protocol.

Intervention	Evidence-informed principle	Practical caution
Low tidal volume ventilation	Use 4–8 mL/kg predicted body weight; commonly start near 6 mL/kg.	Track plateau pressure, gas exchange, and patient–ventilator interaction.

Prone positioning	Use for more than 12 h/day in suitable patients with severe ARDS.	Requires trained staff and prevention of line, airway, and pressure-related complications.
PEEP adjustment	Consider higher PEEP in moderate-to-severe ARDS without prolonged recruitment maneuvers.	Balance recruitment against overdistension and hemodynamic effects.
Fluid management	After shock resolves, avoid unnecessary positive fluid balance when safe.	Do not compromise perfusion; reassess renal function and circulation.
ECMO / rescue therapies	Consider only in selected severe cases after expert review.	Requires specialized resources; risks and expected benefits must be discussed.

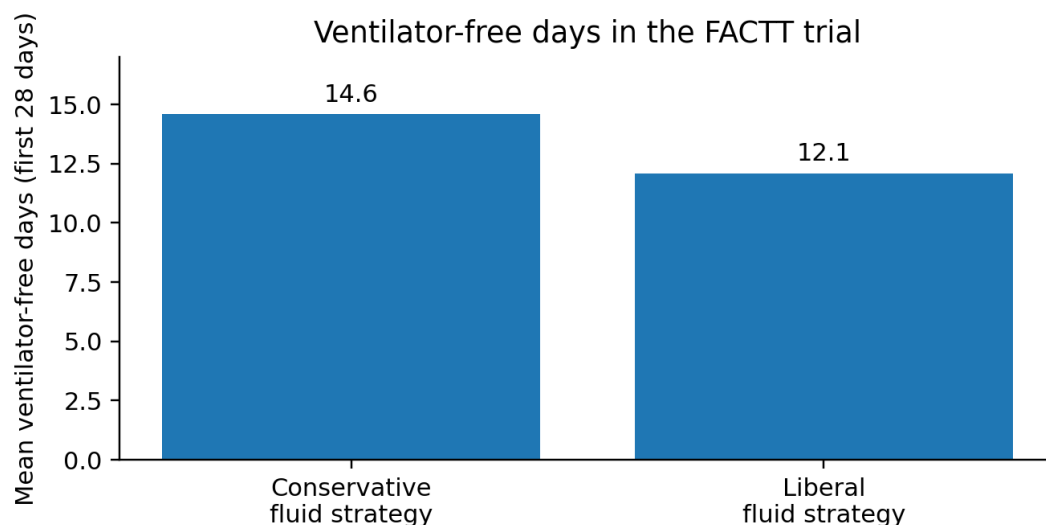


Figure 1. Mean ventilator-free days reported in the FACTT study comparison: conservative fluid management (14.6 days) versus liberal fluid management (12.1 days). The values are study-group averages, not predictions for an individual patient. Conservative fluid management improved ventilator-free days, while the original trial did not demonstrate a statistically significant difference in 60-day mortality [5,6].

7. Complications, Recovery, and Prognosis

Complications arise from severe illness, immobility, infection, and treatment. They may include ventilator-associated pneumonia, barotrauma, delirium, weakness

acquired in the ICU, kidney injury, thromboembolism, and pressure injuries. Risk reduction requires coordinated daily review of sedation and ventilation, infection prevention, appropriate nutrition, mobility when safe, and assessment of organ function. The clinical team must also recognize that oxygenation can improve before strength and endurance return.

Recovery varies considerably. Some people regain their previous function, while others have persistent breathlessness, reduced exercise tolerance, muscle weakness, sleep disturbance, anxiety, depression, or cognitive difficulties after discharge. Follow-up should therefore consider physical rehabilitation, respiratory symptoms, nutrition, and emotional well-being. Family education and clear discharge planning can help patients and caregivers understand that recovery may continue for months.

Mortality is influenced by age, pre-existing disease, the precipitating cause, severity of organ dysfunction, and access to high-quality critical care. A single percentage cannot adequately describe risk for every setting or patient group. Prevention and early treatment of precipitating conditions, timely recognition, and reliable delivery of supportive care remain central priorities.

8. Research Priorities

ARDS remains biologically and clinically heterogeneous, which may explain why treatments that help some patients do not benefit all patients. Research priorities include validating the global definition across diverse health systems, identifying clinically useful biological subgroups, improving noninvasive respiratory support strategies, and determining which patients benefit most from adjunctive treatments. Studies should also examine long-term outcomes rather than focusing only on survival to hospital discharge. More accessible diagnostic pathways may improve recognition where arterial blood gas testing, CT, or advanced respiratory support are limited, but the reliability and prognostic value of these approaches require continued evaluation [2,4].

9. Conclusion

Acute respiratory distress syndrome is a complex form of acute lung injury that can progress rapidly and affect multiple organs. Its core features—diffuse inflammation, alveolar–capillary barrier dysfunction, pulmonary edema, and impaired oxygen transfer—explain both the severity of illness and the need for carefully controlled respiratory support. Diagnosis combines clinical timing, oxygenation assessment, imaging, and exclusion of alternative primary causes, with the newer global definition

broadening recognition in selected non-intubated patients and resource-limited settings. Current management relies on treating the trigger, lung-protective ventilation, prone positioning for appropriate severe cases, individualized PEEP, and thoughtful fluid management after shock has resolved. Because survivors may experience lasting physical and psychological effects, recovery planning and follow-up are integral parts of care. Ongoing research should improve early recognition, personalize treatment, and strengthen long-term outcomes.

References

1. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA*. 2012;307(23):2526–2533. doi:10.1001/jama.2012.5669.
2. Matthay MA, Arabi Y, Arroliga AC, et al. A New Global Definition of Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med*. 2024;209(1):37–47. doi:10.1164/rccm.202303-0558WS. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10870872/>
3. Fan E, Del Sorbo L, Goligher EC, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med*. 2017;195(9):1253–1263. doi:10.1164/rccm.201703-0548ST.
4. Qadir N, Sahetya S, Munshi L, et al. An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome: An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2024;209(1):24–36. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10870893/>
5. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med*. 2006;354:2564–2575. doi:10.1056/NEJMoa062200.
6. Grissom CK, Hirshberg EL, Dickerson JB, et al. Fluid Management With a Simplified Conservative Protocol for the Acute Respiratory Distress Syndrome. *Crit Care Med*. 2015;43(2):288–295. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC4675623/>
7. Thompson BT, Chambers RC, Liu KD. Acute Respiratory Distress Syndrome. *N Engl J Med*. 2017;377:562–572. doi:10.1056/NEJMra1608077.