

EXTRACORPOREAL MEMBRANE OXYGENATION, PRONE POSITIONING, AND HIGH POSITIVE END-EXPIRATORY PRESSURE VENTILATION IN ACUTE RESPIRATORY DISTRESS SYNDROME: A NARRATIVE REVIEW

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Abstract

Acute Respiratory Distress Syndrome (ARDS) remains one of the leading causes of mortality among critically ill patients despite substantial advances in intensive care management. The syndrome is characterized by severe hypoxemia, diffuse alveolar damage, reduced lung compliance, and impaired gas exchange. Mechanical ventilation remains the cornerstone of treatment; however, inappropriate ventilatory strategies may contribute to ventilator-induced lung injury. Consequently, adjunctive therapies such as prone positioning, high positive end-expiratory pressure (PEEP), and extracorporeal membrane oxygenation (ECMO) have emerged as important interventions aimed at improving oxygenation and survival. This narrative review examines the physiological basis, clinical evidence, advantages, limitations, and current role of ECMO, prone positioning, and high PEEP ventilation in the management of ARDS. Current evidence suggests that prone positioning provides a significant mortality benefit in moderate-to-severe ARDS, while ECMO serves as an effective rescue therapy in refractory hypoxemia. High PEEP ventilation improves alveolar recruitment and oxygenation but demonstrates variable effects on survival. An individualized, multidisciplinary approach integrating these strategies appears essential for optimizing outcomes in severe ARDS.

INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a severe inflammatory lung condition characterized by acute onset respiratory failure, bilateral pulmonary infiltrates, and refractory hypoxemia. Since its first description by Ashbaugh and colleagues in 1967, ARDS has remained a major challenge in critical care medicine due to its high morbidity and mortality. Contemporary estimates suggest mortality rates ranging from 30% to 45%, particularly among patients with severe disease. The pathophysiology of ARDS involves diffuse alveolar damage, disruption of the alveolar-

capillary barrier, pulmonary edema, inflammatory cell infiltration, and surfactant dysfunction. These changes result in impaired oxygenation, reduced lung compliance, and severe ventilation-perfusion mismatch. Despite advances in supportive care, management remains challenging, necessitating the use of specialized respiratory support strategies. Among the most widely investigated interventions are high positive end-expiratory pressure (PEEP), prone positioning, and extracorporeal membrane oxygenation (ECMO).

These approaches seek to improve oxygenation, reduce ventilator-induced lung injury, and ultimately improve survival.

Pathophysiology of ARDS

ARDS develops following direct pulmonary insults such as pneumonia, aspiration, and inhalational injury, or indirect causes including sepsis, trauma, and pancreatitis. The inflammatory response increases pulmonary vascular permeability, leading to accumulation of protein-rich edema within the alveolar spaces.

The disease generally progresses through three phases:

Exudative Phase

Characterized by alveolar edema, neutrophilic infiltration, and severe hypoxemia.

Proliferative Phase

Marked by epithelial regeneration and initiation of tissue repair mechanisms.

Fibrotic Phase

Occurs in some patients and may result in permanent pulmonary fibrosis and prolonged respiratory impairment.

Understanding these mechanisms is fundamental for appreciating the rationale behind modern ventilatory strategies.

High Positive End-Expiratory Pressure (PEEP)

Physiological Basis

Positive end-expiratory pressure maintains alveolar patency at end expiration, preventing repetitive alveolar collapse and reopening, a major contributor to ventilator-induced lung injury. By increasing functional residual capacity, PEEP enhances oxygenation and improves pulmonary compliance.

Clinical Evidence

Several studies have demonstrated that higher PEEP levels improve oxygenation and lung recruitment in ARDS. However, evidence regarding mortality reduction remains inconsistent. Meta-analyses have suggested potential benefits in patients with moderate-to-

severe ARDS, whereas others report no significant survival advantage.

Briel et al. demonstrated improved oxygenation with higher PEEP strategies but found variable effects on mortality across patient populations. Similarly, the Cochrane review by Santa Cruz et al. reported uncertain survival benefits despite physiological improvements.

Advantages

- Improved alveolar recruitment
- Enhanced oxygenation
- Reduced cyclic alveolar collapse
- Potential reduction in ventilator-induced lung injury

Limitations

- Risk of alveolar overdistension
- Hemodynamic compromise
- Increased intrathoracic pressure
- Potential barotrauma

Therefore, PEEP should be individualized according to lung recruitability and patient physiology.

Prone Positioning

Physiological Mechanisms

Prone positioning redistributes transpulmonary pressure, resulting in more homogeneous ventilation and improved ventilation-perfusion matching. The maneuver reduces dorsal lung compression caused by the heart and abdominal contents while promoting alveolar recruitment in dependent lung regions.

Additional benefits include:

- Enhanced secretion clearance
- Improved oxygenation
- Reduced ventilator-induced lung injury
- More uniform distribution of tidal volume

Evidence Supporting Prone Positioning

The landmark PROSEVA trial demonstrated a substantial reduction in mortality among patients with severe ARDS treated with prolonged prone positioning. Subsequent meta-analyses confirmed

these findings, particularly when proning sessions exceeded 12–16 hours daily.

Munshi et al. reported significant reductions in mortality among patients with moderate-to-severe ARDS receiving prone ventilation. Similar findings have been replicated in several international studies.

Advantages

- Significant mortality reduction
- Improved oxygenation
- Low cost
- Broad applicability in ICUs

Challenges

- Requires trained personnel
- Risk of pressure injuries
- Accidental displacement of tubes and lines
- Increased workload for ICU staff

Despite these challenges, prone positioning is currently recommended as standard therapy for severe ARDS.

Extracorporeal Membrane Oxygenation (ECMO)

Mechanism of Action

ECMO provides extracorporeal gas exchange by removing deoxygenated blood, oxygenating it through an artificial membrane, and returning it to the circulation. This process permits “lung rest” by allowing clinicians to use ultra-protective ventilation strategies with lower tidal volumes and airway pressures.

Types of ECMO

Veno-Venous ECMO (VV-ECMO)

Used primarily for severe respiratory failure.

Veno-Arterial ECMO (VA-ECMO)

Provides both respiratory and circulatory support.

X- ECMO remains the preferred modality for severe ARDS.

Clinical Evidence

The CESAR and EOLIA trials significantly advanced understanding of ECMO in ARDS management. The EOLIA trial demonstrated

lower mortality and reduced treatment failure among patients receiving early ECMO compared with conventional ventilation.

Recent systematic reviews indicate that ECMO may improve survival in carefully selected patients with severe refractory hypoxemia.

Benefits

- Effective rescue therapy
- Allows ultra-protective ventilation
- Improves oxygenation
- Reduces ventilator-induced lung injury

Risks

- Bleeding complications
- Thromboembolism
- Infection
- Resource-intensive management

Consequently, ECMO should be performed in experienced centers with specialized multidisciplinary teams.

Combining ECMO and Prone Positioning

Growing evidence suggests that combining prone positioning with ECMO may provide synergistic benefits.

Potential mechanisms include:

- Enhanced alveolar recruitment
- Improved ventilation-perfusion matching
- Reduced pulmonary stress and strain
- Better oxygenation during ECMO support

Several recent studies have reported improved survival and greater ventilator-free days among patients managed with combined ECMO-prone strategies compared with conventional approaches. This integrated approach may represent the optimal rescue therapy for severe ARDS unresponsive to standard ventilation.

Current Clinical Recommendations

Current international guidelines recommend:

1. Lung-protective ventilation with low tidal volumes.
2. Appropriate application of PEEP based on recruitability.
3. Early prone positioning in moderate-to-

severe ARDS.

4. Consideration of ECMO for refractory hypoxemia despite optimal conventional therapy.

5. Multidisciplinary management involving intensivists, respiratory therapists, nurses, and physiotherapists.

The choice of intervention should be individualized based on disease severity, resource availability, and patient-specific factors.

Future Directions

Future research should focus on:

- Identifying optimal timing for ECMO initiation.
- Determining ideal proning duration during ECMO.
- Evaluating combined ECMO-prone protocols.
- Developing personalized PEEP titration strategies.
- Investigating long-term functional outcomes among ARDS survivors.
- Assessing cost-effectiveness in resource-limited healthcare systems.

Large multicenter randomized controlled trials remain necessary to further refine ARDS management strategies.

Conclusion

ARDS continues to represent a significant challenge in critical care medicine. High PEEP ventilation, prone positioning, and ECMO each play important roles in the management of severe respiratory failure. Among these interventions, prone positioning has demonstrated the most consistent mortality benefit and should be considered standard therapy in moderate-to-severe ARDS. High PEEP improves oxygenation but requires individualized application to minimize adverse effects. ECMO remains an effective rescue therapy for patients with refractory hypoxemia and may provide additional benefits when combined with prone positioning. An integrated, patient-centered approach utilizing these evidence-based strategies

offers the greatest potential for improving survival and reducing complications in ARDS.

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