JAMA Clinical Guidelines Synopsis

Management of ARDS in Adults

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GUIDELINE TITLE Mechanical Ventilation in Adult Patients With Acute Respiratory Distress Syndrome

DEVELOPER American Thoracic Society (ATS)/European Society of Intensive Care Medicine (ESICM)/Society of Critical Care Medicine (SCCM)

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TARGET POPULATION Hospitalized adults with acute respiratory distress syndrome (ARDS).

SELECTED MAJOR RECOMMENDATIONS

For all patients with ARDS:

- Use lower tidal volumes of 4 to 8 mL/kg per breath, calculated using predicted body weight (PBW) (strong recommendation; moderate confidence in effect estimate).
- Use lower inspiratory pressures, targeting a plateau pressure <30 cm H_2O (strong recommendation; moderate confidence).

For patients with severe ARDS (Pao_2/Fio_2 ratio <100):

- Use prone positioning for at least 12 h/d (strong recommendation; moderate confidence).
- Do not routinely use high-frequency oscillatory ventilation (strong recommendation; high confidence).
- Additional evidence is needed to recommend for or against the use of extracorporeal membrane oxygenation (ECMO) in severe ARDS.

Summary of the Clinical Problem

ARDS is an acute inflammatory lung injury that results in increased vascular permeability. Clinically, this leads to life-threatening acute hypoxemic respiratory failure with bilateral alveolar opacities on chest imaging that are not fully explained by cardiogenic pulmonary edema, pleural effusions, or lung collapse. ARDS is associated with many conditions, including sepsis, aspiration, pneumonia, severe trauma, and overdose. ARDS affects approximately 200 000 individuals and results in 74 500 deaths per year in the United States.[1]

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ARDS management remains largely supportive, with mechanical ventilation forming the cornerstone of therapy. Management of ARDS is clinically challenging because some approaches to mechanical ventilation exacerbate lung injury and increase mortality.[2] ARDS often is managed in community settings without easy access to intensive care specialists.

Characteristics of the Guideline Source

The guideline was developed by the ATS, ESICM, and SCCM with funding from the ATS and ESICM.[3] The committee included experts in ARDS physiology and clinical trials as well as guideline methodologists, a medical librarian, and an ARDS survivor. A formal conflict of interest management policy was followed.

Evidence Base

The guideline committee used Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods (**Table**). PICO (population, intervention, control, and outcomes) questions were constructed and a medical librarian assisted with systematic reviews. In some cases, new meta-analyses were performed. The committee rated recommendations as strong or conditional and classified the level of confidence in evidence of effect estimates.

Benefits and Harms

The guideline strongly recommends lung-protective ventilation for all patients with ARDS, defined as targeting a tidal volume of 4 to 8 mL/kg PBW and a plateau pressure of less than 30 cm H_2O. The ARDSNet trial supporting this recommendation enrolled 861 patients and found a 22% relative reduction in mortality with tidal volumes of 6 mL/kg PBW compared with 12 mL/kg PBW.[2] The guideline identified 8 other relevant trials. When all trials were included, the lung-protective approach was associated with lower mortality (risk ratio [RR], 0.80; 95% CI, 0.66-0.98). Larger tidal volume differences between control and intervention groups were associated with larger improvements in mortality.

The guideline makes 2 important recommendations for severe ARDS, defined as a $Pao_2/Fio2$ ratio of 100 or less. First, these patients should be placed in the prone position for at least 12 hours per day. The recommendation is based largely on the PROSEVA trial, which found that prone positioning reduced 28-day mortality from 32.8% to 16.0% ($P < .001$) in 466 patients with severe ARDS.[4] This will be a practice change for many intensive care units (ICUs) and clinicians; moreover, implementing prone positioning can be logistically challenging. In addition, prone positioning may carry additional risks,

Table. Guideline Rating

Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Fair
Guideline development group composition	Good
Clinical practice guideline–systematic review intersection	Good
Establishing evidence foundations and rating strength for each of the guideline recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Fair
Implementation issues	Fair

including endotracheal tube problems, requirements for increased sedation, less opportunity for early mobilization, and potentially more risk of pressure ulcers. Second, adult patients with moderate to severe ARDS should not routinely receive high-frequency oscillatory ventilation (HFOV). The OSCILLATE trial (N=548) used a higher positive end-expiratory pressure (PEEP) control group and found increased 28-day mortality with HFOV (RR, 1.41; 95% CI, 1.12-1.79)[5]; other pragmatic trials have found no benefit.

The guideline made 2 conditional recommendations for patients with moderate to severe ARDS, suggesting using higher PEEP and recruitment maneuvers, which might in theory open collapsed lung and increase end-expiratory volume. However, shortly after the guideline was published, a large randomized trial found that a strategy of recruitment maneuvers with higher-PEEP titration (vs standard, lower-PEEP care) resulted in increased 28-day mortality (hazard ratio, 1.20; 95% CI, 1.01-1.42).[6]

Discussion

Perhaps the key challenge of ARDS management is that the same intervention that is immediately lifesaving—mechanical ventilation—can also worsen lung injury and increase mortality. Maneuvers that improve short-term parameters like oxygenation or tachypnea may paradoxically worsen survival.

The most important recommendations in the guideline are for low tidal volumes and low inspiratory pressures. There are 2 practical points worth emphasizing. First, tidal volumes should be based on predicted, not actual, body weight. Why? Obesity does not cause the lungs to increase in size, so using actual body weight often results in higher-than-desired tidal volumes and therefore higher mortality. Second, the plateau pressure is a potentially lifesaving parameter to follow in patients with ARDS. This parameter measures the airway pressure after a 0.5-second pause at the end of inspiration, and it reflects the interaction of respiratory system stiffness and the size of the tidal volume. It should be measured regularly in all ARDS patients, and the ventilator should be adjusted to target a plateau pressure of less than 30 cm H_2O. A pocket card summarizing the approach to tidal volume and plateau pressure management used in the seminal ARDSNet trial[2] is freely available and has practical value at the bedside. Management of sedation, analgesia, and strategies for liberation from mechanical ventilation are also crucial to outcomes.[7]

For many clinicians, the strong recommendation for prone positioning may be surprising. The benefit of prone positioning is pathophysiologically plausible: it changes ventilation-perfusion matching and more uniformly distributes tidal volume by changing chest wall (and abdominal) mechanics. While trials of prone positioning were conducted in selected expert centers, this guideline supports judicious dissemination of this practice to other ICUs in the community.

Areas in Need of Future Study

Numerous areas of ARDS management remain important areas for future research, including studies that guide the setting of tidal volume and PEEP using physiology-based parameters such as driving pressure or esophageal pressure and that validate simple tools to guide safe lung recruitment. Even with current knowledge, in a 50-country study, only half of patients with ARDS (n = 3022) were recognized clinically, 60% did not have a plateau pressure measured, and more than one-third received tidal volumes higher than 8 mL/kg PBW.[8] Development of quality measures and quality improvement programs in ARDS is therefore a priority.

Whether spontaneous respiration in ARDS is helpful or harmful remains an area of debate. Most clinicians caring for a patient with severe ARDS must choose whether to initiate neuromuscular blockade. The guideline is silent on this issue. A randomized multicenter trial (N=340) found that adjusted (but not unadjusted) 90-day survival was higher in pharmacologically paralyzed patients with ARDS.[9] A multicenter confirmatory trial is under way suggesting that clinical equipoise remains for this issue. Finally, the guideline also reviewed the evidence relating to ECMO for ARDS but withheld a recommendation because of the rapid pace of technological evolution in extracorporeal techniques as well as numerous ongoing relevant randomized trials.

Related guidelines and other resources

Revised Berlin Definition of ARDS

ARDSNet Tools

ACCCM Guideline: Sedation and Analgesia in the ICU (Pain, Agitation, and Delirium Management) 2013

ARTICLE INFORMATION

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