

Several meta-analyses suggest decreased mortality in patients with a pressure- and volume-limited strategy for established ARDS [353, 354]. The largest trial of a volume- and pressure-limited strategy showed 9% absolute decrease in mortality in ARDS patients ventilated with tidal volumes of 6 mL/kg compared with 12 mL/kg predicted body weight (PBW), and aiming for plateau pressure ≤ 30 cm H₂O [424].

The use of lung-protective strategies for patients with ARDS is supported by clinical trials and has been widely accepted; however, the precise tidal volume for an individual ARDS patient requires adjustment for factors such as the plateau pressure, the selected positive end-expiratory pressure (PEEP), thoracoabdominal compliance, and the patient's breathing effort. Patients with profound metabolic acidosis, high minute ventilation, or short stature may require additional manipulation of tidal volumes. Some clinicians believe it may be safe to ventilate with tidal volumes > 6 mL/kg PBW as long as plateau pressure can be maintained ≤ 30 cm H₂O [429, 430]. The plateau pressure is only truly valuable if the patient is passive during the inspiratory hold. Conversely, patients with very stiff chest/ abdominal walls and high pleural pressures may tolerate plateau pressures > 30 cm H₂O because transpulmonary pressures will be lower. A retrospective study suggested that tidal volumes should be lowered even with plateau pressures ≤ 30 cm H₂O [431] because lower plateau pressures were associated with reduced hospital mortality [432]. A recent patient-level mediation analysis suggested that a tidal volume that results in a driving pressure (plateau pressure minus set PEEP) below 12–15 cm H₂O may be advantageous in patients without spontaneous breathing efforts [433]. Prospective validation of tidal volume titration by driving pressure is needed before this approach can be recommended. Tidal volumes > 6 cc/kg coupled with plateau pressures > 30 cm H₂O should be avoided in ARDS. Clinicians should use as a starting point the objective of reducing tidal volume over 1–2 h from its initial value toward the goal of a “low” tidal volume (≈ 6 mL/kg PBW) achieved in conjunction with an end-inspiratory plateau pressure ≤ 30 cm H₂O. If plateau pressure remains > 30 cm H₂O after reduction of tidal volume to 6 mL/kg PBW, tidal volume may be further reduced to as low as 4 mL/kg PBW. The clinician should keep in mind that very low tidal volumes may result in significant patient-ventilatory dyssynchrony and patient discomfort. Respiratory rate should be increased to a maximum of 35 breaths/min during tidal volume reduction to maintain minute ventilation. Volume- and pressure-limited ventilation may lead to hypercapnia even with these maximum-tolerated set respiratory rates;

this appears to be tolerated and safe in the absence of contraindications (e.g., high intracranial pressure, sickle cell crisis). No single mode of ventilation (pressure control, volume control) has consistently been shown to be advantageous when compared with any other that respects the same principles of lung protection.

Recommendation

50. For adults with sepsis-induced severe ARDS, we **recommend** using an upper limit goal for plateau pressures of 30 cm H₂O, over higher plateau pressures

Strong recommendation, moderate quality of evidence

Rationale

This recommendation is unchanged from the previous guidelines, as no new trials evaluating plateau pressure have been published since then. Of note, the 3 RCTs that guide this recommendation [424, 426, 427] enrolled patients using the criteria from the American-European Consensus Criteria Definition for Acute Lung Injury and ARDS [422] whereas the current document use the 2012 Berlin definition and the terms mild, moderate, and severe ARDS ($\text{PaO}_2/\text{FiO}_2 \leq 300$, ≤ 200 , and ≤ 100 mm Hg, respectively) [423]. These three RCTs compared a strategy of low tidal volume and limited plateau pressure with a strategy using higher tidal volume and plateau pressure; pooled data suggest reduced mortality (RR 0.83; 95% CI 0.70–0.97) and more ventilator-free days (MD 1.8 days; 95% CI 0.35–3.25) in patients managed with low plateau pressures.

A recent systematic review which included five RCTs also identified a strong relationship between plateau pressure and mortality [434]. The recommendation is also supported by observational data. LUNGSAFE, a large international observational study, which reported that plateau pressure correlated with mortality; however, the relationship between the two was not evident when plateau pressure was below 20 cm H₂O [435]. A secondary analysis of five observational studies identified a plateau pressure cut-off value of 29 cm H₂O, above which an ordinal increment was accompanied by an increment of risk of death [436]. We therefore recommend that the upper limit goal for plateau pressure should be less than 30 cm H₂O.

Recommendation

51. For adults with moderate to severe sepsis-induced ARDS, we **suggest** using higher PEEP over lower PEEP

Weak recommendation, moderate quality of evidence