Beyond Low Tidal Volumes

Ventilating the Patient with Acute Respiratory Distress Syndrome

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KEYWORDS

• Acute respiratory distress syndrome • Mechanical ventilation • Lung protective ventilation
• Positive end expiratory pressure

KEY POINTS

- The goal of mechanical ventilation in patients with acute respiratory distress syndrome (ARDS) is minimizing ventilator-induced lung inujury (ie, alveolar overdistension and cyclical recruitment/derecruitment) while providing adequate oxygenation and ventilation.
- An effective conventional mechanical ventilation strategy in patients with ARDS uses low tidal volumes and an open lung strategy employing increased positive end-expiratory pressure (PEEP).
- The optimal level of PEEP in patients with ARDS is unclear, but higher levels may be warranted in patients with moderate/severe ARDS.
- Bedside monitoring techniques (eg, esophageal pressure monitoring and electrical impedance tomography) may help clinicians to individualize the delivery of mechanical ventilation, as well as detect complications.

INTRODUCTION

Since first described by Ashbaugh and colleagues[1] in 1967 as the acute onset of respiratory distress, cyanosis refractory to oxygenation therapy, decreased lung compliance and diffuse pulmonary infiltrates on chest radiography, acute respiratory distress syndrome (ARDS) has been recognized as a life-threatening syndrome associated with significant morbidity[2,3] and mortality[4] that affects many patients admitted to critical care units.

Although several ARDS definitions have been developed and used over time, the most recent was proposed in 2012 by the ARDS Definition Task Force.[5] The Berlin Definition of ARDS requires the development of bilateral opacities on chest imaging within 1 week of a known clinical insult and respiratory failure not fully explained by cardiac failure or fluid overload.[6] The severity of hypoxemia is determined by Pao_2/Fio_2 ratios measured on at least a positive-end expiratory pressure (PEEP) of 5 cm H_2O, resulting in 3 mutually exclusive categories: mild (Pao_2/Fio_2 300–201), moderate (Pao_2/Fio_2 200–101), and severe ($Pao_2/Fio_2 \leq 100$).

Despite the marked derangements in gas exchange, death from refractory hypoxemia is rare and accounts for approximately 13% of deaths in patients with ARDS; sepsis with resulting multiorgan failure remains the leading cause of death.[7] Therefore, although mechanical ventilation

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remains the cornerstone of ARDS management, increased recognition of the potential for injury from mechanical ventilation itself has shifted the focus from restoring normal physiology to mitigating ventilator-induced lung injury (VILI) in ARDS. Ashbaugh and colleagues' observation that ARDS does "not respond to usual and ordinary methods of respiratory therapy" remains relevant and insightful almost 50 years later.

VENTILATOR-INDUCED LUNG INJURY

Classically, the components of VILI include: barotrauma, volutrauma, and atelectrauma. Alveolar overdistention coupled with cyclical recruitment and atelectasis are the primary causes of VILI.[8] Barotrauma is generally recognized as pneumothoraces, pneumomediastinum, and subcutaneous emphysema. The concept of volutrauma originated after animal experiments showed that lung stretch through volume rather than purely high airway pressures was the primary determinant of lung injury.[9] Atelectrauma is thought to result from ventilation at low lung volumes, causing repetitive opening and closing of lung units, altered surfactant function, and regional hypoxia.[8] Collectively, these physical forces can disrupt the epithelial barrier[10] and wound plasma membranes of alveolar cells,[11] leading to increased alveolar–capillary permeability. The resulting increase in the production of inflammatory mediators induces biotrauma at both the local tissue and systemic levels.[12]

Chiumello and colleagues[13] have been influential in framing the understanding of these physiologic descriptions of VILI from a biomechanical perspective. The forces that develop in the lung tissue that react to the transpulmonary pressure (alveolar pressure, pleural pressure) are defined as stress, while the resulting lung deformation is termed strain.[14] Because stress varies in a linear fashion with strain, the relationship of "stress = k × strain" can be translated with clinical variables to be:

$$\textit{Transpulmonary Pressure}\ (\textit{Stress}) = \textit{Specific Lung Elastance} \times \frac{\Delta\, \textit{Volume}}{\textit{FRC}\ (\textit{strain})}$$

Using this relationship and animal data, it has been conjectured that a strain of greater than 2 is harmful and thus provides clinicians with alternate monitoring parameters to avoid VILI.[15]

The evaluation of ventilatory strategies in ARDS has been directly influenced by the understanding of VILI, with the goal of minimizing VILI as much as possible. Although there are several potential adjunctive therapies to mechanical ventilation, such as proning,[16] neuromuscular blockade,[17] and extracorporeal life support,[18] these will be discussed elsewhere in this series.

TARGETING VOLUTRAUMA—LOWERING TIDAL VOLUMES

Both pathologic evidence[19] and radiographic evidence[20] exist demonstrating the heterogeneous distribution of lung injury in patients with ARDS, with relatively more nonaerated lung in gravitationally dependent regions. The remaining aerated nondependent lung regions can be relatively small; quantitative assessment of computed tomography (CT) images measured this aerated portion to be in the order of 200–500 g in severe ARDS, the amount normally found in a healthy 5- or 6–year-old child, the so-called baby lung concept.[21] This baby lung concept, coupled with animal studies demonstrating harm after receiving mechanical ventilation with high tidal volumes,[22] helped inform the design of a number of human clinical trials that tried to reproduce this finding but led to conflicting results. In 2000, the landmark randomized controlled trial (RCT) by the ARDS Network (ARDSNet) was published, demonstrating a nearly 9% absolute risk reduction in short-term mortality with a tidal volume and plateau pressure limited (6 mL/kg predicted body weight [PBW] and 30 cm H_2O) strategy.[23] Interestingly, in addition to more patients breathing without assistance and number of ventilator-free days by day 28, a statistically significant decrease in days without nonpulmonary organ failure (15 vs 12, $P = .006$) was observed.

Subsequently, a meta-analysis including 6 RCTs (1297 patients) comparing ventilation strategies targeting a tidal volume of 7 mL/kg or less and plateau pressures of 30 cmH_2O or less versus ventilation with tidal volumes between 10 and 15 mL/kg has confirmed a significant mortality benefit at 28 days (pooled relative risk [RR] 0.74; 95% confidence interval [CI] 0.51–0.88).[24]

Despite pressure- and volume-limited ventilation becoming the standard of care, the optimal tidal volume and plateau pressure limitations are still unclear, and even strict adherence to the ARDSNet strategy may induce VILI in some patients.[25] For instance, in 30 patients ventilated with the ARDSNet strategy, quantitative CT imaging revealed that a third of these patients still underwent tidal hyperinflation of the aerated nondependent baby lung.[26] Correspondingly, bronchoalveolar lavage concentrations of inflammatory mediators were also significantly elevated in the patients who experienced tidal