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A Few mL's of Prevention: Lung Protective Ventilation Decreases Pulmonary Complications

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The association between mechanical ventilation with high tidal volumes and ventilator-induced lung injury has long been recognized and this understanding has slowly led to changes in the practice of mechanical ventilation.¹⁻³ Lung protective ventilation including tidal volumes targeting 6 ml/kg of predicted body weight (PBW) and plateau pressures 30 cmH₂O is now considered the standard of care for patients with the acute respiratory distress syndrome (ARDS). This change was driven by a landmark randomized controlled trial by the ARDS network of investigators demonstrating lower mortality in patients ventilated with a lung protective ventilation strategy (i.e. tidal volume of 6 ml/kg PBW and plateau pressure 30 cmH₂O) compared to a traditional, and more liberal, ventilation approach (i.e. tidal volume 12 ml/kg PBW and plateau pressure 50 cmH₂O).⁴

Since the publication of that study in 2000, there has been a growing body of evidence that suggests that the use of lung protective ventilation also improves clinical outcomes in patients without ARDS. The use of lower tidal volumes intra-operatively was associated with an almost two-thirds decrease in post-operative complications in a randomized controlled trial of intermediate to high-risk patients undergoing abdominal surgery.⁵ A 2012 meta-analysis of patients without ARDS in both surgical and non-surgical ICUs concluded that mechanical ventilation with low tidal volumes compared to high tidal volumes decreased the risk for lung injury, pulmonary infections and mortality.⁶

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The article by Serpa Neto et al in this issue of *Critical Care Medicine* provides further insight into the potential benefits of low tidal volume ventilation in patients without ARDS.⁷ This patient level meta-analysis examined the association between tidal volumes and the occurrence of a composite outcome of pulmonary complications (i.e. ARDS and pneumonia) in patients without ARDS at the time of intubation. The study analyzed tidal volumes used during the first two days of mechanical ventilation categorized as high (>10ml/kg PBW), intermediate (7-10ml/kg PBW), and low (<7ml/kg PBW). The study concluded that mechanical ventilation with low tidal volumes during the first two days of mechanical ventilation decreased the risk of pulmonary complications compared to high tidal volumes by 28%. While comparison between the low and intermediate tidal volume groups did not achieve statistical significance, the 8% lower risk of complications in the low tidal volume group appears to support a dose-response relationship between tidal volume and the pulmonary complications.

By performing an individual patient data meta-analysis the authors were able to standardize the analysis of data obtained from multiple studies, which is an important strength of this study. They defined a consistent exposure and outcome for all patients included in the analysis and were able to adjust the analysis for important potential confounders including patient severity of illness (e.g. APACHE score, baseline PaO₂/FiO₂ ratio). Furthermore, the analysis included a large sample of both medical and surgical ICU patients who were ventilated for at least 48 hours which improves the generalizability of their findings.

Still, conclusions from this study should be tempered by several limitations. Patients from observational studies comprised the majority (93%) of patients included in the primary analysis which may increase the possibility for bias. Data on several important confounders such as fluid balance and use of blood products was also not available for inclusion in the analysis. Patient data from one of the eight studies identified in the systematic review was unavailable for inclusion in the analysis, potentially influencing the results.

The absence of a high-quality randomized controlled trial to support this practice is a reason for caution. A commonly cited concern is that using low tidal volumes could result in patient discomfort leading to increased sedative use and an increased duration of mechanical ventilation.⁸ However secondary analysis of a randomized controlled trial in ARDS patients showed no difference in sedative use when comparing lung protective ventilation to conventional ventilation.^{9,10} In a recent meta-analysis by the authors of this current study, there was a decrease in the duration of mechanical ventilation in the lung protective ventilation group with no difference in sedative or opioid use when comparing patients with a tidal volume _ 6 ml/kg PBW and _ 10 ml/kg PBW.¹¹

Further defining the relationship between tidal volumes and pulmonary complications is the focus of ongoing research. Two randomized controlled trials are currently enrolling patients and may provide additional evidence for to inform the most appropriate tidal volume for critically ill patients without ARDS. The Preventive Strategies in Acute Respiratory Distress Syndrome (EPALI) trial is a multicenter randomized controlled trial comparing low tidal volume ventilation (4 – 6 ml/kg PBW) to high tidal volumes (8 – 10 ml/kg PBW) in patients at risk for ARDS.¹² The primary outcome of this study is the development of ARDS during

the first 7 days of mechanical ventilation. The Protective Ventilation in Patients without ARDS at Start of Ventilation (PREVENT) trial is a multicenter randomized controlled trial comparing low tidal volume ventilation (4 – 6 ml/kg PBW) to high tidal volumes (8 – 10 ml/kg PBW) in patients without ARDS who are anticipated to require mechanical ventilation for > 24 hours.¹³ The primary end-point is the number of ventilator-free days and alive at day 28. These studies are estimated to complete enrollment in 2016 and 2017, respectively.

So should lung protective ventilation be the default strategy in all critically ill mechanically ventilated patients? The preponderance of available evidence suggests that lung protective ventilation reduces pulmonary complications and improves outcomes. This strategy would also help ensure the early delivery of lung protective ventilation in patients with ARDS including those for whom the diagnosis is delayed as there is recent evidence demonstrating that delaying low tidal volume ventilation worsens outcomes.¹⁴

Tidal volume is an important determinant of the clinical outcomes of mechanically ventilated patients. It is easily measured and readily changed, making it a suitable metric for assessing the quality of care provided to mechanically ventilated patients and for use in quality improvement efforts.¹⁵ Based upon the current evidence, we recommend that mechanically ventilated ARDS patients receive tidal volumes of 6 cc/kg PBW and other patients, excepting those with contraindications to lower tidal volumes, receive tidal volumes of less than 8 cc/kg PBW. Critical care teams should implement systems to improve their ability to consistently provide LPV and routinely monitor the tidal volumes provided to patients in their ICUs.

As we await further evidence to guide our practice tomorrow, we must deliver potentially lifesaving mechanical ventilation and avoid preventable harm today. Although not definitive, the available evidence suggests that using lower tidal volumes reduces pulmonary complications and improves clinical outcomes in broad groups of mechanically ventilated patients. Time will tell the ideal tidal volume for all subgroups of mechanically ventilated patients, but we cannot wait while patient lives are at stake.

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