

Commentary

## Toward a better ventilation strategy for patients with acute lung injury

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### Abstract

Ventilator-induced lung injury is a major outcome determinant of the acute respiratory distress syndrome (ARDS). Ventilatory strategies that limit ventilator-induced lung injury should improve outcome from ARDS. The ARDSnet trial showed improved survival in subjects ventilated with a lower tidal volume. Although this trial developed and tested a rigorous clinical protocol, it did not define the limits to which tidal volume reduction would benefit outcome. It is also not at all clear if it is the reduction in tidal volume or the reduction in plateau airway pressure that confers this benefit. Finally, ventilator-induced lung injury occurs more commonly from repetitive collapse and re-expansion of injured lung units rather than from the overdilatation of persistently aerated lung units. This was not addressed in the trial design. Thus, further study using targeted open-lung strategies are also needed.

**Keywords:** ARDS, outcome, ventilation, ventilator-induced lung injury

The ARDS has been with us as a known entity for over 40 years. It was originally referred to as noncardiogenic pulmonary edema. Although originally thought of as a process of direct alveolar epithelial injury, it is now widely appreciated that almost any insult to the lungs or body can result in ARDS through blood-borne mediators. Inherent in this concept is the realization that ARDS is often part of a systemic inflammatory process. Accordingly, lung-specific therapies, such as mechanical ventilation, if they induce further lung injury, can sustain or promote further lung injury and remote organ system dysfunction. Thus, ventilatory strategies that limit the degree to which ventilator-

induced lung injury occurs should improve outcome in patients who have ARDS. Although simple in its inception, the proof of this theory has proven to be more difficult. In part, the difficulty lies in the heterogeneity of processes that converge to result in the clinical picture of ARDS, and in our inability to define adequately what a lung protective strategy should encompass.

The results of the recent ARDSnet trial [1], which compared higher with lower tidal volume ventilation in patients with ARDS, go a long way to prove that this theory is not only correct, but that the degree to which ventilator-

induced lung injury occurs is probably much greater than previously believed. The authors showed that ventilating at a tidal volume of 6 versus 12 ml/kg conferred a survival advantage of 22%, in a study cohort size of only half of the originally proposed 1600 patients. Several points about this study, and future studies of ventilator support for ARDS patients, deserve mention.

First, the ARDSnet deserves our thanks and gratitude for developing and testing a rigorous clinical trial, whose quality control features should serve as the standard for future clinical trials. Clearly, the devil is in the details. Second, the study did not define the limits to which tidal volume reduction would benefit outcome. Clearly, apneic oxygenation, if associated with adequate carbon dioxide removal, would be the limit, and this might be the best approach. However, no data to date support such an aggressive approach, and mortality may increase if inadequate lung distention allows alveolar de-recruitment to occur. Third, it is not clear at all whether it is the reduction in tidal volume (excursion from expiration to inspiration) or the reduction in plateau airway pressure that confers this benefit. Because barotrauma is probably due to the differential lung stretch of contiguous lung units, tidal volume is probably more relevant than airway pressure, but this too needs to be resolved. Finally, ventilator-induced lung injury occurs more commonly from repetitive collapse and re-expansion of injured lung units than from the over-distention of persistently aerated lung units. Regrettably, none of the previously completed prospective randomized clinical trials used a lung recruitment strategy (open lung approach) before using low tidal volume ventilation. Thus, further study using targeted open lung strategies need to be incorporated into the therapeutic stratification schemes if this important and probably dominant factor is finally to be accounted for.

Can we take the data from the ARDSnet trial to the bedside? I believe that the answer is a cautious 'yes'. Clearly, preventing lung over-distention should be avoided. Using plateau airway pressure limits of 32 cmH<sub>2</sub>O appears to be a reasonable point to be concerned. However, in the ARDSnet trial the resultant hypercapnia in the patients in the lower tidal volume arm of the protocol necessitated a marked increase in respiratory rate so as to keep partial carbon dioxide tension from greatly increasing with its resultant increase in respiratory drive, sympathetic tone and patient anxiety. Thus, lung protective strategies are not without their own risks. Finally, it may well be that even simpler ventilatory approaches that minimize lung injury may confer an even greater survival advantage. However, if they exist, they have not been rigorously tested. Therefore, we are left on the threshold of discovery, knowing only the right direction and a few of the signposts to follow, but not knowing the correct path or our final destination.

## Reference

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