

# Ventilation in acute respiratory distress syndrome: importance of low-tidal volume

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Acute respiratory distress syndrome (ARDS) is a life-threatening syndrome that affects more than 150,000 patients annually in the United States with nearly 40–60% mortality (1-3). Over the past two decades, significant progress has been made in the fields of critical care, mechanical ventilation, fluid management and sedation practices that have impacted the practice of intensive care medicine, including the management of ARDS (3-5). Use of low-tidal volume ventilation (LTVV) has formed the cornerstone of our mechanical ventilation strategies in ARDS patients since the seminal ARDS Network Trial in 2000 (6). Use of tidal volumes of 6 mL/kg of ideal body weight (IBW) *vs.* 12 mL/kg IBW demonstrated lower mortality (31% *vs.* 39.8%,  $P=0.007$ ) and higher ventilatory-free days in the first 28-days ( $12\pm 11$  *vs.*  $10\pm 11$  days;  $P=0.007$ ). Due to the paucity of interventions that have demonstrated mortality benefit in ARDS (7-10), LTVV remains one of the few tried, tested and proven strategies (11,12). Over the past few years, the use of LTVV has gained acceptance in non-ARDS critically ill patients and in settings outside of the intensive care unit (ICU) (13-15).

In the recent article in *Critical Care Medicine*, Weiss *et al.* (16) evaluated the adoption of LTVV at one academic and three community hospitals in urban United States. They performed a retrospective cross-sectional study using a previously validated algorithm to diagnose patients meeting

the Berlin definition of ARDS [bilateral infiltrates based on radiology reports, ARDS risk factors and heart failure based on attending physician notes in the electronic medical record (EMR) and echocardiography reports] (17,18). The primary outcome was determined as the percentage of patients with ARDS with at least one LTVV setting from the time of ARDS onset to extubation, ICU discharge or death; whichever was earliest. The primary outcome of LTVV was defined as 6.5 mL/kg of IBW without inclusion of plateau pressure (as two hospitals did not record plateau pressure). Overall, 70 patients (19.3%) were supported with LTVV after ARDS onset. The mean percentage of time this group received LTVV was 59.1%. Utilizing a lenient cut off of 8 mL/kg IBW, the authors found 54.4% patients receiving LTVV at some point during mechanical ventilation. The use of LTVV has ranged from 15–40% between 1998 and 2014 with notable exceptions being the centers that were involved in the ARDS Network Trials and used LTVV more consistently (16).

Dr. Weiss' study findings reflect present day 'real world' utilization of LTVV (16). It included multiple centers with different clinical practice settings and a multiethnic patient cohort. None of these hospitals relied on a LTVV protocol or order set during the study. While the authors rigorously attempted to identify patients with ARDS, there remained a high rate of discrepancy between identification of ARDS

using EHR and by the attending physicians. Only 12.4% of the ARDS cohort in the study was identified as having ARDS by the attending physicians. LTVV utilization did not differ significantly between the academic and community hospitals; however a majority of patients (282/362; 77.9%) in the cohort were admitted to the academic hospital. Another issue worth noting is the delayed of initiation of LTVV following onset of ARDS (median time 22.1 hours); that has been shown to independently correlate with poor hospital outcomes including mortality (19).

It is pertinent to evaluate barriers against use of LTVV, tools to improve ARDS recognition and the need to develop methods to ensure compliance to a strategy that has proven mortality benefit. Despite robust evidence demonstrating multiple benefits of LTVV in ARDS, the acceptance of this practice is disturbingly low. Major barriers to utilization of LTVV are the inability to recognize and tailor tidal volume to IBW (a function of height and gender) (15,20) and use of non-volume control modes of ventilation (19). Less common barriers to the implementation of LTVV include the fear of increased sedation needs (21,22), lack of acceptance of permissive hypercapnia (20,23,24), management of refractory hypoxemia (23,25), and multidisciplinary team dynamics (20).

Finally, as recognized by the paper from Dr. Weiss, the most important barrier is poor recognition of ARDS by clinicians (16). Delayed recognition of ARDS and delayed application of LTVV is associated with prolonged and often irreversible lung injury (19). Possible approaches to improving ARDS recognition include electronic surveillance tools (18,26), change in ICU staffing models (27) and simplifying diagnostic criteria of ARDS (28). Unfortunately, none of these are particularly effective or easily generalizable to various ICU practice settings. On the other hand, there is a growing evidence of safety and efficacy of LTVV in all mechanically ventilated patients including those ventilated outside ICU (operating room, emergency department) (13,15,16,20,29). Adoption of LTVV to all ventilated patients effectively solves the challenges of timely recognition of ARDS assuring that patients with or without ARDS are not exposed to potentially injurious ventilation. Indeed, a pragmatic approach of using default initial tidal volume settings of 450 mL for adult men and 350 mL in adult women will guarantee adherence to LTVV in the vast majority of patients (19).

Patients at risk of ARDS or suspected ARDS should be treated with volume-controlled modes of ventilation using

IBW to ensure LTVV. The flow, pressure and respiratory rates could be appropriately optimized to aid in patient synchrony. Additionally, in severe cases, use of short-term neuromuscular blockade can result in improved ventilator synchrony and improved patient outcomes (30). Respiratory therapist-driven ventilator management protocols, decision support tools, adoption of quality metrics in policy and targeted provider education offer other pathways towards the goal of improved compliance (29,31-35).

In conclusion, although our understanding of ARDS and its management strategies has evolved significantly over the past decade (4,36), adoption of evidence based mechanical ventilation in real-world practice has been disturbingly slow. Adopting safe default initial ventilator settings is simple yet effective approach to ensure that patients with and without ARDS are not exposed to potentially injurious mechanical ventilation.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

### References

1. Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med* 2005;353:1685-93.
2. Yilmaz M, Gajic O. Optimal ventilator settings in acute lung injury and acute respiratory distress syndrome. *Eur J Anaesthesiol* 2008;25:89-96.
3. Li G, Malinchoc M, Cartin-Ceba R, et al. Eight-year trend of acute respiratory distress syndrome: a population-based study in Olmsted County, Minnesota. *Am J Respir Crit Care Med* 2011;183:59-66.
4. Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med* 2015;372:747-55.
5. ProCESS Investigators, Yealy DM, Kellum JA, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370:1683-93.
6. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and

- the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 2000;342:1301-8.
7. Cepkova M, Matthay MA. Pharmacotherapy of acute lung injury and the acute respiratory distress syndrome. *J Intensive Care Med* 2006;21:119-43.
  8. Ferguson ND, Cook DJ, Guyatt GH, et al. High-frequency oscillation in early acute respiratory distress syndrome. *N Engl J Med* 2013;368:795-805.
  9. Steinberg KP, Hudson LD, Goodman RB, et al. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. *N Engl J Med* 2006;354:1671-84.
  10. Walkey AJ, Wiener RS. Utilization patterns and patient outcomes associated with use of rescue therapies in acute lung injury. *Crit Care Med* 2011;39:1322-8.
  11. Putensen C, Theuerkauf N, Zinserling J, et al. Meta-analysis: ventilation strategies and outcomes of the acute respiratory distress syndrome and acute lung injury. *Ann Intern Med* 2009;151:566-76.
  12. Petrucci N, De Feo C. Lung protective ventilation strategy for the acute respiratory distress syndrome. *Cochrane Database Syst Rev* 2013;(2):CD003844.
  13. Serpa Neto A, Cardoso SO, Manetta JA, et al. Association between use of lung-protective ventilation with lower tidal volumes and clinical outcomes among patients without acute respiratory distress syndrome: a meta-analysis. *JAMA* 2012;308:1651-9.
  14. Futier E, Constantin JM, Paugam-Burtz C, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *N Engl J Med* 2013;369:428-37.
  15. Allison MG, Scott MC, Hu KM, et al. High initial tidal volumes in emergency department patients at risk for acute respiratory distress syndrome. *J Crit Care* 2015;30:341-3.
  16. Weiss CH, Baker DW, Weiner S, et al. Low Tidal Volume Ventilation Use in Acute Respiratory Distress Syndrome. *Crit Care Med* 2016;44:1515-22.
  17. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012;307:2526-33.
  18. Herasevich V, Yilmaz M, Khan H, et al. Validation of an electronic surveillance system for acute lung injury. *Intensive Care Med* 2009;35:1018-23.
  19. Needham DM, Yang T, Dinglas VD, et al. Timing of low tidal volume ventilation and intensive care unit mortality in acute respiratory distress syndrome. A prospective cohort study. *Am J Respir Crit Care Med* 2015;191:177-85.
  20. Rubenfeld GD, Cooper C, Carter G, et al. Barriers to providing lung-protective ventilation to patients with acute lung injury. *Crit Care Med* 2004;32:1289-93.
  21. Truong AD, Fan E, Brower RG, et al. Bench-to-bedside review: mobilizing patients in the intensive care unit--from pathophysiology to clinical trials. *Crit Care* 2009;13:216.
  22. Riker RR, Shehabi Y, Bokesch PM, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. *JAMA* 2009;301:489-99.
  23. Kalhan R, Mikkelsen M, Dedhiya P, et al. Underuse of lung protective ventilation: analysis of potential factors to explain physician behavior. *Crit Care Med* 2006;34:300-6.
  24. Walkey AJ, Wiener RS. Risk factors for underuse of lung-protective ventilation in acute lung injury. *J Crit Care* 2012;27:323.e1-9.
  25. Alhurani RE, Oeckler RA, Franco PM, et al. Refractory Hypoxemia and Use of Rescue Strategies. A U.S. National Survey of Adult Intensivists. *Ann Am Thorac Soc* 2016;13:1105-14.
  26. Schmickl CN, Shahjehan K, Li G, et al. Decision support tool for early differential diagnosis of acute lung injury and cardiogenic pulmonary edema in medical critically ill patients. *Chest* 2012;141:43-50.
  27. Cooke CR, Watkins TR, Kahn JM, et al. The effect of an intensive care unit staffing model on tidal volume in patients with acute lung injury. *Crit Care* 2008;12:R134.
  28. Festic E, Bansal V, Kor DJ, et al. SpO<sub>2</sub>/FiO<sub>2</sub> ratio on hospital admission is an indicator of early acute respiratory distress syndrome development among patients at risk. *J Intensive Care Med* 2015;30:209-16.
  29. Ferguson ND. Low tidal volumes for all? *JAMA* 2012;308:1689-90.
  30. Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. *N Engl J Med* 2010;363:1107-16.
  31. Bourdeaux CP, Thomas MJ, Gould TH, et al. Increasing compliance with low tidal volume ventilation in the ICU with two nudge-based interventions: evaluation through intervention time-series analyses. *BMJ Open* 2016;6:e010129.
  32. Bagga S, Paluzzi DE, Chen CY, et al. Better ventilator settings using a computerized clinical tool. *Respir Care* 2014;59:1172-7.
  33. Wolthuis EK, Korevaar JC, Spronk P, et al. Feedback and education improve physician compliance in use of lung-protective mechanical ventilation. *Intensive Care Med* 2005;31:540-6.
  34. Sjoding MW, Hyzy RC. Recognition and Appropriate

- Treatment of the Acute Respiratory Distress Syndrome Remains Unacceptably Low. *Crit Care Med* 2016;44:1611-2.
35. Yilmaz M, Keegan MT, Iscimen R, et al. Toward the prevention of acute lung injury: protocol-guided limitation of large tidal volume ventilation and inappropriate transfusion. *Crit Care Med* 2007;35:1660-6; quiz 1667.
36. Nava S, Schreiber A, Domenighetti G. Noninvasive ventilation for patients with acute lung injury or acute respiratory distress syndrome. *Respir Care* 2011;56:1583-8.

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