# A Sigh of Relief for ARDS?

Acute lung injury (ALI) is characterized by the acute onset of hypoxemia (ratio of $P_{aO_2}$ to fraction of inspired oxygen [$F_{IO_2}$] $\leq$ 300 mm Hg) and bilateral infiltrates on a frontal chest radiograph, not explained by the presence of left atrial hypertension. ALI associated with the most severe hypoxemia ($P_{aO_2}/F_{IO_2} \leq 200$ mm Hg) is termed acute respiratory distress syndrome (ARDS).[1] ALI and ARDS have a crude incidence of 79 cases and 59 cases per 100,000 persons per year, respectively, and ALI and ARDS cause substantial mortality (34–58%) and economic burden.[2,3]

The lung-protective ventilation strategy, which involves small tidal volume and low airway pressure, is the only intervention found to reduce mortality from ALI and ARDS.[4] However, the lung-protective strategy may be associated with progressive lung derecruitment and worsening oxygenation.[5] *Recruitment* refers to the dynamic process of reopening airless alveoli with an intentional transient increase in transpulmonary pressure. Recruitment maneuvers significantly increase oxygenation in some patients, and have few serious adverse effects.[6] The rationale for recruitment maneuvers in ALI is to improve alveolar recruitment and increase end-expiratory lung volume, which improves gas exchange, reduces overdistention of relatively healthy lung units, and prevents repetitive opening and closing of unstable alveoli, all of which attenuate ventilator-induced lung injury.[7,8]

Despite the physiologic benefits of recruitment maneuvers in ALI, clinical studies have yielded variable results.[9-11] The targets (maximum recruitment vs limiting overdistention), time of initiation (early vs late), duration, optimal pressure, and frequency of recruitment maneuvers are still unclear. Furthermore, the various recruitment-maneuver methods (eg, sustained inflation maneuvers, high pressure controlled ventilation, incremental positive end-expiratory pressure [PEEP], and intermittent sighs) have different physiologic responses in the lungs.[12] In randomized controlled trials, ventilatory strategies that use recruitment and an "open-lung" approach have not demonstrated a mortality benefit over pressure-limited ventilation.[13-15]

In this edition of the Journal, Badet et al present the findings of a single-center trial of sighs and PEEP in patients with ALI/ARDS.[16] They evaluated a method to identify an "optimal" PEEP that would prevent lung derecruitment, and the effects of sustained inflations and sigh breaths (with twice the baseline tidal volume, and a plateau pressure of $<$ 40 cm $H_2O$, every 25 breaths) on lung-volume recruitment. The study was well performed and adds to the growing body of literature on the potential role of recruitment maneuvers and PEEP in the management of ARDS.

See the Original Study on Page 847

Badet et al demonstrate the utility of their simple decremental PEEP test, which uses oxygen desaturation to identify the individualized PEEP that maintains lung recruitment. Their method is easy to perform at the bedside and makes more physiologic sense than other methods of determining PEEP, based on our current understanding of the pathophysiology of ARDS.[17,18] Badet et al found that the PEEP determined via their method maintained the oxygenation benefits of a prior sustained-inflation recruitment maneuver, although not as well as superimposed sighs. The sighs, superimposed on pressure-controlled mechanical ventilation (6 mL/kg) with optimal PEEP, improved the oxygenation and static compliance of the respiratory system, but Badet et al did not address the reasons for those oxygenation and compliance improvements. It has been suggested that sighs and repeated recruitment maneuvers may reverse reabsorption atelectasis, which develops over time, whereas PEEP is effective largely to prevent compressive atelectasis.[9] The variability of tidal volume may represent a limited form of "noisy" ventilation, which is reported to improve respiratory function.[19]

The study by Badet et al has several limitations. The sample size was small and patients were not randomly or successively recruited, which might have caused a biased cohort. The study duration was short: one hour with each strategy. Lung-volume recruitment was not actually measured, and improvement in alveolar recruitment is usually associated with a decrease in $P_{aCO_2}$, which Badet et al did not observe. Furthermore, their measure of improvement (oxygenation) has not been associated with better outcome in ARDS. As yet there is no evidence that recruitment maneuvers impact clinical outcome. The findings from Badet et al are interesting, but their application to clinical practice needs to be critically evaluated.

The return of sighs to the medical literature is an interesting phenomenon. Sighs were originally introduced on the basis of an observation during anesthesia in animals and patients with normal lungs: that breathing with very small tidal volumes decreased the resting lung volume and compliance, and increased the alveolar-arterial oxygen dif-

ference, and that those effects could be reversed by intermittent large breaths (sighs), which recruited alveoli and improved static compliance. Alveolar recruitment can also be achieved by increasing the end-expiratory volume (ie, by applying PEEP). Although sighs were first offered as a setting on mechanical ventilators in the 1960s and 1970s, the increasing use of PEEP reduced the need for sighs. In fact, a 1976 editorial in RESPIRATORY CARE, "The Mechanical Ventilation Sigh Is a Dodo," described the redundancy of sighs with then-current ventilation techniques.[20] The study by Badet et al adds to a small body of literature[9,21] on the potential role of sighs in the modern management of ARDS with pressure-limited ventilation strategies, and suggests a benefit even in the presence of optimal PEEP. More robust clinical trials with well-defined clinical end points are required to clarify the outcome benefit of this approach. Until then, recruitment maneuvers, including sighs, could be considered for individuals with ALI and ARDS, with the understanding that, though oxygenation may improve, there is as yet no documented mortality benefit.

**Philip George MB MRCP**
**Stephen E Lapinsky MB BCh MSc FRCPC**
Intensive Care Unit
Mount Sinai Hospital
Toronto, Ontario, Canada

#### REFERENCES

1. Ware LB, Matthay MA. The acute respiratory distress syndrome. N Engl J Med 2000;342(18):1334-1349.
2. Rubenfeld GD, Herridge MS. Epidemiology and outcomes of acute lung injury. Chest 2007;131(2):554-562.
3. Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, et al. Incidence and outcomes of acute lung injury. N Engl J Med 2005;353(16):1685-1693.
4. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.
5. Richard JC, Maggiore SM, Jonson B, Mancebo J, Lemaire F, Brochard L. Influence of tidal volume on alveolar recruitment. Respective role of PEEP and a recruitment maneuver. Am J Respir Crit Care Med 2001;163(7):1609-1613.
6. Fan E, Wilcox ME, Brower RG, Stewart TE, Mehta S, Lapinsky SE, et al. Recruitment maneuvers for acute lung injury: a systematic review. Am J Respir Crit Care Med 2008;178(11):1156-1163.
7. Lapinsky SE, Mehta S. Bench-to-bedside review: recruitment and recruiting maneuvers. Crit Care 2005;9(1):60-65.
8. Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med 2005;3(6)1:776-784.
9. Pelosi P, Cadringher P, Bottino N, Panigada M, Carrieri F, Riva E, et al. Sigh in acute respiratory distress syndrome. Am J Respir Crit Care Med 1999;159(3):872-880.
10. Lapinsky SE, Aubin M, Mehta S, Boiteau P, Slutsky AS. Safety and efficacy of a sustained inflation for alveolar recruitment in adults with respiratory failure. Intensive Care Med 1999;25(11):1297-1301.
11. Brower RG, Morris A, MacIntyre N, Matthay MA, Hayden D, Thompson T, et al; The ARDS Clinical Trials Network; National Heart, Lung, and Blood Institute; National Institutes of Health. Effects of recruitment maneuvers in patients with acute respiratory distress syndrome ventilated with high positive end-expiratory pressure. Crit Care Med 2003;31(11):3592-2597. Erratum in: Crit Care Med 2004; 32(3):907.
12. Lim SC, Adams AB, Simonson DA, Dries DJ, Broccard AF, Hotchkiss JR, Marini JJ. Intercomparison of recruitment maneuver efficacy in three models of acute lung injury. Crit Care Med 2004; 32(12):2371-2377.
13. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al; National Heart, Lung, and Blood Institute; ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 2004;351(4):327-336.
14. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, Davies AR, Hand LE, Zhou Q, Thabane L, et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2008;299(6):637-645.
15. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, et al; Expiratory Pressure (Express) Study Group. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2008;299(6): 646-655.
16. Badet M, Bayle F, Richard J-C, Guerin C. Comparison of optimal positive end-expiratory pressure and recruitment maneuvers during lung protective mechanical ventilation in patients with acute lung injury/acute respiratory distress syndrome. Respir Care 2009;54;847-854.
17. Hickling KG. Best compliance during a decremental, but not incremental, positive end-expiratory pressure trial is related to open-lung positive end-expiratory pressure: a mathematical model of acute respiratory distress syndrome lungs. Am J Respir Crit Care Med 2001; 163(1):69-78.
18. Maggiore SM, Jonson B, Richard JC, Jaber S, Lemaire F, Brochard L. Alveolar derecruitment at decremental positive end-expiratory pressure levels in acute lung injury: comparison with the lower inflection point, oxygenation, and compliance. Am J Respir Crit Care Med 2001;164(5):795-801.
19. Mutch WA, Harms S, Ruth Graham M, Kowalski SE, Girling LG, Lefevre GR. Biologically variable or naturally noisy mechanical ventilation recruits atelectatic lung. Am J Respir Crit Care Med 2000;162(1):319-323.
20. Fairley HB. The mechanical ventilation sigh is a dodo. Respir Care 1976;21(11):1127-1130.
21. Davis K Jr, Branson RD, Campbell RS, Porembka DT, Johnson DJ II. The addition of sighs during pressure support ventilation. Is there a benefit? Chest 1993;104(3):867-870.

---

The authors have disclosed no conflicts of interest.

Correspondence: Stephen E Lapinsky MB BCh MSc FRCPC, Intensive Care Unit, Mount Sinai Hospital, 600 University Avenue, 18-214, Toronto ON M5G1X5, Canada. E-mail: stephen.lapinsky@utoronto.ca.