Editorial



# "Open the lung and keep it open": a homogeneously ventilated lung is a 'healthy lung'

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The acute respiratory distress syndrome (ARDS) has been a major cause of morbidity and mortality in the intensive care unit (ICU) for over four decades. What was thought to be a universally fatal form of double pneumonia was first identified in 1967 as a unique clinical entity and is now what we call ARDS. Ashbaugh *et al*. first identified ARDS as a unique disease triggered by a collection of pathologic abnormalities from initiating injuries such as sepsis, pneumonia, trauma or burns (1). In addition, this group demonstrated that ARDS mortality could be significantly reduced if positive end expiratory pressure (PEEP) was added to the ventilator strategy (1). Mortality secondary to ARDS was almost 70% from 1967–1979 and has been reduced progressively over the decades [60%: 1980–1989; 50%: 1990–1997] to the current mortality of ~40% [1998-2013] (2). Although we have significantly reduced ARDS mortality from when it was first identified, mortality has not been reduced any further over last 15 years (3).

Pharmacological treatments of ARDS have been largely unsuccessful (4). The most successful therapeutic strategies to date have been proning the patient (5) and low tidal volume (Vt) ventilation strategy (6). Increasing PEEP has not been shown to improve mortality below that of low Vt (7) except in subgroup analysis of the most severe ARDS cases (8). Thus, there is an urgent need to develop new ventilation strategies to reduce ARDS mortality. In 1992, Dr. Lachmann coined a phrase, "*Open the lung and keep it open*", to use as a lung protective strategy (9). The hypothesis behind this statement is that heterogeneous lung inflation, which is a hallmark of ARDS pathology, is a major cause of further lung damage during mechanical ventilation. The corollary to this hypothesis is that if you can open the lung and keep it open, the homogeneously ventilated lung would be protected from ventilator induced lung injury (VILI) and ARDS mortality would be reduced.

Kacmarek *et al*. recently published a pilot randomized controlled clinical trial testing the 'open the lung and keep it open' hypothesis on patients with established ARDS (10). This study compared the standard of care low Vt ventilation strategy (6) with an open lung approach (OLA). Using the OLA, the lung was first recruited and the level of PEEP necessary to keep the lung open following recruitment was individualized to each patient using a decremental PEEP trial. The combination of these two consecutive interventions is what separates the OLA from a simple lung recruitment maneuver using a set pressure over a period of time (i.e., airway pressure set at 40 $cmH_2O$ and held for 40 seconds without PEEP adjustment). In addition, the OLA used in this study differed from studies in which PEEP was set without first recruiting the lung. Without an initial lung recruitment, even with identical PEEP levels, ventilation will be at a much lower end-expiratory lung volume, exacerbating lung heterogeneity (11). Another difference between this study and previous randomized controlled trials (12-14) is that patients were reevaluated 24 hours after ARDS diagnosis to ensure only patients with established ARDS were randomized. Thus, patients enrolled in this study had a more severe lung injury than in previous published trials (12-14). The study showed that the OLA improved oxygenation and reduced driving pressure but did not reduce mortality or ventilator-free days. However, their 60-day (28%) and ICU (25%) mortality in the OLA group was one of the lowest reported for patients with established ARDS. Although the study was initially powered for 600 patients it was terminated with 99 patients in the OLA groups and 101 patients in the ARDS net low Vt group for a number

of logistical reasons. However, the promising results in the secondary endpoints support the need for a multicenter trial comparing OLA against the low Vt standard of care.

This is an important study since it supports our current understanding of the pulmonary pathophysiology associated with ARDS and the role played by mechanical ventilation in either preventing or exacerbating this initial lung injury. A recent review on the impact of mechanical ventilation during progressive acute lung injury shows that a physiologically based ventilation strategy can block all of the pathologic tetrad that are the hallmarks of ARDS (15). Multiple combinations of mechanical breath parameters, most often Vt and PEEP, in many animal models of ARDS have been shown to reduce pulmonary vascular permeability, pulmonary edema, preserve surfactant function and stabilize alveoli, minimizing strain-induced tissue damage known as atelectrauma (15). Thus, the physiologic foundation for protective mechanical ventilation is well established and all that is necessary is to identify the optimal combination of mechanical breath parameters (e.g., airway pressures, volumes, flows, rates and the duration that they are applied to the lung during both inspiration and expiration) that maximize lung tissue protection.

To this end, Gattinoni's group recently published two papers using an engineering analysis to determine the impact of the mechanical breath on the lung injury (16,17). They demonstrated that the applied stress, which for the lung is the Vt, impacts: (I) lung anatomy resulting in either collapse and heterogeneity or recruitment and homogeneous ventilation; (II) the energy load placed upon the lung and (III) dynamic strain (e.g., the change in lung size and shape in response to the applied stress) on lung tissue. Their studies showed that if the volumetric threshold (i.e., the limit of inspiratory capacity) was exceeded VILI occurred, secondary to stress rupture (pneumothorax). However, if the lower limit of inspiratory capacity was reached, but not exceeded, excessive dynamic strain (high Vt plus low PEEP) caused VILI, whereas a high static strain (low Vt plus high PEEP) did not (16). In addition, Protti *et al.* showed that PEEP was lung protective as long as it was associated with reduced Vt, increasing static strain but reducing dynamic strain (17).

Would the OLA be lung protective using this engineering analysis? The plateau pressures in the Kacmarek study (10) were less than 30 $cmH_2O$, suggesting that the inspiratory capacity was not exceeded and thus preventing VILI due to stress rupture. Also the PEEP was higher (static strain) and the Vt was lower (dynamic strain) on days 1 and 3, thus stabilizing the lung and minimizing dynamic strain, which was shown to be the major mechanism of VILI (16,17). Gattinoni's group also stressed that in ARDS the "inhomogeneity factor" with uneven distribution of volumes and pressures could induce local stress/strain relationships double that of the entire lung. Thus, recruiting the lung before application of an appropriate and personalized PEEP to keep the lung open would result in improved homogeneity, further protecting from VILI (10). The improvements in lung function using the OLA in the Kacmarek study make sense from a physiologic standpoint, supporting further work with this protective lung strategy.

From a physiologic standpoint if conventional mechanical ventilation (CMV) is used to ventilate patients with established ARDS, the OLA strategy should be optimal to, 'open the lung and keep it open'. However, an alternative strategy would be to, 'Never let the lung collapse'. Recent studies suggest that the preferred strategy in patients at high-risk would be to reduce the incidence of ARDS, using a preemptive mechanical ventilation strategy. This preemptive strategy would apply protective mechanical ventilation as soon as the patient is intubated, before the development of acute lung injury (18). With an ARDS mortality still at ~40%, with no decrease in over 15 years, reducing ARDS incidence is a very appealing approach. In addition to a preemptive low Vt strategy using CMV (18) others have shown reduced ARDS incidence in a high-fidelity, clinically applicable animal ARDS model (19) and a clinical statistical analysis (20) using preemptive airway pressure release ventilation (APRV).

In conclusion, based on our current knowledge of lung pathophysiology the OLA seems optimal for patients on CMV with established ARDS. Hopefully, improved preemptive ventilation strategies designed to reduce ARDS incidence may render the very difficult job of ventilating the ARDS patient obsolete, greatly reducing the morbidity and mortality of this serious medical problem.

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## Footnote

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## References


1. Ashbaugh DG, Bigelow DB, Petty TL, et al. Acute respiratory distress in adults. Lancet 1967;2:319-23.
2. Villar J, Sulemanji D, Kacmarek RM. The acute respiratory distress syndrome: incidence and mortality, has it changed? Curr Opin Crit Care 2014;20:3-9.
3. Villar J, Blanco J, Kacmarek RM. Current incidence and outcome of the acute respiratory distress syndrome. Curr Opin Crit Care 2016;22:1-6.
4. Boyle AJ, Mac Sweeney R, McAuley DF. Pharmacological treatments in ARDS; a state-of-the-art update. BMC Med 2013;11:166.
5. Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368:2159-68.
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. Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med 2004;351:327-36.
8. Briel M, Meade M, Mercat A, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA 2010;303:865-73.
9. Lachmann B. Open up the lung and keep the lung open. Intensive Care Med 1992;18:319-21.
10. Kacmarek RM, Villar J, Sulemanji D, et al. Open lung approach for the acute respiratory distress syndrome: a pilot, randomized controlled trial. Crit Care Med 2016;44:32-42.
11. Suter PM, Fairley B, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. N Engl J Med 1975;292:284-9.
12. Meade MO, Cook DJ, Guyatt GH, 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;299:637-45.
13. Mercat A, Richard JC, Vielle B, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2008;299:646-55.
14. Talmor D, Sarge T, Malhotra A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359:2095-104.
15. Nieman GF, Gatto LA, Habashi NM. Impact of mechanical ventilation on the pathophysiology of progressive acute lung injury. J Appl Physiol (1985) 2015;119:1245-61.
16. Protti A, Andreis DT, Monti M, et al. Lung stress and strain during mechanical ventilation: any difference between statics and dynamics? Crit Care Med 2013;41:1046-55.
17. Protti A, Andreis DT, Milesi M, et al. Lung anatomy, energy load, and ventilator-induced lung injury. Intensive Care Med Exp 2015;3:34.
18. Neto AS, Simonis FD, Barbas CS, et al. Lung-protective ventilation with low tidal volumes and the occurrence of pulmonary complications in patients without acute respiratory distress syndrome: a systematic review and individual patient data analysis. Crit Care Med 2015;43:2155-63.
19. Roy S, Habashi N, Sadowitz B, et al. Early airway pressure release ventilation prevents ARDS-a novel preventive approach to lung injury. Shock 2013;39:28-38.
20. Andrews PL, Shiber JR, Jaruga-Killeen E, et al. Early application of airway pressure release ventilation may reduce mortality in high-risk trauma patients: a systematic review of observational trauma ARDS literature. J Trauma Acute Care Surg 2013;75:635-41.


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