“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 cmH₂O 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
Thus stabilizing the lung and minimizing dynamic strain, the Vt was lower (dynamic strain) on days 1 and 3, to stress rupture. Also the PEEP was higher (static strain). The plateau pressures in the Kacmarek study (10) were less than 30 cmH₂O, suggesting that the inspiratory capacity was not exceeded and thus preventing VILI due to static strain. 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).

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 cmH₂O, 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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