The Complexity of Interpreting Plateau Pressure in ARDS

In the early years of lung-protective ventilation, it was thought that limiting plateau pressure (P_{plat}), a signifier of alveolar stress, was important for improving survival in patients with ARDS. However, there were no clinical data and no agreement on the limit. A 1993 consensus conference recommended that P_{plat} be limited to 35 cm H_2O.[1] This was based on the assumption that, despite heterogeneous lung injury, it was probably safe to ventilate the lungs at or below total lung capacity, which would correspond to a P_{plat} of 30–35 cm H_2O.[2] Others suggested that a more liberal P_{plat} limit of 40–50 cm H_2O might be reasonable in severe ARDS.[3-5]

It is astonishing to witness the change that has occurred in our approach to targeting P_{plat} since the seminal ARMA trial.[6] Since then, a tidal volume (V_T) targeted between 4 and 8 mL/kg is generally used to keep P_{plat} at $\leq$ 30 cm H_2O. Post-ARMA studies suggest that not only does lung-protective ventilation decrease the likelihood of developing ARDS,[7] but also that there may not be an unambiguously safe P_{plat} in patients with established ARDS.[8,9]

The study by Chan et al[10] in this issue of RESPIRATORY CARE specifically examines the importance of limiting P_{plat} in patients with sepsis. Their primary finding was that during the first 24 h of mechanical ventilation, the mean P_{plat} was higher in nonsurvivors despite being $<$ 30 cm H_2O. Moreover, at 24 h, those subjects with a P_{plat} of $>$ 25 cm H_2O had nearly a 3-fold higher mortality risk. These findings are similar to those in subjects with established ARDS, wherein despite achieving a V_T of 6 mL/kg, subjects with a P_{plat} of 28–30 cm H_2O had higher regional pulmonary hyperinflation and pro-inflammatory mediator release associated with higher mortality compared with subjects with a P_{plat} of 25–26 cm H_2O.[9] We also observed a trend toward higher mortality during lung-protective ventilation related to a mean P_{plat} of ~25 cm H_2O versus 27–29 cm H_2O during the first week of ARDS.[11,12] When viewed together, these studies suggest that just achieving a P_{plat} of $\leq$ 30 cm H_2O may not be sufficient to optimize survival from ARDS or sepsis.

An intriguing finding of Chan et al[10] was that nonsurvivors were actually managed more closely to lung-protective ventilation goals in terms of mean V_T and PEEP compared with survivors. Nonsurvivors were sicker as judged by significantly higher Acute Physiology and Chronic Health Evaluation II scores, larger positive fluid balance, and lower respiratory system compliance. Thus the interpretation of what the higher P_{plat} in nonsurvivors signified in this study is not altogether clear.

Both P_{plat} and respiratory system compliance are convenient but crude surrogates for lung stress. As these variables are system measurements (ie, lung and chest wall compliance exists in series), their physiologic validity in terms of lung stress rests upon the assumption that chest wall compliance remains normal. In ARDS, that assumption is precarious, as most studies examining pulmonary mechanics reported that chest wall compliance in ARDS was reduced by 50–80%.[13]

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This is particularly relevant when managing ARDS associated with systemic capillary leak (eg, sepsis, trauma, burns). These patients often require aggressive fluid resuscitation to maintain systemic perfusion, which, in consequence, aggravates fluid extravasation into the extracellular compartment, thus reducing both lung and chest wall compliance. Mortality in critically ill patients (including those with sepsis or ARDS) is associated with increased extravascular lung water[14,15] and impaired alveolar fluid clearance.[16] Conservative fluid management has been shown to reduce mortality[17] or to be associated with a trend toward reduced mortality in ARDS.[18]

Furthermore, recent research into ventilator-associated lung injury has uncovered an important contribution from altered pulmonary hemodynamics. In brief, the combination of elevated pulmonary arterial pressures (transmitted to extra-alveolar vessels) with high inflation pressures amplifies transmicrovascular pressures sufficient to cause stress fractures in the pulmonary endothelium. The critical pressure gradient needed to induce capillary stress failure is likely influenced by the deleterious effects of surfactant depletion and inflammation on the integrity of the base-

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ment membrane.[19] Thus, the interpretation of controlling P_{plat} in ARDS is highly contextualized and includes ambiguities in a popular classification scheme.

It is conceptually convenient to designate ARDS as either direct (pulmonary) injury caused by pneumonia, aspiration, contusion, or inhalation injury or indirect (extrapulmonary or blood-borne) injury caused by sepsis, non-thoracic trauma, pancreatitis, or transfusion reactions. These distinctions in etiology are conjoined with observed differences in pulmonary mechanics attributed to the underlying pathogenesis.[20] In brief, direct injury is characterized by alveolar consolidation, which ostensibly occurs with relatively lower potentially recruitable lung tissue. In contrast, indirect injury appears more amenable to recruitment because it is characterized by congestive and compressive atelectasis.

This scheme has been useful in providing a general guide for applying higher PEEP and recruitment maneuvers in different etiologies of ARDS. Unfortunately, it is also likely to be an oversimplification of a complex problem. Pneumonia is the leading cause of both ARDS and sepsis (accounting for ~50% of cases),[21] thus considerably blurring an otherwise elegant classification scheme. More importantly, on average, the alveolar-capillary membrane is only 0.6 μm thick,[22] making it implausible that the inflammatory response to parenchymal injury would result in such distinct manifestations depending upon which side of the barrier was initially injured.

The major distinction between pulmonary and extrapulmonary ARDS is the effect of abdominal distention on chest wall compliance.[20,23] Aggressive volume infusion tends to cause abdominal distention, resulting in decreased chest wall compliance and lung compression.[24] Patients with intra-abdominal injuries, pancreatitis, extensive burns, or sepsis would more likely exhibit the mechanical problems we classify as extrapulmonary ARDS. However, we have observed obese patients with ARDS (both from H1N1 and bacterial pneumonia) whose response to high PEEP and recruitment maneuvers was indistinguishable from that of similarly treated patients with so-called extrapulmonary ARDS.

Furthermore, these ambiguities lend support for measuring esophageal pressure (P_{es}) to estimate end-inspiratory and end-expiratory transpulmonary pressure in ARDS. This would likely improve the implementation of lung-protective ventilation (at least in the subset of patients suspected of having reduced chest wall compliance), as it would allow for the estimation of gross transpulmonary pressure when setting both V_T and PEEP ($P_{plat} - P_{es}$ end inspiration; PEEP $- P_{es}$ end expiration). A further refinement would be integrating dead-space measurements with transpulmonary pressure measurements, as the combination may help in both identifying and balancing lung recruitment and overdistention. However, as others have pointed out,[25] measuring P_{es} has important limitations. It requires relatively extensive knowledge of pulmonary mechanics, as well as bedside experience to master its ambiguities.

Notwithstanding these challenges, the importance of measuring chest mechanics in ARDS will likely gain importance and should provide professional growth opportunities for respiratory therapists. For now, the take-home message for managing ARDS or sepsis is that, when feasible, V_T should be targeted to achieve a P_{plat} goal of 25 cm H_2O.

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