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Still Looking for Best PEEP

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The recruitment of airless and/or closed lung units is one of the central tenets of the open lung protective approach to mechanical ventilation in acute respiratory distress syndrome (ARDS). Recruitment strategies seek to “open” collapsed lung units in order to reduce parenchymal strain by distributing a given volume of inspired gas across a greater number of alveoli. In addition, epithelial injury from interfacial stress may be prevented by minimizing atelectrauma, which arises as a consequence of the repeated opening and collapse of unstable lung units.¹ Parenchymal strain, in turn, an index of tissue deformation, is closely linked to alveolar tidal expansion and is the single most important risk factor of Ventilator Induced Lung Injury². Strain-sensitive injury mechanisms include both an alteration in pulmonary vascular barrier properties leading to alveolar flooding and surfactant dysfunction, as well as tensile stress mediated effects on cell and tissue integrity and associated pro-inflammatory mechanotransduction responses. Unfortunately many popular terms including atelectrauma, alveolar overdistension, hyperinflation, volutrauma and biotrauma capture only selected aspects of this complex mechanobiology. Uncertainty in the causal pathways involving physical input and tissue responses are not always clear which yields controversy in the choice of ventilation mode, setting and recruitment strategy.

In order to recruit atelectatic alveoli, injured lungs must typically be inflated using high applied pressures followed by the application of Positive End Expiratory Pressure (PEEP) to prevent loss of the recruitment gains. Despite concerted efforts to define the optimal recruitment and PEEP management strategy, clinical trials on the topic have so far failed to provide clear guidance.^{3–5} In the absence of compelling data, one could reach any one of following conclusions: 1) PEEP management decisions have a much smaller impact on lung protection than for example the choice of applied tidal volume; 2) means of assessing alveolar recruitment have limited specificity; 3) atelectrauma is less prevalent than alternative biophysical lung injury mechanisms; 4) the possible benefit of aggressive recruitment strategies is all too often offset by the risk of hemodynamic compromise and/or potentially injurious stresses applied to already open units.

Underlying each of these conclusions are assumptions about the topographical distribution of lung mechanical properties and therefore stress and strain in injured lungs. The most

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widely cited model of regional lung mechanics in ARDS is one proposed by Gattinoni⁶. Accordingly, the injured lung is like a wet sponge, which is heavy and therefore collapses under its own weight. The model is appealing in its simplicity and predicts gravitational gradients in lung density, which can be readily observed in computed tomography (CT) images of ARDS patients lying supine. The model assumes that the pressure required to reexpand a collapsed region of the lung is largely a function of the weight of the overlying lung tissue and as such offers a testable hypothesis about the impact of PEEP on regional lung volumes and ventilation. In this issue of *Anesthesiology* Cressoni et al. report the results of experiments designed to explore the relationships between lung recruitability and CT based estimates of superimposed lung compressive pressure in patients with ARDS.⁷ Contrary to predictions, “heavy lungs” were no less recruitable than “light ones” leading the authors to conclude that PEEP management targets are not informed by CT based estimates of lung density.

The “wet sponge” model has been challenged on both theoretical⁸ and experimental grounds⁹. The original challenge arose out of concern for the confounding influence of alveolar edema on CT density. More importantly, the physics of recruitment cannot be understood without considering the effects of external compressive forces (e.g. elevated pleural pressure) and surface tension on the opening pressure of the closed segments. Surface forces generated by air-liquid interfaces at occlusion sites, be they located in small airways, alveolar ducts or alveolar entrance rings, must be overcome before luminal pressure within the closed segment can rise and counteract compressive forces. If the occluded segment also contains trapped gas and therefore behaves like wet foam, the computational approach to the problem becomes quite challenging, but the fundamental mechanism responsible for impeding recruitment, namely surface tension, remains the same. The lack of correlation between CT based density estimates and lung recruitability does not seem so surprising if one considers 1) that it is nearly impossible to quantify extent and distribution of occluding liquid plugs in the dichotomously branching airway tree, 2) that CT imaging cannot inform about the liquid vs. solid nature of the material that occludes or fills the affected lung segment 3) that the segment of interest is also exposed to unknown traction forces that are exerted by surrounding lung parenchyma and 4) that in the supine posture the weight of the abdomen imposes a lung-compressive stress, which raises pleural pressure, but is not accounted for by chest wall compliance.

While to a clinician the preceding arguments may seem esoteric and directed largely at physiologists, they do motivate a reappraisal of the risks and goals of prevailing ventilator management strategies. Cressoni et al. make the compelling argument that the rationale for using high PEEP in low recruiters is relatively weak and point out that none of the existing PEEP management trials have stratified patients according to lung recruitability. If the primary objective of raising PEEP is to minimize the risk of atelectrauma, then efficacy ought to be linked to recruitability. Without affecting alveolar recruitment, the adverse consequences of high PEEP on hemodynamics and alveolar wall stress will likely dominate the treatment response. Indeed, some post hoc and meta-analyses have suggested that high levels of PEEP are associated with harm in patients with mild ARDS.^{10,11} Cressoni et al may not have silenced the debate how to best individualize the approach to PEEP management. However, they should be congratulated for having reminded us that the

determinants of regional lung mechanics are complex, and that measures of global lung function may not reveal them.

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