PEEP Titration: New Horizons

Most respiratory practitioners agree that PEEP helps to recruit and maintain alveoli that would otherwise collapse or suffer tidal inflation and deflation. PEEP thus reduces atelectrauma, shear forces, and systemic inflammatory mediator release. These benefits are balanced against consequences. PEEP can lead to overdistention of lung units, especially those that remain normal in the midst of heterogeneous lung injury. High PEEP does not always translate to an "open lung"; several studies have shown that atelectasis actually increases when PEEP is set above the optimal level, due to ventilator-induced lung injury or collapse in dependent areas in the setting of overdistention of others.[1-3] Animal studies have described the cellular level pathophysiology for PEEP above and below levels that achieve optimal oxygenation and elastance. Low[4-6] and high PEEP[5,6] ventilation in mice increased histological lung injury, including edema, hemorrhage, and inflammation. PEEP can have adverse hemodynamic effects related to reduced right-ventricle filling and increased afterload on the right ventricle.[7]

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The majority of reports regarding PEEP selection have been in the setting of ARDS. Clinical trials designed to determine the optimal PEEP have centered on high PEEP versus lower PEEP. Two of these trials used pre-set PEEP/F_{IO_2} tables,[8,9] and one titrated PEEP to a plateau pressure of 28–30 cm H_2O regardless of oxygenation.[10] These trials utilized PEEP levels higher than those in the traditional ARDS Network PEEP/F_{IO_2} tables. A meta-analysis of these trials found that higher PEEP decreased the in-hospital mortality by 5% in the subgroup of patients with moderate and severe ARDS.[11,12] High PEEP also decreased the use of rescue therapies and improved oxygenation early in the intervention.

There is a complementary body of data from trials suggesting alternative approaches to individualize PEEP in patients with ARDS. These trials have targeted a variety of variables for PEEP titration: end-expiratory transpulmonary pressure,[13] dead space,[14] dynamic compliance,[15] stress index,[16] electrical impedance tomography,[17] computed tomography,[18] and ultrasonography.[19] Some of these trials compared an alternative approach to obtain optimal PEEP to the traditional ARDS Network F_{IO_2}/PEEP table and found higher applied PEEP. In general, when a variable other than oxygenation was optimized, compliance and oxygenation also improved. These trials were too small to identify a mortality benefit.

PEEP titration has been evaluated in other settings. These data depend heavily on mechanical and animal data rather than clinical trials. In airway obstruction, the role of PEEP depends on patient interaction with the ventilator. For the spontaneously breathing patient, intrinsic PEEP (auto-PEEP) is an important concern. In flow-triggered or pressure-triggered ventilation the patient must overcome auto-PEEP before achieving the trigger threshold, which substantially increases the effort required to trigger the ventilator. By setting the applied PEEP just below the measured auto-PEEP, the effort required to trigger the ventilator is reduced,[20] as discussed in the "waterfalls" editorial by Tobin and Lodato.[21] Less regional variation in auto-PEEP and recruitment of dependent and collapsed lung units may explain this potential benefit. The role of PEEP in the passively ventilated patient with airway obstruction is less clear. However, PEEP is of likely benefit, for the reasons described above, and is commonly applied. Despite theoretical benefits in airway obstruction, adverse effects of applied PEEP are possible. Lung compliance is relatively normal in COPD and asthma, and even a low PEEP may result in overdistention. This concern has been addressed in small animal studies.[22] A role for PEEP is more widely accepted in COPD than in asthma. The mechanism of obstruction (parenchymal destruction vs bronchiole inflammation and smooth muscle constriction), as well as the presence of mucus plugging, plays a role in this distinction.[23]

Intra-abdominal hypertension is another widely recognized complication of critical care practice. Recent preclinical work investigated setting PEEP relative to the measured intra-abdominal pressure, in animal models.[24-27] In swine with intra-abdominal hypertension and normal lungs, PEEP set at half the intra-abdominal pressure returned the functional residual capacity (FRC) to the value seen with normal intra-abdominal pressure. In an oleic acid injury model, PEEP set at half the intra-abdominal pressure improved oxygenation but did not significantly improve FRC. In detergent or oleic acid injured lungs, PEEP set 1:1 to intra-abdominal pressure improved FRC but was associated with hypotension, most likely related to elevated intrathoracic pressure. A clinical study examining a mix-

ture of pulmonary and non-pulmonary ARDS patients with grade I-II intra-abdominal hypertension (intra-abdominal pressure of 12–20 mm Hg) found that PEEP of approximately half the intra-abdominal pressure increased lung and respiratory system elastance but did not improve oxygenation.[28] Most clinical studies in ARDS have not accounted for intra-abdominal pressure explicitly, although some have specifically examined the contribution of the chest wall to airway pressure requirements.[29] Studies regarding optimum titration of PEEP in patients with lung injury and intra-abdominal hypertension are ongoing.

There has been some examination of PEEP in extrapulmonary intrathoracic processes as well. Pleural effusion is commonly encountered clinically, but the data regarding optimal use of PEEP is limited. Evaluation has primarily been in animal models. In uninjured lungs with unilateral large effusions (26 mL/kg), PEEP of 10 cm H_2O improved FRC to the baseline level. Computed tomography data suggest that PEEP recruited dependent lung units in the ipsilateral and contralateral lungs and decreased tidal recruitment in areas directly compressed by effusion.[30] These changes were not evident on static compliance measurements, suggesting that FRC improvement may be a better marker of optimal PEEP in this setting.

In this issue of RESPIRATORY CARE, Pintado et al describe a method of titrating PEEP based on "best compliance," as determined by tidal volume divided by the difference between plateau pressure and PEEP.[31] In comparison to patients receiving PEEP according to the ARDS Network F_{IO_2}/PEEP table, Pintado et al found significantly fewer days of multi-organ system dysfunction and hemodynamic failure, as well as more ventilator-free days. There was a trend toward decreased mortality. Average PEEP level was similar in both groups. Eighty percent of patients in the treatment group, however, had a different PEEP than would have been assigned according to the ARDS Network protocol.

Previous trials have assessed compliance through dynamic measurement or the inflection point on the pressure-volume curve. Pintado et al report that this is the first published clinical study of using best static compliance for PEEP titration. A multicenter trial is now underway evaluating decremental PEEP titration based on best static compliance.[32] This is an attractive method for PEEP titration and uses techniques that are universally understood. Theoretically, targeting the best static compliance should identify an area on the pressure/volume curve that minimizes atelectasis and overdistention. In addition, static compliance accounts for chest wall compliance, as patients with decreased chest wall compliance would likely benefit from increased PEEP to prevent derecruitment.[29]

It is notable, given previous data that "high PEEP" strategies decreased mortality in ARDS,[11] that the average PEEP was similar between the groups in the Pintado et al study. This is consistent with mechanistic data that imply that a moderate level of PEEP avoids the dangers of both overdistention and tidal recruitment. In addition, it addresses the dichotomy of ARDS into recruitable and non-recruitable types: patients with highly recruitable lung injury would benefit from a higher PEEP strategy, while those with non-recruitable pathology would be best served with a moderate PEEP that prevents air-space collapse, but nothing further.

PEEP titration as described by Pintado et al aims for the middle ground. This approach is clinically feasible but labor intensive, relative to simply following the PEEP/F_{IO_2} table developed for the ARDS Network study group. These results are impressive, given use of a time-tested ventilatory strategy as a control group, but require duplication with a larger sample size.

There are additional questions regarding PEEP titration on the horizon. Prone ventilation reduced ARDS mortality in a recent trial.[33] However, a lower PEEP/F_{IO_2} algorithm first used by the ARDS Network[34] was employed, so the mortality benefit compared to the supine position with a higher PEEP strategy has not been identified. In addition, PEEP titration may be different in prone patients, given previous studies suggesting that prone patients with ARDS are more recruitable and require less PEEP to achieve a given P_{aO_2}/F_{IO_2}.[35] Ongoing discussion on position, non-pulmonary factors, and respiratory insufficiency outside ARDS that may affect ventilator strategy suggests that PEEP titration requires further research.

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