

With or Without ARDS: Evidence Regarding PEEP levels

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Positive end-expiratory pressure (PEEP) is defined as the alveolar pressure above atmospheric pressure that exists at the end of expiration, and it comprehends the intrinsic PEEP and extrinsic PEEP [1]. Intrinsic PEEP is a dynamic hyperinflation, which may lead to gas trapping, increased end expiration pressure, and hemodynamic instability [1]. It can also be subdivided in static, measured by occluding the airway at end-expiration, and dynamic, measured by recording the change in pressure required to initiate lung inflation [2]. Extrinsic PEEP is an adjustable variable provided by the mechanical ventilator and involves the application of a resistance to expiration in order to produce positive airway pressure, which could stabilize airways, prevent premature airway closure, improve ventilation and reduce gas trapping [1].

Patients with acute respiratory distress syndrome (ARDS) present several structural and functional abnormalities in the lungs. Among these, the repetitive opening and closing of alveolar units that collapses at the end of expiration, known as *atelectrauma*, is an important driver to ventilator-induced lung injury (VILI) [3,4]. Results from preclinical studies using animals [3,5] and studies in humans [6,7] support the use of PEEP to prevent or at least minimize atelectrauma. Indeed, PEEP could counteract the pressure exerted by the lung upon itself and decreases the pulmonary edema by reducing venous return and increasing interstitial pressure [8], reducing the risk of end-expiratory cyclical collapse and VILI. However, beyond a certain point, PEEP can be harmful, leading to alveolar over distension [9] and cardiac depression [10].

According to a recent meta-analysis that analyzed randomized clinical trials (RCT) comparing higher versus lower levels of PEEP in patients with ARDS, high levels of PEEP did not reduce hospital mortality, produced no significant difference in the risk of barotrauma, but rather improved oxygenation during the first days of ventilation [11]. Nevertheless, an individual patient data meta-analysis found reduction in hospital mortality with the use of high levels of PEEP when considering only patients with moderate-to-severe ARDS [12]. Taken all together, the evidence suggests that more severe ARDS patients could benefit from higher levels of PEEP during mechanical ventilation.

In patients without ARDS, the impact of PEEP on outcome is less understood. Use of lower tidal volumes in this group of patients could promote atelectasis, even more with a longer duration of ventilation, which could be a reason to use higher levels of PEEP

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[13]. However, in this group of patients specially, higher levels of PEEP may induce hemodynamic compromise and hyperinflation, as such maybe causing more harm than benefit [10]. Although it could be that higher levels of PEEP may benefit certain ICU patients, like obese patients or patients with increased chest wall elastance, robust evidence for any suggestion on the best level of PEEP in ICU patients without ARDS is lacking [13].

In a recent systematic review and meta-analysis assessing the association between PEEP levels and outcomes in patients without ARDS at the onset of mechanical ventilation, higher levels of PEEP were not associated with lower in-hospital mortality or shorter duration of ventilation [14]. Nonetheless, the use of high levels of PEEP decreased the incidence of ARDS and the occurrence of hypoxemia during follow-up. However, the heterogeneity among included studies was moderate to high and the quality of the available evidence ranged from low to very low. Nevertheless, the impact of PEEP in this group of patients is still matter of debate [14].

When discussing patients without ARDS, the group of patients undergoing mechanical ventilation for general anesthesia for surgery is of paramount importance. It is known that

postoperative complications after surgery are an important cause of morbidity and even mortality [15]. In particular, the development of postoperative pulmonary complications is strongly associated with a worse postoperative outcome [16]. Postoperative ARDS is the most feared postoperative pulmonary, and recent observational studies [17,18] suggest that the incidence of postoperative ARDS is maybe even higher than the incidence of sepsis-associated ARDS. Therefore, it is important that normal lungs undergoing mechanical ventilation during the surgical procedure are not damaged by inadequate intraoperative ventilation strategies [19].

Data regarding the use of PEEP during surgical procedures are conflicting. Three large randomized trials of intraoperative ventilation showed that low tidal volume and high levels of PEEP reduced postoperative pulmonary complications [19-21]. In this scenario, tidal volume reduction could induce atelectasis and consequently could increase harm by tidal recruitment of those lung parts that collapse at the end of expiration. Higher levels of PEEP could stabilize these parts during the respiratory cycle. Nevertheless, a recent RCT showed that, during low tidal volume ventilation, a strategy using high levels of PEEP during open abdominal surgery does not protect against postoperative pulmonary complications [22]. Indeed, it could lead to more hemodynamic instability, need of fluid and of vasoactive drugs [23].

It may be incorrect to assume that beneficial or harmful effects of PEEP are linear. Like with many physiologic effects the effects of PEEP could be U-shaped [24-26], meaning that too low as well as too high levels of PEEP could be harmful, and that the best level of PEEP is somewhere in between. Notably, the final shape of the curve could very well depend on severity of lung injury, with less severe patients presenting some degree of over distention with the use of higher levels of PEEP [9]. Also non-pulmonary effects of PEEP should be held in account, as high levels could reduce afterload of the left ventricle of the heart but at the same time decrease preload and increase afterload of the right ventricle [10]. Furthermore, the effects of PEEP on the systemic circulation depend not only on how much lung tissue is recruited but also on lung volume, since if the lung volume is below the functional residual capacity at end expiration, an increase in the level of PEEP likely increases the cardiac output [10,14].

In conclusion, the level of PEEP should not be defined according to general characteristics of the patients. A more individualized strategy with PEEP titration according to lung mechanics and lung recruitability could produce better results, leading to better outcomes in patients undergoing mechanical ventilation. When discussing the use of PEEP in patients undergoing mechanical ventilation, one size does not fit all.

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