Editorial

Optimum positive end-expiratory pressure 40 years later

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In 1975, Suter and colleagues published a fascinating study trying to determine the "optimum" level of end-expiratory pressure (PEEP) in patients with acute respiratory failure receiving mechanical ventilation.[1] The fascinating aspect of the paper was that they proposed a physiological model of the acute respiratory distress syndrome (ARDS) based on the relationship between lung volume, respiratory mechanics (compliance), dead space, cardiac output, and shunt and oxygenation. This model is still very useful today. Some of the messages of this paper should not be forgotten: Although increasing PEEP seemed to be beneficial, it had a double effect and above a certain value, PEEP was probably more risky than beneficial, with increase in dead space and reduction in cardiac output and oxygen delivery. The message about oxygen delivery was important, stressing that what really mattered was not the level of PaO_2 in the blood but the quantity of oxygen carried by hemoglobin, as measured by oxygen transport. Therefore, increasing PaO_2 at the expense of a decrease in cardiac output would result in a net negative effect in terms of oxygen delivered to the tissue. If the goal of PEEP is to increase oxygenation, this makes a lot of sense and continuing to look at PaO_2 without considering cardiac output is conceptually a major limitation.[2] In addition, a positive relationship between shunt, i.e. the percentage of cardiac output passing through non-ventilated areas, and cardiac output was demonstrated.[3] Dantzker, a few years later, even suggested that an important reason for the observed improvement in oxygenation with PEEP in ARDS was the reduction in cardiac output and the shunt–cardiac output relationship.[4] It was also demonstrated later, however, that maintaining cardiac output with inotropic agents had significant benefits of PEEP on oxygenation.[5]

Suter *et al*. suggested in their study that this "optimum" PEEP in terms of oxygen delivery was characterized by a similar level of optimum compliance and dead space. In a nice physiological study, in this issue El-Baradey and El-Shamaa compared what could be the optimum PEEP level based on the best compliance versus the lower dead space in a series of 30 patients with ARDS.[6] They found that dead space values resulted in slightly lower PEEP levels. The results differ somehow from some previous studies. Though these results are definitely interesting, several comments are required to better place them into perspective.

- Physiological measurements are often complex to interpret because most of them are interrelated. For instance, you cannot set a rule for VT titration based on plateau pressure without deciding PEEP titration at the same time. Therefore, the results of such measurements may vary depending on what is selected first. Similarly, compliance values are influenced by the amplitude of the tidal volume used and where the volume starts and ends on the global pressure–volume curve.[7] In this study, the authors selected Vt of 6 ml/kg or lower
- Compliance is not easy to interpret because the value

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of any measurement may be influenced by the amount of intratidal recruitment. In other terms, compliance may appear relatively high because you reopen a large number of closed alveoli during the maneuver used, adding areas of "infinite compliance" when they pop open.[7] Once alveoli are fully open and kept open, paradoxically, compliance may appear lower, even if alveoli have been recruited.[8] A progressive reduction in compliance may primarily indicate distension of already open alveoli, decrease in the amount of ongoing recruitment, or both. This makes the use of compliance relatively difficult to interpret when incremental PEEP values are used. In this study, the authors tried to recruit the lungs before doing their stepwise PEEP titration, which may have helped to minimize the problem, although the effects of recruitment maneuvers are often transient[9]

- Dead space is also influenced by hemodynamics. Indeed, alveolar dead space is influenced by the amount of the so-called zone 2 regions, as described by West,[10] in which alveolar pressure becomes higher than the venous pressure, creating a zone with ventilation but no perfusion. Therefore, dead space depends both on the amount of alveolar pressure (plateau pressure at end inspiration) and of central venous pressure. In other terms, fluid loading, by increasing vascular pressure, may help to "recruit" capillaries[11] and decrease dead space. The optimum dead space may thus depend on intravascular volume status and venous pressure. It is not surprising that the concordance between optimum dead space and optimum compliance is not the same across different studies, simply because fluid status may differ. Of note, the authors measured alveolar dead space (based on the difference between $PaCO_2$ and $PetCO_2$) and not physiological dead space. The alveolar dead space is also influenced by shunt[12]
- Therefore, for the same lung, depending on volume status, cardiac output, and tidal volume used, the same PEEP titration tests may give different results. Although, individually, these parameters make sense, the course for an optimum PEEP level based on these measurements may still continue for another 40 years for these reasons.

Underlying the debate around PEEP titration in mechanical ventilation is this central question: What exactly is the purpose of PEEP? While ensuring gas exchange and oxygen delivery are adequate, clinicians must also strive to prevent ventilator-induced lung injury (VILI). This latter priority may well be the more important determinant of patient outcome. A rational physiological approach to titrating PEEP will aim to optimize some valid surrogate measure of VILI. Despite the interesting insights of the present study, it remains unclear whether VILI is more effectively prevented by improving compliance or minimizing dead space (or targeting some other parameter). While compliance might be correlated with tidal stress and strain within the lung, regional lung inhomogeneity (which dramatically amplifies alveolar stress) was recently shown to correlate with physiological dead space.[13] Thus, the question remains, what should be our target when setting PEEP?

The role of PEEP may well be predominantly to keep the lung open, as a way to minimize cycling opening and closing phenomena.[14] In this sense, one of our primary goals should be to determine whether the level of PEEP we give to a patient has a significant effect on keeping some parts of the lung open and avoiding derecruitment. Whether oxygenation at the bedside is sufficient to ascertain this response[15] or whether we need to use more sophisticated measurements estimating recruitment,[16] is an important question for future studies.

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