



Recruiting the Acutely Injured Lung: How and Why?

The beneficial effects of positive end-expiratory pressure (PEEP) on oxygenation in acute respiratory distress syndrome (ARDS) were very soon attributed to the “recruitment of gas exchange airspaces and prevention of terminal airway closure” (1). In 1975, Suter proposed “optimal PEEP” as the value at which the best compliance was obtained, indicating that recruitment outweighed PEEP’s potentially adverse hemodynamic effects. Indeed, best compliance was associated with the highest tissue oxygen transport (DO_2 ; i.e., the product of arterial oxygen content and Q) and with lowest dead space (2). This physiology-based approach integrated key considerations of lung mechanics, hemodynamics, and gas exchange. With passing time, the PaO_2/FiO_2 ratio displaced oxygen transport to assess the benefit of PEEP, and hemodynamic status became relatively neglected (3). These days, the focus of ventilatory strategy is primarily concentrated on the recruitment-PEEP pairing, which is central to the prevention of atelectrauma (4) and to the open-lung strategy (5). Therefore, recruitment for the last 5 decades has held a central role in setting PEEP during mechanical ventilation.

Although the word recruitment, as currently used, is perceived as an unambiguous concept, its meaning and quantification differ sharply depending on assessment method. Recruitment with the computed tomography scan-based approach is quantified by the amount of tissue that regains aeration from the gasless state (6) or as a reduced radio-density in well-defined anatomical regions (7). In contrast, the respiratory mechanics approach measures recruitment not only as the gas entering newly opened units but also as the gas entering previously opened units that improve their compliance at higher PEEP (Figure 1). Therefore, the computed tomography scan- and respiratory mechanics-based methods measure different entities and, not surprisingly, often provide discordant results (8).

Several investigators assessed recruitment by assuming that the change in compliance at different PEEP levels is only a result of the recruitment of previously collapsed units (9–13). Although this assumption is not completely correct (8, 14), such gas-based methods illustrate how PEEP improves the overall inflation by increasing the lung compliance. This is a result of both the enrollment of new pulmonary units and the improved compliance of ones already open.

In this issue of the *Journal*, Chen and colleagues (pp. 178–187) (15) suggest that a simplified variant of such gas-based tidal mechanics methods may help clinicians to extract and separate the appropriately targeted reopened element by calculating a novel recruitment:inflation compliance ratio. This index, based on the passive deflation properties of a single tidal breath delivered from two levels of PEEP, aims to separate recruiting responses to the PEEP increment from nonrecruiting responses of simple distention

of units already open at the lower PEEP value. Correlations with oxygen exchange and hemodynamic tolerance in their cohort of tested patients with ARDS, as well as with a more laborious research method for tracking unit opening, suggested the potential clinical use of this single-breath recruitment-to-inflation index.

A second intriguing observation in this report is the apparently high incidence (almost one in three) of near-complete end-expiratory airway closure, as indicated by failure of initially building airway pressure to initiate any detectable inspiratory flow. Although regional closure of lung units and regional air trapping have been demonstrated previously in patients with ARDS of this severity who are ventilated at very low PEEP levels (16, 17), extension to the entire lung and into a higher PEEP range is a relatively recent inference (18) and conceptually seems rather difficult to explain, given the wide range of transpulmonary forces encountered within the acutely injured lung. If auto-PEEP and airway closure are prominent features, the proposed recruitment-to-inflation index must be adjusted to account for them to prevent serious calculation errors. Chen and colleagues are right in highlighting the preliminary, rather than clinically validated, nature of their report. The described technique, although conceptually innovative and thought-provoking, depends heavily on the accuracy, timing, and alignment of the pressure and flow measurements made by the ventilator, as well as on assumptions regarding tissue properties of lung and chest wall that are open to question.

However determined, bedside estimates of recruitment do not account for coexisting hyperinflation and hemodynamic impairment, which are nearly unavoidable prices to pay when PEEP is increased into its higher range. The key issue when dealing with the potential for recruitment, however, is to define its relationship with PEEP, whose level, in turn, relates both to oxygenation and to atelectrauma prevention. Let us assume, for example, that recruitability is correctly determined to be 10%, 20%, or 40% of the lung mass/volume. How should this guide PEEP selection?

The oxygenation, in most cases, is a relatively minor problem: A moderate PEEP level is usually adequate and seldom impairs hemodynamics. Recruitability and oxygenation, contrary to common belief, are usually weakly correlated, as also reflected in data from the present study, in which the R^2 of the recruitment to inflation index and PaO_2 was only 0.12. It must be kept in mind that for a fixed FiO_2 , oxygenation depends uniquely on the ventilation/perfusion ratio (i.e., the perfusion has an equal role as the ventilation). Indeed, it has been shown that the PaO_2 improvement with PEEP may sometimes be primarily a result of the decreased perfusion, even in absence of recruitment (19–21).

More important, we do not know which is the optimal PEEP that prevents atelectrauma of some pulmonary units while avoiding the volotrauma of some others (22). In an unselected ARDS population, it is consistently established in large clinical trials that the risks and benefits of preventing atelectrauma (higher PEEP) are equivalent to the ones of preventing volotrauma (lower PEEP) (23–25), at least within the PEEP range that has been tested (~7–15 cm H_2O). In contrast, at higher PEEP levels, the risk for

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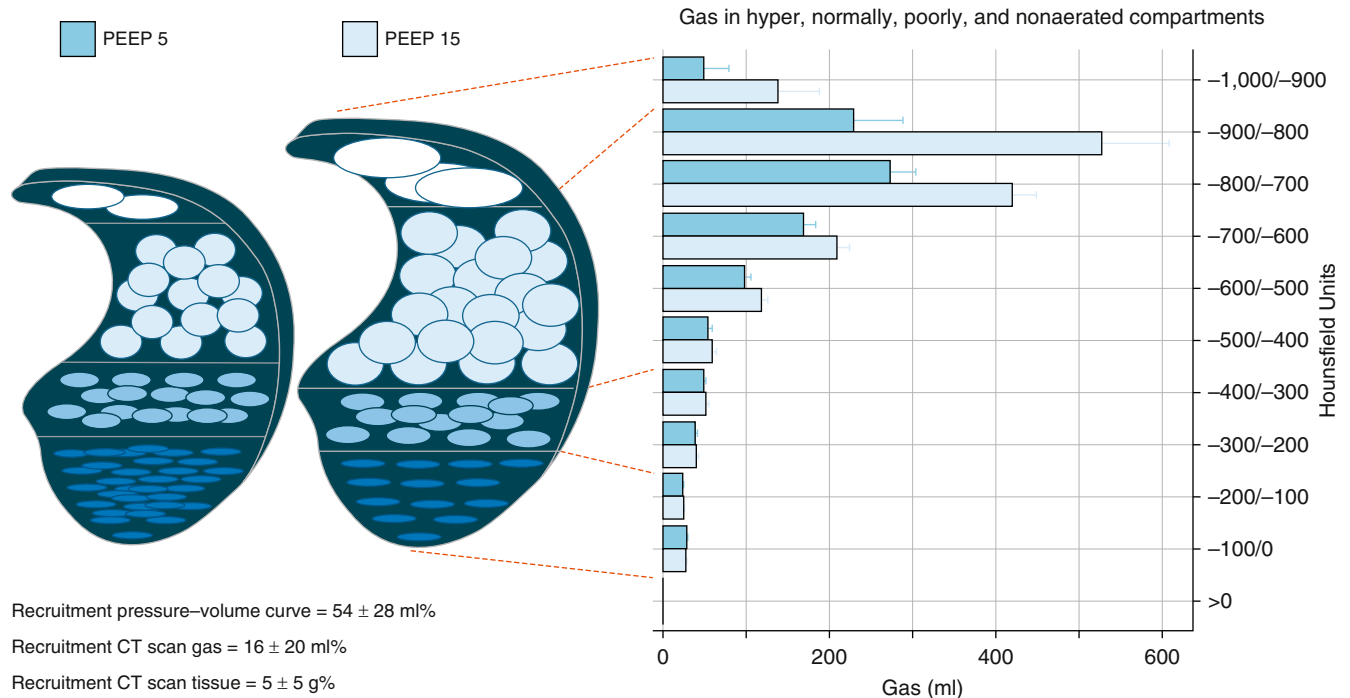


Figure 1. Schematic representation of the gas-mass redistribution within the lungs after an increase of positive end-expiratory pressure (PEEP) from 5 cm H₂O (darker blue, left) to 15 cm H₂O (lighter blue, right). On the right, we show the histogram related to the quantitative analysis of the computed tomography (CT) scan in the two conditions. Although we observe a very minor increase in gas volume in the poorly aerated compartments, we observe a significant amount of gas volume increase in the normally and hyperinflated lung compartments. The gas-based method includes a portion of the gas present in the already aerated compartment as a recruited volume. In contrast, the CT scan–based method considers recruitment to be the difference in nonaerated tissue (0/–200 HU, dark blue, dependent) between 5 and 15 cm H₂O. The method difference leads to large differences in the recruitment computation.

volotrauma exceeds the benefits of atelectrauma prevention (26). It is possible, however, that in a selected population of PEEP responders (i.e., patients with high potential for recruitment), the higher PEEP may provide advantages, as signaled by meta-analysis of the lower versus higher PEEP trials (27). Unfortunately, the definition of recruiters and nonrecruiters is usually based on the median value of a given population, which may be widely variable. In unselected patients with ARDS, we found 9% recruitability of nonaerated tissue (28), whereas in extracorporeal membrane oxygenation patients, Camporota, using the same method, found a median value nearly threefold greater (29). Chen and colleagues report a median recruitment:inflation ratio of 0.5, ranging from 0 to 2. In face of such extreme variability, any simple recruitable–nonrecruitable dichotomy must be considered arbitrary and interpreted cautiously (30).

In our view, therefore, the authors' efforts to individualize the PEEP setting based on highly relevant bedside physiology is both well taken and welcome. Fifty years of investigation have demonstrated the dangers of raising airway pressures unnecessarily and without tracking all parameters (lung recruitment, hemodynamics, and hyperinflation) that are most closely aligned to PEEP's clinical objectives and hazards. Examining the worth and costs of fixating on the clinical objective of "optimized" recruitment alone deserves to be just as carefully scrutinized. ■

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References

1. Falke KJ, Pontoppidan H, Kumar A, Leith DE, Geffin B, Laver MB. Ventilation with end-expiratory pressure in acute lung disease. *J Clin Invest* 1972;51:2315–2323.
2. Suter PM, Fairley B, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. *N Engl J Med* 1975;292:284–289.
3. Jardin F, Vieillard-Baron A. Right ventricular function and positive pressure ventilation in clinical practice: from hemodynamic subsets to respirator settings. *Intensive Care Med* 2003;29:1426–1434.

4. Tremblay L, Valenza F, Ribeiro SP, Li J, Slutsky AS. Injurious ventilatory strategies increase cytokines and c-fos m-RNA expression in an isolated rat lung model. *J Clin Invest* 1997;99:944–952.
5. Lachmann B. Open up the lung and keep the lung open. *Intensive Care Med* 1992;18:319–321.
6. Gattinoni L, Pesenti A, Avalli L, Rossi F, Bombino M. Pressure-volume curve of total respiratory system in acute respiratory failure. Computed tomographic scan study. *Am Rev Respir Dis* 1987;136:730–736.
7. Lu Q, Constantin JM, Nieszkowska A, Elman M, Vieira S, Rouby JJ. Measurement of alveolar derecruitment in patients with acute lung injury: computerized tomography versus pressure-volume curve. *Crit Care* 2006;10:R95.
8. Chiumello D, Marino A, Brioni M, Cigada I, Menga F, Colombo A, et al. Lung recruitment assessed by respiratory mechanics and computed tomography in patients with acute respiratory distress syndrome: what is the relationship? *Am J Respir Crit Care Med* 2016;193:1254–1263.
9. Ranieri VM, Eissa NT, Corbeil C, Chassé M, Braidy J, Matar N, et al. Effects of positive end-expiratory pressure on alveolar recruitment and gas exchange in patients with the adult respiratory distress syndrome. *Am Rev Respir Dis* 1991;144:544–551.
10. Dellamonica J, Lerolle N, Sargentini C, Beduneau G, Di Marco F, Mercat A, et al. PEEP-induced changes in lung volume in acute respiratory distress syndrome: two methods to estimate alveolar recruitment. *Intensive Care Med* 2011;37:1595–1604.
11. Patroniti N, Bellani G, Cortinovis B, Foti G, Maggioni E, Manfio A, et al. Role of absolute lung volume to assess alveolar recruitment in acute respiratory distress syndrome patients. *Crit Care Med* 2010;38:1300–1307.
12. Gattinoni L, Pelosi P, Suter PM, Pedoto A, Vercesi P, Lissoni A. Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease: different syndromes? *Am J Respir Crit Care Med* 1998;158:3–11.
13. Maggiore SM, Jonson B, Richard JC, Jaber S, Lemaire F, Brochard L. Alveolar derecruitment at decremental positive end-expiratory pressure levels in acute lung injury: comparison with the lower inflection point, oxygenation, and compliance. *Am J Respir Crit Care Med* 2001;164:795–801.
14. Stahl CA, Möller K, Steinmann D, Henzler D, Lundin S, Stenqvist O. Determination of 'recruited volume' following a PEEP step is not a measure of lung recruitability. *Acta Anaesthesiol Scand* 2015;59:35–46.
15. Chen L, Del Sorbo L, Grieco DL, Junhasavasdikul D, Rittayamai N, Soliman I, et al. Potential for lung recruitment estimated by the recruitment-to-inflation ratio in acute respiratory distress syndrome: a clinical trial. *Am J Respir Crit Care Med* 2020;201:178–187.
16. Brochard L, Martin GS, Blanch L, Pelosi P, Belda FJ, Jubran A, et al. Clinical review: respiratory monitoring in the ICU. A consensus of 16. *Crit Care* 2012;16:219.
17. Koutsoukou A, Bekos B, Sotiropoulou C, Koulouris NG, Roussos C, Milic-Emili J. Effects of positive end-expiratory pressure on gas exchange and expiratory flow limitation in adult respiratory distress syndrome. *Crit Care Med* 2002;30:1941–1949.
18. Chen L, Del Sorbo L, Grieco DL, Shklar O, Junhasavasdikul D, Telias I, et al. Airway closure in acute respiratory distress syndrome: an underestimated and misinterpreted phenomenon. *Am J Respir Crit Care Med* 2018;197:132–136.
19. Lemaire F, Gastine H, Regnier B, Teisseire B, Rapin M. Changes in intrapulmonary shunting with alterations in pulmonary vascular resistance. *Anesthesiology* 1977;47:315–316.
20. Lynch JP, Mhyre JG, Dantzker DR. Influence of cardiac output on intrapulmonary shunt. *J Appl Physiol* 1979;46:315–321.
21. Dantzker DR, Lynch JP, Weg JG. Depression of cardiac output is a mechanism of shunt reduction in the therapy of acute respiratory failure. *Chest* 1980;77:636–642.
22. Del Sorbo L, Tonetti T, Ranieri VM. Alveolar recruitment in acute respiratory distress syndrome: should we open the lung (no matter what) or may accept (part of) the lung closed? *Intensive Care Med* 2019;45:1436–1439.
23. Brower RG, Lancken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al.; National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med* 2004;351:327–336.
24. Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL, et al.; Expiratory Pressure (Express) Study Group. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 2008;299:646–655.
25. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, et al.; Lung Open Ventilation Study Investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA* 2008;299:637–645.
26. Cavalcanti AB, Suzumura EA, Laranjeira LN, Paisani DM, Damiani LP, Guimaraes HP, et al.; Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial I. Effect of lung recruitment and Titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. *JAMA* 2017;318:1335–1345.
27. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. *JAMA* 2010;303:865–873.
28. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. *N Engl J Med* 2006;354:1775–1786.
29. Camporota L, Caricola EV, Bartolomeo N, Di Mussi R, Wyncoll DLA, Meadows CIS, et al. Lung recruitability in Severe acute respiratory distress syndrome Requiring extracorporeal membrane oxygenation. *Crit Care Med* 2019;47:1177–1183.
30. Constantin JM, Jabaudon M, Lefrant JY, Jaber S, Quenot JP, Langeron O, et al.; AZUREA Network. Personalised mechanical ventilation tailored to lung morphology versus low positive end-expiratory pressure for patients with acute respiratory distress syndrome in France (the LIVE study): a multicentre, single-blind, randomised controlled trial. *Lancet Respir Med* 2019;7:870–880.

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