CURRENT OPINION

Selecting the 'right' positive end-expiratory pressure level

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Purpose of review
To compare the positive end-expiratory pressure selection aiming either to oxygenation or to the full lung opening.

Recent findings
Increasing positive end-expiratory pressure in patients with severe hypoxemia is associated with better outcome if the oxygenation response is greater and positive end-expiratory pressure tests may be performed in a few minutes. The oxygenation response to recruitment maneuvers was associated with better outcome in patients with acute respiratory distress syndrome from influenza A (H1N1). If, after recruitment maneuver, the recruitment is not sustained by sufficient positive end-expiratory pressure, the lung will unavoidably collapse. Several papers investigated the positive end-expiratory pressure selection according to the deflation limb of the pressure–volume curve. It is still questionable whether to consider oxygenation or respiratory mechanics change as the best marker for adequate selection. A growing interest is paid to the estimate of transpulmonary pressure, although no consensus is available on which methodology is preferable. Finally, the positive end-expiratory pressure adequate for full lung opening may be computed combining the computed tomography scan variables and the chest wall elastance.

Summary
When compared, most of the methods give the same positive end-expiratory pressure values in patients with higher and lower recruitability. The positive end-expiratory pressure/inspiratory oxygen fraction tables are the only methods providing lower positive end-expiratory pressure in lower recruiters and higher positive end-expiratory pressure in higher recruiters.

Keywords
acute respiratory distress syndrome, computed tomography scan, esophageal pressure, oxygenation, positive end-expiratory pressure

INTRODUCTION

The physiology of positive end-expiratory pressure (PEEP) and its application in pulmonary edema was described by Barach *et al.* in 1938 [1]; however, its widespread clinical use began with Gregory *et al.* in pediatric patients [2] and became routine practice in the treatment of acute respiratory distress syndrome (ARDS) [3]. The target of PEEP application was to improve oxygenation; the concern was the cardiac output decrease, as described in detail by Cournand *et al.* in 1948 [4]. The decrease of cardiac output, moreover, is a mechanism that, *per se*, may improve oxygenation as described by Lemaire *et al.* [5], and confirmed by Dantzker *et al.* [6]. The best compromise to reconcile the oxygenation needs with the hemodynamic was described by Suter *et al.* [7]. These authors found that the best oxygen transport, a variable which associates oxygenation and cardiac output, is reached when the PEEP provides the best respiratory system compliance. Suter's PEEP selection according to oxygenation and respiratory system compliance has been rediscovered several times over the decades, up to the most recent papers.

In the 1990s, a new concept for PEEP use emerged, in the framework of 'lung protective strategy', starting, in our opinion, from a paper of Webb and Tierney

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KEY POINTS

- PEEP selection methods based on PEEP/FiO_2 tables are the only discriminating factors between patients with higher and lower recruitability.
- To keep the lung fully open, similar PEEP is required in patients with higher and lower potential for lung recruitment.
- PEEP selection using the inspiratory limb of the volume–pressure curve is conceptually wrong because inspiratory pressure reflects the opening pressure, whereas PEEP relates to the closing pressure of the lung.
- PEEP selection along the deflation limb of the volume–pressure curve makes more sense, but the use of oxygenation or compliance changes as a marker of adequate PEEP is questionable.
- Tailoring PEEP according to the ARDS severity, as defined by the Berlin definition, may be a reasonable approach: 5–10 cmH_2O PEEP in mild patients, 10–15 cmH_2O PEEP in moderate patients and 15–20 cmH_2O PEEP in severe patients.

[8], who described, in rats, a 'protective' effect of PEEP against damage of mechanical ventilation. The mechanism of lung protection was attributed primarily to the prevention of intratidal opening and closing based on a theoretical background provided by Mead *et al.* [9], whereas the transduction of mechanical stimuli to the inflammatory reaction was first described by Slutsky [10]. Therefore, in the context of 'open the lung and keep it open' [11], the target of PEEP was no more the oxygenation but the prevention of the intratidal collapse and decollapse.

We will describe, first, the PEEP selection according to oxygenation and, second, the PEEP selection according to the lung protective strategy, and, finally, we will attempt to describe how these different methods were compared and which are the conclusions reached so far.

SELECTING POSITIVE END-EXPIRATORY PRESSURE TO IMPROVE OXYGENATION

Setting PEEP based on PEEP/FiO_2 tables is likely the most diffused method, introduced by the ARDS Network [12] and LOVs study [13]. Higher and lower PEEP, selected by these tables, have been compared in large trials recently reviewed in a Cochrane analysis [14]. The authors concluded that the outcome was unrelated to the PEEP level and (what a surprise!) the higher the PEEP, the higher is the oxygenation. The oxygenation response to PEEP has been studied in a secondary analysis [15▪] of the LOVs [13] and ExPress [16] trials and in H1N1 patients [17]. These studies reported that the relation between oxygenation response following PEEP adjustment and decreased mortality was strongest in patients with more severe baseline hypoxemia (PaO_2/FiO_2 <150 mmHg) subjected to increased PEEP. All of these data corroborate the belief that higher PEEP could be of benefit in the most severe patients with ARDS [18,19] in whom the lung recruitability (and PEEP response) is higher [20]. It is important to note that oxygenation response to PEEP changes may be tested in a few minutes [21].

SELECTING POSITIVE END-EXPIRATORY PRESSURE TO PROTECT THE LUNG

Setting a PEEP value sufficient to keep the lung open throughout the respiratory cycle is one of the main issues of the 'lung protective strategy'. Several approaches have been proposed through the years for this purpose, from the traditional use of the volume–pressure curve to the use of transpulmonary pressure and the imaging technologies.

Respiratory mechanics-based positive end-expiratory pressure selection: the volume–pressure curve of the respiratory system

The volume–pressure curve has been largely used to individualize the PEEP selection hypothesizing that the lower inflection point indicates the end of recruitment, whereas the upper inflection point indicates the beginning of hyperinflation. Although, for decades, the PEEP was set using the inflation limb of the respiratory system curve, more recently the attention has been focused on the deflation limb. At the same pressure, the inspiratory volume is lower than the expiratory one, and, conversely, the pressure required to reach a given volume is greater along the inspiratory limb than along the expiratory one. The 'extra pressure' required during the inflation is dissipated in the system to overcome the surface tension and the tissue resistances and, eventually, to open up the collapsed lung regions.

The inspiratory limb of the volume–pressure curve: the recruitment maneuver

In contrast with previous beliefs, it has been shown consistently, in humans [22] and in different animal species [23,24], that recruitment is not limited to the pressure around the inflection point of the inspiratory volume–pressure curve but occurs along the entire curve. This indicates that the collapsed units open up at different opening pressures. As an example, at the inflation of 30 cmH_2O, a consistent part of the potentially recruitable lung, which may be estimated from 15% to 30%, remains closed. To open up these regions, opening pressures spanning from 30 to 45–60 cmH_2O are required [22,25]. Therefore, the recruitment maneuver may open up different amounts of recruitable lung if performed at 30, 40 or 60 cmH_2O inflation pressure. Liu *et al.* [17] reported that, if the recruitment maneuver (at 30 cmH_2O for 60 s) resulted in better oxygenation, the patients with influenza A (H1N1)-associated ARDS had a better chance of survival. The same group [26] found, in a canine model, that hyperinflation after recruitment maneuver was greater in the surfactant model rather than in the oleic acid model. Engel *et al.* [27] compared two recruitment maneuvers (at 45 and 15 cmH_2O PEEP) with no recruitment. These authors concluded that recruitment maneuvers improve oxygenation with less hemodynamic impairment and inflammatory reaction at lower PEEP. Actually, the authors defined as recruitment the application of two different PEEP levels, which are expiratory phenomena related to the deflation limb of the volume–pressure curve. This fact underlines the confusion originating by concepts such as 'recruitment with PEEP.' Actually, recruitment occurs during inspiration and PEEP maintains open, if sufficient, what has been previously recruited. If the PEEP is insufficient, the recruitment is not sustained and the lung will unavoidably collapse again, as confirmed by Kheir *et al.* [28]. Keenan *et al.* [29], reviewing the recruitment issue, wisely concluded, in our opinion, that recruitment maneuvers should be guided by individual clinician experience and patients' factor.

Therefore, although the recruitment must be tailored on the inspiratory limb of the volume–pressure curve, tailoring PEEP in the same limb is misleading. Hata *et al.* [30–33] provided a systematic review of three randomized trials that used the inflation limb of the pressure–volume curve to tailor PEEP selected above the lower inflection point. The authors suggested a possible outcome benefit, although the limited number of patients prevents any real conclusion. In our opinion, in all of these studies, there is a fundamental bias. First, the authors assume that recruitment is complete or near complete above the lower inflection point, which is not true; second, when the lower inflection point cannot be identified, a PEEP approximately 15–16 cmH_2O was used. To be consistent with the hypothesis, PEEP should have been set equal to 0 cmH_2O.

The expiratory limb of the volume–pressure curve

In the last few years, several papers investigated the effects of PEEP selection on the deflation part of the volume–pressure curve, usually setting PEEP at the pressure values corresponding to the best compliance or before the oxygenation decrease. It must be noted, however, that, first, because of the sigmoid shape of the deflation limb, the compliance is always higher in the middle part of the lung, even in normal lungs. Second, the derecruitment starts, in ARDS, at very high deflation pressures (20 cmH_2O), as shown by the closing pressure curve, both in humans and in experimental animals [22,23], to continue at lower pressures along the deflation limb. Actually, in supine patients with ARDS, when PEEP is decreased, the most dependent lung regions along the sternum–vertebral direction collapse first and then the less dependent regions, as shown with the regional computed tomography (CT) scan analysis [34], and recently confirmed in 51 patients with ARDS [35▪]. This makes the use of a single unique pressure point as a marker of derecruitment highly questionable. How the commonly used physiological variables are different if measured at the same pressure during inflation or during deflation has been recently emphasized by Bikker *et al.* [36].

The lung mechanics-based positive end-expiratory pressure selection

The interest in ventilator-induced lung injury and the stress/strain applied to the lung structures renewed the attention on the esophageal pressure measurement and its clinical use in the framework of the lung protective strategy. Moreover, the use of CT scan allowed a better characterization of the lung status and the individualization of the mechanical ventilation settings.

The transpulmonary pressure-based positive end-expiratory pressure selection

The recognition that the distending pressure of the lung is the transpulmonary pressure led to a series of studies in which the PEEP level was selected to maintain the transpulmonary pressure positive through the whole respiratory cycle, to maintain the lung always open. Because the transpulmonary pressure is the difference between the airway and the pleural pressure, the estimate of this variable is mandatory and the only clinical tool available is the measurement of the esophageal pressure.

The indications and the limits of using esophageal pressure as a surrogate of pleural pressure have been reviewed by Brochard [37▪] and by Keller and Fessler [38]. Two approaches have been proposed to estimate the pleural pressure from the esophageal pressure measurement. The first one assumes that the absolute values of esophageal pressure equal the pleural pressure. To take into account the weight of the mediastinum, a correction factor of $-5\,cmH_2O$ may be applied. The second method considers the variation of the esophageal pressure equal to the variations of the pleural pressure. Therefore, after measuring the chest wall elastance, the Δpleural pressure may be estimated as the change in airway pressure times the ratio of the chest wall to the total respiratory system elastance [35▪]. Gulati *et al.* [39▪] compared these two methods for estimating pleural pressure on the same group of patients. They concluded that the two methods cannot be considered interchangeable. Moreover, chest wall and respiratory system elastances may vary unpredictably with changes in PEEP.

The computed tomography scan-based positive end-expiratory pressure selection

The assumption behind the CT scan-based PEEP selection is that the primary reason for lung collapse in ARDS is the excessive lung weight that compresses the dependent lung regions. Therefore, the CT scan-derived PEEP is computed as the pressure sufficient to overcome the maximal hydrostatic pressure superimposed on the most dependent lung regions and the pressure necessary to lift up the chest wall [35▪]. Cressoni *et al.* found, however, that, in severe ARDS, the CT scan-derived PEEP ranged from 7 to $28\,cmH_2O$, averaging $16\pm5\,cmH_2O$ in mild ARDS, $16\pm5\,cmH_2O$ in moderate ARDS and $18\pm5\,cmH_2O$ in severe ARDS, and was unrelated to the lung recruitability, that is, to keep open 1 or 100 pulmonary units collapsed in the dependent lung regions, approximately the same PEEP is required.

COMPARISON BETWEEN DIFFERENT MODES OF POSITIVE END-EXPIRATORY PRESSURE SELECTION

In the last years, several papers compared different PEEP selection methods. In Table 1, we summarize the methods in comparison, their targets, and the authors' conclusions. Briefly, Chiumello *et al.* found that, within all of the bedside PEEP selection methods tested, the only one that provides appropriately lower PEEP in the less recruitable patients was the high PEEP arm of the ARDSNet table. All of the other systems, including the CT-derived PEEP, provide similar values in patients with higher or lower potential for lung recruitment. Other authors, instead of recruitability, targeted PEEP to other variables. Yang *et al.* found that better oxygenation was provided by applying a positive transpulmonary pressure than following the ARDSNet table. Huang *et al.*, during a decremental PEEP trial, measured stress index, static lung compliance, oxygenation and the inflection point in the inspiratory limb of the volume–pressure curve. These authors concluded that stress index and oxygenation methods set PEEP at higher values than indicated by the highest compliance and the inflection point. In turn, Pintado *et al.* found that the best compliance method, compared with the ARDSNet table, resulted in decreased organ dysfunction with a trend toward a better outcome. In addition to respiratory system compliance and transpulmonary pressure during decremental PEEP trial, Rodriguez *et al.* found that alveolar dead space could add further information; in fact, it increased when transpulmonary pressure became negative and oxygenation deteriorated. In a series of papers, in humans [49] and in pigs [36,45], during the PEEP changes, in addition to the usual variables such as dynamic compliance, transpulmonary pressure, oxygenation parameters and dead space, the electrical impedance tomography was applied. As expected, all of these studies showed that, when applying PEEP, we have unavoidably to compromise between regional overdistension and regional collapse. Finally, in postoperative patients, Ferrando *et al.* [47] found advantages setting PEEP during a decremental PEEP trial according to the best compliance instead of using a constant value equal to $5\,cmH_2O$ PEEP, whereas Hansen *et al.* [48], in cardiovascular patients, found that $8\,cmH_2O$ PEEP was substantially similar to $5\,cmH_2O$ PEEP.

It is evident that the different methods do provide different PEEP values as they explore different properties of the system. The target of the oxygenation method is to provide an oxygen saturation approximately 90% without negative hemodynamic effects. The PEEP level to reach this target is usually lower than the one required for mechanical targets, because the complete opening of the lung is not necessary. The stress index and the ExPress study methods aim to sustain a complete recruitment by setting PEEP approximately at the level of the upper inflection point of the inspiratory volume–pressure curve, where it loses its linearity. The healthier the lung, however, the higher is the pressure set with these two methods [40▪]. Using the deflation part of the volume–pressure curve is physiologically sound, but the variable to be considered for setting PEEP is questionable. Some authors proposed as a signal of derecruitment the decrease of oxygenation. This is not necessarily true because the changes in intrathoracic pressure are associated with changes in hemodynamics, which may influence oxygenation changes [5,6]. In contrast, some authors consider the decrease in respiratory system compliance as the beginning of derecruitment. Even in normal lung, however, the compliance during deflation first increases, then

Table 1. Positive end-expiratory pressure selection methods reported in recent literature

Author	Population	PEEP selection method	Targets	Conclusions
Chiumello *et al.* [35■,40■]	Patients with ARDS	Increased recruitment strategy of the ExPress study	Airway pressure up to 28–30 cmH_2O or PEEP = 20 cmH_2O at constant tidal volume 6 ml/kg IBW	PEEP/FiO_2 table is the only method providing appropriately lower/higher PEEP in lower/higher recruiters
		Stress index	PEEP at which the time–pressure curve loses its linearity	
		Esophageal pressure	PEEP was set equal to the absolute value of esophageal pressure measured at functional residual capacity	
		LOV study	PEEP selected according to a PEEP/FiO_2 table, targeting SaO_2 between 88% and 93%	
		CT-derived	PEEP = maximal superimposed pressure	
Yang *et al.* [41]	Patients, with and without IAH	Transpulmonary pressure	Transpulmonary pressure = 0–10 cmH_2O at end expiration, according to a sliding scale based on PaO_2 and FiO_2	Transpulmonary pressure method provided higher PEEP than PEEP/FiO_2 table with better oxygenation and respiratory mechanics
		ARDSNet protocol	PEEP selected according to a PEEP/FiO_2 table	
Gulati *et al.* [39■]	Patients with ARDS	Pes-based method	End-expiratory transpulmonary pressure of 0 cmH_2O	Absolute esophageal pressure or chest wall compliance method to set transpulmonary pressure does not yield similar results
		E_{CW}-based method	End-inspiratory transpulmonary pressure of 26 cmH_2O	
Huang *et al.* [42]	Pulmonary patients with ARDS	Oxygenation	PEEP decremented until $PaO_2/FiO_2 < 400$ mmHg or >5% difference in PaO_2/FiO_2 between two consecutive PEEP reduction	PEEP titration by stress index might be more beneficial for pulmonary patients with ARDS after a recruitment maneuver
		Stress index	Optimal PEEP was set to obtain a stress index value between 0.9 and 1.1	
		Cst	PEEP was reduced in steps of 2 cmH_2O starting from 20 cmH_2O, until the lowest PEEP level providing the maximal Cst	
		LIP + 2 cmH_2O	Optimal PEEP = LIP + 2 cmH_2O	
Pintado *et al.* [43]	Patients with ARDS	Compliance-guided PEEP	The highest static compliance was considered to be the best PEEP during an incremental trial. If at two different PEEPs the static compliance was identical, the one with the lowest plateau was chosen	PEEP setting by highest compliance is better than by PEEP/FiO_2 table to decrease organ dysfunction
		ARDSNet protocol	PEEP selected according to a PEEP/FiO_2 table	
Rodriguez *et al.* [44]	Patients with ARDS	Crs	The best Crs PEEP was defined as the highest value of PEEP producing the higher Crs during the decremental titration maneuver	Negative values of transpulmonary pressure during decremental PEEP are associated with increased V_D/V_T and high risk of collapse
		Transpulmonary pressure	The PEEP value corresponded to an expiratory Ptp of 0	
		Dead space		

Blankman *et al.* [45]	Postcardiac surgery patients	Dynamic compliance PaO_2/FiO_2 ratio EIT	Decremental PEEP trial. An even distribution of tidal volume to the nondependent and dependent lung regions Decremental PEEP trial. Highest value Decremental PEEP trial. Highest value	In postcardiac surgery patients, the EIT-derived ITV index was comparable with dynamic compliance to indicate 'best' PEEP, that is, avoids overdistension of the nondependent regions
Bikker *et al.* [36]	Pigs (healthy and after ALI induction)	Crs EELV Transpulmonary pressure PaO_2 Dead space Shunt Electrical impedance	Best PEEP at maximum compliance Best PEEP at maximum EELV Best PEEP was defined at transpulmonary pressure equal to or exceeding zero during end expiration Best PEEP at maximum PaO_2 Best PEEP at lowest dead space Best PEEP at lowest shunt Minimal lung collapse and overdistension	'Best' PEEP levels are comparable with the different PEEP selection methods. EIT provides information on gas distribution
Wolf *et al.* [46]	Pigs (ARDS)	ARDSNet protocol Electrical impedance	PEEP selected according to a PEEP/FiO_2 table Regional EIT-derived compliance was used to maximize the recruitment of dependent lung and minimize overdistension of nondependent lung areas	EIT-guided ventilation resulted in improved respiratory mechanics, improved gas exchange and reduced histologic evidence of ventilator-induced lung injury in an animal model
Ferrando *et al.* [47]	Patients undergoing thoracic surgery	Dynamic compliance 5 cmH_2O	PEEP decrement trial at 2 cmH_2O steps until the maximal dynamic compliance was obtained	During one-lung ventilation, best compliance method is better than 5 cmH_2O PEEP to preserve oxygenation and lung mechanics
Hansen *et al.* [48]	Mechanically ventilated patients after isolated coronary artery bypass grafting or combined CABG and valve operations	5 cmH_2O 8 cmH_2O		The use of 8 cmH_2O PEEP instead of 5 cmH_2O does not seem beneficial
Mauri *et al.* [49]	Patients recovering from ARDS after switch to pressure support ventilation	Clinical PEEP (7 ± 2 cmH_2O) Clinical PEEP + 5 cmH_2O	More homogeneous distribution by EIT	Higher PEEP and lower pressure support provides more homogeneous ventilation and, possibly, better ventilation/perfusion matching

The table summarizes the results of recent studies comparing different PEEP selection methods. It reports the methods compared, their targets and the authors' conclusions. ALI, acute lung injury; ARDS, acute respiratory distress syndrome; CABG, coronary artery bypass graft; Crs, respiratory system compliance; Cst, static pulmonary compliance; CT, computed tomography; E_{CW}, chest wall elastance; EELV, end-expiratory lung volume; EIT, electrical impedance tomography; FiO_2, inspiratory oxygen fraction; IBW, ideal body weight; ITV, intratidal gas distribution; LIP, lower inflection point; PEEP, positive end-expiratory pressure; Pes, esophageal pressure; Ptp, transpulmonary pressure; SaO_2, arterial oxygen saturation; V_D/V_T, dead space.

stays constant and, then, decreases again, according to the sigmoid shape of the volume–pressure curve, independent of recruitability. The use of positive transpulmonary pressure as a guide for PEEP selection assumes that esophageal pressure equals the pleural pressure. Unfortunately, in our opinion, this assumption is far from true, because the esophageal pressure is highly positive in most patients with ARDS, which, according to the theory, should have their lung completely collapsed, sometimes even at the end of inspiration. The changes of esophageal pressure, in contrast, better reflect the changes of pleural pressure. Therefore, useful information can be acquired to judge the real distending pressure of the lung once the chest wall compliance has been estimated. Finally, the CT-derived PEEP is physiologically appealing, but we do not have any proof that it should be used as a guide for therapy. It simply tells us that in ARDS, from mild to severe, if we want to keep the whole lung completely open, either a few or hundreds of units, approximately the same pressure must be used. There is no clinical sense, in our opinion, to use high pressure either in patients with higher recruitability or in patients with lower recruitability, and, unfortunately, the CT scan-derived PEEP is unrelated to recruitability.

CONCLUSION

'The best PEEP' does not exist. To pretend and claim that we may find a PEEP level that avoids intratidal recruitment–derecruitment, providing in the meantime the best compliance, best oxygenation and lowest dead space, without causing hyperinflation and affecting hemodynamics, reflects a wishful dream that has nothing to do with the reality. Therefore, in our opinion, we should use a 'better PEEP' approach as a reasonable compromise among oxygenation, hemodynamics status and intratidal opening and closing. Because the latter phenomenon depends quantitatively on the lung recruitability, which is a function of the lung severity, the best compromise should be the use of higher PEEP in severe ARDS (range 15–20 cmH_2O), lower PEEP in mild ARDS (range 5–10 cmH_2O) and intermediated in moderate ARDS, paying attention to the chest wall elastance and hemodynamic impairment [50]. This pragmatic approach [50], supported by decades of studies and experience, is likely as effective as the more laborious PEEP trials that do not provide, at the end, anything else than reported range of values.

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Conflicts of interest

The authors do not have conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. Barach AL, Martin J, Eckman M. Positive pressure respiration and its application to the treatment of acute pulmonary edema. Ann Intern Med 1938; 12:754–795.
2. Gregory GA, Kitterman JA, Phibbs RH, *et al.* Treatment of the idiopathic respiratory-distress syndrome with continuous positive airway pressure. N Engl J Med 1971; 284:1333–1340.
3. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967; 2:319–323.
4. Cournand A, Motley HL, Werko L, Richards DW. Physiologic studies of the effect of intermittent positive pressure breathing on cardiac output in man. Am J Physiol 1948; 126:162–174.
5. Lemaire F, Harf A, Simonneau G, *et al.* Gas exchange, static pressure–volume curve and positive-pressure ventilation at the end of expiration. Study of 16 cases of acute respiratory insufficiency in adults. Ann Anesthesiol Fr 1981; 22:435–441.
6. 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.
7. 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.
8. Webb HH, Tierney DF. Experimental pulmonary edema due to intermittent positive pressure ventilation with high inflation pressures. Protection by positive end-expiratory pressure. Am Rev Respir Dis 1974; 110:556–565.
9. Mead J, Takishima T, Leith D. Stress distribution in lungs: a model of pulmonary elasticity. J Appl Physiol 1970; 28:596–608.
10. Slutsky AS. Ventilator-induced lung injury: from barotrauma to biotrauma. Respir Care 2005; 50:646–659.
11. Bone RC. The ARDS lung. New insights from computed tomography. JAMA 1993; 269:2134–2135.
12. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301–1308.
13. Meade MO, Cook DJ, Guyatt GH, *et al.* 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.
14. Santa CR, Rojas JI, Nervi R, *et al.* High versus low positive end-expiratory pressure (PEEP) levels for mechanically ventilated adult patients with acute lung injury and acute respiratory distress syndrome. Cochrane Database Syst Rev 2013; 6:CD009098.
15. ▪ Goligher EC, Kavanagh BP, Rubenfeld GD, *et al.* Oxygenation response to positive end-expiratory pressure predicts mortality in acute respiratory distress syndrome. A secondary analysis of the LOVS and ExPress trials. Am J Respir Crit Care Med 2014; 190:70–76.

It may be of some interest to note that in patients with ARDS enrolled in the classical trials with more severe hypoxemia, the extent of oxygenation response following PEEP adjustment is associated with outcome.

16. Mercat A, Richard JC, Vielle B, *et al.* 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.
17. Liu X, Ma T, Qu B, *et al.* Efficacy of lung recruitment maneuver with high-level positive end-expiratory pressure in patients with influenza-associated acute respiratory distress: a single-center prospective study. Curr Ther Res Clin Exp 2013; 75:83–87.
18. Phoenix SI, Paravastu S, Columb M, *et al.* Does a higher positive end expiratory pressure decrease mortality in acute respiratory distress syndrome? A systematic review and meta-analysis. Anesthesiology 2009; 110:1098–1105.
19. Briel M, Meade M, Mercat A, *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.

20. Gattinoni L, Caironi P, Cressoni M, *et al.* Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med 2006; 354:1775–1786.
21. Chiumello D, Coppola S, Froio S, *et al.* Time to reach a new steady state after changes of positive end expiratory pressure. Intensive Care Med 2013; 39:1377–1385.
22. Crotti S, Mascheroni D, Caironi P, *et al.* Recruitment and derecruitment during acute respiratory failure: a clinical study. Am J Respir Crit Care Med 2001; 164:131–140.
23. Pelosi P, Goldner M, McKibben A, *et al.* Recruitment and derecruitment during acute respiratory failure: an experimental study. Am J Respir Crit Care Med 2001; 164:122–130.
24. Quintel M, Pelosi P, Caironi P, *et al.* An increase of abdominal pressure increases pulmonary edema in oleic acid-induced lung injury. Am J Respir Crit Care Med 2004; 169:534–541.
25. Borges JB, Okamoto VN, Matos GF, *et al.* Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006; 174:268–278.
26. Yang Y, Chen Q, Liu S, *et al.* Effects of recruitment maneuvers with PEEP on lung volume distribution in canine models of direct and indirect lung injury. Mol Biol Rep 2014; 41:1325–1333.
27. Engel M, Nowacki RM, Reiss LK, *et al.* Comparison of recruitment manoeuvres in ventilated sheep with acute respiratory distress syndrome. Lung 2013; 191:77–86.
28. Kheir JN, Walsh BK, Smallwood CD, *et al.* Comparison of 2 lung recruitment strategies in children with acute lung injury. Respir Care 2013; 58:1280–1290.
29. Keenan JC, Formenti P, Marini JJ. Lung recruitment in acute respiratory distress syndrome: what is the best strategy? Curr Opin Crit Care 2014; 20:63–68.
30. Hata JS, Togashi K, Kumar AB, *et al.* The effect of the pressure–volume curve for positive end-expiratory pressure titration on clinical outcomes in acute respiratory distress syndrome: a systematic review. J Intensive Care Med 2014; 29:348–356.
31. Amato MB, Barbas CS, Medeiros DM, *et al.* Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338:347–354.
32. Ranieri VM, Suter PM, Tortorella C, *et al.* Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 1999; 282:54–61.
33. Villar J, Kacmarek RM, Perez-Mendez L, Aguirre-Jaime A. A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. Crit Care Med 2006; 34:1311–1318.
34. Gattinoni L, D'Andrea L, Pelosi P, *et al.* Regional effects and mechanism of positive end-expiratory pressure in early adult respiratory distress syndrome. JAMA 1993; 269:2122–2127.
35. ■ Cressoni M, Chiumello D, Carlesso E, *et al.* Compressive forces and computed tomography-derived positive end-expiratory pressure in acute respiratory distress syndrome. Anesthesiology 2014; 121:572–581.

This paper shows that compressive forces are similar in patients with lower and higher recruitability. Therefore, a CT-scan derived PEEP is inappropriately similar in higher and lower recruiters.

36. Bikker IG, Blankman P, Specht P, *et al.* Global and regional parameters to visualize the 'best' PEEP during a PEEP trial in a porcine model with and without acute lung injury. Minerva Anestesiol 2013; 79:983–992.
37. ■ Brochard L. Measurement of esophageal pressure at bedside: pros and cons. Curr Opin Crit Care 2014; 20:39–46.

Excellent review on the use of esophageal pressure as a surrogate of pleural pressure.

38. Keller SP, Fessler HE. Monitoring of oesophageal pressure. Curr Opin Crit Care 2014; 20:340–346.
39. ■ Gulati G, Novero A, Loring SH, Talmor D. Pleural pressure and optimal positive end-expiratory pressure based on esophageal pressure versus chest wall elastance: incompatible results. Crit Care Med 2013; 41:1951–1957.

This paper underlines problems related to the estimate of transpulmonary pressure at the bedside.

40. ■ Chiumello D, Cressoni M, Carlesso E, *et al.* Bedside selection of positive end-expiratory pressure in mild, moderate, and severe acute respiratory distress syndrome. Crit Care Med 2014; 42:252–264.

Only the PEEP selected by the 'high PEEP' arm of the LOV study is appropriately lower or higher in patients with lower or higher recruitability.

41. Yang Y, Li Y, Liu SQ, *et al.* Positive end expiratory pressure titrated by transpulmonary pressure improved oxygenation and respiratory mechanics in acute respiratory distress syndrome patients with intra-abdominal hypertension. Chin Med J (Engl) 2013; 126:3234–3239.
42. Huang Y, Yang Y, Chen Q, *et al.* Pulmonary acute respiratory distress syndrome: positive end-expiratory pressure titration needs stress index. J Surg Res 2013; 185:347–352.
43. Pintado MC, de Pablo R, Trascasa M, *et al.* Individualized PEEP setting in subjects with ARDS: a randomized controlled pilot study. Respir Care 2013; 58:1416–1423.
44. Rodriguez PO, Bonelli I, Setten M, *et al.* Transpulmonary pressure and gas exchange during decremental PEEP titration in pulmonary ARDS patients. Respir Care 2013; 58:754–763.
45. Blankman P, Hasan D, Groot JE, Gommers D. Detection of 'best' positive end-expiratory pressure derived from electrical impedance tomography parameters during a decremental positive end-expiratory pressure trial. Crit Care 2014; 18:R95.
46. Wolf GK, Gomez-Laberge C, Rettig JS, *et al.* Mechanical ventilation guided by electrical impedance tomography in experimental acute lung injury. Crit Care Med 2013; 41:1296–1304.
47. Ferrando C, Mugarra A, Gutierrez A, *et al.* Setting individualized positive end-expiratory pressure level with a positive end-expiratory pressure decrement trial after a recruitment maneuver improves oxygenation and lung mechanics during one-lung ventilation. Anesth Analg 2014; 118:657–665.
48. Hansen JK, Anthony DG, Li L, *et al.* Comparison of positive end-expiratory pressure of 8 versus 5 cm H2O on outcome after cardiac operations. J Intensive Care Med 2014. [Epub ahead of print]
49. Mauri T, Bellani G, Confalonieri A, *et al.* Topographic distribution of tidal ventilation in acute respiratory distress syndrome: effects of positive end-expiratory pressure and pressure support. Crit Care Med 2013; 41:1664–1673.
50. Gattinoni L, Carlesso E, Brazzi L, *et al.* Friday night ventilation: a safety starting tool kit for mechanically ventilated patients. Minerva Anestesiol 2014; 80:1046–1057.

