Bedside evaluation of pressure–volume curves in patients with acute respiratory distress syndrome

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Purpose of review

To describe the physiologic and diagnostic utility of static pressure–volume curves of the respiratory system at the bedside in patients with acute lung injury or acute respiratory distress syndrome.

Recent findings

The pressure–volume curve of the respiratory system is a useful tool for the measurement of respiratory system mechanics in patients with acute lung injury or acute respiratory distress syndrome. The pressure–volume curve has a sigmoid shape, with lower and upper points on the inspiratory limb and a point of maximum curvature on the expiratory limb. Visual and mathematical pressure–volume curve analysis may be useful for understanding individual lung mechanics and for selecting ventilator settings. Among the different techniques for acquiring pressure–volume curves at the bedside, the constant slow flow method is the simplest to perform, the most clinically reliable and has the fewest limitations.

Summary

Measurement of pressure–volume curves at the bedside in critically ill patients with acute lung injury or acute respiratory distress syndrome should be considered a useful respiratory monitoring tool to assess physiologic lung status and to adjust ventilator settings, when appropriate, to minimize superimposed lung injury associated with mechanical ventilators.

Keywords

acute lung injury, lung mechanics, mechanical ventilation, pressure–volume curve

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Abbreviations

ARDS	acute respiratory distress syndrome
Cinf	inflection compliance
LIP	lower inflection point
P–V	pressure–volume
PEEP	positive end-expiratory pressure
UIP	upper inflection point

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Introduction

The pressure–volume curve of the respiratory system is a physiologic method to characterize in static conditions the mechanical properties of the lungs in patients with acute respiratory failure. After the initial description of the adult respiratory distress syndrome, pressure–volume (P–V) curves were immediately used to describe the best combination of positive end-expiratory pressure (PEEP), tidal volume and the respective effects of these parameters on the increase in lung volume as well as to track the evolution of the respiratory system mechanics as the disease progressed [1–3]. Translational research has since shown that overdistension and repetitive opening and closing of alveolar units contribute to progressive lung injury, and that this damage is not distinguishable from the original disease [4,5]. Ventilator strategies focused on preventing alveolar end-expiratory collapse and limiting the tidal volume of each breath to avoid overdistension can attenuate ventilator-induced lung injury (VILI) [6]. P–V curves of the respiratory system performed at the bedside can help clinicians to accomplish these objectives.

Physiologic meaning

The usual shape of the quasi-static respiratory system P–V curve in acute respiratory distress syndrome (ARDS) patients is more or less sigmoidal, with an upward concavity at low inflation pressure and a downward concavity at higher inflation pressure [1]. The characteristic parameters of the P–V curves (lower and upper inflection points) were initially estimated by visual and manual means. Different methods have been proposed to attempt to standardize the definitions of these points. The most rigorous approach is the one proposed by Venegas *et al.* [7] based on fitting the P–V curve to the equation:

$$V = a + \left[\frac{b}{1 + e^{-(P-c)/d}}\right],$$

where V is volume, P is pressure, a is residual volume, b is total capacity, c is point of highest compliance and d is proportional to the pressure range within which most of the volume change takes place. Lower and upper inflection points, named lower (Pcl) and upper (Pcu) corner points by these authors, are calculated from the estimated curve using these two equations:

$$\mathrm{Pcl} = c - 2d$$

$Pcu = c + 2d$.

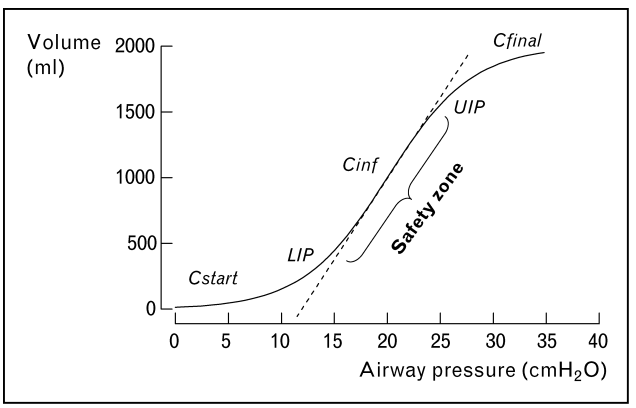
The P–V curve consists of three segments:

(1) An initial flat segment that reflects a very low compliance, indicating collapse of peripheral airways or alveolar units.
(2) A segment with a steeper slope; the transition between these two segments, which can be more or less abrupt, is the lower inflection point (LIP). This high and stable compliance over the linear segment following the LIP during inflation may be explained by continuing recruitment.
(3) At large volumes and high pressures, the slope decreases and the compliance approaches zero when the respiratory system is distended; the point at which a decrease in compliance can be identified is the upper inflection point (UIP).

If ventilation is conducted over the linear portion of the P–V curve, between the LIP and UIP, it may prevent both end-expiratory collapse and end-inspiratory overdistension (Fig. 1). In this figure, the LIP is the pressure corresponding to the intersection between starting compliance (Cstart) and inflection compliance (Cinf). Cinf is the slope of the curve in the most linear part. The UIP is the pressure corresponding to the intersection between Cinf and final compliance (Cfinal). Cfinal decreases with respect to Cinf because overdistension occurs at high lung volume. The portion of the curve above the LIP and below the UIP is proposed as the safety zone to avoid cyclic collapse (adequate PEEP) and overdistension (low tidal volume).

Based on mathematical models and studies performed in patients with acute lung injury [8–11], several authors suggested that LIP reflects the alveolar threshold opening pressures rather than the end-expiratory collapse and recruitment should continue on the linear portion of the P–V curve and end or diminish at the UIP without significant lung overdistension.

Figure 1 Theoretic pressure–volume curve of the respiratory system



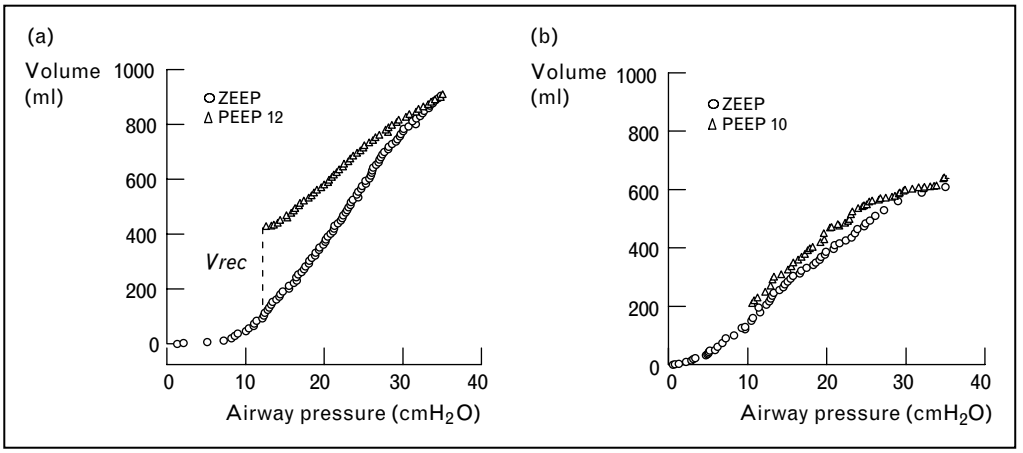
Cfinal, final compliance; Cinf, inflection compliance; Cstart, starting compliance; LIP, lower inflection point; UIP, upper inflection point.

Finally, when recruitment ends or diminishes, the slope of the curve decreases, a UIP can be seen and this does not only indicate overdistension. The deflation limb on the P–V curve has been less studied, maybe due to the absence of an accurate tracing method. Hickling [10] also found that after full lung recruitment, the maximum P–V slope during a decremental PEEP trial with a low tidal volume may be a useful method to determine open-lung PEEP in ARDS and to set the level of PEEP that avoids lung derecruitment. Albaiceta *et al.* [12] traced both limbs of the P–V curve by means of a stepwise change in airway pressure in 12 ARDS patients with early lung injury and obtained a computed tomography (CT) scan slice for every pressure level. Interestingly, they showed that whereas aeration and recruitment are parallel phenomena along inflation, loss of aeration and derecruitment has a threshold at the point of maximum curvature on the deflation limb, regardless of the origin of the ARDS. The application of this point in determining the PEEP level required to achieve the highest normal aerated tissue and the lowest derecruitment – in other words, 'to keep the lung open' – remains to be determined, however.

Are P–V curves useful in ARDS patients when no LIP or UIP is discernible in the graph? Vieira *et al.* [13] and Rouby *et al.* [14] showed that the presence or absence of a LIP on the P–V curve was associated with differences in lung morphology. In patients with no LIP, normally aerated lung areas coexisted with nonaerated lung areas and increasing levels of PEEP resulted in lung overdistension rather than in additional alveolar recruitment. In patients with a LIP, air and tissue were more homogeneously distributed within the lungs and increasing PEEP resulted in additional recruitment without lung overdistension. Clinicians might observe ARDS patients with low respiratory system compliance that exhibit a straight P–V curve not modified with the application of PEEP. Essentially in this context, what the diagnostic P–V tool shows is lung overdistension without a marked alveolar recruitment associated with the PEEP application (Fig. 2). The P–V curves of the respiratory system recorded with zero PEEP and PEEP are superimposed on the volume axes. The first point on the P–V curve drawn with PEEP corresponds to the increase in lung volume induced by PEEP. Recruited volume is the volume difference between the two curves at any pressure above the first point in the P–V curve. Both curves tend to join at high lung volume and pressure segments, suggesting that maximum lung volume is reached.

Figure 2 Pressure–volume curves obtained with and without positive end-expiratory pressure in two patients with acute respiratory distress syndrome

Panel (a) shows the application of positive end-expiratory pressure (PEEP) in a patient with a predominant effect of alveolar recruitment. Panel (b) shows the application of PEEP in a patient with a predominant effect of overdistension. Vrec, recruited volume; ZEEP, zero end-expiratory pressure.



Methods of measurement at the bedside

The first method used for measuring P–V curves was the supersyringe [1,3]. This consists of connecting a supersyringe to the endotracheal tube after reaching relaxation of the lung volume and then insufflating volume in regular steps (about 50–100 ml each) with 2–3 s pauses to allow quasi-static conditions while measuring airway pressure. Once airway pressure reaches 40 cmH_2O, insufflation is stopped and deflation is performed in the same way. The main disadvantages of this method are that it needs additional equipment, the patient must be disconnected and it does not take into account variations in lung volume due to continuing gas exchange, changes in gas temperature and humidity, or compression and decompression of the gas. Another method proposed is the multiple-occlusion technique [15], which consists of periodically interrupting tidal breathing at different lung volumes to obtain each P–V curve point. Normal tidal breathing is resumed for a few breaths and another different point is obtained. Both limbs can be obtained with this method and no disconnection is required; more importantly, no correction for oxygen consumption is needed. To avoid the problem of disconnection from the ventilator, Albaiceta *et al.* [16] proposed tracing the inspiratory and expiratory limb by increasing and decreasing the continuous airway positive pressure using inductive plethysmography to assess the lung volume. This method assumes the absence of any thorax-to-periphery blood shift. A dynamic P–V curve can be measured using the continuous slow flow method [17–19,20•], which entails delivering a selected volume at a very low constant inspiratory flow after an expiration with a duration and end-expiratory airway pressure defined by the user. This method is simple to perform, it is already included in the software of some ventilators, the effect of the oxygen consumption is not avoided, and the patient does not need to be disconnected or paralyzed [21•].

Effects of chest wall and abdomen in pressure–volume curve interpretation

Mechanical properties of the respiratory system vary greatly with the underlying disease responsible for acute lung injury/ARDS. If abdominal distension is present, the mechanical properties of the chest wall contribute to the derangement of respiratory system mechanics. In this condition, the UIP of the static P–V curve of the respiratory system is clearly underestimated. Ranieri *et al.* [22] performed static P–V curves of the respiratory system in ARDS patients and found an increase in respiratory system compliance with inflation volume in those with medical ARDS. The contrary occurred in surgical ARDS patients, in whom a decrease in compliance was found with inflation volume. Static inflation P–V curves of the chest wall and abdomen also differed between medical and surgical ARDS patients. Surgical ARDS patients had decreased chest-wall compliance and flattened abdominal P–V curves. Surgical abdominal decompression caused an upward and leftward shift of the P–V curves of the respiratory system, chest and abdomen, indicating an improvement in compliance. These data suggest that the flattening of the P–V curves of the respiratory system observed in some ARDS patients may be due in part to the decrease in chest-wall compliance related to abdominal distension that prohibits the descent of the diaphragm [23]. Data from Ranieri *et al.* [22] showed that the values of tidal volume that corresponded to the UIP were about 28% greater when estimated from the lung P–V as opposed to the respiratory system P–V curve.

The severity and changing conditions of some patients may require the determination of lung P–V curves (and therefore an esophageal balloon) to find the tidal volume that ensures an inflation pressure above PEEP in the lower vicinity of the UIP. At the bedside, esophageal

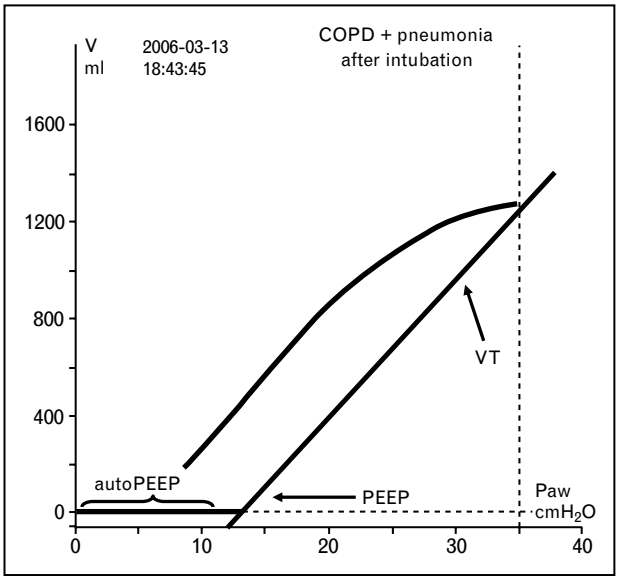
balloons are rarely used because information is difficult to interpret and for technical reasons as well. In this scenario, recognition of decreased thoracic compliance is usually suspected using clinical criteria such as generalized edema, abdominal distension or restrictions in chest-wall expansion. In line with these comments, Gattinoni *et al.* [24] found a marked increase in chest-wall elastance (the opposite of compliance) in patients with extrapulmonary ARDS (peritonitis, polytrauma) compared with patients with pulmonary ARDS (pneumonia, hemorrhagic alveolitis), and the estimated recruitment at 15 cmH_2O PEEP was nil in pulmonary ARDS and reached 293 ml in extrapulmonary ARDS. The different respiratory mechanics and response to PEEP observed are consistent with a prevalence of consolidation in pulmonary ARDS as opposed to prevalent edema and alveolar collapse in extrapulmonary ARDS.

The contribution of the chest wall could also be manifested in the LIP. Mergoni *et al.* [25] found that the contribution of the chest wall could be as high as 4.8 cmH_2O. This finding suggests physiologic explanations (chest wall) other than recruitment for the LIP of the respiratory system P–V curve. Interestingly, recruited volume could also be found in patients with no LIP and only those patients with a LIP in the lung P–V curve showed an improvement in gas exchange with PEEP application [26]. Lower values of LIP attributable to the chest wall should not mislead intensivists when determining the best level of PEEP in ARDS patients. Usually, the LIP caused by collapse/opening of diseased alveoli is much higher than the LIP caused by alterations in chest-wall mechanics. Finally, if expiratory time is too short and autoPEEP is still present due to dynamic hyperinflation or airflow limitation, a sudden increase in pressure without a parallel increase in lung volume is depicted in the P–V tracing [27] (Fig. 3). Despite a long expiratory time programmed in the ventilator previous to initiation of the P–V maneuver, an initial increase in pressure with no increment in lung volume is observed due to the presence of dynamic hyperinflation and autoPEEP.

Setting the ventilator using pressure–volume curves

The response to PEEP plus inspired tidal volume on lung recruitment depends on the cause of the lung injury or differences in lung morphology [13,24,28••]. In ARDS, different populations of alveoli may coexist. First, there is a group of alveoli recruitable by PEEP and tidal volume that can contribute to the LIP observed in the P–V curve if it is large enough. Second, there is a group of alveoli recruitable at the high airway pressures produced by high tidal volume or airway pressure and stable at end-expiration if PEEP is sufficiently high. Third, there is a group of alveoli recruitable at the very high airway

Figure 3 Pressure–volume curve obtained with a Galileo ventilator (Hamilton) in a patient with pneumonia and associated airflow obstruction



COPD, chronic obstructive pulmonary disease; Paw, airway pressure; V, volume; PEEP, positive end-expiratory pressure; VT, tidal volume.

pressures [29] of cyclic positive pressure ventilation but that collapse, again, at end-expiration because their threshold closing pressure is higher than the applied PEEP level. In the light of these considerations, the best selection of PEEP and tidal volume remains controversial, although a strategy based on the mechanical properties of the respiratory system seems appropriate provided that oxygen delivery to the peripheral tissues is preserved [30].

Among the few positive clinical trials performed in large populations of ARDS patients, three studies have shown interesting data when tidal volume and PEEP were selected in accordance with the findings obtained from P–V curves drawn in zero PEEP conditions. Amato *et al.* [31] provided the first demonstration that setting the ventilator according to the measured mechanics of the respiratory system can have a significant impact on clinical outcome in patients with ARDS. These authors compared a group of ARDS patients ventilated using a lung protective approach, which involved setting the PEEP above the LIP and tidal ventilation (6 ml/kg) in the linear portion of the respiratory system P–V curve (i.e. between the lower and the upper inflection points) with a group of ARDS patients ventilated in a conventional manner, using the lowest possible PEEP and a high tidal volume (12 ml/kg). Compared with conventional ventilation, the protective strategy was associated with improved survival at 28 days. Factors influencing the relative risk of death were the severity

of the disease and ventilatory strategy, specifically PEEP and driving pressure (the difference between plateau pressure and PEEP). Villar *et al.* [32•] found that a mechanical ventilation strategy with a PEEP level set on day 1 above the LIP and a low tidal volume had a beneficial impact on outcome in patients with severe and persistent ARDS compared with a strategy with a higher tidal volume and relatively low PEEP. Finally, Ranieri *et al.* [33] found that the group of ARDS patients randomized to receive tidal volume and PEEP based on the P–V curve had a reduction in plasma and bronchoalveolar-lavage concentrations of IL-6, soluble TNF-alpha receptor 75 and IL-1 receptor antagonist, whereas in the control group, an increase in several of these inflammatory mediators was observed.

Avoiding high tidal volume in ARDS and setting PEEP and FiO_2 using a predefined table combination based on different patients' hemoglobin oxygen saturation has improved survival in a large number of ARDS patients [34,35]. Within this framework of hard clinical evidence, however, clinical judgment and application of respiratory physiology at the bedside are also important. A recent study by the Acute Respiratory Distress Syndrome Network [35] compared the traditional lower end-expiratory pressure strategy with a higher end-expiratory pressure strategy (FiO_2 and PEEP were predefined in each arm) in ARDS patients ventilated with low tidal volumes. Clinical outcomes were similar whether lower or higher PEEP levels were used. Grasso *et al.* [36•] sequentially applied both the lower ($9 \pm 2\,cmH_2O$) and higher ($16 \pm 1\,cmH_2O$) PEEP strategy in 19 ARDS patients. In nine recruiters, the higher end-expiratory pressure strategy resulted in significant alveolar recruitment (587 ± 158 ml), improvement in arterial oxygenation (150 ± 36 to 396 ± 138 mmHg), and reduction in static lung elastance. In 10 nonrecruiters, however, alveolar recruitment was minimal, oxygenation did not improve and static lung elastance significantly increased. The increase in oxygenation, the reduction in static lung elastance and the shape of the P–V curve during the lower PEEP strategy were independently associated with alveolar recruitment. If a moderate/high PEEP level is used in an attempt to keep all alveoli open, the level of tidal volume should not exceed the UIP in the P–V curve because recruitment is nonsignificant and further hyperinflation will clearly cause overdistension, as demonstrated by CT scan [20•]. Roupie *et al.* [37] observed a mean UIP value of $26 \pm 6\,cmH_2O$ in 25 ARDS patients, and when a tidal volume of 10 ml/kg was used, 80% showed a plateau pressure that exceeded the UIP value. Based on this criterion, many patients would need reduction in tidal volume, which would result in hypercapnia.

Recently, Terragni *et al.* [38••] found that limiting tidal volume to 6 ml/kg predicted body weight and plateau pressure to $30\,cmH_2O$ may not be sufficient to avoid superimposed lung injury in ARDS patients characterized by a larger nonaerated compartment. Therefore, the protocol to set mechanical ventilation proposed by the Acute Respiratory Distress Syndrome Network to ventilate ARDS patients [34,35] could be further improved by periodic assessment of respiratory mechanics and the effects of PEEP on recruitment by using P–V curves at the bedside. Moreover, the advanced technology built into ventilators allows construction of P–V curves under anesthesia alone with acceptable variability and no serious adverse effects [20•,21•].

Conclusion

Measurement of respiratory system mechanics in patients with ARDS is important for assessing the status of the disease and for choosing the appropriate ventilator settings. Static inflation P–V curves of the respiratory system showing a concave LIP have been used to select the appropriate level of PEEP, which has decreased mortality when used with a lower tidal volume in some human ARDS studies. Nevertheless, several important questions remain to be answered, such as the periodicity of the P–V curve measurement, and limitations such as the complexity of the procedure and usually uncertainties regarding the interpretation must be overcome. As technological advances have simplified the P–V procedure, P–V curve measurement should be considered a useful respiratory monitoring tool for refining ventilator settings to minimize the devastating effects of ventilator-associated lung injury.

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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

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 358).

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