Review

Measurement of pressure–volume curves in patients on mechanical ventilation: methods and significance

Qin Lu and Jean-Jacques Rouby

University of Paris VI, Paris, France

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Abstract

Physiological background concerning mechanics of the respiratory system, techniques of measurement and clinical implications of pressure–volume curve measurement in mechanically ventilated patients are discussed in the present review. The significance of lower and upper inflection points, the assessment of positive end-expiratory pressure (PEEP)-induced alveolar recruitment and overdistension and rationale for optimizing ventilatory settings in patients with acute lung injury are presented. Evidence suggests that the continuous flow method is a simple and reliable technique for measuring pressure–volume curves at the bedside. In patients with acute respiratory failure, determination of lower and upper inflection points and measurement of respiratory compliance should become a part of the routine assessment of lung injury severity, allowing a bedside monitoring of the evolution of the lung disease and an optimization of mechanical ventilation.

Keywords: acute lung injury, acute respiratory distress syndrome, compliance, lower inflection point, mechanical ventilation, method, positive end-expiratory pressure, pressure–volume curve, upper inflection point

Introduction

Assessment of respiratory (combined chest wall and lung) pressure–volume curves permits analysis of the static mechanical properties of the respiratory system. The static pressure–volume curves are impaired in acute respiratory distress syndrome (ARDS). Three abnormalities are characteristic [1]: the appearance of an initial inflection point, which corresponds to the opening pressure of the collapsed bronchoalveolar zones; reduction of the slope of the ascending limb, which indicates the loss of lung aeration that characterizes acute lung injury [2]; and lowering of the volume that corresponds to the upper inflection point, which increases the risk of mechanical ventilation-induced over-distension [3]. The lower inflection point determines the minimal level of PEEP at which alveolar recruitment starts [2]. The upper inflection point determines the pressure level that is not to be exceeded in order to avoid barotrauma and/or ventilator-associated lung injury [4]. In critically ill patients, measurement of pressure–volume curves has been suggested as a method for assessing the severity of lung injury and for monitoring the evolution of lung disease. It can also guide the ventilatory adjustments to optimize mechanical ventilation [5].

Physiological background

Elasticity and resistance of the respiratory system

The anatomy of the respiratory system comprises of three passive structures (the lung, the chest wall and the

ARDS = acute respiratory distress syndrome; CT = computed tomography; FRC = function residual capacity; HU = Hounsfield units; PEEP = positive end-expiratory distress syndrome; ΔP = driving pressure; $\Delta V/\dot{V}$ = change in volume/flow; ZEEP = zero end-expiratory pressure.

airways) and one active structure (the respiratory muscles). These structures possess the mechanical properties of elasticity and resistance. Elasticity reflects the relation between the driving pressure (ΔP) and the change in the volume (ΔV). The elasticity of the respiratory system (lung and chest wall) is quantified by compliance ($\Delta V/\Delta P$) or elastance ($\Delta P/\Delta V$). The elastance of the respiratory system is equal to the elastance of the lungs plus the elastance of the chest wall. Resistance represents the relation between the driving pressure and the gas flow ($\dot{V}$), and is quantified by the following equation: resistance = $\Delta P/\Delta \dot{V}$.

Inflation of the respiratory system requires opposition of the forces of resistance, inertia and elastance, which act on the chest wall and the lungs. The force required for this is generated by the respiratory muscles during spontaneous ventilation, by the ventilator during controlled ventilation, or by both when the patient is on a partial mode of ventilatory support. One of the characteristic features of the respiratory system is that the chest wall and the lung, which constitute the passive structures, cannot be dissociated anatomically from the active structure constituted by the respiratory muscles. As a result, the resistive and elastic properties of the respiratory system can be evaluated only when the respiratory muscles are inactive. In ventilated patients, this can be achieved by sedation or muscle paralysis.

The resistive forces can be measured by the end-inspiratory occlusion method [6]. After end-inspiratory clamping, an analysis of the pressure signal reveals a decline in the airway pressure that occurs in two steps: a rapid initial decline that corresponds to the resistive forces of the airways and the endotracheal tube, and a progressive secondary decline that represents the resistive forces of the lung tissue, which depend on its viscoelastic properties. Measurement of the resistance of the respiratory system helps to evaluate the severity of the airway disease. In ARDS, the increase in the respiratory resistance is essentially due to a reduction in the aerated lung volume, which in turn modifies the viscoelastic properties of the tracheobronchial tree [7]. In the majority of patients there is no true active bronchoconstriction and the specific respiratory resistance [the measured resistance divided by the functional residual capacity (FRC)] is normal.

In acute respiratory failure, the impairment of the respiratory mechanics involves mainly the elastic component of the respiratory system. As a consequence, the measurement of respiratory pressure–volume curves should be done under static or quasistatic conditions in order to eliminate the resistive component. To achieve this, an end-inspiratory occlusion is performed with an end-inspiratory pause that is of sufficient duration (>3 s) to equalize the pressure between bronchial and alveolar compartments. Under these conditions, the intratracheal pressure reflects the alveolar pressure and the respiratory compliance can be calculated as the change in the lung volume divided by the change in the intratracheal pressure between end-inspiration and end-expiration, both measured at zero flow.

The pressure–volume relationship permits assessment of the mechanical properties of the respiratory system at different levels of lung inflation. This can be accomplished by static methods such as the inspiratory occlusion method [8] and the super-syringe method [1], or by a quasistatic method that is based on the inflation of the lung at a constant low flow. When the latter technique is used, the resistive component must be taken into account when analyzing the pressure–volume curves [9,10].

Intrinsic positive end-expiratory pressure

Another factor that can influence the interpretation of the pressure–volume curve is the presence of an intrinsic PEEP, which is defined as the presence of a positive alveolar pressure at end-expiration. Intrinsic PEEP results from a difference between the actual expiratory time and the expiratory time required for complete expiration of the tidal volume. Intrinsic PEEP may be generated by a very short expiratory time and/or a slow expiration due to high bronchial resistance or an abnormally high respiratory compliance. The presence of intrinsic PEEP may result in an error of the measurement of the compliance if the alveolar pressure at end-expiration is higher than the intratracheal pressure. In other words, if the intrinsic PEEP is not subtracted from the measured intratracheal pressure, the difference between the end-inspiratory and end-expiratory pressures may be overestimated, and consequently the respiratory compliance may be underestimated [11].

Intrinsic PEEP due to a short expiratory time and an incomplete emptying of the lung at end-expiration may also interfere with the measurement of the lower inflection point on the pressure–volume curve [10]. Kacmarek *et al* [12] compared the differences between extrinsic and intrinsic PEEP, in terms of the distribution of the end-expiratory airway pressures in a lung model with four compartments that had different time constants. Those investigators showed that, in the presence of an extrinsic pressure, the end-expiratory pressures were equal in all of the four compartments, whereas they were unequal when the same level of expiratory pressure was applied as an intrinsic pressure. At an intrinsic PEEP of 12.7 cmH_2O, the slow lung unit had an end-expiratory pressure of 15.8 cmH_2O, whereas the fast lung unit had an end-expiratory pressure of 10.1 cmH_2O. In other words, the positive pressure generated by the intrinsic PEEP may cause an over-distension of lung areas that have a prolonged time constant and a low recruitment of lung areas that have a short time constant where PEEP is expected to keep the alveoli open. When measuring pressure–volume curves, it is essential to empty the lungs completely by a prolonged expiration before inflating the respiratory system.

Lung and chest wall

The mechanical properties of the respiratory system depend on the mechanical characteristics of the lung and the chest wall. The compliance of the chest wall is determined by the ratio $\Delta V/\Delta P$, where ΔP is the pleural pressure, which is approximated by the measurement of oesophageal pressure. The compliance of the lung is measured by the same principle, where ΔP is the transpulmonary pressure, which is defined as the difference between the alveolar and the pleural pressures. In patients with acute lung injury, the impairment of the respiratory compliance may, in part, be due to a decrease in the compliance of the chest wall [13].

Techniques of measurement of the pressure–volume curves

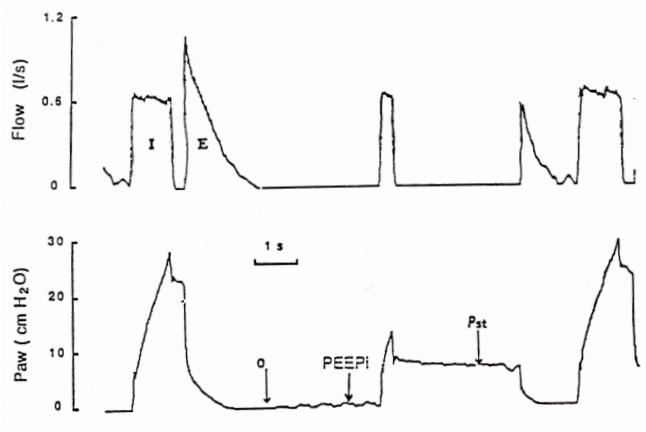
Static methods

The super-syringe technique

This static method consists of inflation of the lungs in steps of 50–100 ml up to 1.5 or 3.0 l starting from the FRC [1]. The volume of gas administered is determined by the displacement of the piston. The airway pressure is measured by a pressure transducer, with zero referred to the atmospheric pressure. The patients are sedated, paralyzed and ventilated at a fractional inspired oxygen of 1.0 without any PEEP for 15 min before the measurement, and the syringe is filled beforehand with humidified oxygen. A few seconds of disconnection of the patient from the ventilator is necessary to empty the lungs completely. The syringe is then connected to the endotracheal tube and the inflation manoeuvre is started from the FRC. The interval between two successive inflations should be 3 s in order to ensure a stable plateau pressure. The same maneuver can be performed during deflation in successive steps of 50–100 ml. The pressures and the volumes are recorded simultaneously and the pressure–volume curve is constructed from the obtained data. The entire procedure takes about 60 s.

The super-syringe technique was largely utilized during the 1980s to describe the different stages of ARDS [1,2]. This method has some disadvantages, however; the patient has to be disconnected from the ventilator and there is a loss of lung volume during the inflation procedure due to the consumption of the oxygen contained in the syringe. The errors in measurement that occur with the use of the super-syringe technique have been evaluated by Dall'Ava-Santucci *et al* [14] and Gattinoni *et al* [15]. Those investigators compared the variations in lung volumes obtained using the syringe technique with those measured by inductance plethysmography (Respitrace, NIMS Inc, Miami, FL, USA). The pressure–volume curves obtained with Respitrace exhibited lesser degrees of hysteresis (difference between the lung volumes during inflation and deflation for the same level of pressure), and the compliance during deflation was higher (73 versus 67 ml/cmH_2O). This difference was observed only if the duration of the inflation was prolonged (>45 s) and is related to the gas exchange that occurs in the lung during the manoeuvre; the loss of lung volume due to oxygen uptake is only partially compensated for by the carbon dioxide production [15]. A rapid inflation of less than 40 s helps to minimize this error [14]. The temperature and the humidity of the gas in the syringe may also influence the measurement of the pressure–volume curve. Administration of unwarmed and unhumidified gas causes a displacement of the curve to the left [15,16].

Figure 1



Inspiratory occlusion technique as described by Levy *et al* [8]. The patient is on controlled ventilation with a constant flow. Between two measurements, the lung volume is standardized by maintaining the ventilatory parameters constant. The intrinsic PEEP (PEEPi) is determined before each inflation followed by an end-inspiratory occlusion. The plateau pressure (Pst) is obtained a few seconds after the occlusion. From Levy *et al* [8].

The inspiratory occlusion technique

The inspiratory occlusion technique was developed in the late 1980s and was initially described by Levy *et al* [8]. It consists of measurement of plateau pressures that correspond to different tidal volumes during successive end-inspiratory occlusions. This technique is performed using a mechanical ventilator equipped with facilities for end-inspiratory and end-expiratory occlusions. It is not necessary to disconnect the patient from the ventilator, and the loss of volume due to lung oxygen uptake is negligible because each measurement lasts only 3 s. The patient is ventilated in a volume-controlled mode with a constant flow. Between two measurements, the ventilation is normalized by using the same ventilatory parameters. The different tidal volumes are administered in a randomized sequence. These tidal volumes are obtained by changing the respiratory rate while maintaining the inspiratory flow constant (lengthening or shortening the duration of inflation). The intrinsic PEEP is determined before each inflation to ensure that the lung volume and the end-expiratory pressure are stable. The

occlusion manoeuvre is performed at end-inspiration and the plateau pressure is measured after a few seconds of occlusion. The pressure–volume curve is constructed from the different plateau pressures that correspond to the administered volumes (Fig. 1).

The inspiratory occlusion technique offers the advantage of avoiding disconnection of the patient from the ventilator and it allows the measurements from any level of PEEP. Since the start of the 1990s, this technique has been extensively used to determine the lower and upper inflection points on the pressure–volume curve [4,5] and to quantify the effect of PEEP on alveolar recruitment in patients with ARDS [17,18]. The time required to perform the manoeuvre is around 15 min, however, which renders the technique cumbersome in clinical practice.

The quasistatic method using a continuous inflation at a constant flow

The simplest technique to obtain the pressure–volume curve in a critically ill patient without having to disconnect the patient from the ventilator is to inflate the respiratory system by a constant flow delivered by the ventilator [9,10]. This is a quasistatic technique. It can be performed on any intensive care ventilator that is equipped with a constant flow generator, and that has software and a display screen for plotting and analyzing the pressure–volume curve. This technique is derived from a dynamic method proposed by Suratt and co-workers [19,20] and is based on the assumption that when the lungs are inflated at a constant inspiratory flow, the change in the airway pressure is inversely proportional to the compliance of the respiratory system. Those investigators compared the quasistatic technique at a constant flow with the static technique, and showed that the compliances obtained by the two methods are closely correlated. Ranieri *et al* [17] later studied the pressure–volume curves in patients with ARDS and showed that curves obtained by the constant flow technique, like those obtained by the inspiratory occlusion technique, permit the determination of PEEP-induced alveolar recruitment or over-distension. If high constant flows that range between 20 and 60 l/min are used, however, only the slope of the pressure–volume curve can be reliably measured; upper and lower inflection points are overestimated because of the resistive effect generated by the high flow [9,10]. Utilization of constant flows less than 10 l/min can reproduce conditions close to those obtained with static methods [10].

In the 1980s, Mankikian *et al* [21] compared the pressure–volume curves obtained by the super-syringe technique with those obtained by the constant flow technique, using a very low flow of 1.7 l/min delivered by a special flow generator that was connected directly to the patient's endotracheal tube. Those investigators showed that the curves obtained using the two methods were identical. It must be emphasized that, in order to obtain such a low flow, a period of 60 s was required to inflate the lungs, which may have resulted in a loss of lung volume during the manoeuvre caused by oxygen uptake by the lungs. In other words, this technique illustrates one of the drawbacks of the super-syringe technique, although the resistive component with such a low flow is negligible.

Fifteen years later, Servillo *et al* [9] compared this technique using a higher constant flow of 15 l/min with the inspiratory occlusion technique. The flow was delivered by a Servo 900C computerized prototype ventilator (Siemens-Elema AB, Solna, Sweden). Those authors showed that the pressure–volume curve obtained using the constant flow technique was shifted to the right when compared with the curve obtained using the inspiratory occlusion method because of the resistive factor. The slopes of the curves were similar between the two methods, but the 15 l/min constant flow method was associated with an overestimation of the upper and lower inflection points.

Two solutions have been proposed to obviate the resistive factor when quasistatic methods are used: subtraction of the resistive pressure in the connecting tubes and in the airways from the measured total pressure; and reduction of the constant flow.

The first method was described by Servillo *et al* [9] and Jonson *et al* [22] and requires a complex computerized system that includes a computer-controlled Servo Ventilator 900C (Simens-Elema AB, Solna, Sweden), a ventilator–computer interface and an IBM-compatible computer. The ventilator–computer interface allows the computer to supervise the ventilator settings and collect inspiratory and expiratory flows and airway pressure signals. A constant or oscillating low flow (200 ml/s) is then administered to the patient after a prolonged expiration (4 s). The pressure–volume curve is analyzed using the Excel spreadsheet (Microsoft Corporation) and plotted after subtracting resistive pressure in the connecting tubes and airways from the total airway pressure (P_{tot}), which is measured by a pressure transducer included in the ventilator. The tracheal pressure (P_{trach}) and the elastic pressure (P_{el}) are calculated using the following equations:

$$P_{trach} = P_{tot} - P_{res(tube)} = P_{tot} - [(K_1 \times \dot{V}) + (K_2 \times \dot{V}^2)] \quad (1)$$

$$P_{el} = P_{trach} - P_{res} = P_{trach} - (R_{rs} \times V_t) \quad (2)$$

In Equation 1, inspiratory flow ($\dot{V}$) is measured using a pneumotachograph that is included in the ventilator, and K_1 and K_2 are determined *in vitro* for each type of tube and connection in order to calculate the resistive pressure that is related to the connecting and endotracheal tubes [$P_{res(tube)}$]. In Equation 2, tidal volume (V_t) is measured

using a pneumotachograph that is included in the ventilator, P_{res} is the resistive pressure in the airway and R_{rs} is the inspiratory resistance of the respiratory system, which can be calculated as the quotient between area of the pressure–volume loop and area of the flow–volume loop when a constant flow is administered, or as the quotient between pressure and flow when an oscillating inspiratory flow is used during the insufflation [22].

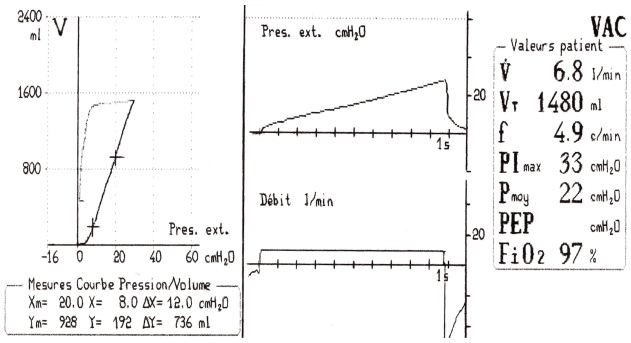
Servillo *et al* [9] compared the constant flow method (allowing subtraction of the resistive pressure) with the inspiratory occlusion method, and found a good agreement between both methods as far as respiratory compliance, and lower and upper inflection points are concerned.

The second method employed to obviate the resistive factor when quasistatic methods are used involves reduction of the constant flow. A recent study compared the quasistatic method using two constant flows (3 and 9 l/min) with the super-syringe technique and the inspiratory occlusion technique in patients with acute respiratory failure [10]. The constant flows were obtained through the regulating device of a César ventilator (Taema, Antony, France) equipped with a display screen and software capable of plotting and analyzing the pressure–volume curves. The ventilator was set in a volume-controlled mode with a constant inspiratory flow, a tidal volume of 500 or 1500 ml, an inspiration:expiration ratio of 80% and a respiratory frequency of 5 breaths/min. With these particular ventilatory settings, a constant flow of either 3 or 9 l/min was delivered over a period of 9.6 s and the pressure–volume curves were displayed real-time on the screen of the ventilator. The measurement of the respiratory compliance (slope of the pressure–volume curve between the two inflection points) and the determination of the upper and lower inflection points were carried out with the help of two mobile cursors available on the ventilator display screen. The entire procedure took 2 min and was performed without disconnecting the patient from the ventilator (Fig. 2).

That study showed that the pressure–volume curves obtained at a constant flow of 3 l/min matched those obtained using the static methods. When a constant flow of 9 l/min was used, there was a slight shift of the curve to the right due to the resistive factor (Fig. 3). The lower inflection point measured using the quasistatic method with a constant flow of 9 l/min was slightly higher than that obtained using the static methods, but the difference was not statistically significant. The slopes of the curves were similar for both flows and also between the quasistatic and static methods. The resistive pressures induced by the two constant flows, which were defined as the initial increase in the airway pressure until the inspiratory flow becomes constant, were 1.0 ± 1.0 and 1.8 ± 2.1 cmH_2O, respectively. These results, which have been confirmed by a second study [23], show that the influence of the resistive factor on the pressure–volume curves obtained using the quasi–static method is not clinically relevant if the flow administered is less than 9 l/min.

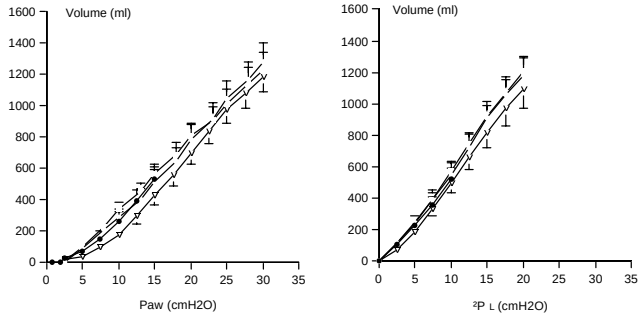
The continuous flow technique presents a number of advantages over the super-syringe and the inspiratory occlusion techniques: it does not require disconnection of the patient from the ventilator; it does not modify the lung volume before performing the manoeuvre; the construction of the pressure–volume curve on the ventilator screen

Figure 2



Recording obtained from the ventilator display screen (César ventilator, Taema, Antony, France) during measurement of the pressure–volume curve with a constant flow technique (9 l/min). The diagram on the right shows that the patient is ventilated in a volume controlled (VAC) mode at a constant inspiratory flow with a tidal volume of 1480 ml, a respiratory frequency of 4.9 breaths/min and a fractional inspired oxygen of 97%. These settings deliver a constant flow of 9 l/min (diagram in the middle) over a period of 9.6 s. The pressure–volume curve is seen on the left side of the screen. The lower inflection point and the slope are determined with the help of two cursors. From Lu *et al* [10].

Figure 3



Respiratory (left panel) and pulmonary (right panel) pressure–volume curves obtained by the supersyringe technique (O), the inspiratory occlusion technique (□) and the constant flow technique at 3 (●) and 9 (▽) l/min flow. The curves obtained using the constant flow technique at 9 l/min are slightly shifted to the right due to the generation of a resistive pressure. The curves obtained by the other methods are not significantly different. From Lu *et al* [10].

takes only 10 s and the entire procedure, including the analysis of the characteristics of the pressure–volume curves, takes around 2 min; the loss of volume due to oxygen uptake by the lungs is negligible; and the technique is simple to carry out at the bedside without the need for any special equipment other than a respirator. The software for freezing and analyzing the pressure–volume curve is not available on most intensive care ventilators, however. Systems are being developed that deliver constant flows between 0 and 10 l/min and that include software that allow analysis of the pressure–volume curves; such future ventilators should facilitate routine measurement of the pressure–volume curves at the bedside

Measurement of chest wall pressure–volume curve and lung pressure–volume curve

The chest pressure–volume curve is constructed by plotting lung volumes against pleural pressures that are estimated from oesophageal pressures. Oesophageal pressure can be measured by using either a balloon or a water-filled catheter. A catheter that incorporates a thin-walled balloon inflated with air (10 cm long, 1 cm in circumference) or a water-filled catheter is inserted into the mid-oesophagus and is connected to a pressure transducer. The patient is kept in the half-sitting position in order to minimize the effect of weight of the mediastinum in the supine position. Before measurement, an 'occlusion test' consisting of a series of three to five spontaneous occluded inspiratory efforts is recommended [24]. A ratio between oesophageal pressure changes and occluded inspiratory pressure changes that is close to 1 indicates that the catheter is properly positioned and that oesophageal pressure is an acceptable reflection of pleural pressure. The lung pressure–volume curve is constructed by plotting lung volumes against transpulmonary pressures (differences between airway and oesophageal pressures).

Clinical implications of the pressure–volume curves

General shape of the curve

In normal individuals the curve has a sigmoidal shape. It is linear in its initial part when the pressure–volume relation is measured from the FRC [1]. During spontaneous ventilation, the total compliance of the respiratory system, including the chest wall and the lung, is 100 ml/cmH_2O. The lung compliance is around 200 ml/cmH_2O [25]. In anaesthetized ventilated normal individuals, the total compliance of the respiratory system is slightly decreased (70–80 ml/cmH_2O) [13]. The respiratory compliance reflects the elastic properties of the respiratory system, and quite often that of the lungs. A stiff lung (as seen in ARDS) has a low compliance, whereas a highly distensible lung (as seen in an emphysematous patient) has a very high compliance. In healthy persons, the upper inflection point occurs at a lung volume of 3 l above the FRC, which defines the total lung capacity. The upper inflection point corresponds to the pressure above which pulmonary overdistension commences [26]. On the pressure–volume curve, this point is situated around 30 cmH_2O. Lastly, the loop formed by the pressure–volume curves in inflation and deflation indicates the presence of hysteresis [1].

The different components of the pressure–volume curve in acute respiratory distress syndrome

Significance of the lower inflection point

In ARDS, the initial part of the pressure–volume curve is not linear. The pressure corresponding to the intersection of two lines that represent the minimal and maximal compliance is defined as the lower inflection point [2,5]. The significance of the lower inflection point has been studied both in lung models and in patients with ARDS.

Using a mathematical ARDS lung model, Hickling *et al* [3] showed that the lower inflection point reflects both gravitational superimposed pressure and alveolar threshold opening pressure, the latter playing the most important role. The lower inflection point is not able to predict optimum PEEP accurately, because there is a continuous alveolar recruitment on the linear portion of the curve. According to Jonson *et al* [27], a marked lower inflection point indicates the pressure at which many collapsed alveoli are opening at the same time. On the other hand, the absence of a lower inflection point on the pressure–volume curve signifies an inhomogeneous lung having many different time constants and alveolar threshold opening pressures. In this configuration, the different alveolar compartments are opened one after another as far as the pressure increases, so that the lower inflection point is not clearly defined on the pressure–volume curve.

In patients with ARDS, the lower inflection point can be related either to the chest wall or to the lung parenchyma. Between 0 and 5 cmH_2O, the lower inflection point may result from the impairment of viscoelastic properties of the chest wall due to positive fluid balance, abdominal distension, oedema of soft tissue and pleural effusion [28]. In supine position, an upward displacement of the diaphragm resulting from an increased abdominal pressure induces an increase in the stiffness of the chest wall and a decrease in the chest wall compliance [13,29].

Only the presence of a lower inflection point on the pulmonary pressure–volume curve identifies the existence of a massive reopening of previously collapsed bronchoalveolar regions. In such a situation, application of a PEEP that is equal to or greater than the pressure corresponding to the lower inflection point results in significant alveolar recruitment and decrease in pulmonary shunt. It may avoid mechanical ventilation-induced lung injury resulting from the repeated opening and closure of the terminal bronchioles during each respiratory cycle [30]. Sometimes the lower inflection point cannot be clearly identified on the

respiratory pressure–volume curves in patients with a true acute respiratory failure. As a consequence, the PEEP level is often chosen on the basis of arterial oxygenation criteria.

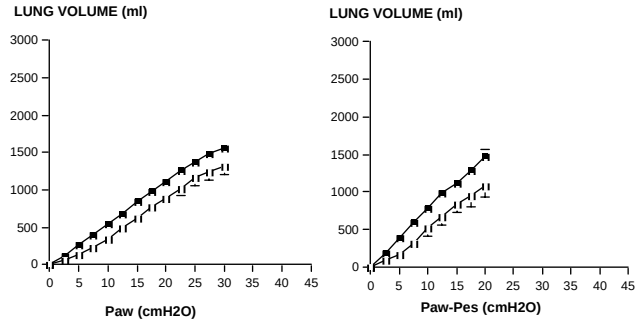
Vieira *et al* [31] compared the respiratory mechanics, computed tomography (CT) morphology of the lung and the radiological appearances in two groups of patients with or without a lower inflection point on their pulmonary pressure–volume curves. In that study, the analysis of the pulmonary morphology was performed by a technique involving measurement of the CT attenuation (pulmonary density) using a fast spiral scanner. According to previous studies [32–35] lung zones with a CT attenuation between −1000 and −900 Hounsfield units (HU) are considered as over-distended, those between −900 and −500 HU are considered as aerated, those between −500 and −100 HU as poorly aerated, and those between −100 and +100 HU as nonaerated.

In the study by Vieira *et al* [31], the aetiology of the lung injury and the haemodynamic and respiratory parameters were not different between groups. However, the patients with a lower inflection point were younger, their respiratory compliance was lower, and their Murray's score and mortality tended to be higher (Fig. 4). The total lung volume as well as the volume of lung tissue (comprising a mixture of alveolar septa, pulmonary and bronchial vessels, bronchi, various bronchopulmonary cells and pulmonary blood volume) were similar between the two groups, suggesting that the degree of pulmonary inflammation was similar in patients with or without a lower inflection point. On the other hand, the patients with a lower inflection point had a much smaller volume of normally aerated lung and a much higher volume of poorly and nonaerated lung. Their lungs were characterized by extensive diffuse radiological opacities, which were homogeneously distributed. In these patients, the volumetric distribution of CT attenuations was monophasic, with a peak at 7 HU (close to the CT attenuation of water) and the chest radiograph was characterized by diffuse pulmonary hyperdensities. In patients without a lower inflection point, the volumetric distribution of CT attenuations was biphasic with a peak at −727 HU and another at 27 HU. The chest radiograph showed opacities predominating in the lower lobes. In this latter group of patients, the aeration of the upper lobes appeared relatively well preserved. In both groups, PEEP induced an alveolar recruitment that was associated with lung over-distension only in those without a lower inflection point. Although the reasons for such differences in pulmonary morphology remain unknown, their effect on respiratory mechanics is marked. For the managing physician, these differences imply different ventilatory strategies in these two groups.

Significance of the upper inflection point

Experimental studies [36] have shown that the pulmonary lesions induced by mechanical ventilation are related to high tidal volumes. A ventilatory strategy based on the reduction of tidal volume has been proposed to avoid this risk. This strategy consists of titrating the tidal volume in such a way that the maximal alveolar pressure does not exceed the pressure that corresponds to the upper inflection point. The upper inflection point is defined as the pressure on the linear part of the pressure–volume curve beyond which the slope of the curve decreases. It indicates the end of alveolar recruitment and the beginning of pulmonary over-distension [3]. Like the lower inflection point, however, the upper inflection point is not always present on the pressure–volume curve. This phenomenon was studied in a mathematical lung model developed by Hickling *et al* [3]. Those authors suggested that the absence of an upper inflection point does not necessarily suggest the absence of over-distension. It is rather a result of continued alveolar recruitment above the upper inflection point, which masks its presence.

Figure 4



Respiratory (left panel) and pulmonary (right panel) pressure–volume curves at ZEEP in patients with acute respiratory failure or ARDS presenting with ($n = 8$, □) or without ($n = 6$, ■) a lower inflection point. Both the compliances were significantly lower in patients with a lower inflection point. Paw, airway pressure measured the trachea; Pes, oesophageal pressure measured in the lower third of the oesophagus. From Vieira *et al* [31].

Respiratory pressure–volume curve, alveolar recruitment and pulmonary over-distension

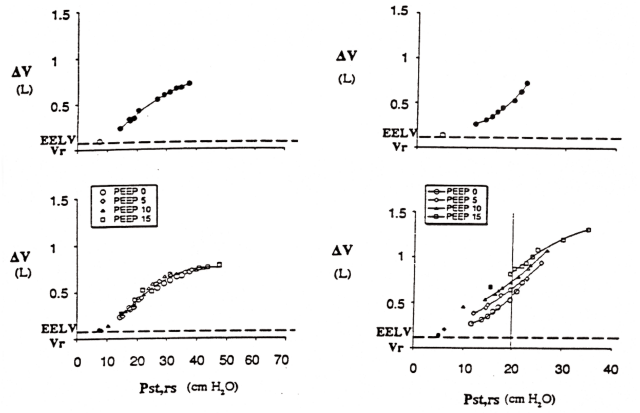
Ranieri *et al* [18] showed that an analysis of the pressure–volume curves in zero end-expiratory pressure (ZEEP) conditions permits prediction of whether PEEP induces alveolar recruitment or over-distension. A respiratory pressure–volume curve in ZEEP with upward convexity signifies a reduction in respiratory compliance as the lung volume increases. In these patients, the pressure–volume curve in PEEP conditions superimposes the curve obtained in ZEEP, implying the lack of any alveolar recruitment and the presence of over-distension. Conversely, a curve with its convexity downward in ZEEP conditions signifies progressive alveolar recruitment when the lung volume increases. In these patients, the application of PEEP induces an upward shift of the curve, indicating alveolar recruitment.

The volume of recruited lung according to Ranieri *et al* [18] can be quantified from the pressure–volume curves measured in ZEEP and PEEP. After determining the difference in end-expiratory lung volume between ZEEP and PEEP, the curves are placed on the same pressure and volume axes and the recruited lung volume is calculated as the difference in the volumes between ZEEP and PEEP for the same alveolar pressure (Fig. 5). An alveolar pressure of 15 or 20 cmH_2O is often chosen for this purpose [17,18]. Using this method, Jonson *et al* [22] quantified the amount of alveolar recruitment at two levels of pressure (15 and 30 cmH_2O) in a series of patients with acute lung injury. The authors showed that recruitment induced by PEEP was greater at 15 cmH_2O than at 30 cmH_2O (205 and 78 ml, respectively). The respiratory compliance in ZEEP was always higher than the respiratory compliance in PEEP. These results suggest a continuous alveolar recruitment of previously collapsed lung units during insufflation in ZEEP and a distension or over-distension of previously open lung units at higher level of pressure in PEEP.

In fact, the technique proposed by Ranieri *et al* [18] measures the total increase in gas volume resulting from PEEP. It does not permit differentiation of PEEP-induced alveolar recruitment from PEEP-induced distension and/or over-distension [31,35]. The measurement of pulmonary CT attenuation from a spiral CT scan permits differentiation of PEEP-induced alveolar recruitment from over-distension. Vieira *et al* [31] quantified the decrease in lung volume with a CT attenuation between −100 and +100 HU (the recruited lung volume according to Gattinoni *et al* [33]) and the increase in lung volume with a CT attenuation of less than −900 HU (the over-distended volume according to Vieira *et al*) following PEEP administration in patients with acute respiratory failure. In these patients, the PEEP level was fixed at 2 cmH_2O above the lower inflection point. As Figure 6 shows, in some patients alveolar recruitment was accompanied by an over-distension of the lung territories that were previously aerated. These results clearly demonstrate that PEEP can induce alveolar recruitment and lung over-distension simultaneously.

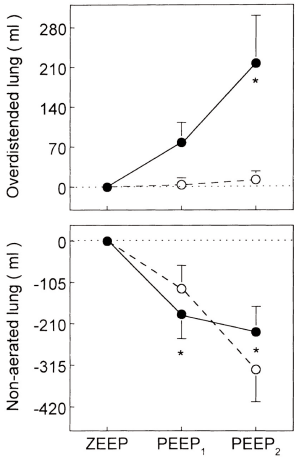
One option to avoid PEEP-induced over-distension could be to restrict the increase in lung volume in previously aerated lung areas by decreasing the compliance of the upper part of the chest wall. Turning the patient to the prone position results in a significant decrease in the chest wall compliance [37]. A significant relationship has been found by Pelosi *et al* [37] between prone position-induced improvement in arterial oxygenation and the decrease in chest wall compliance observed after turning the patient. In addition, the value of chest wall compliance in the supine position seems to be a predictive factor of the improvement in arterial oxygenation after the prone position is assumed; the greater the chest wall compliance in the supine position, the greater the improvement in arterial oxygenation. In

Figure 5



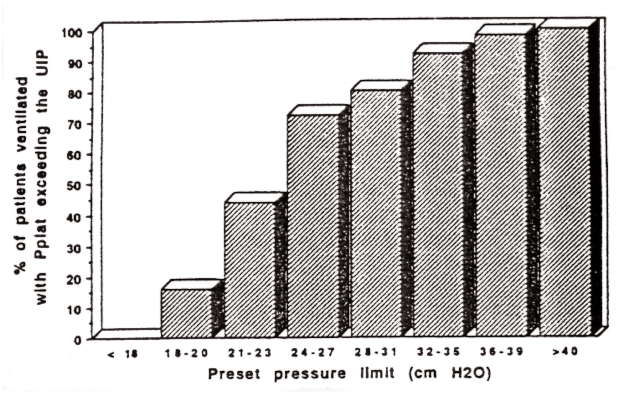
Pressure–volume curves obtained in ZEEP conditions and at PEEP values of 5, 10 and 15 cmH_2O in two patients with ARDS. In the patient who had a convex curve in ZEEP conditions (top left panel), PEEP did not induce any alveolar recruitment. When the different PEEP levels were applied the pressure–volume curves appeared superimposed on the curve obtained in ZEEP conditions, indicating an over-distension of the lung (bottom left panel). In the patient who had a concave curve in ZEEP conditions (top right panel) PEEP displaced the curve upwards, indicating alveolar recruitment (bottom right). The increase in lung volume between ZEEP and PEEP for a given alveolar pressure (20 cmH_2O) is the recruited lung volume. From Ranieri *et al* [17].

Figure 6



Changes in the volume of overdistended areas (upper panel) and in the volume of nonaerated areas (lower panel) induced by two PEEP levels in patients with ($n=8$, ○) and without ($n=6$, ●) a lower inflection point. $PEEP_1$, lower inflection point +2 cmH_2O or +10 cmH_2O in the absence of lower inflection point; $PEEP_2$, lower inflection point +7 cmH_2O or +15 cmH_2O in the absence of a lower inflection point. The lung volumes were measured by an analysis of the volume distribution of CT attenuations with a spiral thoracic CT scan. Alveolar recruitment is defined as the reduction of the nonaerated lung zones with a CT attenuation ranging between −100 and +100 HU. Pulmonary over-distension is defined as the appearance of lung regions with CT attenuation less than −900 HU. In patients without a lower inflection point, increasing levels of PEEP are associated with PEEP-induced lung over-distension. From Vieira *et al* [31].

Figure 7



Percentage of patients with ARDS and ventilated with PEEP in whom the plateau pressure exceeds the upper inflection point. In 50% of the patients, the upper inflection point is attained or exceeded for a plateau pressure of 25 cmH_2O. From Roupie *et al* [4].

other words, by limiting the expansion of the compliant part of the rib cage, the prone position tends to limit PEEP-induced over-distension and to promote alveolar recruitment in the caudal parts of the lung.

Respiratory pressure–volume curve and optimization of ventilatory settings

The presence or the absence of a lower inflection point on the pressure–volume curve should influence the choice of ventilatory settings [31]. In the absence of a lower inflection point on the lung pressure–volume curve, as observed when upper lobes remain fairly aerated and lower lobes are essentially nonaerated, the patient is at risk of lung over-distension at high levels of PEEP, and a PEEP around 10 cmH_2O should be administered because it represents a good compromise between PEEP-induced alveolar recruitment and over-distension. When a lower inflection point is present on the lung pressure–volume curve, as observed when loss of gas is homogeneously distributed within the lungs, a PEEP level far above the lower inflection point should be tested because the probability of a significant alveolar recruitment is largely predominant over the risk of over-distension.

Based on the consensus of experts, the European–American Consensus Conference of 1993 [38] recommended limiting the plateau pressure to 35 cmH_2O in patients with ARDS. Clinical studies [4,9,39] have shown that the upper inflection point in severe ARDS is at around 26 cmH_2O and can vary from 18 to 40 cmH_2O depending on the severity of the lung injury (Fig. 7). As a consequence, there is no 'magic number' that defines the risk of over-distension. In each individual, the upper inflection point varies according to the pressure–volume curve, and thus routine measurement of pressure–volume curves appears to be a critical element for implementing a protective ventilatory strategy.

Conclusion

The mortality of patients suffering from ARDS, despite a steady decline, remained high at 40–60% at the end of the 1990s. A recent randomized prospective study [5] has demonstrated that use of a 'protective ventilatory strategy' ameliorates lung function and decreases the mortality in patients with ARDS. This strategy combines application of a PEEP higher than the lower inflection point and administration of tidal volumes less than 6 ml/kg to limit the end-inspiratory pressures to below 40 cmH_2O. Even though the results of that study need to be confirmed by larger studies, the concept of recruiting while protecting the lung is already adopted by most centres and has become an important element of the therapeutic arsenal in patients with severe ARDS. In order to achieve this, measurement of the compliance and determination of the upper and lower inflection points on the pressure–volume curves at the patient's bedside should become a part of the routine monitoring of patients with acute respiratory failure. The continuous flow technique is a simple and reliable method that facilitates routine assessment of the pressure–volume curves and should be available on most intensive care ventilators.

References

1. Matamis D, Lemaire F, Harf A, *et al*: **Total respiratory pressure-volume curves in the adult respiratory distress syndrome.** *Chest* 1984, **86**:58–66.
2. 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.
3. Hickling KG: **The pressure–volume curve is greatly modified by recruitment.** *Am J Respir Crit Care Med* 1998, **158**:194–202.
4. Roupie E, Dambrosio M, Servillo G, *et al*: **Titration of tidal volume and induced hypercapnia in acute respiratory distress syndrome.** *Am J Respir Crit Care Med* 1995, **152**:121–128.
5. Amato MBP, Barbas CSV, Mediros 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.
6. Bates JHT, Rossi A, Milic-Emili J: **Analysis of the behavior of the respiratory system with constant inspiratory flow.** *J Appl Physiol* 1985, **58**:1840–1848.
7. Broseghini C, Bradolese R, Poggi R, *et al*: **Respiratory resistance and intrinsic positive end-expiratory pressue (PEEPi) in patients with the adult respiratory distress syndrome (ARDS).** *Eur Respir J* 1988, **1**:726–731.
8. Levy P, Similowski T, Corbeil C, *et al*: **A method for studying the static volume-pressure curves of the respiratory system during mechanical ventilation.** *J Crit Care* 1989, **4**:83–89.
9. Servillo G, Svantesson C, Beydon L, *et al*: **Pressure–volume curves in acute respiratory failure. Automated low flow inflation versus occlusion.** *Am J Respir Crit Care Med* 1997, **155**:1629–1636.
10. Lu Q, Vieira S, Richecoeur J, *et al*: **A simple automated method for measuring pressure-volume curve during mechanical ventilation.** *Am J Respir Crit Care Med* 1999, **159**:275–282.
11. Rossi A, Gottfried SB, Zocchi L, *et al*: **Measurement of static compliance of the total respiratory system in patients with acute respiratory failure during mechanical ventilation.** *Am Rev Respir Dis* 1985, **131**:672–677.
12. Kacmarek RM, Kirmse M, Nishimura M, Mang H, Kimball WR: **The effects of applied vs auto-PEEP on local lung unit pressure and volume in a four-unit lung model.** *Chest* 1995, **108**:1073–1079.
13. Pelosi P, Cereda M, Foti G, Giacommi M, Pesenti A: **Alterations of lung and chest wall mechanics in patients with acute lung injury:**

effects of positive end-expiratory pressure. *Am J Respir Crit Care Med* 1995, **152**:531–537.
14. Dall'Ava-Santucci J, Armaganidis A, Brunet F: **Causes of error of respiratory pressure-volume curves in paralyzed subjects.** *J Appl Physiol* 1988, **64**:42–49.
15. Gattinoni L, Mascheroni D, Basilico E, *et al*: **Volume/pressure curve of total respiratory system in paralyzed patients: artifacts and correction factors.** *Intens Care Med* 1987, **13**:19–25.
16. Sydow M, Burchardi H, Zinserling J, *et al*: **Improved determination of static compliance by automated single volume steps in ventilated patients.** *Intens Care Med* 1991, **17**:108–114.
17. Ranieri VM, Giuliani R, Flore T, Dambrosio M, Milic-Emili J: **Volume–pressure curve of the respiratory system predicts effects of PEEP in ARDS: 'occlusion' versus 'constant flow' technique.** *Am J Respir Crit Care Med* 1994, **149**:19–27.
18. Ranieri VM, Mascia LM, Fiore T, *et al*: **Cardiorespiratory effects of positive end-expiratory pressure during progressive tidal volume reduction (permissive hypercapnia) in patients with acute respiratory distress syndrome.** *Anesthesiology* 1995, **83**:710–720.
19. Suratt PM, Owens DH, Kilgore WT, Harry RR, Hsiao HS: **A pulse method of measuring respiratory system compliance.** *J Appl Physiol* 1980, **49**:1116–1121.
20. Suratt PM, Owens DH: **A pulse method of measuring respiratory system compliance in ventilated patients.** *Chest* 1981, **80**:34–8.
21. Mankikian B, Lemaire F, Benito S, *et al*: **A new device for measurement of pulmonary pressure-volume curves in patients on mechanical ventilation.** *Crit Care Med* 1983, **11**:897–901.
22. Jonson B, Richard JC, Straus C, *et al*: **Pressure–volume curves and compliance in acute lung injury.** *Am J Respir Crit Care Med* 1999, **159**:1172–1178.
23. Rodriguez L, Marquer B, Mardrus P, *et al*: **A new simple method to perform pressure-volume curves obtained under quasi-static conditions during mechanical ventilation.** *Intens Care Med* 1999, **25**: 173–179.
24. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J: **A simple method for assessing the validity of the esophageal balloon technique.** *Am Rev Respir Dis* 1982, **126**:788–791.
25. Permutt S, Martin HB: **Static pressure–volume characteristics of lungs in normal males.** *J Appl Physiol* 1960, **15**:819–825.
26. Rahn H, Otis AB, Chadwick LE, Fenn WO: **The pressure–volume diagram of the thorax and lung.** *Am J Physiol* 1946, **146**:161–178.
27. Jonson B, Svantesson C: **Elastic pressure–volume curves: what information do they convey?** *Thorax* 1999, **54**:82–87.
28. Mergoni M, Martelli A, Volpi A, *et al*: **Impact of positive end-expiratory pressure on chest wall and lung pressure-volume curve in acute respiratory failure.** *Am J Respir Crit Care Med* 1997, **156**: 846–854.
29. Mutoh T, Lamm WJ, Embree LJ, Hildebrandt J, Albert RK: **Volume infusion produces abdominal distension, lung compression, and chest wall stiffening in pigs.** *J Appl Physiol* 1992, **72**:575–582.
30. Muscedere JG, Mullen JBM, Gan K, Slutsky AS: **Tidal ventilation at low airway pressure can augment lung injury.** *Am J Respir Crit Care Med* 1994, **149**:1327–1334.
31. Vieira S, Puybasset L, Lu Q, *et al*: **A scanographic assessment of pulmonary morphology in acute lung injury: signification of the lower inflection point detected on the lung pressure–volume curve.** *Am J Respir Crit Care Med* 1999, **159**:1612–1623.
32. Gattinoni L, Pesenti A, Torresin A, *et al*: **Adult respiratoy distress syndrome profiles by computed tomography.** *J Thorac Imag* 1986, **1**:25–30.
33. Gattinoni L, Pelosi P, Crotti S, Valenza F: **Effects of positive end-expiratory pressure on regional distribution of tidal volume and recruitment in adult respiratory distress syndrome.** *Am J Respir Crit Care Med* 1995, **151**:1807–1814.
34. Umamaheswara Rao GS, Gallart L, Law-koune J-D, *et al*: **Factors influencing the uptake of inhaled nitric oxide in patients on mechanical ventilation.** *Anesthesiology* 1997, **87**:823–834.
35. Vieira S, Puybasset L, Richecoeur J, *et al*: **A lung computed tomographic assessment of positive end-expiratory pressure-induced lung overdistension.** *Am J Respir Crit Care Med* 1998, **158**:1571–1577.
36. Dreyfuss D, Soler P, Basset G, Saumon G: **High inflation pressure pulmonary edema. Respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure.** *Am Rev Respir Dis* 1988, **137**:1159–1164.
37. Pelosi P, Tubiolo D, Mascheroni D, *et al*: **Effects of the prone position on respiratory mechanics and gas exchange during acute lung injury.** *Am J Respir Crit Care Med* 1998, **157**:387–393.
38. Slutsky AS: **Consensus conference on mechanical ventilation – January 28–30, 1993 at Northbrook, Illinois, USA.** *Intens Care Med* 1994, **20**:150–162.
39. Richecoeur J, Lu Q, Vieira S, *et al*: **Expiratory washout vs optimization of mechanical ventilation during permissive hypercapnia in patients with severe acute respiratory distress syndrome**. *Am J Respir Crit Care Med* 1999, **160**:77–85.

Authors' affiliation: Surgical Intensive Care Unit Pierre Viars, Department of Anesthesiology, La Pitié-Salpêtrière Hospital, University of Paris VI, Paris, France

Correspondence: Dr Q Lu, MD, PhD, Réanimation Chirurgicale Pierre Viars, Département d'Anesthésie, Hôpital de la Pitié-Salpêtrière, 47–83 boulevard de l'Hôpital, 75013 Paris, France.
Tel: +33 1 42 17 73 05; fax: +33 1 42 17 73 26;
e-mail: qin.lu@psl.ap-hop-paris.fr