Measuring respiratory mechanics in ARDS

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Summary

Mechanical ventilation is necessary in most patients affected by the acute respiratory distress syndrome (ARDS). Unfortunately, mechanical ventilation itself can cause lung damage as a result of ventilator-induced lung injury (VILI). The cyclical recruitment and de-recruitment of atelectatic lung regions (atelectrauma), lung overdistension (volutrauma) and *de-novo* inflammation caused by a combination of the two (biotrauma) are likely participants in the development of VILI. Increasing experimental evidence suggests that the risk of VILI may be decreased by careful titration of ventilator support guided by monitoring pulmonary mechanics. Airway pressure (Paw) is the simplest signal available to monitor mechanics in ARDS. In combination with measurements of lung volume, Paw allows to plot volume-pressure curves (VP curves) and to record end-expiratory pressure and end-inspiratory pressure during zero flow (Pplat). In the past it was assumed that VP curves could give accurate information on lung recruitment and overdistension. Those assumptions, however, have been proven incorrect. Similarly, it is incorrect to consider Pplat an accurate index of overdistension. In this review we will examine some of the available tools to monitor pulmonary mechanics in ARDS. The critical interpretation of the data recorded with these tools, their limitations and the potentials use of these data in setting the ventilator will be discussed as well.

KEY WORDS: Acute Respiratory Distress Syndrome; monitoring; respiratory mechanics; Ventilator-Induced Lung Injury.

Introduction

The acute respiratory distress syndrome (ARDS) is a form of noncardiogenic pulmonary edema that results from acute damage to the alveoli (1). Most patients with this syndrome will die if they do not receive supplemental oxygen and mechanical ventilation (2, 3). By reversing life-threatening hypoxemia and alleviating the work of breathing, mechanical ventilation buys time for the lungs to heal (3). Mechanical ventilation can also cause lung damage by several mechanisms, including alveolar rupture and alveolar hemorrhage, especially when high airway pressures are used for ventilation (4, 5). In these patients, the damage to the lungs caused by mechanical ventilation is known as ventilator-induced lung injury (VILI) (5). Mounting experimental evidence suggests that the risk of VILI may be decreased by a careful titration of ventilator support guided by monitoring pulmonary mechanics in ARDS (5-8).

Ventilator-induced lung injury (VILI) may be considered as a "de-novo" biotrauma caused by cyclical recruitment and de-recruitment of atelectatic lung regions (atelectrauma), and lung overdistension (volutrauma).

Pressure Volume curves in ARDS

A useful first step in understanding the impact of monitoring pulmonary mechanics in ARDS is to examine the pressure-volume relationship of the respiratory system in these patients. As shown in Figure 1, the pressure-volume curve in patients with ARDS can have a sigmoid shape with two discrete bends (9). The lower bend is called lower inflection point (LIP) and the upper bend is called upper inflection point (UIP) (9).
In the past the LIP was thought to be the critical pressure needed to reopen most of previously collapsed airways and alveoli. The UIP was thought to be the critical pressure beyond which alveolar overdistension occurs. That meant that tidal ventilation was thought to be safe as long as it was delivered within these two points. We now know that these are oversimplifications because recruitment of collapsed lung units continues above LIP (10) and above UIP (11).

Examination of pressure-volume (P-V) curves is the first step of monitoring pulmonary mechanics in ARDS. However, P-V curves are difficult to interpret due to many confounders.

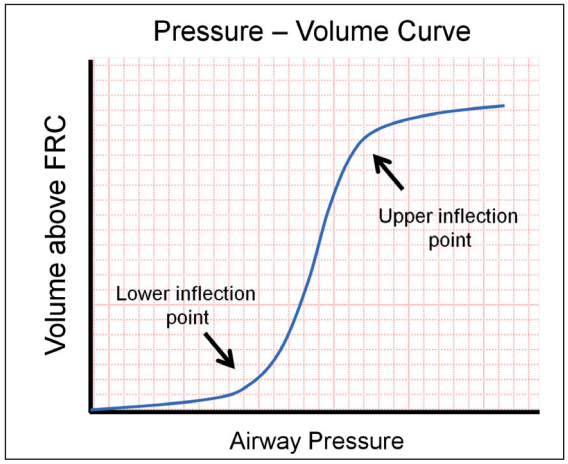

Figure 1 - Schematic representation of a pressure-volume curve of the respiratory system in a patient with ARDS. In these patients, the pressure-volume curve can have a sigmoid shape with two discrete bends above functional residual capacity. The lower bend is called lower inflection point and an upper bend is called upper inflection point. In 1995, Roupie et al. (AJRCCM 1995;152:121) reported that using conventional tidal volumes (9-12 mL/kg), and a mean PEEP of 10 cm H_2O, more than 70% of patients with ARDS had an end-inspiratory plateau airway pressure exceeding upper inflection point. Reducing tidal volumes to 6 mL/kg brought the end-inspiratory plateau airway pressure below upper inflection point. This was the first study to demonstrate the relevance of reduction in tidal volume for lung protection.

Ventilation that continues beyond the UIP can cause lung injury (5). This type of lung injury is known as "barotrauma" or lung trauma caused by excessive pressure applied to the lungs (5). Some investigators, however, prefer the term "volutrauma" (lung trauma caused by excessive distension of the lungs) because – they note – it is not the pressure at the airway opening that causes lung injury but the distention of the lung (12).

Ventilation that starts below the LIP is associated with cyclical collapse and reopening of lung units. This cyclical collapse and reopening causes a type of lung damage know as "atelectrauma" (13). In addition to biophysical injury (volutrauma and atelectrauma), investigators now posit that injurious ventilatory strategies associated with overdistension of the lung and with repeated recruitment and de-recruitment of collapsed lung units can also lead to the release of inflammatory mediators, including TNF- , interleukin-6, prostaglandins, leukotrienes and reactive oxygen species (13). According to those investigators, these inflammatory mediators cause a biochemical injury termed "biotrauma" (13). At a local level inflammatory mediators can lead to recruitment of a number of cells, including neutrophils (14). In addition, inflammatory mediators can translocate from the lung into the systemic circulation and this may lead to distal organ dysfunction and death (4, 13).

At one time, investigators advocated obtaining pressure-volume curves to properly select ventilator settings in patients with ARDS (15). Unfortunately, pressure-volume curves are difficult to generate because they require heavy sedation and paralysis (16). In addition they can cause hypoxemia at low lung volumes, derecruitment at low levels of positive end-expiratory pressure (PEEP) and hemodynamic compromise (decrease of venous return) (16). Pressure volume curves are also difficult to interpret due to many confounders. These confounders include expiratory flow limitation (17), abnormal chest-wall mechanics (18), continuous recruitment of collapsed lung units above LIP (10) and above UIP (11) and focal vs. non-focal distribution of ARDS (6, 19). Not surprisingly, most experts around the world use pressure-volume curves only for research purposes but not in clinical practice (Figure 2).

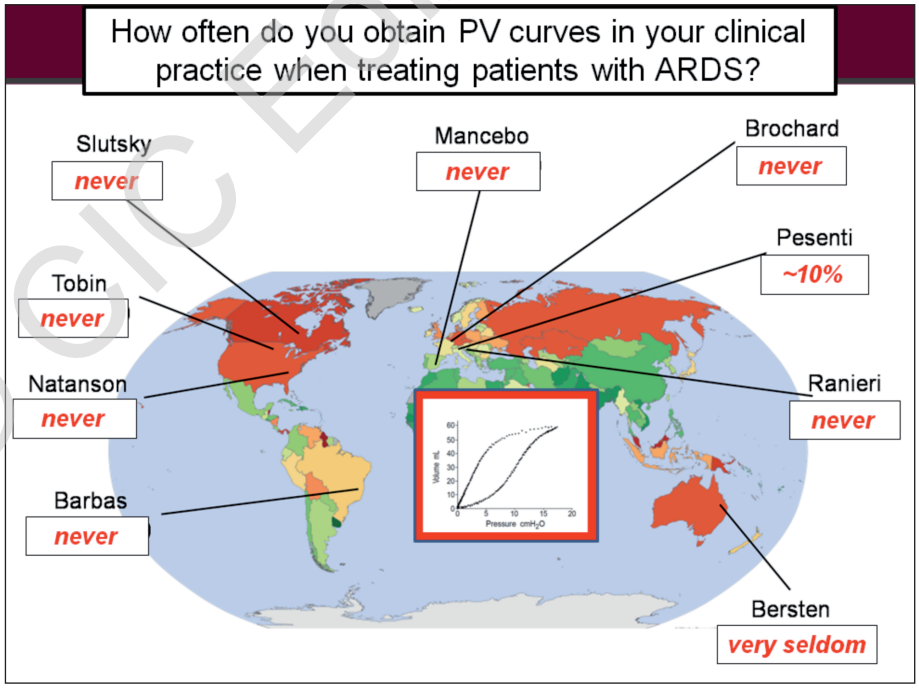

Figure 2 - Pressure volume curves are difficult to generate and to interpret. This is why most international experts do not use them in their daily clinical practice (Franco Laghi, personal communication, November 2010).

Monitoring pulmonary mechanics to limit overdistension (Volutrauma)

Following the seminal study of Amato et al. (15), the ARDS Network published the result of a large multicenter trial of 861 patients with ARDS (20). In the study, one group of patients was randomized to mechanical ventilation with small tidal volumes (6 ml/kg of ideal body weight or IBW) and a plateau airway pressure (Pplat) recorded following an inspiratory pause of 0.5 seconds of 30 cm H_2O or less. A second group of patients was randomized to traditional tidal volumes (12 ml/kg IBW) and a Pplat of 50 cm H_2O or less (20). The trial was stopped when an interim analysis revealed that lowering tidal volume and Pplat decreased mortality by 22%. In a subsequent meta-analysis, Eichacker et al. (21) concluded that the most important aspect in setting the tidal volume in ARDS is to use tidal volumes that produce a Pplat between 28 and 32 cm H_2O.

Plateau airway pressure (Pplat) is used to estimate transpulmonary pressure (lung stretching). In some patients a higher stiffness of the chest wall may cause grossly overestimation of lung stretching.

Pplat is used to estimate transpulmonary pressure (lung stretching). A high Pplat usually signifies excessive lung stretching, and a low Pplat signifies less lung stretching. Unfortunately, the value of Pplat is determined not only by the stiffness of the lung but it is also determined by the stiffness of the chest wall. In some patients, including those who are obese, pregnant or who have tense ascites, the stiffness of the chest wall can be significant. In these patients, Pplat may be very high without this signifying that the lungs are truly overdistended (volutrauma). That is, in patients with a chest wall that is stiffer than normal the simple measurement of Pplat will cause physicians to grossly overestimate lung stretching. In these patients it may necessary to measure transpulmonary pressure using esophageal pressure tracings (see below).

Transpulmonary pressure is calculated by subtracting alveolar pressure from pleural pressure (Figure 3). In clinical practice, it is unrealistic to perform direct measurements of alveolar pressure and direct measurements of pleural pressure. Instead, airway pressure is used as a substitute of alveolar pressure, and esophageal pressure is used as a substitute of pleural pressure.

If a clinician wants to know the extent of lung stretching at ***end-inhalation*** he/she will have to record Pplat plus the corresponding esophageal pressure at ***end-inhalation***. Of note, the value of Pplat already comprises any external PEEP applied to the patient and any intrinsic PEEP the patient may have. This means that it would be wrong to include in the calculation of transpulmonary pressure any correction for external PEEP or intrinsic PEEP. It has been reasoned that in patients with ARDS, tidal volume should be titrated to keep the transpulmonary pressure in the physiologic range – i.e., transpulmonary pressure <25 cm H_2O while the patient is in the supine position (7, 22).

The use of small tidal volumes in ARDS causes a reduction of CO_2 clearance and a reduction in lung recruitment. These phenomena are responsible for an initial worsening in lung compliance and ventilation/perfusion matching when instituting low-tidal volume ventilation (20). In other words, permissive hypercapnia and permissive atelectasis/hypoxemia are the trade-offs we have to accept to improve the outcome of patients with ARDS (20). Of interest, new experimental evidence suggests that permissive hypercapnia may itself be lung-protective (23). Hypercapnia causes intracellular acidosis, which, in turn, has many potential protecting effects on injured alveolar cells. These potential protecting effects include the inhibition of xanthine oxidase (with consequent decrease in the production of free radicals), inhibition of the activity of NF-kB (with consequent decrease in cytokine production) and inhibition of capsase-3 that results in less apoptosis (23).

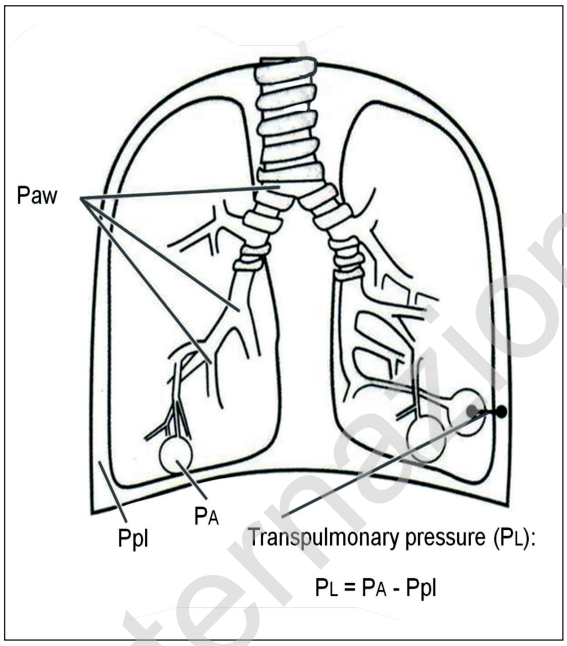

Figure 3 - Transpulmonary pressure or P_L (lung stretching) is calculated by subtracting alveolar pressure (PA) from pleural pressure (Ppl). In clinical practice, airway pressure (Paw) substitutes alveolar pressure and esophageal pressure substitutes pleural pressure.

Monitoring pulmonary mechanics to limit cyclical recruitment-derecruitment (Atelectrauma)

The central question here is "what aspects of pulmonary mechanics should we monitor to avoid atelectrauma?". Stated differently the question is "what aspects of pulmonary mechanics should we monitor to set PEEP in ARDS?". This is a difficult question that can be answered only tentatively.

The various strategies used to set PEEP in ARDS include:

1. Monitoring oxygenation and using a sliding-scale (table) developed by a panel of experts to adjust PEEP and FiO_2 in discrete steps to maintain adequate arterial oxyhemoglobin saturation (24, 25).
2. Monitoring respiratory system compliance while titrating PEEP (optimal PEEP defined as the PEEP associated with maximal compliance) (26, 27).

3. Monitoring the shape of the airway pressure signal during lung inflation with constant airflow (optimal PEEP defined as the PEEP associated with a linear rise in airway pressure or "stress index = 1") (6).
4. Monitoring Pplat while titrating PEEP (optimal PEEP defined as the highest PEEP associated Pplat of 28-30 cm H_2O) (28).
5. Monitoring an estimate of transpulmonary pressure measured with an esophageal balloon (optimal PEEP defined as the PEEP associated with positive transpulmonary pressure at ***end-exhalation*** while keeping transpulmonary pressure in the physiologic range of <25 cm H_2O) (7).

Investigators have reported encouraging results (tendency to improve survival) in patients with ARDS ventilated with a tidal volume of 6 ml/kg IBW in whom PEEP was titrated according to the mechanical characteristics of each individual patient.

Except for the first strategy listed above, all the other strategies are based on two ideas, first, to monitor the mechanical characteristics of the individual patient with ARDS and, second, set PEEP accordingly.
Investigators have reported encouraging results (tendency to improve survival) in patients with ARDS ventilated with a tidal volume of 6 ml/kg IBW in whom PEEP was titrated according to the mechanical characteristics of each individual patient (7, 28). In contrast, titrating PEEP using a sliding-scale (table) designed to adjust PEEP and FiO_2 in discrete steps to maintain adequate arterial oxyhemoglobin saturation has not improved survival (24, 25).

Monitoring pulmonary mechanics to limit biotrauma

To posit that monitoring a particular aspect of pulmonary mechanics can give an insight to the risk of developing biotrauma implies the existence of a not yet well identified link between pulmonary mechanics and biotrauma. Monitoring tools that have triggered interest in this regard include the quantification of the *end-inspiratory strain of the lung* (29, 30) and the computation of the so-called *driving pressure* (31).

1. End-inspiratory strain: according to continuum mechanics, a branch of classic mechanics that deals with solids and fluids, the transformation of a body from a reference configuration to a current configuration is called *deformation*. This is quantified as the displacement between particles in the body relative to a reference length or *strain*. In the case of the lungs undergoing mechanical ventilation *end-inspiratory strain* is defined as the change in lung volume relative to the resting volume (29, 30). This means that to calculate the end-inspiratory strain of the lung it is necessary to measure the end-expiratory lung volume and tidal volume (30). In mechanically ventilated patients, measurements of end-expiratory lung volume can be performed using the helium dilution technique, the nitrogen washout/washin technique and with spiral computed tomography (32, 33). (Whether strain should be calculated while patients are on PEEP or not remains controversial) (34).
Cyclical *end-inspiratory strain* associated with inflation to total lung capacity is injurious to healthy lungs (29). This occurs when the resting lung volume (the baby lung in case of ARDS) is increased by two-fold to three-fold (29, 35). In patients with ARDS damage has been reported with *end-inspiratory strains* well below this upper limit (29). Such observation implies the presence of inhomogeneous distribution of local *end-inspiratory strain* (29).
2. Driving pressure: this pressure is calculated as the difference between Pplat and PEEP. This means that one of the determinants of driving pressure is end-inspiratory lung strain: the greater the strain the greater the driving pressure.
Post-hoc analysis of several clinical investigations suggests that driving pressures above 15-20 cm H_2O are conducive to increased mortality in ARDS (Figure 4) (4, 7, 15, 20, 24, 25, 28, 36-40). It would be tempting to speculate that the excess mortality in those studies was due, at least in part, to excessive strain and biotrauma. For several reasons such speculation cannot be either accepted or refuted. First, the link between strain and driving pressure is indirect. Second, the value of Pplat required to calculate driving pressure is not only a function of lung mechanics but it is also a function of chest wall mechanics (see section on volutrauma). Third, no study has prospectively determined the impact of different driving pressures on ARDS outcome. Fourth, ventilator settings (such ventilator mode, as PEEP, respiratory rate, FiO_2) in the investigations summarized in Figure 4 varied from study to study (4, 7, 15, 20, 24, 25, 28, 36-40). This makes it impossible to dissect the effect of driving pressure from other ventilator variables on patient outcome. In other words, while it would seem reasonable to aim for a driving pressure below 15-20 cm H_2O (5, 15, 41) it is necessary to bear in mind that such threshold is based on conjecture, biological plausibility and post hoc analysis of studies not designed to identify the ideal driving pressure to use in patients with ARDS.

The quantification of the end-inspiratory strain of the lung and the computation of the so-called driving pressure has been suggested to limit biotrauma, but the link between pulmonary mechanics and biotrauma has not yet been identified.

Conclusion

In patients with ARDS mechanical ventilation can be lifesaving yet it can also exacerbate lung injury (VILI). Current knowledge suggests that preventing VILI during mechanical ventilation requires avoidance of cyclical opening and closing of unstable lung units and avoidance of excessive stretching of lung parenchyma. Growing experimental evidence suggests that these goals may be

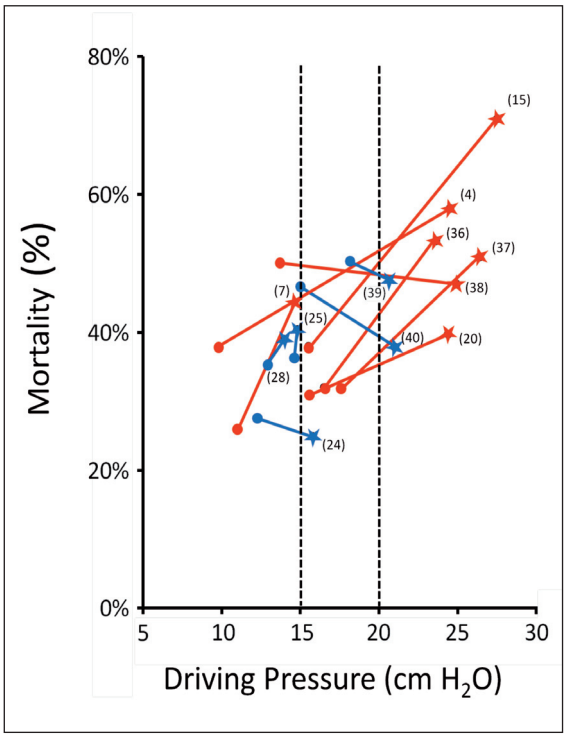

Figure 4 - Mortality of patients with ARDS plotted against driving pressure in twelve clinical studies designed to compare some type of conventional ventilation against different lung-protective strategies (4, 7, 15, 20, 24, 25, 28, 36-40). For each study, the circle indicates the combination of mortality and driving pressure recorded with protective strategy and the star indicates the combination of mortality and driving pressure recorded with conventional ventilation. In blue are studies where there was no difference in mortality between protective strategy and conventional ventilation. In red are studies were the mortality with conventional ventilation was greater than with protective strategy. In most instances, mortality was the highest when driving pressure of the conventional ventilation group was more than 20 cm H_2O and it was the lowest when driving pressure of the lung-protective strategy group was less than 15 to 20 cm H_2O (Modified from Bugedo and Bruhn) (41).

achieved by a careful titration of ventilator support guided by monitoring pulmonary mechanics (5-8).

Acknowledgements and disclosures

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