

Optimizing Perioperative Ventilation Support with Adequate Settings of Positive End-Expiratory Pressure

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1. Introduction

1.1 Mechanical ventilation

Mechanical ventilation is often employed to replace spontaneous breathing of patients under general anesthesia. Even after operation, the patient still needs ventilation support until the respiratory muscles regain full function. A ventilator delivers a certain amount of air flow through a facial mask or tracheal tube to the patient whose respiratory system fails to function properly due to the effects of anesthetics or diseases. Based on the difference in breath initiation, mechanical ventilation can be divided into two categories: controlled ventilation and assisted ventilation. In this chapter, we focus on controlled mechanical ventilation, under which the patient is not able to trigger a valid breath and the ventilator overtakes all the workload of respiratory muscles. Respiratory parameters such as respiratory rate (RR), inspiratory-to-expiratory time ratio (I:E), tidal volume (V_t) (or minute volume) are controlled by the ventilator.

Traditionally, controlled mechanical ventilation can either be volume controlled (VCV) or pressure controlled (PCV). Ideal respiratory signals obtained in a healthy human during VCV and PCV are shown in Fig. 1. In the VCV mode, a patient receives constant flow from the ventilator until a preset V_t is reached. A severe drawback of VCV is missing control of the peak airway pressure. Airway pressure (P_{aw}) depends on respiratory system compliance and resistance. In patients with certain lung diseases, such as acute lung injury (ALI), the same setting of V_t as in patients with healthy lungs may lead to a higher peak P_{aw} with the potential to further injure the lung. Therefore, VCV is often applied with a pressure limitation. Once the peak P_{aw} rises above this limit, the ventilator will stop delivering gas even if the preset V_t is not yet reached. In the PCV mode, a maximum airway pressure (P_{max}) is defined. Inspiration ends when P_{max} is reached i.e. the flow driven by the pressure difference decreases to zero. PCV may be superior to VCV in patients requiring one-lung

anesthesia (Tuğrul *et al.*, 1997). However, the V_i is not controlled by the ventilator in the PCV mode, but determined by the preset maximum pressure and respiratory system mechanics. There is no guarantee that sufficient gas will be delivered into the lung. Hence, V_i and minute volume that the patient receives must be monitored. In reality, the respiratory signals measured by the ventilator do not look exactly like the ideal tracings shown in Fig. 1. Signals are subjected to various error sources, such as environmental noise, sense dysfunction, and calibration failure and they also depend on individual physiological or pathophysiological properties of the patient's respiratory system.

Respiratory signal analysis is helpful for the clinician and beneficial to the patient. Lung diseases influence tidal ventilation, which is reflected in the P_{aw} , air flow and respiratory volume signals. Based on a shape analysis of respiratory signals, clinical diagnosis can be supported. For example, the flow-volume curve of a patient with cystic fibrosis during forced respiration, measured by body plethysmography, is plotted in Fig. 2. Low expiratory flow rates compared to the normal values at 75%, 50% and 25% of volume capacity indicate airway obstruction in this patient.

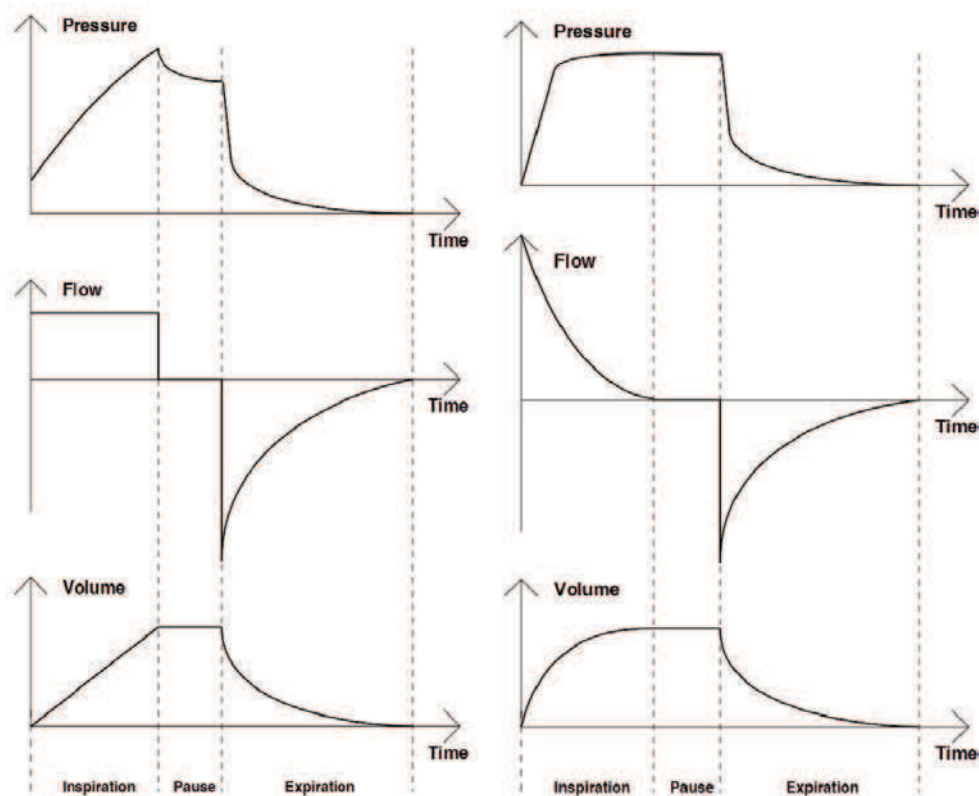


Fig. 1. Ideal respiratory signals (airway pressure, air flow and respiratory volume) of a healthy human under volume controlled (left) and pressure controlled (right) ventilation mode.

To better understand the respiratory system, many mathematical models were proposed (Gillis and Lutchen, 1999, Lutchen and Costa, 1990). The simplest one is based on the first order equation of motion:

$$P_{aw}(t) = V(t) / C_{rs} + V'(t) \times R_{rs} + P_0 \tag{1}$$

where P_{aw} , V and V' denote airway pressure, volume and airway flow, C_{rs} and R_{rs} represent respiratory system compliance and resistance, respectively; P_0 is the pre-existing pressure in the lung. With the measured respiratory signals, lung mechanics (C_{rs} and R_{rs}) can be calculated. These measures provide a better insight into the lung status and thereby help the physicians to establish diagnosis and make adequate therapeutical decisions.

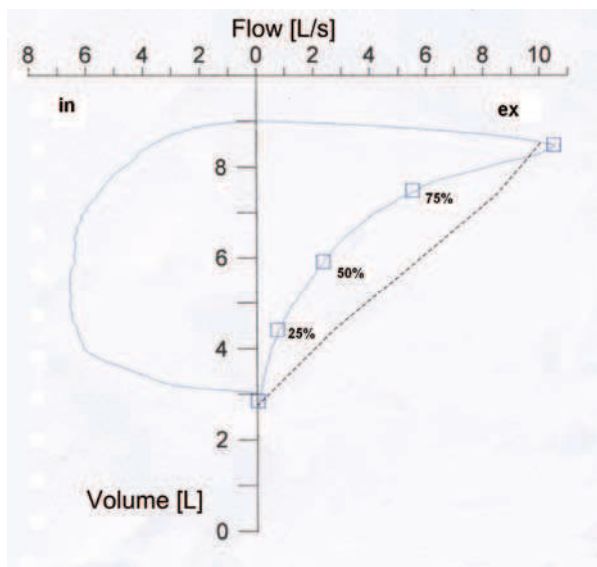


Fig. 2. Flow-volume curve of a patient with cystic fibrosis during forced respiration. The inspiration phase is depicted on the left side and expiration on the right side of the vertical axis. Rectangle points indicate maximal expiratory flow, expiratory flow at 75%, 50%, 25% of vital capacity and the end of expiration, from top to bottom respectively. The dashed-line shows the normal reference of expiratory flow rate with respect to this patient’s age, height and weight.

At different locations i.e. the airway opening, the trachea or at the alveoli, pressure measurements are of interest. If the patient is intubated, tracheal pressure (P_{trach}) is sometimes more desired than P_{aw} since the endotracheal tube contributes significantly to total airflow resistance, and thus affects the R_{rs} calculation (Guttmann *et al.*, 1993). Alveolar pressure (P_{alv}) is a decisive factor of alveolar recruitment/derecruitment. P_{alv} is usually calculated by subtracting total resistive pressure from P_{aw} or P_{trach} . Typical examples of different pressure-volume curves based on P_{aw} , P_{trach} and P_{alv} are plotted in Fig. 3. Note that at the start of inspiration and expiration, the signals are disturbed due to the non-ideal mechanics of the ventilator.

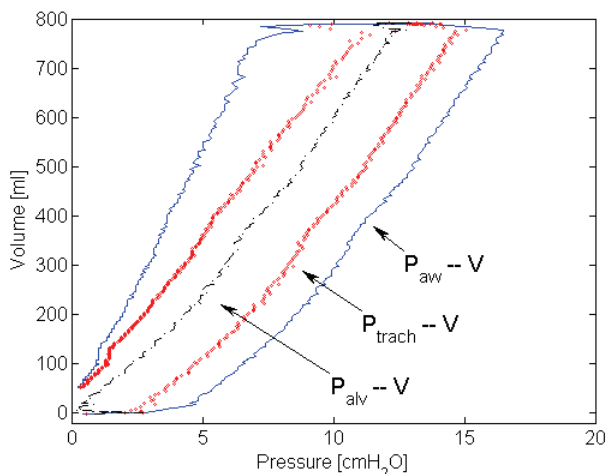


Fig. 3. Three pressure-volume curves obtained in a lung healthy patient undergoing orthopedic surgery. P_{aw} (blue line): airway pressure; P_{trach} (red circle): tracheal pressure; P_{alv} (black dashed line): alveolar pressure.

1.2 Lung protective ventilation strategy

When patients are generally anesthetized, the alveoli in the dependent lung regions may collapse while non-dependent regions remain open. With the help of sufficient external pressure delivered by a ventilator during inspiration, some of the collapsed lung regions may be opened up (i.e. they are recruited) but already open regions may be overinflated. Neither atelectasis nor hyperinflation of lung regions is beneficial in most clinical cases, however, one or the other or a mixture of both processes is inevitable to a certain degree. During expiration, while gas is exhaled, the alveolar pressure drops, which may lead to alveolar collapse (i.e. derecruitment) of the dependent lung regions. Different types of ventilator-induced lung injury (VILI) are therefore observed during mechanical ventilation (Dreyfuss and Saumon, 1998, Uhlig and Frerichs, 2008), such as shear stress trauma caused by cyclic recruitment/derecruitment, barotrauma and pulmonary edema caused by high ventilation pressure. As one of many perioperative complications, acute respiratory distress syndrome (ARDS) was found developed in 3.1% of patients after thoracic surgery and carrying a high mortality rate of over 30% (Grichnik and D'Amico, 2004, Phua *et al.*, 2009). Various lung protective ventilation strategies have therefore been proposed, including high positive end-expiratory pressure (PEEP) combined with low V_t (Brower *et al.*, 2004, Brochard *et al.*, 1998, The Acute Respiratory Distress Syndrome Network, 2000), permissive hypercapnia (Hickling *et al.*, 1990), and recruitment maneuvers (Lachmann, 1992), to reduce the adverse consequences of mechanical ventilation. In this chapter, we focus on optimization of PEEP.

PEEP was introduced to maintain the once recruited atelectatic areas open and thereby reduce the risk of hypoxemia, cyclic recruitment/derecruitment and biotrauma (Gattinoni *et al.*, 2001, Slutsky and Tremblay, 1998). Figure 4 illustrates the effect of PEEP on keeping the lung open. In healthy subjects, although the pulmonary alveoli increase their size at the end of inspiration and decrease at the end of expiration, the shape of alveoli doesn't change

thanks to the pulmonary surfactant. However, in patients with lung injury or with other types of lung disease as well as during thoracic surgery, some alveoli collapse at the end of expiration when the pressure drops below a critical value, and reopen in the next inspiration when the pressure rises above a certain opening pressure. To avoid cyclic recruitment/derecruitment (open/collapse) and to “keep the lung open”, an adequate PEEP is applied (Fig. 4B). At the end of expiration, P_{aw} doesn't drop to 0 cmH₂O (relative to atmospheric pressure). Instead, the pressure is held by the ventilator at a preselected positive level. The recruited lung regions remain aerated, which leads to a better oxygenation.

2. PEEP optimization

2.1 History

In 1960's, Ashbaugh *et al.* proposed the use of PEEP to improve oxygenation in a clinical syndrome characterized by atelectasis and hypoxemia (Ashbaugh *et al.*, 1967). The use of PEEP has become widespread ever since that study. Suter and his colleagues later published the concept of “optimal” PEEP (Suter *et al.*, 1975). Because at that time, cardiac output and blood gas measurements were not always available, they suggested that maximizing tidal compliance could be used to identify a PEEP level, at which oxygen delivery was optimized. In the past three decades, a multitude of physicians and scientists dedicated themselves to identify the best PEEP levels for patients under surgeries (Beiderlinden *et al.*, 2003, Berendes *et al.*, 1996, Bensenor *et al.*, 2007), as well as patients with variable diseases, such as ALI or ARDS (Badet *et al.*, 2009, Huh *et al.*, 2009), morbid obesity (Bohm *et al.*, 2009, Erlandsson *et al.*, 2006), chronic obstructive pulmonary disease (COPD) (Glerant *et al.*, 2005, Mancebo *et al.*, 2000), brain-injury (Shapiro and Marshall, 1978, Huynh *et al.*, 2002), including infants (Greenough *et al.*, 1992, Dimitriou *et al.*, 1999). Although different terminologies and end-points for optimizing PEEP were used (Villar, 2005), most of the approaches tried to obtain the best oxygenation while minimizing VILI as outcome. A lower mortality rate and a better quality of life would be the most desirable goals of therapies. While PEEP has experimentally been shown to reduce VILI, there is no consent in the literature if a suitable PEEP is able to reduce mortality (Miller *et al.*, 1992, DiRusso *et al.*, 1995, Brower *et al.*, 2004), due to the fact that the effect of PEEP is hard to be assessed independently.

It remains under debate how to titrate an adequate PEEP level in individual patients, despite the widely used application of PEEP in clinical practice (Rouby *et al.*, 2002). Increase of PEEP may prevent alveolar derecruitment in dependent areas but may lead to hyperinflation in the non-dependent areas, which may trigger pulmonary inflammation (Terragni *et al.*, 2007). Besides, high PEEP levels may reduce cardiac output (Baigorri *et al.*, 1994) and impair the hemodynamic stability (Herff *et al.*, 2008). Therefore, as also stated by Rouby and Brochard in an editorial (Rouby and Brochard, 2007), one goal of setting PEEP is to find a suitable level, high enough to keep the lung open while minimizing adverse side effects.

Generally speaking, the current available methods of PEEP titration can be mainly divided into three categories: They are based on 1) arterial blood gases such as partial pressure of oxygen in arterial blood (PaO_2) and oxygen saturation (SpO_2); 2) lung mechanics such as dynamic compliance and static pressure-volume (P/V) curve; 3) imaging techniques such as computed tomography (CT) and electrical impedance tomography (EIT). In the following, representative methods within these three categories are introduced and their assets and drawbacks discussed.

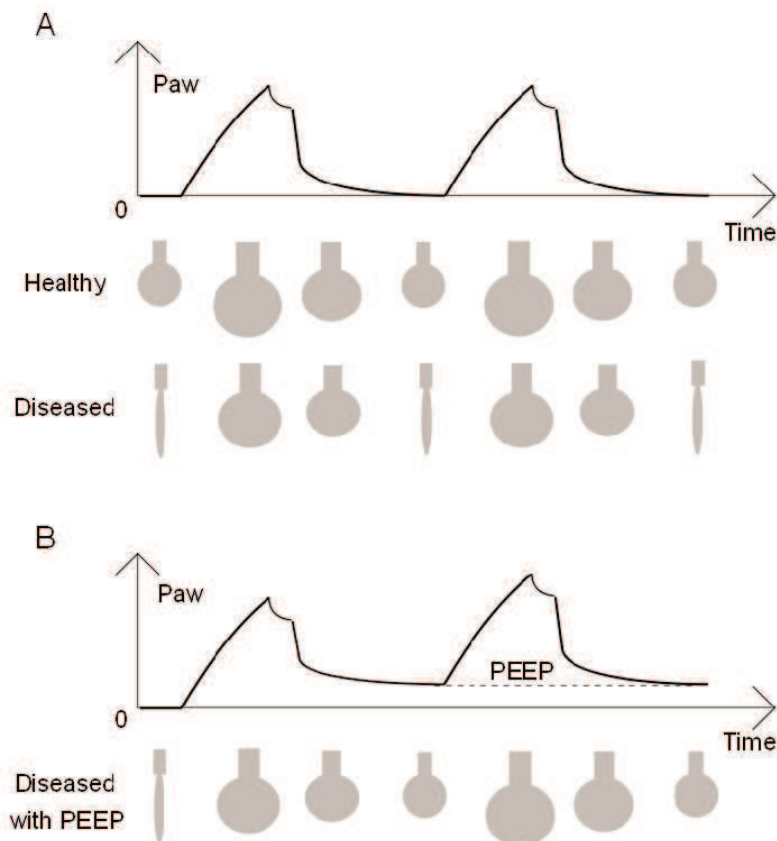


Fig. 4. The effect of positive end-expiratory pressure (PEEP) on keeping the alveoli open. A: Under controlled mechanical ventilation without PEEP, alveoli of a healthy subject stay open throughout the whole breathing cycle, while the alveoli of a patient with lung disease collapse at the end of expiration. B: When PEEP is applied, the recruited alveoli will no longer collapse at the end of expiration in a patient with lung disease.

2.2 Optimizing PEEP with blood gas analysis

One of the main goals of PEEP selection is to optimize oxygenation. Therefore, it is reasonable to guide the PEEP settings by analyzing blood gases (Girgis *et al.*, 2006, Borges *et al.*, 2006, Luecke *et al.*, 2005). It was suggested that “best” PaO₂ (maximum value) indicates the “optimal” PEEP in many studies (Borges *et al.*, 2006, Suarez-Sipmann *et al.*, 2007). Toth *et al.* suggested setting PEEP at the level where PaO₂ starts to drop rapidly during a decremental PEEP trial (Toth *et al.*, 2007). A typical course of PaO₂ values obtained during a decremental PEEP trial in an experimental model of ALI is shown in Fig. 5. PEEP decreased from 30 cmH₂O to 5 cmH₂O in steps of 5 cmH₂O. Decrease of PaO₂ implies worse aeration and oxygenation. Optimal PEEP is defined at the pressure level before PaO₂ decreases significantly.

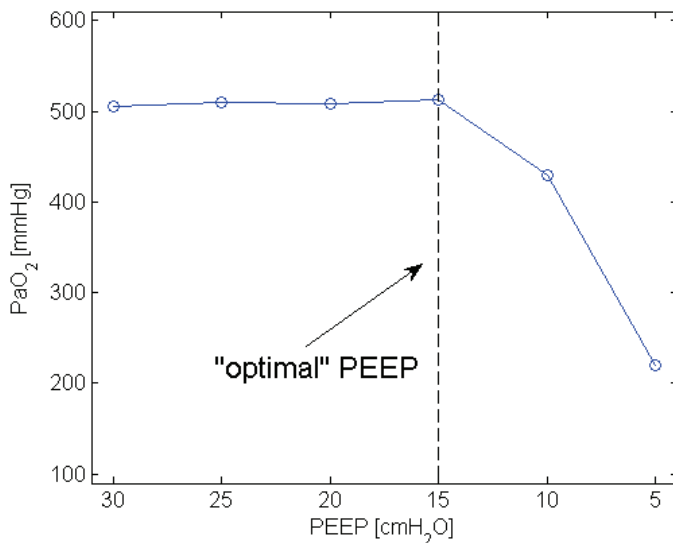


Fig. 5. Change of PaO₂ during a decremental PEEP trial in a porcine model of acute lung injury. Vertical dashed line indicates the optimal PEEP level with respect to PaO₂.

Luecke *et al.* argued that improving only PaO₂ was not good enough, the elevation of PaCO₂ should not be ignored (Luecke *et al.*, 2005). Girgis *et al.* have shown in twenty ALI/ARDS patients that the PaO₂/FiO₂ ratio was improved by tuning FiO₂ after a recruitment maneuver and monitoring the SpO₂ changes during decremental PEEP titration (Girgis *et al.*, 2006). SpO₂ values were measured by pulse oximetry, which is a noninvasive method, however, less precise than direct measurement of arterial oxygen saturation. Rouby concluded in a review that the highest PaO₂ and SaO₂ at the lowest FiO₂ indicated the right PEEP level (Rouby *et al.*, 2002). Caramenz *et al.* have compared ten different parameters for setting PEEP following a recruitment maneuver, including blood gas analysis and lung mechanics (Caramenz *et al.*, 2009). The results of PEEP selection using C_{rs}, PaO₂ with or without PaCO₂ were statistically indistinguishable (Caramenz *et al.*, 2009). Statistically significant differences may have not been revealed due to the small number of studied subjects (n = 14) and high variation. Although these studies indicate that PaO₂ is a possible criterion for setting PEEP, precise blood gas analysis is invasive and discontinuous and, thus, not suitable for continuous bedside monitoring.

2.3 Optimizing PEEP with lung mechanics

The P/V curve has been introduced to individualize V_t and PEEP settings in patients with ARDS by Matamis *et al.* in 1984 (Matamis *et al.*, 1984). In this concept, a lower inflection point (LIP) and an upper inflection point (UIP) are identified on the inflation limb of the P/V curve (Fig. 6B). The LIP was considered to be the pressure level at which massive alveolar recruitment occurs (Jonson and Svantesson, 1999); UIP was considered to be the pressure level indicating alveolar overdistension (Roupie *et al.*, 1995). In consequence, a ventilation strategy was developed to keep the lung open (by setting PEEP above LIP) and to minimize overdistension (by restricting V_t such that peak pressure is smaller than UIP)

(Dambrosio *et al.*, 1997, Hermle *et al.*, 2002). Takeuchi *et al.* proposed that setting PEEP at LIP + 2 cmH₂O might be more appropriate (Takeuchi *et al.*, 2002). However, studies indicate that LIP is only the beginning of recruitment and the UIP is not a reliable marker of overdistension (Crotti *et al.*, 2001, Hickling, 2002, Downie *et al.*, 2004). New findings suggest that it may be better to set PEEP according to UIP on the deflation limb of the P/V curve (Albaiceta *et al.*, 2004). In order to obtain quasi-static P/V curves, the normal ventilation process has to be interrupted by performing a specific respiratory maneuver such as low-flow inflation (Servillo *et al.*, 1997), super-syringe inflation (Matamis *et al.*, 1984) or SCASS, i.e. static compliance by automated single steps (Sydow *et al.*, 1991), (Fig. 6A). As pointed out by LaFollette *et al.*, the key to bedside application is acquiring a dynamic curve, which is easier and more applicable, instead of a static one (LaFollette *et al.*, 2007).

Respiratory system compliance C_{rs} or elastance E_{rs} ($C_{rs}=1/E_{rs}$) can be measured quasi-statically by airway occlusion (D'Angelo *et al.*, 1991) or dynamically by applying linear least-squares regression on the first order equation of motion (Eq. 1) (Iotti *et al.*, 1995). Considering the limitation of static C_{rs} (Stenqvist *et al.*, 2008) and the significant difference between static and dynamic C_{rs} (Stahl *et al.*, 2006), it is the dynamic lung mechanics that should be monitored. Many studies have shown that "optimal" PEEP may be obtained by identifying maximal dynamic C_{rs} , or minimal E_{rs} (Fig. 7) (Suter *et al.*, 1975, Carvalho *et al.*, 2008, Stahl *et al.*, 2006). Hickling demonstrated with a mathematical model of an ARDS lung that maximizing C_{rs} during a decremental PEEP trial may be more suitable to indicate the "optimal" PEEP (Hickling, 2001). Several studies support this result (Suarez-Sipmann *et al.*, 2007, Hanson *et al.*, 2009).

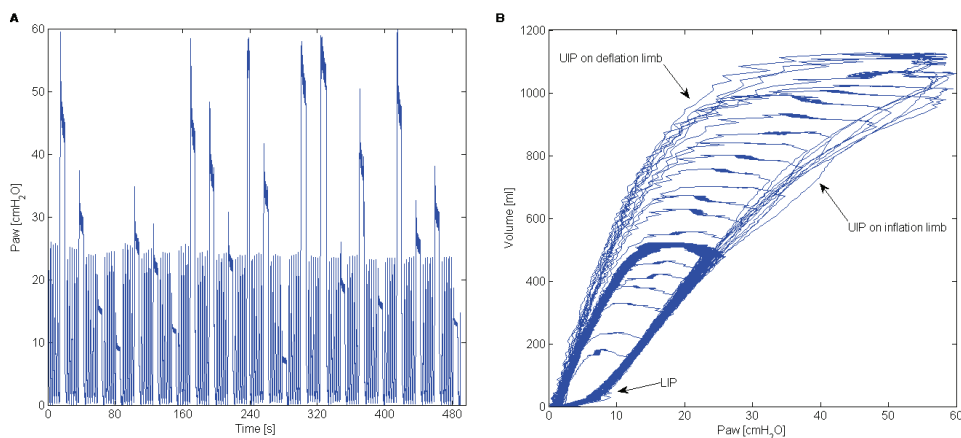


Fig. 6. A: Airway pressure (P_{aw}) of an ARDS patient during the SCASS maneuver to determine static compliance by automated single steps (Sydow *et al.*, 1991) and B: the corresponding P/V curves with lower inflection point (LIP) and upper inflection point (UIP) marked on both inflation and deflation limbs.

Methods other than P/V curve and maximum dynamic compliance are rarely used in clinical practice. Mols *et al.* suggested that the intra-tidal compliance-volume curve, calculated by the SLICE method (Guttman *et al.*, 1994), was able to indicate the ongoing recruitment and overdistension of alveoli in the lung (Mols *et al.*, 1999). The shapes of the

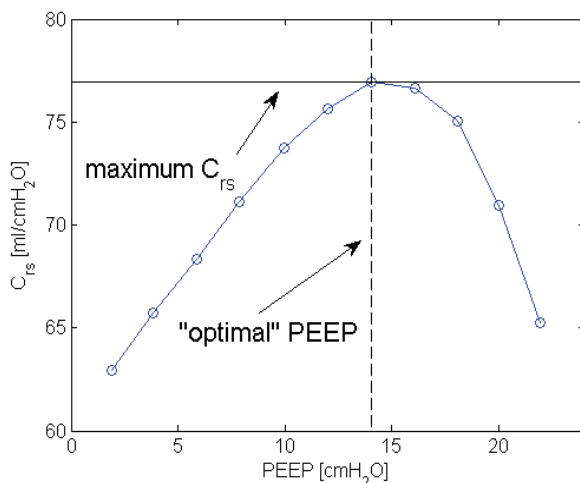


Fig. 7. Mean dynamic respiratory system compliances (C_{rs}) of a sedated patient under mechanical ventilation at different PEEP levels. Dashed line indicates the “optimal” PEEP level, at which C_{rs} is maximum.

compliance-volume curves are classified into three categories: 1) a decrease in slope indicates overdistension; 2) an increase in slope indicates recruitment; 3) a quasi-horizontal compliance-volume curve indicates a suitable PEEP setting (Mols *et al.*, 1999). However, the method has not yet been evaluated for clinical relevance. Ranieri *et al.* used the pressure-time curve as an index to predict pulmonary stress (Ranieri *et al.*, 2000). This method requires phases with constant air flow which limits its applicability. Nevertheless, these methods have brought the importance of pulmonary mechanical stress into focus. Talmor *et al.* estimated the transpulmonary pressure with help of esophageal balloon catheters and set PEEP to such a level that transpulmonary pressure stayed between 0 and 10 cmH₂O during end-expiratory occlusion, and less than 25 cmH₂O during end-inspiratory occlusion (Talmor *et al.*, 2008). They observed improvement of PaO₂/FiO₂ ratio and C_{rs} compared to the group guided according to the ARDS network standard-of-care recommendations. This finding is interesting, but the placement of esophageal balloon catheters needs additional effort in clinical care. Therefore, this method will only become accepted if advantages over other methods using C_{rs} and blood gas analysis are outweighing the extra burden of complex handling.

2.4 Optimizing PEEP with imaging techniques

CT has a very good spatial resolution and is able to show the distribution of the tissue density in the chest, thereby providing primarily morphological data. Hence, CT is the gold standard for assessment of tidal volume distribution in injured lungs and many validation studies were done by comparing various methods with the CT results (Gattinoni *et al.*, 2006, Carvalho *et al.*, 2008, Suarez-Sipmann *et al.*, 2007, Meier *et al.*, 2008). Figure 8 shows two chest CT images of a patient under mechanical ventilation at two different PEEP levels. Higher aeration and reversal of lung collapse in the dependent lung regions were detected at a PEEP level of 15 cmH₂O (Fig. 8, right) compared to that of 5 cmH₂O (Fig. 8, left).

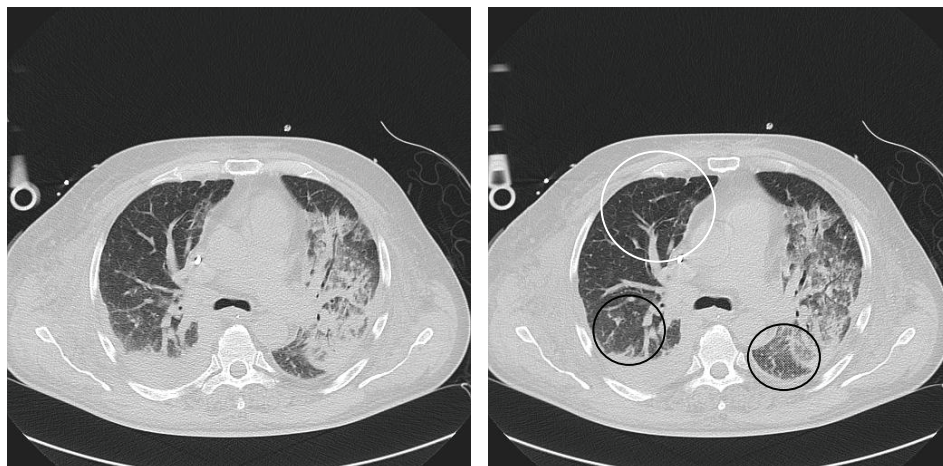


Fig. 8. CT images of a patient under mechanical ventilation at two different PEEP levels. Left: PEEP=5 cmH₂O; Right: PEEP=15 cmH₂O. Pneumonic infiltrates in the left lung and intrapleural fluid accumulation are discernible. Lung aeration is increased, e.g. in the anterior region of the right lung (white circle) and dependent lung regions are recruited (black circles) at the higher PEEP level.

Unfortunately, application of CT imaging for bedside monitoring is limited due to complex handling (e.g. large equipment) and radiation exposure of patients. Hertzog *et al.* have reported a case study using mobile CT scanners to optimize PEEP in a 6-month-old premature infant (Hertzog *et al.*, 2001). However, even with the development of low-dose CT, radiation exposure makes it practically impossible to use CT to guide PEEP titration at the bedside.

In contrast to CT, the relatively new imaging technique, electrical impedance tomography (EIT) is noninvasive and radiation-free. EIT utilizes the phenomenon that changes in regional air content modify electrical impedance of lung tissue (Nopp *et al.*, 1993). Small alternating electrical currents are applied at the chest wall surface during examination and the resultant potential differences are measured. The distribution of electrical impedance within the chest can be determined from these data. Although EIT has a relatively low resolution, it has the potential to monitor regional lung aeration and to visualize regional ventilation distribution dynamically at the bedside (Zhao *et al.*, 2010). Thus, EIT may provide additional information to individualize protective ventilation strategies by titrating PEEP.

Several applications of EIT for selecting PEEP were recently proposed. Erlandsson and colleagues used EIT to set PEEP in morbidly obese patients by maintaining a stable end-expiratory lung volume, and suggested that the corresponding PEEP level was optimal (Erlandsson *et al.*, 2006). Although the PaO₂/FiO₂ ratio and C_{rs} increased in these patients, this "optimal" PEEP need not be the best oxygenation point. Besides, the identification of stable, horizontal end-expiratory EIT values may be difficult. Luepschen and colleagues modified the centre of gravity index from Frerichs *et al.* (Frerichs *et al.*, 1998) to evaluate functional lung opening and overdistension of the lung tissue in an animal model of lavage-induced acute lung injury (Luepschen *et al.*, 2007). Dargaville *et al.* have applied EIT during an incremental and decremental PEEP trial to identify the PEEP level at which the most

homogeneous distribution of regional C_{rs} and ventilation was observed in healthy, injured and surfactant-treated lungs (Dargaville *et al.*, 2010). Zhao and colleagues applied the global inhomogeneity (GI) index (Zhao *et al.*, 2009) to facilitate the PEEP titration in mechanically ventilated patients undergoing orthopedic surgery (Zhao *et al.*, 2010) (Fig. 9). Lowhagen *et al* proposed the assessment of intratidal ventilation distribution using EIT to identify optimal PEEP level in patients with ALI/ARDS (Lowhagen *et al.*, 2010). These results are promising but they still need to be confirmed in further larger studies on lung injured patients. Other EIT-based methods assessing regional lung filling characteristics (Grant *et al.*, 2009, Hinz *et al.*, 2007) have also shown potential to guide PEEP setting. As stated by Dueck in a review article, EIT is helpful in achieving the balance between alveolar recruitment and hyperinflation for patients with severe lung injury (Dueck, 2006). Although the use of EIT is limited to scientific research and clinical experiments, EIT has the potential to gain acceptance from more physicians and become a useful tool in clinical routine in the future.

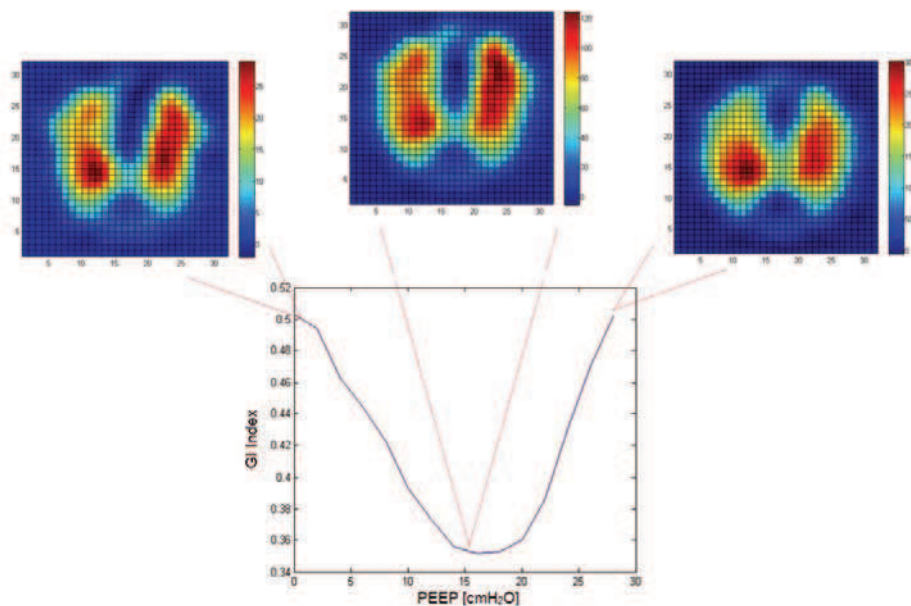


Fig. 9. PEEP titration guided by ventilation homogeneity based on electrical impedance tomography (EIT) (Zhao *et al.*, 2010). Top: EIT images at different PEEP levels (from left to right: PEEP = 0, 15, 28 cmH₂O). The color bars at the right side of each image indicate the magnitude of change in relative impedance during ventilation. Lung regions with the highest ventilation are coded in red. Bottom: global inhomogeneity (GI) index (Zhao *et al.*, 2009) versus PEEP. The minimum value of GI index implies the PEEP level at which ventilation distribution is most homogeneous.

2.5 Combination of PEEP setting indices

Individualized PEEP titration is important, especially in patients with severe lung injury (Kallet and Branson, 2007). Methods discussed in this chapter focused on different aspects: C_{rs} and P/V curves represent the global mechanical properties of the respiratory system;

blood gas analysis provides a direct view on the oxygenation status; CT and EIT evaluate the local ventilation distribution. Obviously, it is rational to combine these different variables to guide PEEP titration. We suggest selecting PEEP according to a weighted combination of C_{rs} , GI index (EIT analysis) and SpO_2 (or PaO_2) to include all available information on the patient's lung status. The disease state of the patient and strategic treatment goals may lead to different weighted combinations. A practical way to define these weighting factors is still warrant and should be achieved in the future with further studies.

Besides, ventilator settings, such as tidal volume (Suter *et al.*, 1978) and inspired oxygen concentration (FiO_2) (Rouby *et al.*, 2002) may strongly influence the "optimal" level of PEEP. The National Institutes of Health's ARDS Network has developed a recommendation in form of a PEEP/ FiO_2 titration table to adjust these variables (Brower *et al.*, 2004). As mentioned before, lung protective ventilation strategies are more than just PEEP optimization. The patients will also benefit from adequate tidal volumes and body positioning which may additionally limit hyperinflation and reduce the amount of non-aerated lung tissue.

3. Summary

Perioperative ventilation support is indispensable for patients under thoracic surgery. Inadequate settings of ventilation support may cause a number of problems, including hypoxemia, shear stress trauma, barotraumas and pulmonary edema. A suitable PEEP level maintains dependent lung regions open and thereby improves oxygenation and reduces the risk of inflammation. The selection of optimal PEEP is still under debate. We propose to combine indices of lung mechanics, blood gas analysis and imaging techniques to titrate PEEP. Besides, application of PEEP should be complemented with other strategies (e.g. low tidal volume, appropriate body positioning, recruitment maneuver), to achieve the best outcome of the patient.

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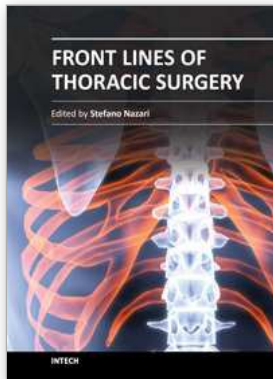
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