Current Anesthesiology Reports (2019) 9:452–458
https://doi.org/10.1007/s40140-019-00350-z

THORACIC ANESTHESIA (T SCHILLING, SECTION EDITOR)

Positive End-Expiratory Pressure (PEEP), Tidal Volume, or Alveolar Recruitment: Which One Does Matter in One-Lung Ventilation?

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Published online: 24 October 2019

Abstract

Purpose of Review This review attempts to focus on protective ventilation approaches during one-lung ventilation (OLV) and will summarize recent findings.

Recent Findings Recent studies have demonstrated the importance of low tidal volume (low TV) and reduced driving pressure during OLV. Along with low TV, correct use of positive end-expiratory pressure (PEEP) seems to have a vital role in terms of protecting the ventilated lung. PEEP decremental trial and the use of electrical impedance tomography are prominent techniques for individualizing the PEEP. The use of alveolar recruitment maneuvers (ARMs) is furthermore recommended. Nevertheless, there are several studies published considering negative effects of ARM.

Summary Although small tidal volumes are highly recommended during OLV, it is not possible for low TV to be beneficial unless an optimal PEEP is applied. Use of ARM is still under debate. Yet, it seems to be the only way for preventing injurious tidal recruitment, which is known to be harmful to the lungs.

Keywords One-lung ventilation · Lung protective ventilation · Individualized PEEP · Ventilator-induced lung injury

Introduction

One-lung ventilation (OLV) is a technique that excludes a single lung from ventilation and leaves it deflated and collapsed. The indications for OLV include the need for "lung isolation" and "lung separation." Lung isolation aims to protect one lung from a pathological process that harms the other lung such as hemorrhage and infection etc., while the main target in lung separation is surgical exposure [1]. OLV is not only performed in thoracic surgery but also in other procedures like cardiac interventions, esophagectomy, and others, where lung deflation is required for surgical intervention.

This article is part of the Topical Collection on *Thoracic Anesthesia*

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Previously, guidelines had suggested the use of rather high tidal volume (TV) and zero end-expiratory pressure (ZEEP) for the management of OLV [2]. This non-protective approach was logical at the time when frequency of hypoxemia during OLV was higher than 25% [3]. This is because PEEP application can result in a diversion of blood flow to the non-ventilated, collapsed lung while the use of low tidal volumes without PEEP may cause severe atelectasis in the ventilated lung. In line with this, use of ZEEP and high TVs (more than 10 ml/kg) was a main strategy to prevent hypoxemia. Use of high TVs has been shown to provide a better aeration and oxygenation with a cost of increased mechanical stress, even when a 5 cm H_2O PEEP is applied [4]. However, with major developments in anesthesia techniques and the routine use of fiber optic bronchoscopes, the incidence of hypoxemia during OLV has decreased to less than 5% [5]. This result allowed the clinicians to focus on another important concern, acute lung injury (ALI).

ALI incidence during OLV is shown to be 2% when it is diagnosed with the most recent ARDS consensus criteria, while the mortality of ALI which develops after OLV is reported to be 54.5% [6]. Simplified, the two preceding sentences indicate that when one hundred patients undergo OLV, one of them is expected to die.

Therefore, prevention of ALI during OLV has become the main issue for clinicians. Furthermore, the incidence of postoperative pulmonary complications after surgeries reaches up to 23%. Indeed, this ratio is much higher in patients undergoing OLV [7•].

This review attempts to focus on ALI and protective ventilation during OLV and summarizes recent findings regarding these issues.

ALI During OLV

Previous studies have demonstrated that lung injury after thoracic surgery is more significant in the ventilated lung when compared with non-ventilated one that undergoes a surgical procedure [8]. This finding indicates that mechanical ventilation can be more hazardous than the surgery itself. Furthermore, one-lung ventilation itself has shown to cause a greater damage when compared with two-lung ventilation [9].

Mechanical ventilation harms the lung due to several mechanisms which involve volutrauma, barotrauma, atelectrauma, and biotrauma [10]. Volutrauma and barotrauma are the results of over-distension of alveoli based on high TVs/pressures and/or high PEEP settings applied inadequately. Increased strain and stress which accompanies overdistention has been found to be the main pathogenesis in VILI [10]. While the non-dependent lung areas face with overdistension, dependent regions are exposed to cyclic opening and closing which result in atelectrauma [11]. All these explained mechanisms may lead to a release of cytokines and other inflammatory mediators that eventually cause biotrauma.

In the light of such information, we can name three steps for protecting the lung from ventilator-induced lung injury (VILI). [1] Open the closed alveoli (alveolar recruitment maneuvers), [2] keep them open (application of PEEP), and [3] avoid overinflation (use of low TVs). If we can re-open the atelectatic areas and manage to keep them open, there will be no cyclic opening and closing. Also, when all alveoli are open, we will be able to deliver the same "low" TV with a less driving pressure and thus prevent the overdistension of alveoli. These are the three main components of protective ventilation (Fig. 1).

Regarding VILI, a new concept called "ergotrauma" has been recently presented by Gattinoni et al. [12]. This concept combines the effects of volume, pressure, respiratory rate, and flow for explaining the importance of mechanical power during ventilation. They hypothesize that the cumulative energy applied to the lungs is the main factor that triggers the induction of VILI. This approach obviously needs to be studied broadly.

Components of Protective Ventilation During OLV

Low Tidal Volume

In 1998, Amato et al. demonstrated that the use of low TV ventilation can effectively reduce mortality in ARDS patient [13]. Since then, low TV strategy has been used widely in different patient groups in operating rooms and intensive care units (ICUs). The strategy was demonstrated to reduce pulmonary complications in patients without ALI in ICUs [14] and in patients with healthy lungs undergoing surgery [15–18]. Different study groups have demonstrated the beneficial effect of low TV during OLV as well. Low TV ventilation was associated with decreased inflammatory response [19] and less postoperative respiratory failure [20, 21]. This is not surprising, since use of high TVs is already hazardous for two lungs. Applying this amount of TV to only one lung should obviously result with worse outcomes [9, 22].

Accordingly, Qutub et al. compared different TVs (4, 6, and 8 ml/kg) with 5 cm H_20 PEEP in terms of extravascular lung water content (EVLW) in patients undergoing VATS under OLV [23]. They enrolled 13 patients per group and demonstrated that in the 4 ml/kg TV group, EVLW was significantly lower than other groups' EVLW values. On the other hand, Blank et al. retrospectively examined the effects of TV on postoperative pulmonary complications (PPC) [24••]. They found TVs to be inversely related with PPC frequency. Yet, they did not assign this negative result solely to low TV but rather concluded that insufficient PEEP with low TV was hazardous as the PEEP values used were mostly less than 5 cm H2O.

Lastly, Tahan et al. performed a meta-analysis regarding the effect of low TV in OLV. They included 14 articles in the analysis, and as major result, low TV strategy was found to be related with reduction in infiltrates and with better oxygenation postoperatively [25••]. Yet, this study failed to demonstrate any difference in terms of PPC frequency possibly due to heterogeneity between the patient study groups. Although authors have mostly chosen 5–6 ml/kg ideal or predicted body weight for low TV strategy, there is still a need for prospective randomized controlled studies which compare different TV values with a standardized PEEP value because all of the aforementioned studies were designed with different PEEP settings in different groups, or with such PEEP values that are probably ineffective. Despite all these studies performed, we still do not know how low we should keep the "low" TVs or how to individualize it. Obviously, it should be considered that a TV of even 56 ml/kg for the "one" lung means almost 10–12 ml/kg in total. In fact, these volumes are not in line with those demonstrated to be protective in two-lung ventilation [16, 17].

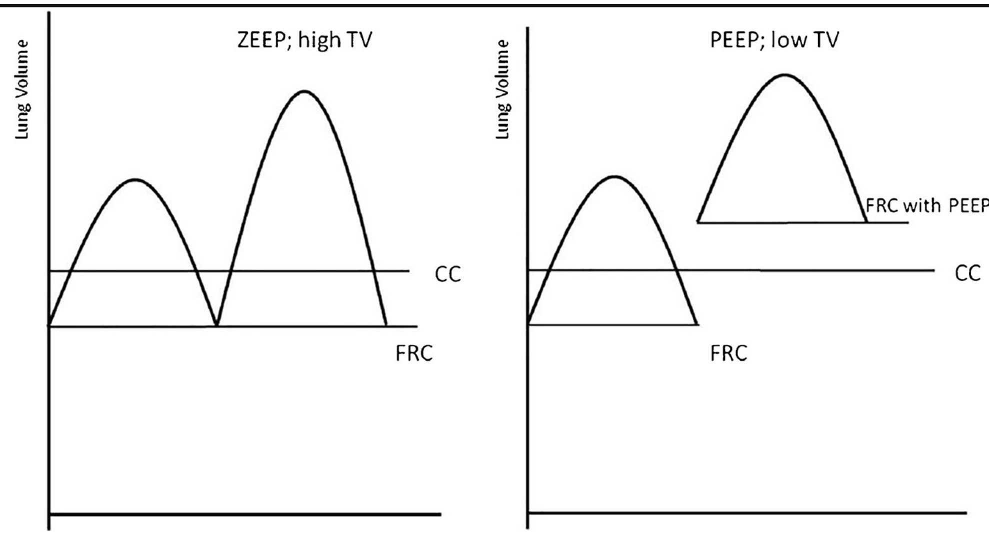

Fig. 1 Effects of conventional (ZEEP + High TV) and protective (PEEP + Low TV + ARM) ventilation strategies on the lungs. Right: functional residual capacity (FRC) falls below closing capacity (CC) due to anesthesia and positioning, during mechanical ventilation. Cyclic recruitment of the alveoli is inevitable under such a condition. High TVs are needed for obtaining a better oxygenation (Note the difference between two areas above the CC line). Left: Applying PEEP after an ARM while keeping TV low. PEEP obtains an FRC above the CC and so cyclic recruitment along with atelectasis is avoided. Low TVs are enough for maintaining a better oxygenation than the one with ZEEP, with a less driving pressure. Reprinted from *Best Practice & Research Clinical Anaesthesiology*, Volume 29, Issue 3, Şentürk M, Slinger P, Cohen E, "Intraoperative mechanical ventilation strategies for one-lung ventilation," pages 357-369, ©2015, with permission from Elsevier.

Which One Matters More, Pressure or Volume?

Recent studies have pointed out the importance of driving pressure which is defined as the difference between plateau pressure and PEEP. It is currently considered the best predictor of VILI in ARDS patients [26•]. In a recent retrospective meta-analysis, Neto et al. demonstrated that driving pressure was associated with PPCs while the effects of TV and PEEP were found to be not significant in healthy patients undergoing surgery [27••]. In patients undergoing OLV, Amar et al. concluded that when peak and plateau pressures are kept limited along with a restrictive fluid therapy, there should not be a difference in terms of PPCs between the groups with the TVs of less than 8 ml/kg and more than 8 ml/kg [28]. In line with these results, in a survey study conducted by Kidane et al., most anesthesiologist defined low airway pressures as the primary strategy of lung protective ventilation during OLV [29]. Well-designed prospective studies are needed to determine whether pressure or volume is more important during lung-protective ventilation in OLV.

Positive End Expiratory Pressure

In the past, PEEP studies were mostly designed to evaluate the effects on oxygenation. They showed that the application of PEEP could increase [30], decrease [31], or even could not change [32] the paO_2 values. Because of the concerns, such as dangerous overdistention and diversion of blood away from the ventilated lungs [33], the application of PEEP was limited to restoring hypoxemia [34]. Regarding oxygenation, Slinger et al. demonstrated that the application of PEEP is useful when end-expiratory pressure was close to the lower inflection point (LIP) [35]. This is the best way for avoiding alveolar collapse and overdistension at the same time. Similarly, Ferrando et al. offered the PEEP decrement trial for individualizing the PEEP value in accordance with the best compliance, and found this method to provide a better oxygenation [36].

Recently, Park et al. published study results which released the first data regarding the effect of PEEP on PPCs [37•]. They have demonstrated that, when compared with conventional protective OLV with a 5 cm H_2O PEEP, individualization of PEEP in accordance with driving pressure resulted in less PPCs. There are two ongoing randomized controlled trials which aim to evaluate effects of different PEEP values on PPCs. PROTHOR compares 5 cm H_2O (with no RM) and 10 cm H_2O (with RM) of PEEP under OLV with a low tidal volume approach [38••]. On the other hand, iPROVE-OLV compares 5 cm H_2O of PEEP with individualized PEEP in accordance with best compliance [39]. Hopefully, they will be able to reveal the effect of PEEP on patient outcomes. Lastly, regarding the diversion of blood away from the dependent lung, Spadaro et al. have demonstrated that high values of PEEP (up to 15 cm H_2O) can be used safely for improvement of pulmonary dynamics without any effects on intrapulmonary shunt fraction [40].

How to Individualize the PEEP?

The aim of PEEP application is to prevent the lungs from cycling recruitment and de-recruitment (atelectrauma) by keeping the alveoli open all the time. Yet, adjusted pressure can also cause overdistension (and volutrauma) in some of the alveoli while protecting others from atelectrauma. Therefore, clinicians should adjust such PEEP values which may benefit the patients most while balancing atelectrauma and volutrauma. Imaging techniques and lung mechanics can be used for achieving this goal.

Imaging Techniques Computed tomography (CT) scans, ultrasound, and electrical impedance tomography (EIT) are useful techniques for evaluating overinflation, atelectasis, and the homogeneity of aeriation. Therefore, one can think that PEEP values can be optimized with these imaging techniques [41]. Performing a CT scan requires an intense work and ultrasound can only explore the lungs partially, so the clinical use of these tools is limited. On the other hand, EIT has been gaining a great interest among clinicians since it can be performed at the bedside [42].

Lung Mechanics Best compliance (the lowest driving pressure) and stress index have been used for individualizing PEEP adjustment [43]. Best compliance method was mentioned previously in this review [36].

Stress index method relies on the shape of the pressure-time curve during volume-controlled ventilation [44]. A linear increase in the pressure curve suggests alveolar recruitment without overdistension and defines the stress index = 1 situation. An upward concavity in the pressure-time curve is a surrogate for decreasing compliance during inspiration and suggests overdistension (stress index > 1). Conversely, a downward concavity in the curve (an increase in compliance as the lungs are inflated, stress index < 1) suggests tidal recruitment which means that the patient can benefit from a higher PEEP.

Alveolar Recruitment Maneuvers

When atelectasis occurs (mostly in the dependent pulmonary regions as a result of compression), shunt fraction increases due to increased ratio of areas that are perfused but not ventilated. On the other hand, in non-dependent parts, alveoli start to distend more than usual since now the same tidal volume is delivered to a smaller number of alveoli. As a result, driving pressure and plateau pressure increase together with dead space, all resulting in overdistension. Recruitment maneuvers have demonstrated to decrease the shunt fraction and so hypoxia [45, 46], improve the distribution of ventilation with a reduction in dead space [4, 45], and decrease the ventilation pressures which theoretically cause less strain and stress that are the main cause of baro/volutrauma.

We still do not have enough data regarding the effect of alveolar recruitment maneuvers (ARM) on PPCs or other long-term outcomes. There is one RCT study that has demonstrated the positive effects of RMs on inflammatory parameters [47]. On the other hand, Amar et al. published retrospective data from which they concluded that RMs can possibly cause a non-significant increase in mortality (p = 0.06) [48]. This study was limited by a small sample size and a lack of data regarding the cause of death. Yet, authors have speculated that the increased mortality might have resulted from overdistension, which was the cause for increased inflammation and surgical manipulation. Obviously, there is an urgent need for well-designed RCTs which aims to reveal the effects of ARMs on patient outcomes.

For recruiting the closed alveoli, performing a positive pressure above the upper inflexion point is necessary [49]. Although squeezing the ventilation bag to keep the pressure at 40 cm H_2O is the simplest way [50], this approach is being abandoned day by day. Performing ARM by increasing PEEP up to 20 cm H_2O gradually with a driving pressure maintained at 20 cm H_2O is widely gaining interest [51]. Along with individualized PEEP, this is probably the most effective way to achieve the best pulmonary mechanics. Ferrando et al. have used the stepwise PEEP increment strategy together with individualized PEEP adjustment in line with the best compliance in patients undergoing OLV and obtained a better oxygenation with lower driving pressures in the intervention group when compared with the control group [36].

Combinations of Low TV, PEEP, and ARM

In a double blind RCT, Marret et al. demonstrated that the use of low TV and PEEP (5 ml/kg and 5-8 cm H_2O, respectively) was related to improved patient outcomes when compared with high TV without PEEP (10 ml/kg TV and zero PEEP) [52]. Yang et al. obtained similar results in a RCT that was performed in patients undergoing lung cancer surgery [53]. Michelet et al. have also revealed the positive effect of low TV + PEEP (5 ml/kg TV and 5 cm H_2O PEEP) approach on inflammation parameters, extravascular lung water content, and oxygenation when compared with conventional (9 ml/kg TV + ZEEP) approach in patients undergoing OLV [54]. It is now accepted that the use of low TV and PEEP together has beneficial effects. Yet, as previously mentioned studies outline, using low TV with low or un-individualized PEEP have no effects on outcome and can even be more hazardous when compared with a high TV and low PEEP strategy [24••, 28]. From this point of view, using the low TV and optimal PEEP combination correctly is probably what mostly matters. We still do not know the definition of "optimal PEEP", but studies demonstrate that it can vary widely among patients. Therefore, we strongly advise it to be individualized in accordance with the best compliance [49] or electrical impedance tomography findings [55]. What is the best way to adjust the best PEEP? This question will be a cornerstone for designing future studies.

The use of ARMs along with the combination of low TV and optimal PEEP defines the “open lung approach (OLA)” during one long ventilation. If the lungs are not completely open, low TV will not be low enough since this volume will be distributed only to open alveoli inhomogenously and overdistension will be inevitable with an increasing driving pressure. This is probably why driving pressure has found to be related with patient outcomes in ARDS patients [26•]. From this point of view, it might not be possible for low TV strategy to be effective unless the lungs are completely open. In a recent descriptive, multicenter study in which 690 patients were enrolled, iPROVE network investigators have demonstrated that open lung approach with individualized PEEP can result in less PPCs when compared with available findings [56••]. Verbeek et al. conducted a RCT trial using the open lung approach (stepwise recruitment, 10 cm H*2*O PEEP and 4–5 ml/kg TV during OLV) in 748 patients undergoing lung transplantation surgery [57]. They compared this approach with a conventional lung-protective strategy (5 cm H_2O PEEP, 4 ml/kg TV without ARM) and found OLA to be related with reduced duration of mechanical ventilation. Licker et al. retrospectively compared two strategies designed as 5 ml/kg TV + 6 cm H_2O PEEP + ARM and 7 ml/kg TV + 3 cm H_2O PEEP. They found significantly better results with the former strategy in terms of hospital stay, ICU admission and ALI [20].

Conclusion

Does protective ventilation really protect the lungs? The PROVHILO [58] and PROBESE [59] trials did not result in line with previously aforementioned studies that support the positive effects of lung protective ventilation. So the answer of this question is, we still do not know it for sure. We define the components of “lung protective ventilation” as low tidal volumes, optimal PEEP settings, and ARM. Today, we have enough evidence to believe in protective effects of the mentioned components during OLV and so we strongly advice their use in the operating theatre. The best way to stay away from over-distension and tidal recruitment is to apply these components correctly. Yet, 10 years from now, it is possible for this strategy to be named as “conventional” instead of “lung protective.”

Compliance with Ethical Standards

Conflict of Interest Taner Abdullah and Mert Şentürk declare they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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