Ventilator management using esophageal balloon pressure measurements

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ABSTRACT

Mechanical ventilation provides essential support for patients with acute respiratory failure and provides time for these patients to recover from the primary disorder. Ventilator strategies need to provide adequate oxygenation and avoid barotrauma. This trauma develops when some regions of the lungs are overinflated and develops when some regions are underinflated and have cyclical opening and closing during the respiratory cycle. The ARDS network trial demonstrated that a low tidal volume and low pressure strategy improved outcomes. Subsequent trials have tried to determine the optimal PEEP level in patients with moderate to severe ARDS. The use of esophageal balloons provides information about the transpulmonary pressure at the end of inspiration and the transpulmonary pressure at the end of expiration. However, available studies to date do not demonstrate a definite improvement in outcomes in patients with ventilator adjustments based on esophageal pressures. Beitler et al. randomized 200 patients with moderate to severe ARDS into one group in which PEEP titration was based on esophageal balloon pressure measurements, and a second group in which PEEP titration was based on a high FiO_2/PEEP table studied in earlier trials. There were no differences in mortality between the two groups. Reanalysis of this information after the trial was completed suggested that transpulmonary pressures in the range of –2 to +2 cm H_2O at the end of expiration were associated with improved outcomes compared to pressures outside that range. Two trials have studied lung recruitment maneuvers with PEEP adjustments based on optimal compliance levels or on the PEEP level at which desaturation occurred; neither approach improved outcomes. Mechanical ventilation strategies based on the underlying pathophysiology provide clinicians with a better understanding of lung disease and the hazards of mechanical ventilation. However, recent trials have not identified new strategies which reduce mortality.

Keywords: Mechanical ventilation, pleural pressure, esophageal balloon, PEEP, transpulmonary pressure

INTRODUCTION

The use of lung mechanics can help evaluate and manage patients who require mechanical ventilation. Standard pressure measurements include the peak pressure, the plateau pressure, and the PEEP level measured at the proximal airway. However, this information is not adequate to calculate the transpulmonary pressure or the transchest wall pressure. Measuring intrapleural pressure provides the information necessary to calculate these pressures.[1] The measurement of transpulmonary pressure at the end of inspiration and at the end of expiration provides important information about lung distending pressures. In particular, calculation of the transpulmonary pressure at the end of exhalation provides reasonable

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conjecture regarding the possibility that regions of the lung are collapsing at the end of exhalation because there is inadequate distending pressure. In this circumstance, there will be cyclical opening and closing of airways which has the potential to cause lung injury and aggravate the underlying pathology associated with the current problem requiring mechanical ventilation. This leads to the important question of how to measure intrapleural pressures.

Intrapleural pressure is not a uniform pressure throughout the thoracic space.[1] It depends on the patient's position, the location in the pleural space, elastic recoil of the lung, elastic recoil of the chest wall, and other external factors, including the presence of pleural effusions and increases in intra-abdominal pressure secondary to obesity and or intra-abdominal processes, such as ascites. For example, a patient with significant ascites and increased intra-abdominal pressure has this pressure transmitted into the pleural space which increases pleural pressure. Consequently, some regions of the thorax in that patient will have positive intrapleural pressures throughout the respiratory cycle, especially at the end of exhalation. This promotes collapse of lung regions and creates regions of ventilation perfusion-mismatch resulting in hypoxemia.

In experimental models, intrapleural pressure has been measured with small catheters and with sensors placed in the pleural space, an approach not possible in patients.[1] The intra-esophageal pressure provides a reasonable estimate of the intrapleural pressure, especially in the mid lung zone. In patients in the supine position, the intrapleural pressure is likely lower or more negative in nondependent superior regions of the lung and is more positive or less negative in dependent inferior regions of the lung. Consequently, intra-esophageal pressure does not adequately reflect the intrapleural pressures throughout the thorax in patients in the supine position on mechanical ventilation. In addition, this pressure is increased by the weight of the mediastinum and heart on the esophagus. With advances in ventilator technology, it is possible to connect esophageal balloons to the ventilator to calculate intra-esophageal pressure and use that information to calculate transpulmonary pressures and transthoracic wall pressures.[2]

Clinical studies

PEEP adjustments using esophageal balloons to measure intrapleural pressure

Beitler et al. randomized 200 patients with moderate to severe ARDS into either a "treatment" group in which PEEP titration was based on esophageal balloon pressure measurements or a "control" group in which PEEP titration was based on a high FiO_2/PEEP table studied in earlier trials.[3] These two groups of patients had a median age of 58 and 57.5 years and median APACHE 2 scores of 27 and 28, respectively. Baseline pressure measurements in the esophagus at the end of inspiration were 19 and 18 cm H_2O and 16 and 15 cm H_2O at the end of expiration in the two groups. The transpulmonary pressures were 8 and 9 cm H_2O at the end of inspiration and 0 and –1 cm H_2O at the end of expiration. After initiation of ventilator management by protocol, the PEEP level was increased by a mean of 3 cm H_2O in the esophageal pressure guided group and by a mean of 3 cm H_2O in the empiric FiO_2/PEEP group. In the esophageal pressure group, PEEP was increased by up to 20 cm H_2O and decreased by as much as 12 cm H_2O after the first adjustments. In the group managed using an empiric FiO_2/PEEP table, PEEP was increased by as much as 13 cm H_2O and decreased by as much as 5 cm H_2O. In the esophageal pressure guided group, the highest PEEP was 36 cm H_2O. In the empiric FiO_2/PEEP table group, the maximum PEEP level was limited to 24 cm H_2O.

Over the first 7 days of management, there were no differences in any pressure measurements between the two groups. There were no significant differences between the two groups in the primary outcome, which was a combination of death and days free from mechanical ventilation through day 28. Mortality and the number of ventilator-free days were not different between the two groups. Patients in the esophageal pressure guided PEEP group were less likely to receive rescue therapy than patients in the empiric high FiO_2/PEEP table group. There were no differences in shock-free days through day 28, and there were no differences in barotrauma or acute kidney injury. The authors concluded that this study does not support the use of esophageal pressure guided PEEP titration in patients with moderate to severe ARDS. By trial design, prone positioning was prohibited in this study unless it was used as a rescue therapy.

These investigators reanalyzed this trial by splitting the patients into two cohorts, based on the median APACHE 2 score which was 27.5.[4] At the baseline, these two cohorts had similar PaO_2/FiO_2 ratios, tidal volumes, respiratory rates, PEEP levels, plateau pressures, driving pressure, and esophageal pressures. The patients in the high APACHE 2 score cohort required vasopressors more frequently at baseline. Patients with low APACHE 2 scores had improved survival when ventilator adjustments were made using the esophageal pressure guided PEEP protocol. In the patients with high APACHE 2 scores, survival improved but not significantly in the group managed with a high empiric high FiO_2/PEEP table. Patients in the low APACHE 2 score cohort had more ventilator-free days when managed by the esophageal pressure guided protocol. Patients in the high APACHE cohort had more ventilator-free days and more shock-free days when managed by the empirical high FiO_2/PEEP table.

When the entire cohort was analyzed based on end-expiratory transpulmonary pressures averaged over the first three days, patients with an end expiratory pressure ±2 cm H_2O had improved survival. This analysis suggests that patients with a lower severity of illness have improved outcomes when PEEP levels are based adjusted based on esophageal pressure measurements. More importantly, adjusting the transpulmonary pressure at the end of expiration to a range of –2 to +2 cm H_2O appears to result in better survival than pressures outside this range. These observations suggest that an optimal transpulmonary pressure at the end of expiration both improves gas exchange and limits the potential for barotrauma and may improve the hemodynamic status and reduce shock.

Dianti et al. used a systematic review and network meta-analysis to analyze the association of PEEP and lung recruitment strategies with mortality in acute respiratory distress syndrome.[5] The comparisons included a lower PEEP strategy, a higher PEEP strategy without lung recruitment, a higher PEEP strategy with a brief lung recruitment, and a higher PEEP strategy with prolonged lung recruitment, and an esophageal pressure guided strategy. This analysis indicated that a higher PEEP strategy without lung recruitment resulted in better survival than a lower PEEP strategy. In none of these comparisons did an esophageal pressure guided strategy reduce mortality.

PEEP ADJUSTMENTS USING ALTERNATIVE TECHNIQUES

Cavalcanti et al. compared outcomes in a study of 1010 patients with moderate to severe ARDS using either lung recruitment and titrated positive end-expiratory pressure or low PEEP on mortality.[6] These investigators used lung recruitment with an additional PEEP level of 25 cm H_2O for 1 minute, then 35 cm H_2O for 1 minute, and then 45 cm H_2O for 2 minutes. They used decremental titration with the PEEP level starting at 23 cm H_2O in a volume-controlled mode of ventilation. They decreased PEEP by 3 cm H_2O down to 11 cm H_2O and measured static respiratory system compliance to determine the optimal pressure. The PEEP level associated with the best compliance +2 cm H_2O was then considered the optimal PEEP. This was followed by a new recruitment in pressure-controlled ventilation at 45 cm H_2O for 2 minutes. After 3 episodes of cardiac arrest using this approach, they changed the protocol to lower levels of PEEP for shorter periods of time. The mortality in the experimental group was 55.3%, and mortality in the control low PEEP group was 49.3% ($P = 0.041$). In addition, the experimental group had a decreased number of ventilator-free days, an increased risk of pneumothorax, and an increased risk of barotrauma. Consequently, this study indicated that routine use of lung recruitment maneuver and PEEP titration did not improve outcomes.

Hodgson et al. used the lung recruitment protocol in which patients were placed on PEEP at 20 cm H_2O, then 30 cm H_2O, and then to 40 cm H_2O for 2 minutes at each step.[7] This was followed by a decrease in PEEP levels from 25 cm H_2O by 2.5 cm H_2O intervals for 3 minutes at each step until the peripheral O_2 saturation decreased by 2% or more. The patients were then placed on a PEEP level that was 2.5 cm H_2O higher than the level at which they had desaturation. The study included 115 patients but was stopped earlier than expected because of a publication of study by Cavalcanti et al.[6] There was no difference in the mean number of ventilator-free days between the groups treated with the recruitment strategy and the group treated with protective ventilation. There was also no difference in mortality or the frequency of barotrauma. The experimental group did have an increase in the number of new cardiac arrhythmias.

These 2 studies used the lung recruitment maneuvers to recover atelectatic zones and then PEEP titration to maintain recruitment through two different strategies to determine the optimal PEEP level. One involves determining the best lung compliance, and the other involved determine in a PEEP level at which desaturation occurred. Neither study demonstrated any significant benefit using lung recruitment maneuvers. The one study did report an increased mortality rate in these patients, but the explanation for these adverse outcomes is uncertain. It is possible that higher PEEP levels result in adverse hemodynamic effects or results in increased barotrauma and lung injury.

Due to operator-dependent issues and technicalities, such as the proper placement of the esophageal catheter and the difficulty of obtaining accurate measurements in patients with/without multiorgan failure, with/without severe ARDS, or in prone versus supine positions, esophageal manometry to guide PEEP management is used in few ICUs and often on a case by case basis.[8–13] Some investigators have developed air-filled esophageal catheters without a balloon (instead using a disposable catheter that allows reproducible esophageal pressures) to facilitate minimally invasive, inexpensive, and rapidly available means of promoting this technique for ventilator management.[14,15] The Pleural Pressure Working Group (PLUG) continues to work on consolidating knowledge on esophageal pressure measurements and suggesting how these measurements could be used to monitor mechanical ventilation in critically ill patients. Currently, there are nine clinical trials investigating the use of esophageal balloon catheters listed on ClinicalTrials.gov (Clinical Trials on Esophageal Balloon Catheters). Only seven trials are active and are being conducted in various countries; these trials are focused on specific patient subgroups to better understand ventilation strategies in patients with chest wall disease, obesity, intra-abdominal hypertension, or undergoing abdominal surgeries. Two of the special situations are considered below.

Special circumstances

Obesity

Obese patients have decreased lung volumes, including total lung capacity, functional residual capacity, and vital capacity. Owens et al. measured esophageal pressure differences in sitting and supine positions in obese and non-obese subjects.[16] Twenty-five individuals with a body mass index (BMI) > 25 kg/m^2 and 11 individuals with end < 25 kg/m^2 were recruited. The average end-expiratory esophageal pressures sitting and supine were greater in the BMI > 25 kg/m^2 group than the < 25 kg/m^2 group (sitting –0.1 ± 2.1 vs. –3.3 ± 1.2 cmH$_2$O; supine 9.3 ± 3.3 vs. 6.9 ± 2.8 cmH$_2$O, respectively). There were no differences in changes in the esophageal pressures when changing from a sitting to a supine position in the 2 groups.

Behazin et al. studied respiratory system mechanics in obese patients undergoing surgery by making pressure measurements prior to the surgical procedure.[17] The patients had been intubated, undergone general anesthesia, and had complete paralysis. These investigators estimated the pleural pressure by determining the airway pressure needed to start lung inflation. Therefore, this method estimates the lowest pleural pressure found in the chest at a relaxation volume. The threshold pressure needed to start inflation of the lung in obese patients ranged from 0.6 to 14 cm H$_2$O and from 0.2 to 0.9 cm H$_2$O in control patients. The esophageal pressure at relaxed lung volume ranged from 3 to 25.7 cm H$_2$O in obese patients and from 0.7 to 12.2 cm H$_2$O in control patients. In all subjects, there was a significant correlation between the esophageal pressure at a relaxed lung volume and the pressure needed to initiate ventilation. Gastric pressure in obese patients ranged from 6.7 to 17 cm H$_2$O, and there was a good correlation between gastric pressure and esophageal pressure at end expiration and at end inspiration.

Chest wall compliance in obese patients with similar to control patients, but lung compliance was substantially lower in obese patients than in control patients. The BMI was positively correlated with lung elastance in all subjects. This analysis suggests that the effect of obesity on the chest wall largely involves mass loading, and that obesity does not change chest wall properties or compliance. The assumption that the initial pressure associated with the onset of a change in lung volume assumes that the pleural pressure is uniform throughout the thorax and that lung properties are uniform throughout the lung parenchyma. In fact, the intrapleural pressure depends on the location in the thorax and the position of the patient. In the supine position, the heart and mediastinum can compress the esophagus and increase the intra-esophageal pressure. In addition, the intrapleural pressure is more negative at the apex in the upright position and in the anterior region in the supine position. The opening pressure in collapsed airways also affects the pressure requirement to initiate changes in lung volume. However, regardless of these considerations, the intrapleural pressure in obese patients is higher than in normal control patients and in some patients can be extremely positive. In these severely obese patients, there was not a significant correlation between BMI and the pressure needed to initiate increases in lung volumes.

Mezidi et al. investigated transpulmonary pressure differences between obese and non-obese critically ill, mechanically ventilated COVID-19 patients.[18] Eight obese and seven non-obese patients in French university hospital intensive care units were included in the study. To obtain a positive expiratory transpulmonary pressure, obese patients required a PEEP $\geq$ 16 cm H_2O; non-obese patients required a PEEP $\geq$ 10 cm H_2O. Inspiratory transpulmonary pressure, driving transpulmonary pressure, plateau pressure, and respiratory system driving pressure were higher in non-obese patients with high PEEP ($\geq$18 cm H_2O). Chest wall and lung elastances were not statistically different between the 2 groups.

Obi et al. randomized morbidly obese adults with tracheostomy requiring mechanical ventilation to either a strategy in which PEEP was adjusted using esophageal balloon pressures or was adjusted to obtain the best (highest) static compliance.[19] The adjustment with the esophageal balloon aimed to have the end-expiratory transpulmonary pressure in the range of 0 to 5 cm H_2O. The goal of the study was to determine the success rate of tracheostomy collar trials with the rationale was that the optimal PEEP level would minimize atelectasis. The median BMI in the esophageal balloon group was 68.4 kg/m^2. The median BMI in the optimal compliance group was 73.9 kg/m^2. Using esophageal balloons, PEEP was increased from 14 to 27 cm H_2O. Transpulmonary pressure increased from a mean value of –11.2 cm H_2O to a positive value of 0.7 cm H_2O. In the group with the adjustments made based on optimal compliance, the PEEP was increased from 14 to 24 cm H_2O, and the static compliance increased from 36 ml/cm H_2O to 67 ml/cm H_2O.

There was no significant difference between the groups in the percentage of patients weaned by day 30. Eight patients were weaned in the esophageal balloon group, and nine patients were weaned in the optimal compliance group. Patients in the esophageal balloon group were weaned more quickly than those in the optimal compliance group. The reason for this result is not clear from this study, but it is possible that adjusting PEEP based on esophageal balloon pressures identifies optimal PEEP levels more quickly and reduces atelectasis more quickly. During these tracheostomy collar trials, the patient had a speaking valve in place to provide small amounts of intrinsic PEEP. The PEEP level used in this trial was high in both groups, and the final static compliance was high in both groups. There were no adverse effects associated with high PEEP levels. In both groups of pressure support level needed to provide ventilator support was significantly decreased after the PEEP adjustment.

In summary, these studies demonstrate that intrapleural pressures are higher in obese patients and that these patients likely require higher PEEP levels to prevent lung collapse at the end of exhalation.

Intra-abdominal hypertension

Intra-abdominal hypertension (IAH, defined as a sustained increase in intra-abdominal pressure

≥ 12 mm Hg) affects organs in the abdominal cavity and outside the abdomen. Increased intra-abdominal pressure decreases cardiac output and venous return and increases cardiac pressures and affects lung mechanics mostly due to the cephalad movement of the diaphragm. The shift in the diaphragm decreases the end-expiratory volumes and lung compliance and increases dead-space ventilation. These changes can require increased levels of PEEP to maintain adequate ventilation.[20–22] Higher PEEP levels are usually required in patients with IAH to reduce alveolar decruitment, but the best approach to PEEP titration in these patients is still under investigation.[20,22]

There is limited literature on the use of esophageal manometry to titrate PEEP levels in patients with IAH. One trial consisting of 60 people attempted to study esophageal pressures to guide PEEP settings in intubated patients with abdominal hypertension, but the results have not been formally published (ClinicalTrials.gov Identifier: NCT01825304). Kubiak et al. demonstrated that pigs with IAH produced by intraperitoneal CO_2 insufflation had a linear increase in plateau pressure with increases in intra-abdominal pressure, but no change in transpulmonary pressures calculated using the esophageal pressure as an estimate of intrapleural pressure.[23] These investigators concluded that using plateau pressures to make changes in ventilation may lead to underventilation in patients with intra-abdominal hypertension.

Ni et al. studied pigs with increased intra-abdominal pressure generated by nitrogen insufflation undergoing mechanical ventilation in the volume-assist mode and adjusted PEEP levels based on esophageal pressures.[24] They demonstrated that PaO_2, systemic oxygen delivery, and pulmonary compliance increased significantly after adjustment in comparison to the baseline levels before adjustment. This study demonstrated that in porcine models of IAH using transpulmonary measurements based on esophageal manometry improved oxygen metabolism and static compliance. Others have also studied the utility of measuring transpulmonary pressures through esophageal pressure balloons in explaining how different levels of PEEP influence recruitment during tidal ventilation in the presence of IAH.[25,26] Clearly, more clinical studies are needed to analyze the use of esophageal pressure measurements as a surrogate of intrapleural in humans with IAH to manage PEEP titration during ventilator management. However, these protocols will need a large number of patients to determine important outcomes, such as ICU mortality or length of ICU stay.

Summary

Most patients requiring mechanical ventilation have a heterogeneous distribution of lung disease which ranges from cystic structures to lung consolidation. Consequently, a given ventilator pressure will have nonuniform effects on lung parenchyma and results in a nonuniform distribution of the tidal volume. This creates situations in which some regions are under ventilated resulting in low V/Q units and atelectasis and some regions are over ventilated resulting in high V/Q units and possible barotrauma. Measuring a transpulmonary pressure at both the end of inspiration and at the end of expiration potentially provides important information. This is particularly true in patients with a significant chest wall disease and patients with abdominal disorders, such as obesity, ascites, and intra-abdominal hypertension. Measuring intra-esophageal pressure provides an index of pleural pressure. However, multiple factors influence this pressure, including patient position and the weight of the heart and mediastinum. Pleural pressure is never uniform throughout the thorax, and no available clinical methods can provide information about regional intrapleural pressures. Finally, esophageal pressure measurements have not resulted in improved outcomes in available studies in patients with moderate to severe respiratory failure done by experts with this measurement.

Clinicians should remember that in most cases they have little or no information about the intrapleural pressure and its effect on gas exchange. The best approach to adjusting in PEEP involves attention to the lowest FiO_2 which results in adequate O_2 saturation, a plateau pressure below 30 cm H_2O, and the driving pressure at or below 14 cm H_2O. In addition, management of patients with moderate to severe ARDS using the prone position for 16 hours/day may improve outcomes by reducing atelectasis in the lung bases.[27]

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