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Positive end-expiratory pressure (PEEP)

Authors: Rommel Sagana, MD, Robert C Hyzy, MD

Section Editor: Polly E Parsons, MD **Deputy Editor:** Geraldine Finlay, MD

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INTRODUCTION

Positive end-expiratory pressure (PEEP) is used therapeutically during mechanical ventilation (extrinsic PEEP). It can also be a complication of incomplete expiration and airtrapping (intrinsic PEEP).

Clinical aspects of extrinsic and intrinsic and PEEP are discussed in this topic review. High levels of PEEP that have been investigated in patients with acute respiratory distress syndrome as well as the application of PEEP in patients with dynamic hyperinflation from asthma and chronic obstructive pulmonary disease are described separately. (See "Invasive mechanical ventilation in acute respiratory failure complicating chronic obstructive pulmonary disease", section on 'Dynamic hyperinflation' and "Invasive mechanical ventilation in adults with acute exacerbations of asthma", section on 'Adding extrinsic PEEP to offset intrinsic PEEP' and "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Further titration/increase in PEEP (high PEEP)'.)

DEFINITION

Positive end-expiratory pressure (PEEP) is the alveolar pressure above atmospheric pressure that exists at the end of expiration. There are two types of PEEP:

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Extrinsic PEEP – PEEP that is provided by a mechanical ventilator is referred to as applied PEEP

 Intrinsic PEEP – PEEP that is secondary to incomplete expiration is referred to as intrinsic PEEP or auto-PEEP

APPLIED (EXTRINSIC) PEEP

Applied PEEP is usually one of the first ventilator settings chosen when mechanical ventilation is initiated. It is set directly on the ventilator. (See "Overview of initiating invasive mechanical ventilation in adults in the intensive care unit", section on 'Indications'.)

Indications — The optimal level of applied PEEP in most mechanically ventilated patients is unknown. Typically, a small amount of PEEP is applied routinely in most patients undergoing mechanical ventilation (3 to 5 cm H₂O; also known as "physiologic" PEEP; although technically zero PEEP is physiologic). In select populations (eg, acute respiratory distress syndrome), PEEP is applied to prevent cyclic opening and closing of alveoli (and thereby prevent ventilator-induced lung injury) and to maintain adequate oxygenation (>5 cm H₂O; "supraphysiologic" PEEP). The potential benefits of applied PEEP are best studied in acute respiratory distress syndrome (ARDS).

Routine mechanical ventilation — Low levels of applied PEEP are indicated for most patients undergoing mechanical ventilation. PEEP mitigates end-expiratory alveolar collapse (a consequence of the endotracheal tube bypassing the glottic apparatus) and may reduce the incidence of ventilator-associated pneumonia and lung injury [1,2]. A randomized trial of 131 nonhypoxemic (partial pressure of arterial oxygen to fraction of inspired oxygen ratio [PaO₂/FiO₂] >250) patients undergoing mechanical ventilation received either applied PEEP at 5 to 8 cm H₂O (85 percent received 5 cm H₂O) or no applied PEEP [2]. Applied PEEP was associated with a lower incidence of ventilator-associated pneumonia (9 versus 25 percent) and a lower likelihood of developing hypoxemia (19 versus 54 percent). There were no differences in mortality, length of intensive care unit (ICU) stay, or length of hospital stay. Applied PEEP is associated with decreased leakage of posterior pharyngeal secretions into the lower airway, providing a potential mechanism for this benefit [3].

Acute respiratory distress syndrome — Applied PEEP, usually at levels ≥5 cm H₂O, are indicated in most patients with acute respiratory distress syndrome (ARDS) and other types of hypoxemic respiratory failure. The major benefit for applied PEEP in this

population is improvement in oxygenation. There has been significant research done in an attempt to determine the optimal PEEP in patients with ARDS. Most trials titrate PEEP while holding other ventilator settings constant. Data suggest optimal PEEP may depend on the tidal volume. Changing the tidal volume done during a best PEEP trial may lead to different best PEEP settings in the same patient [4]. Studies in a pediatric population appear to validate the use of applied PEEP as pediatric intensivists generally use less PEEP and higher fractions of inspired oxygen (FiO₂) than what is recommended by the ARDS Network (ARDSNet). A trial demonstrated that pediatric patients with ARDS managed with lower PEEP relative to FiO₂ than recommended by the ARDSNet model had higher mortality [5].

The benefits, harms, and application of applied PEEP in this clinical setting are discussed separately. (See "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Further titration/increase in PEEP (high PEEP)' and "Ventilator management strategies for adults with acute respiratory distress syndrome".)

Patients with auto-peep — Applied PEEP can mitigate the effects of auto-PEEP (also known as intrinsic PEEP) in patients who have an expiratory airflow limitation (eg, acute exacerbations of asthma and chronic obstructive pulmonary disease). The application of extrinsic PEEP in patients with auto-PEEP should always be less than the measured auto-PEEP (50 percent or no greater than 80 percent). The use of applied PEEP in this setting is discussed in greater detail, separately. (See 'Treatment' below and "Invasive mechanical ventilation in acute respiratory failure complicating chronic obstructive pulmonary disease", section on 'Dynamic hyperinflation' and "Invasive mechanical ventilation in adults with acute exacerbations of asthma", section on 'Adding extrinsic PEEP to offset intrinsic PEEP'.)

Cardiogenic pulmonary edema — Applied PEEP has been used in patients with cardiogenic pulmonary edema to improve cardiac function. However, the data indicate that PEEP provides little additional benefit beyond the positive pressure ventilation alone. This was illustrated by a trial of 12 patients receiving mechanical ventilation, during which left ventricular performance was assessed by echocardiography before and after applied PEEP was increased by 10 cm H₂O [6]. Left ventricular performance did not change when applied PEEP was increased.

Intraoperative patients — The optimal strategy for mechanically ventilating patients intraoperatively is described separately. (See <u>"Mechanical ventilation during anesthesia in adults"</u>.)

Postoperative patients — The application of PEEP has been employed in postoperative patients in an effort to prevent atelectasis and atelectrauma that can occur in injured lung when undergoing ventilation [7-9].

The application of PEEP as an alveolar recruitment maneuver may be beneficial in the postoperative setting. One single center study of 320 patients who had undergone elective cardiac surgery and were mechanically ventilated for hypoxemia compared an intensive recruitment strategy with a moderate strategy [9]. An intensive strategy consisted of two rounds (four hours apart) of three cycles of 60 second lung inflation with PEEP 30 cm H₂O, pressure controlled ventilation, driving pressure 15 cm H₂O, respiratory rate 15/minute, inspiratory time 1.5 seconds, and fraction of inspired oxygen 0.4 followed by low tidal volume ventilation and a PEEP setting of 8 cmH₂O, while a moderate strategy consisted of two rounds (four hours apart) of three cycles of 30 second inflation with continuous positive pressure at 20 cm H₂O, and fraction of inspired oxygen 0.6 followed low tidal volume ventilation and a PEEP setting of 8 cm H₂O. Intensive recruitment maneuvers resulted in fewer pulmonary complications (severity score 1.8 versus 2.1), and decreased ICU length of stay (3.8 versus 4.8 days) and mortality (2.5 versus 4.9 percent), without increasing the incidence of barotrauma. Flaws in the study design including small sample size, and lack of adjustment for confounding variables and control group, as well as poor generalizability limit interpretation such that further trials demonstrating similar benefit are needed before aggressive recruitment maneuvers can be routinely recommended in the postoperative setting.

Additional details regarding recruitment in patient with ARDS are provided separately.

Other — Applied PEEP has also been used in patients with flail chest (to stabilize the chest wall) or tracheobronchomalacia (to maintain patency of the airways during expiration) with mixed results [1].

Contraindications — There are no absolute contraindications to applied PEEP. However, applied PEEP can have adverse consequences (especially at high levels) and should be used cautiously in patients who have intracranial abnormalities, unilateral or focal lung disease, hypotension, hypovolemia, pulmonary embolism, dynamic hyperinflation without airflow limitation, or a bronchopleural fistula. It may also have undesirable consequences in patients undergoing prone ventilation.

Intracranial disease — Increased intrathoracic pressure due to applied PEEP could theoretically decrease cerebral venous outflow, leading to increased intracranial

pressure, decreased mean arterial pressure, or both. The end result may be decreased cerebral perfusion pressure and neurologic deterioration.

Whether this actually occurs is uncertain. Observational studies with patients who had acute stroke or acute subarachnoid hemorrhage found that incremental elevation of applied PEEP was associated with diminished cerebral perfusion pressure (due to decreased mean arterial pressure) [10,11]. In contrast, another observational study with patients who had traumatic brain injury found that applied PEEP was associated with increased cerebral perfusion pressure (due to decreased intracranial pressure) [12]. The reason for the conflicting results is uncertain, but may be related to varying effects of the different intracranial abnormalities.

Given the uncertainty that exists, it is prudent to monitor both the mean arterial blood pressure and intracranial pressure (if available) whenever applied PEEP is used in a patient with an intracranial abnormality. Reduction of applied PEEP should be considered if the mean arterial blood pressure decreases or intracranial pressure increases. (See "Evaluation and management of elevated intracranial pressure in adults".)

Focal lung disease — Applied PEEP can worsen hypoxemia in patients with focal lung disease (eg, pneumonia). This probably occurs because the applied PEEP compresses intra-alveolar capillaries in the uninvolved lung, diverting blood flow to the injured lung [13]. This increases intrapulmonary shunting.

Hypotension — Positive pressure ventilation increases intrathoracic pressure, which can decrease venous return, reduce cardiac output, and potentially cause hypotension [14]. This is exacerbated by applied PEEP, especially in hypovolemic patients. In euvolemic patients, applied PEEP up to 20 cm H₂O is generally well tolerated from a hemodynamic standpoint, as demonstrated by a trial of eight patients with ARDS [15]. Incremental increases of applied PEEP from 10 to 20 cm H₂O caused hypotension in only one patient, while gastric mucosal perfusion (a marker of systemic hypoperfusion) and cardiac index were unchanged in the remaining patients. A technique is being developed that estimates the cardiac output from changes in the pulmonary shunt at different levels of PEEP; the technique is not yet available for routine clinical use [16]. (See "Physiologic and pathophysiologic consequences of mechanical ventilation", section on 'Hemodynamics'.)

Hyperinflation without flow limitation — Applied PEEP should not be used to treat auto-PEEP that exists in the absence of an expiratory flow limitation. Applied PEEP in

this setting can worsen alveolar pressure and increase the risk of complications such as pulmonary barotrauma or hypotension.

Prone patients — In patients who are mechanically ventilated in the supine position, 10 cm H₂O of applied PEEP is associated with similar redistribution of ventilation and blood flow to the dependent (ie, dorsal) portion of the lung, thereby maintaining a constant amount of ventilation-perfusion (V/Q) mismatch [17]. In contrast, in patients who are mechanically ventilated in the prone ventilation, 10 cm H₂O of applied PEEP is associated with a redistribution of blood flow to the dependent (ie, ventral) portion of the lung that is out of proportion to the redistribution of ventilation, thereby exacerbating the V/Q mismatch. This suggests that supraphysiologic applied PEEP may be less beneficial, or potentially harmful, in patients undergoing prone ventilation.

Tools for titrating applied PEEP — The titration of PEEP is critical for managing patients with ARDS. Most experts use oxygenation using the strategy outlined in the ARMA trial (<u>table 1</u>). However, several tools are available but with the exception of utilizing oxygenation, most of the tools listed below are not suitable for routine use nor has their use been associated with improved outcomes:

- Oxygen For the initial setting of PEEP, we use the strategy outlined in ARMA [18] (table 1), a strategy associated with improved outcomes. (See "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Positive end-expiratory pressure (PEEP) and fraction of inspired oxygen'.)
- **Esophageal pressure** Esophageal pressure (P_{ES}) is an estimate of pleural pressure. It can be measured with an esophageal balloon catheter and then used to calculate the transpulmonary pressure:

Transpulmonary pressure = airway pressure - pleural pressure

The transpulmonary pressure can then be adjusted by titrating applied PEEP, since airway pressure is related to applied PEEP. Titrating applied PEEP to an end-expiratory transpulmonary pressure between 0 and 10 cm H_2O may reduce cyclic alveolar collapse, while maintaining an end-inspiratory transpulmonary pressure \leq 25 cm H_2O may reduce alveolar overdistension [19].

The value of measuring esophageal pressure was evaluated in two trials:

An initial trial (EPvent) randomly assigned 61 patients with ARDS to one of the following mechanical ventilation strategies [19]:

- Adjustment of the FiO₂ and applied PEEP to achieve specific transpulmonary pressures, as measured with an esophageal balloon during an end-expiratory occlusion maneuver
- Adjustment of the FiO₂ and applied PEEP according to a table of ventilator combinations, an approach similar to that used in the ARMA trial described above (<u>table 1</u>)

Both strategies were designed to maintain a PaO₂ between 55 and 120 mmHg (7.32 to 16 kPa), or an oxyhemoglobin saturation between 88 and 98 percent. The group whose applied PEEP was guided by esophageal pressure measurements was managed with significantly higher total PEEP (18 versus 12 cm H₂O) and had a significantly higher PaO₂/FiO₂ ratio (280 versus 191 mmHg [37.2 versus 25.4 kPa]), both assessed at 72 hours. The esophageal pressure group also had an almost statistically significant reduction in 28-day mortality (17 versus 39 percent, adjusted relative risk 0.46, 95% CI 0.19-1.00). There was no difference in the number of ICU-free days or ventilator-free days. However, this study had an unblended single-center design and was stopped early for benefit which may have overestimated the true effect.

• In a multicenter phase 2 confirmatory trial (EPvent-2) of 200 patients with severe ARDS (arterial oxygen tension/fraction of inspired oxygen [PaO₂/FiO₂] ratio ≤200 mmHg), P_{ES}-guided titration of PEEP was compared with empirical high PEEP-FiO₂ titration (eg, similar to that in the table (table 2) (see "Ventilator management strategies for adults with acute respiratory distress syndrome", section on 'Open lung ventilation')) [20]. The goal oxygenation was to maintain a PaO₂ between 55 and 80 mmHg (7.32 to 10.7 kPa), or an oxyhemoglobin saturation between 88 and 93 percent. P_{ES}-guided PEEP titration did not improve the composite outcome of death and the number of mechanical ventilation-free days but did decrease the need for rescue therapy (eg, prone positioning, recruitment maneuvers, extracorporeal membrane oxygenation, inhaled pulmonary vasodilators), perhaps indicating improved oxygenation with P_{ES}-guided PEEP strategies. The rate of barotrauma was no different between the groups (5 versus 6 percent).

We believe P_{ES}-guided PEEP should not be used routinely in most centers. Improved oxygenation alone is insufficient to warrant a change in routine clinical practice [18,21]. It is difficult for most centers to justify the inconvenience and cost of obtaining the necessary equipment and expertise without more certain evidence of

clinical benefit. However, in centers that already have the necessary equipment and expertise, P_{ES}-guided PEEP may be helpful in the management of patients with ARDS, especially if there are concerns that airway pressures do not accurately reflect distending pressures in the lung (eg, when there is external compression of the lung due to abdominal compartment syndrome, chest wall deformities, or large pleural effusion).

- Pressure-volume (PV) curves In many patients with early ARDS, PV curves appear flat at low lung volumes (low compliance), become steeper at higher lung volumes (higher compliance), and then flatten again at even higher lung volumes (figure 1). The lower inflection point is the transition from low to higher compliance, while the upper inflection point is the transition from higher to low compliance. There are two methods of titrating applied PEEP that require a PV curve:
 - The first method involves using a level of applied PEEP that is slightly above the lower inflection point (<u>figure 1</u>) [22-24]. The trials of open lung ventilation described above are examples of this method. Specifically, they used an applied PEEP that was 2 cm H₂O greater than the lower inflection point that was chosen.
 - The second method involves using a level of applied PEEP that matches the pressure at which lung compliance is maximized. This is determined from the PV curve (slope equals compliance) or by stepwise titration of applied PEEP with calculation of compliance at each step [25,26]. Compliance is calculated using the equation Crs = VT/(Ppl PEEP), where Crs is the compliance, VT is the tidal volume, and Ppl is the plateau airway pressure. Measurement of the plateau airway pressure is described separately. (See "Diagnosis, management, and prevention of pulmonary barotrauma during invasive mechanical ventilation in adults", section on 'Prevention'.)

Regardless of which method is chosen, inflation beyond the upper inflection point can result in alveolar overdistension and pulmonary barotrauma, as well as impaired cardiac filling and oxygen delivery [27].

There are significant limitations to using PV curves to identify the level of applied PEEP necessary for open lung ventilation [25,28-33]. Among the limitations, the lower inflection point cannot be identified in some patients and neuromuscular blockade or apneic-level sedation is generally required to accurately construct a PV curve [25,29]. A novel approach to plotting a PV curve that doesn't require

neuromuscular blockade has been used in several clinical trials [34,35]. Following five cycles of controlled ventilation, the inspiratory to expiratory ratio is set to 80 percent, the respiratory rate is set to five breaths per minute, and the tidal volume is set to 500 mL [36]. Inspiratory flow is then administered for 9.6 seconds, during which a PV curve is generated on the ventilator screen. From this curve, the lower inflection point can be determined. This approach appears promising but requires validation.

- Lung ultrasound The effects of applied PEEP on lung aeration can be directly visualized by lung ultrasound [37]. While this may prove useful in the future, additional experience is necessary before lung ultrasound is used to titrate PEEP in patients with ARDS.
- Oxygen delivery Applied PEEP can be titrated to a maximum oxygen delivery (DO₂). This method involves calculating the DO₂ at each level of applied PEEP, then using the applied PEEP that corresponds with the best DO₂ for ongoing mechanical ventilation. The calculation of DO₂ is discussed elsewhere. (See "Oxygen delivery and consumption".)

AUTO (INTRINSIC) PEEP

Incomplete expiration prior to the initiation of the next breath causes progressive air trapping (ie, dynamic hyperinflation). This accumulation of air increases alveolar pressure at the end of expiration, which is referred to as auto-PEEP.

This section focuses on auto-PEEP that develops during mechanical ventilation. Auto-PEEP that develops during spontaneous breathing is discussed separately. (See "Dynamic hyperinflation in patients with COPD".)

Causes — There are three common situations during which auto-PEEP develops: high minute ventilation, expiratory flow limitation, and expiratory resistance.

High minute ventilation — A high minute ventilation is caused by large tidal volumes, a high respiratory rate, or both. Either alteration can create auto-PEEP.

• Large tidal volumes increase the volume that must be exhaled prior to the next breath. The larger the tidal volume, the less likely that the full tidal volume will be exhaled before the onset of the next breath.

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High respiratory rates decrease the duration of expiration. The faster the respiratory rate, the shorter the expiratory time and the less likely that the full tidal volume will be exhaled before the onset of the next breath.

Expiratory flow limitation — An expiratory flow limitation exists when expiratory flow is slowed by airway narrowing due to collapse, bronchospasm, inflammation, or remodeling (<u>figure 2</u>). It increases the likelihood that the full tidal volume will not be exhaled before the onset of the next breath and auto-PEEP will develop.

Most patients with chronic obstructive pulmonary disease (COPD) have an expiratory flow limitation. As a result, such patients are prone to developing auto-PEEP when mechanical ventilation is initiated [38].

A patient's expiratory flow limitation is not routinely assessed in critical care units because it requires neuromuscular paralysis, specialized techniques, or both to be measured [39,40]. However, it appears that expiratory flow limitation is more prominent when patients are supine rather than semirecumbent [40].

Expiratory resistance — Expiratory resistance is conceptually similar to expiratory flow limitation in that it slows expiration and increases the likelihood that the full tidal volume will not be exhaled before the onset of the next breath. However, expiratory resistance is unrelated to the airways. Examples of expiratory resistance include a narrow diameter or kinked endotracheal tube, inspissated secretions, exhalation or PEEP valves, and patient-ventilator asynchrony. (See "Overview of initiating invasive mechanical ventilation in adults in the intensive care unit", section on 'Follow- up'.)

Potential sequelae — Auto-PEEP increases intrathoracic pressure, which can decrease venous return, reduce cardiac output, and potentially cause hypotension. This is most pronounced in hypovolemic patients. (See <u>"Physiologic and pathophysiologic consequences of mechanical ventilation"</u>, section on 'Hemodynamics'.)

Auto-PEEP can also cause alveolar overdistension, increasing the likelihood of pulmonary barotrauma and ventilator-associated lung injury. Alveolar overdistension can also cause hypoxemia if V/Q mismatch increases due to compression of adjacent pulmonary blood vessels. (See "Diagnosis, management, and prevention of pulmonary barotrauma during invasive mechanical ventilation in adults" and "Ventilator-induced lung injury".)

Finally, auto-PEEP increases the work required for a patient to trigger a ventilator breath when pressure-triggering is being used. This is because the patient must generate

enough negative pressure to overcome the trigger sensitivity plus the auto-PEEP, rather than the trigger sensitivity alone (figure 3). As an example, a patient whose auto-PEEP is 8 cm H₂O and whose ventilator has a trigger sensitivity of -2 cm H₂O needs to generate -10 cm H₂O of negative pressure to trigger a breath. In contrast, a patient who has no auto-PEEP only needs to generate the -2 cm H₂O of negative pressure that is necessary to overcome the trigger sensitivity. Inability to trigger breaths may cause patient-ventilator asynchrony, dyspnea, and insufficient ventilation [41]. (See "Overview of initiating invasive mechanical ventilation in adults in the intensive care unit", section on 'Trigger sensitivity' and "Overview of initiating invasive mechanical ventilation in adults in the intensive care unit", section on 'Follow- up'.)

Assessment — Auto-PEEP can be detected using ventilator-generated flow versus time graphs, or palpation plus auscultation of the chest. With flow versus time graphs, the upstroke that indicates inspiratory flow will begin before the expiration tracing reaches zero flow if auto-PEEP exists. With palpation and auscultation, inspiratory airflow will be heard before the expiratory airflow ceases. Palpation and auscultation can confirm that auto-PEEP is present, but it is unreliable for determining its absence [42].

Another approach exists that can quantitate the auto-PEEP. Specifically, the auto-PEEP is determined by measuring the end-expiratory alveolar pressure and then subtracting the applied PEEP:

Auto-PEEP = end-expiratory alveolar pressure - applied PEEP

The end-expiratory alveolar pressure is measured by applying an end-expiratory breath hold and reading the airway pressure directly from the ventilator during the breath hold. The applied PEEP is set on the ventilator.

Auto-PEEP is difficult to quantitate accurately, as illustrated by the following examples:

- Widespread airway closure in patients with severe asthma can falsely lower the end-expiratory alveolar pressure measurement [43]. As a result, marked dynamic hyperinflation and auto-PEEP may be unrecognized.
- Expiratory muscle activity in non-paralyzed patients can falsely elevate the endexpiratory alveolar pressure measurement (<u>figure 4</u>) [44]. This can lead to the inappropriate and potentially harmful treatment of presumed auto-PEEP. (See 'Treatment' below.)

The second situation described above can be avoided by carefully palpating for the absence of expiratory muscle activity prior to measuring the end-expiratory alveolar

pressure [45]. This coincides with the onset of inspiration because the expiratory muscle must relax in order for the inspiratory muscles to decrease intrathoracic pressure [46].

Treatment — Steps should be taken to correct auto-PEEP as soon as it is identified. Initial efforts should focus on determining and treating the underlying cause. When auto-PEEP persists despite management of its underlying cause, applied PEEP may be helpful if the patient has an expiratory flow limitation.

When a high minute ventilation is the presumed cause of auto-PEEP, the minute ventilation should be decreased by lowering the tidal volume or respiratory rate. This frequently requires a strategy of permissive hypercapnia. (See "Permissive hypercapnia during mechanical ventilation in adults".)

When an expiratory flow limitation due to obstructive airways disease is the presumed cause of auto-PEEP, the duration of expiration should be prolonged. This can be accomplished by increasing the inspiratory flow, decreasing the tidal volume, or decreasing the respiratory rate.

Treatment with bronchodilators, steroids, and antibiotics may also be beneficial. In a study of 25 patients with COPD and acute respiratory failure, expiratory flow limitation was present in 96 percent of the patients at the initiation of mechanical ventilation [47]. The prevalence of expiratory flow limitation decreased to 47 percent at the time of extubation and 40 percent at the time of ICU discharge, indicating that expiratory flow limitation may respond to therapy. (See "Management of exacerbations of chronic obstructive pulmonary disease".)

When increased expiratory resistance is the presumed cause of auto-PEEP, the source of increased resistance should be identified and corrected. This may require sedation, pharmacologic paralysis, or replacement of the endotracheal tube or ventilator tubing.

Applied PEEP — Small amounts of applied PEEP can decrease auto-PEEP in patients who have an expiratory flow limitation [48-50]. This can be conceptualized as the applied PEEP holding open the narrowed airways during expiration, improving expiratory airflow, and allowing more complete expiration prior to the onset of the next breath. Additional benefits of using applied PEEP to offset auto-PEEP include decreased oxygen consumption and improved gas exchange. The latter is due to opening the small airways in the dependent lung zones and distributing inspired gas more homogeneously [51-53].

Applied PEEP should always be less than the measured auto-PEEP [54]. Otherwise, alveolar pressure may increase, placing the patient at increased risk for complications such as pulmonary barotrauma or hypotension (figure 5). One study even suggested that applied PEEP does not need to exceed the measured auto-PEEP for this to occur. Rather, it can occur if the applied PEEP is greater than 85 percent of the measured auto-PEEP [55]. Given the potential inaccuracy of auto-PEEP measurements, it is prudent to set applied PEEP to a level that is less than 50 percent of the measured auto-PEEP. Research has shown that mechanical ventilation with PEEP induces longitudinal atrophy by displacing the diaphragm in caudal direction and reducing the length of fibers. As a result, muscle fibers generate less force causing diaphragm weakness [56]. This may exacerbate diaphragm weakness in critically ill patients thus prolonging mechanical ventilation. This advocates for maintaining the lowest required PEEP setting.

Applied PEEP should not be used to counter auto-PEEP in patients who do not have an expiratory flow limitation. Applied PEEP may increase alveolar pressure and increase the risk of both barotrauma and hemodynamic compromise in this setting [57].

SUMMARY AND RECOMMENDATIONS

Positive end-expiratory pressure (PEEP) is the alveolar pressure above atmospheric
pressure that exists at the end of expiration. PEEP that is applied through a
mechanical ventilator is referred to as applied PEEP (also called extrinsic PEEP),
whereas PEEP that is secondary to incomplete exhalation is referred to as autoPEEP (also called intrinsic PEEP). (See 'Definition' above.)

Applied PEEP — The optimal level of PEEP in most populations is unknown. In general:

- A small amount of applied PEEP (3 to 5 cm H₂O) is used in most mechanically ventilated patients to mitigate end-expiratory alveolar collapse. (See <u>'Indications'</u> above.)
- A higher level of applied PEEP (>5 cm H₂O) is sometimes used to improve hypoxemia or reduce ventilator-associated lung injury in patients with acute respiratory distress syndrome or other types of hypoxemic respiratory failure, and offset the effects of auto-PEEP in patients with expiratory airflow limitation. (See <u>'Indications'</u> above.)

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Improvement in P:F ratio with a higher level of applied PEEP is associated with improved mortality in patients with moderate-to-severe ARDS. (See <u>'Indications'</u> above.)

There are no absolute contraindications to applied PEEP. However, applied PEEP
can have adverse consequences (especially at high levels) and should be used
cautiously in patients with intracranial abnormalities, unilateral or focal lung disease,
hypotension, hypovolemia, dynamic hyperinflation without airflow limitation, or a
bronchopleural fistula. (See <u>'Contraindications'</u> above.)

Auto-PEEP

- There are three common situations during which auto-PEEP develops: high minute ventilation, expiratory flow limitation, and expiratory resistance. (See <u>'Causes'</u> above.)
- Auto-PEEP increases intrathoracic pressure, which can decrease venous return, reduce cardiac output, and potentially cause hypotension. It can also cause alveolar overdistension, increasing the likelihood of pulmonary barotrauma and ventilatorassociated lung injury. Finally, auto-PEEP increases the work required for a patient to trigger a ventilator breath if pressure-triggering is being used. (See <u>'Potential</u> <u>sequelae'</u> above.)
- Auto-PEEP can be detected using ventilator-generated flow versus time graphs or by palpation and auscultation of the chest. It can be detected and quantitated by measuring the end-expiratory alveolar pressure and then subtracting the applied PEEP. (See 'Assessment' above.)
- Steps should be taken to correct auto-PEEP as soon as it is identified. Initial efforts should focus on determining and treating the underlying cause. When auto-PEEP persists despite management of its underlying cause, applied PEEP may be helpful if the patient has an expiratory flow limitation. (See <u>'Treatment'</u> above.)
- For patients with auto-PEEP and an expiratory flow limitation, we suggest administering applied PEEP at a level that is 50 percent of the measured auto-PEEP (**Grade 2C**). (See 'Treatment' above.)

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Topic 1642 Version 18.0

GRAPHICS

Low tidal volume ventilation in patients with acute respiratory distress syndrome

Initial ventilator settings											
Calculate predicted body weight (PBW)											
Male = 50 + 2.3 [height (inches) - 60] OR											
50 + 0.91 [height (cm) - 152.4]											
Female =	45.5 + 2.3 [height (inches) - 60] OR										
45.5 + 0.91 [height (cm) - 152.4]											
Set mode to volume assist-control											
Set initial tidal volume to 6 mL/kg PBW											
Set initial ventilator rate ≤35 breaths/min to match baseline minute ventilation											
Subsequent tidal volume adjustment											
Plateau pressure goal: Pplat ≤30 cm H ₂ O											
Check inspiratory plateau pressure with 0.5 second inspiratory pause at least every four hours and after each change in PEEP or tidal volume.											
If Pplat $>$ 30 cm H ₂ O, decrease tidal volume in 1 mL/kg PBW steps to 5 or if necessary to 4 mL/kg PBW.											
If Pplat <25 cm $\rm H_2O$ and tidal volume <6 mL/kg, increase tidal volume by 1 mL/kg PBW until Pplat >25 cm $\rm H_2O$ or tidal volume = 6 mL/kg.											
If breath stacking (autoPEEP) or severe dyspnea occurs, tidal volume may be increased to 7 or 8 mL/kg PBW if Pplat remains \leq 30 cm $\rm H_2O$.											
Arterial oxygenation and PEEP											
Oxygenation goal: PaO ₂ 55 to 80 mmHg or SpO ₂ 88 to 95 percent											
Use these FiO ₂ /PEEP combinations to achieve oxygenation goal:											
FiO ₂	0.3	0.4	0.5	0.6	.6 0.7 0.8 0.9 1.0			1.0			
PEEP	5	5 to 8	8 to 10	10	10 to 14	14 14 14 to 18 18 to 24					
PEEP should be applied starting with the minimum value for a given FiO ₂ .											

Pplat: plateau pressure; PaO_2 : arterial oxygen tension; SpO_2 : oxyhemoglobin saturation; PEEP: positive end-expiratory pressure; FiO2: fraction of inspired oxygen.

Adapted from: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000; 342:1301.

Graphic 57072 Version 4.0

Titration of PEEP

Higher PEEP/lower FiO ₂																	
Step:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
FiO ₂	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.6	0.7	0.8	0.8	0.9	1.0	1.0
PEEP	5	5	8	10	12	14	16	16	18	20	20	20	20	22	22	22	24

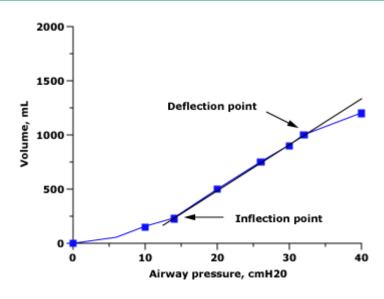
PEEP: positive end-expiratory pressure; ${\rm FiO}_2$: fraction of inspired oxygen.

Adapted from:

- 1. Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. NEJM 2004; 351:327.
- 2. Meade MO, Cook DJ, Guyatt GH. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2008; 299:637.

Graphic 118834 Version 1.0

Pressure-volume curve in ARDS

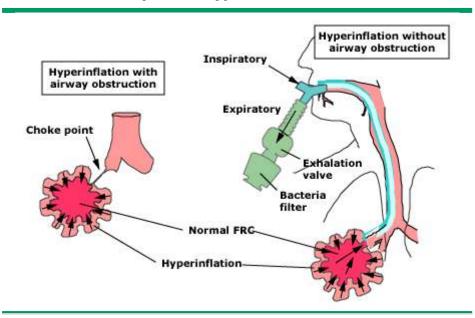


Pressure-volume curve in a patient with acute respiratory distress syndrome (ARDS). The slope of the curve is flat at low and high airway pressures (ie, below the inflection point and above the deflection point). In these areas, increases in airway pressure produce minimal increases in lung volume. Compliance is maximized on the straight part of the curve. The deflection point is defined as the level at which the curve begins to divert from a straight line. Above this threshold, the lung is likely to begin to become overdistended. Mechanical ventilation is considered optimal when it takes place on the straight part of the curve between the inflection and deflection points.

Redrawn from Brunet, F, Jeanbourquin, D, Monchi, M, et al, Am J Respir Crit Care Med 1995; 152:524.

Graphic 72036 Version 1.0

Auto-PEEP and dynamic hyperinflation



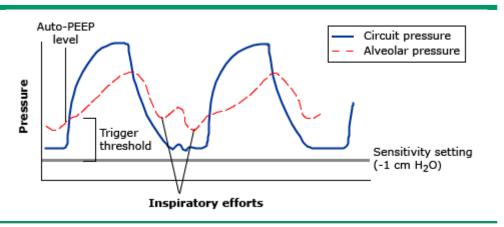
This diagram shows the presence of auto-PEEP and dynamic hyperinflation with and without expiratory flow limitation. The diagram on the left displays the circumstance of expiratory flow limitation as reflected in proximal airway collapse ("choke point"). In the diagram on the right, expiratory flow limitation has not taken place although the patient manifests auto-PEEP and dynamic pulmonary hyperinflation as a function of increased expiratory resistance from the endotracheal tube, exhalation valve, and bacteria filter. The application of PEEP in the patient with expiratory flow limitation would be expected to improve expiratory airflow. However, in conditions without the presence of expiratory limitation, the application of PEEP would potentially worsen dynamic hyperinflation and increase the risk of barotrauma.

PEEP: positive end-expiratory pressure.

Adapted from Puritan-Bennett 1994, Form AA-1888.

Graphic 77948 Version 2.0

Trigger threshold for auto-PEEP



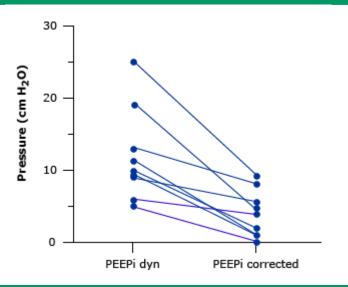
Effect of auto-PEEP on elevation of the triggering threshold in a mechanically ventilated patient with obstructive airways disease. This figure representation shows airway pressure over time. The solid blue line demonstrates the circuit pressure as measured by the ventilator manometer, and the dashed red line is the alveolar pressure. In the absence of auto-PEEP, the sensitivity setting of -1 cm H₂O would be achieved by the patient making inspiratory efforts at the end of expiration, when airway pressure is at its minimum. In the presence of auto-PEEP, alveolar pressure remains positive. In this setting, the patient's inspiratory effort needs to decrease airway pressure not only by the -1 cm H₂O sensitivity set on the machine, but also by the amount of positive alveolar pressure (auto-PEEP). In this figure, the patient's inspiratory efforts are insufficient to trigger the ventilator, and the patient is "locked out," being unable to get a breath because of an inability to overcome the elevated effective triggering threshold rendered by auto-PEEP.

PEEP: positive end-expiratory pressure.

Adapted from Puritan-Bennett 1994, Form AA-1888.

Graphic 64640 Version 4.0

Spuriously elevated intrinsic PEEP



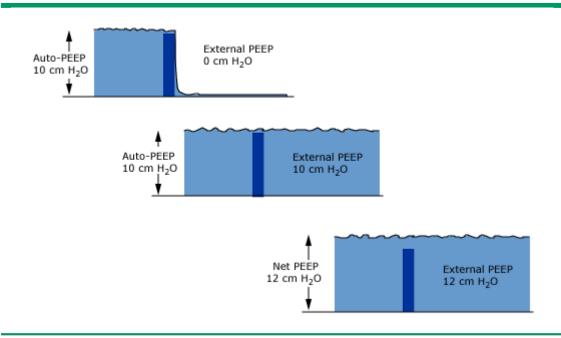
Individual values of intrinsic PEEP (auto-PEEP) measured on esophageal tracings (PEEPi dyn) compared with values obtained after subtracting for the rise in gastric pressure resulting from expiratory muscle activity (PEEPi corrected). The difference shown represents the contribution of expiratory muscle activity to the measured auto-PEEP. The corrected auto-PEEPi would be that component of auto-PEEP expected to be responsive to the application of PEEP. Thus, the presence of expiratory muscle activity can lead to the erroneous impression of a higher level of auto-PEEP and to the application of PEEP in an amount which might result in worsened dynamic pulmonary hyperinflation.

PEEP: positive end-expiratory pressure.

Redrawn from Lessard MR, Lofaso F, Brochard L. Am J Respir Crit Care Med 1995; 151:562.

Graphic 79638 Version 2.0

External positive end-expiratory pressure (PEEP) with auto-PEEP



The use of external positive end-expiratory pressure (PEEP) in the setting of auto-PEEP may be conceptualized by the "waterfall over a dam" analogy. In this analogy, the presence of dynamic hyperinflation and $10 \text{ cm H}_2\text{O}$ of auto-PEEP is represented in the top panel by the reservoir of water trickling over the dam represented by the solid block. In the middle panel, as long as the external PEEP is less than or equal to the amount of auto-PEEP, the amount of water in the upstream reservoir, representing dynamic hyperinflation, does not increase. However, once the amount of water in the reservoir does increase (bottom panel), dynamic hyperinflation worsens. Additional experimental studies done by others suggest that this effect occurs once the external PEEP is greater than approximately 85 percent of the amount of auto-PEEP.

Redrawn from Tobin MJ, Lodato RF, Chest 1989; 96:449.

Graphic 72568 Version 2.0

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