MECHANICAL VENTILATION IN OBSTRUCTIVE LUNG DISEASE

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Severe airflow obstruction is one of the most common causes of acute respiratory failure encountered in medical ICUs. Although most patients with life-threatening exacerbations of asthma or chronic obstructive pulmonary disease (COPD) respond to a noninvasive approach, in certain instances, endotracheal intubation and mechanical ventilatory support are necessary for survival. Although often lifesaving, mechanical ventilation of patients with severe airflow obstruction is associated with many complications that may result in serious morbidity or even death. An important cause of ventilator-related complications is excessive dynamic pulmonary hyperinflation, a process that occurs primarily in the setting of severe airflow obstruction. In addition, patients may suffer complications related to the drugs used to treat underlying airway disease or to facilitate ventilatory support by inducing relaxation of respiratory muscles.

This article review selected topics relevant to the use of mechanical ventilation in patients with severe airflow obstruction. Areas discussed include the bedside assessment of respiratory system mechanics, the ventilatory determinants of dynamic pulmonary hyperinflation, the role of controlled hypoventilation with permissive hypercapnia, and the delivery of bronchodilators during mechanical ventilation. Weaning from mechanical ventilation and the use of noninvasive ventilation are covered elsewhere in this issue.

RESPIRATORY MECHANICS

Derangements in lung mechanics and gas exchange typically are worse in fulminant asthma than in exacerbations of COPD. In addition, the pathophysiology of airflow obstruction in asthma and COPD may differ in certain respects. Nonetheless, the basic physiologic principles that govern the bedside assessment of lung mechanics in the setting severe airflow obstruction are common to both conditions.

Airway Pressures

The fundamental pathophysiologic abnormality in severe airflow obstruction is a marked increase in airway resistance that leads to a decrease in the rate of expiratory flow and resultant pulmonary hyperinflation. Because of the increase in airway resistance and lung volume, volume-cycled mechanical ventilation of patients with severe airflow obstruction typically is associated with a marked increase in airway pressure, including peak pressure, plateau pressure, and auto (intrinsic)-positive end-expiratory pressure (auto-PEEP).

During occlusion of the proximal airway at end inspiration, airway pressure falls from a preocclusion peak pressure to a lower postocclusion plateau pressure, the latter representing the elastic recoil pressure of the respiratory system at end inspiration. The difference between the two pressures, or the inspiratory flow resistive pressure, is a function of the resistance of the
entire respiratory system (including the endotracheal tube) and the inspiratory flow rate (v1). In patients with obstructive airway disease, pulmonary hyperinflation and increased flow resistive properties contribute to increased peak pressure. In contrast, the plateau pressure is independent of inspiratory flow resistive properties. An elevation in plateau pressure during mechanical ventilation of patients with asthma or COPD reliably indicates the presence of pulmonary hyperinflation. This is because plateau pressure represents the sum of end-expiratory alveolar pressure (auto-PEEP) and tidal elastic recoil pressure (V_t x respiratory system elastance), and patients with obstructive lung disease typically have normal respiratory system elastance. Analysis of the decay in pressure following end-inspiratory airway occlusion reveals two components-a rapid drop to an initial pressure (P_1) followed by subsequent slower decline to a final pressure (P_2) (Fig. 1). The initial drop in pressure, a result of sudden interruption of flow, depends on V1 and the intrinsic airway resistance. The subsequent slower decrease in pressure is caused by two factors-gas redistribution within the lung and the dissipation of pressure related to viscoelastic properties of the pulmonary parenchyma and chest wall (stress relaxation). In a normal lung, little gas redistribution takes place during airway occlusion, and a plateau in airway pressure is reached quickly. In the setting of severe airflow obstruction, in contrast, there is considerable inhomogeneity in airway resistance, leading to regional differences in the rates of filling and emptying of lung units. As a result, local alveolar volumes and pressures vary throughout the lung and significant gas redistribution takes place during an airway occlusion. The relatively large amount of gas redistribution in asthma and COPD is reflected in an increase in the P_1 - P_2 difference and in a greater amount of time required before a final plateau in pressure is achieved during conditions that stop airflow. Auto-PEEP can be quantified in a variety of ways (discussed in the article by Ranieri et al). Most commonly used is the static methods in which the airway is occluded at the end of a passive expiration while the next ventilator breath is delayed. If expiratory flow is present, a positive pressure that represents the average end-expiratory elastic recoil pressure of the respiratory system will be recorded. The recorded value underestimates the end-expiratory alveolar pressure of some units and overestimates that of others. Assuming that the patient is relaxed, the presence of auto-PEEP always indicates that there is dynamic hyperinflation-i.e., end-expiratory lung volume is greater than the equilibrium (relaxed) volume. An alternative way of assessing auto-PEEP is the dynamic method. The latter technique measures auto-PEEP as the amount of pressure required to initiate flow once inspiration has begun, as assessed with an esophageal balloon during spontaneous or machine-assisted breaths, or by monitoring of airway pressure during controlled breaths. Severe airflow obstruction is characterized by considerable regional variation in mechanical time constants. With different rates of emptying, regional end-expiratory alveolar pressure varies throughout the lung. One consequence of this variability in end-expiratory alveolar pressure is that simultaneous measurements of auto-PEEP by the static and dynamic methods yield different values, with that of the static technique being higher. The dynamic method records auto-PEEP as the pressure required to initiate flow in lungs units with the lowest end-expiratory alveolar pressure. Static auto-PEEP more closely reflects the average end-expiratory alveolar pressure after gas redistribution. Although the dynamic method may be useful for assessing the effect of auto-PEEP on work of breathing, static measurements probably are better at assessing the overall degree of dynamic hyperinflation. A second consequence of inhomogeneity is an increase in the duration of airway occlusion required to measure static auto-PEEP accurately. When auto-PEEP develops in the setting of acute lung injury caused by high minute ventilation (V_E) without flow limitation, alveolar and proximal airway pressures equilibrate rapidly following airway occlusion. As previously discussed in regard to measurement of plateau pressure, however, equilibration may require several seconds in the setting airflow obstruction (see Fig. 1). Use of a brief airway occlusion may
lead to a gross underestimation of end-expiratory alveolar pressure. An additional factor that may increase the time to equilibration is the presence of the ventilator circuit.

**Figure 1.** Proximal airway pressure recording during an end-inspiratory airway occlusion and during an end-inspiratory occlusion.

Indeed, with a highly compliant ventilator circuit, the large compressible volume of gas may cause measured auto-PEEP to underestimate end-expiratory alveolar pressure, even when a prolonged occlusion is used. Measurements of airway pressures have been reported in many studies involving patients with asthma and COPD. Two relatively large studies have reported on initial peak pressure and plateau pressure in patients with asthma. Approximately 50 patients were evaluated in each, and average values for ventilator settings were similar (V̇ about 12 mL/kg, respiratory rate about 14 breaths/minute, and V1 about 80 L/minute). Plateau pressure was measured with a 0.5-second inspiratory pause. Average initial values for peak and plateau pressure were approximately 64 and 25 cm H₂O in one study and 66 and 26 cm H₂O in the second study, with considerable variation among patients. Data on airway pressures in COPD generally have included smaller numbers of patients. In one study, eight patients with an acute exacerbation of COPD were studied on the first day of mechanical ventilatory support. Average values for peak pressure, plateau pressure, and auto-PEEP were 47, 26, and 14 cm H₂O, respectively. In three other studies, average values ranged from 32 to 42 cm H₂O for peak pressure, 18 to 25 cm H₂O for plateau pressure, and 5 to 12 cm H₂O for auto-PEEP.

**Airway Resistance**

Inspiratory and expiratory resistances are approximately equal in the normal lung, but expiratory resistance may exceed inspiratory resistance greatly in obstructive airway disease and influences the degree of pulmonary hyperinflation at a given V̇. Nonetheless, inspiratory resistance is simpler to measure, and most studies have focused on measurements of the resistance to flow during mechanical inflation of the respiratory system.

The most common method for evaluating airway resistance is by interruption of flow immediately following the delivery of a tidal breath, a maneuver that eliminates the contribution of airway resistance to airway pressure recorded proximally. Inspiratory resistance is calculated as the quotient of the drop in pressure during airway occlusion and V̇. In a simplified, single-compartment model of the respiratory system, in which the airways are viewed as rigid pipes and lung parenchyma and chest wall have constant elastic properties, the calculated resistance would reflect only the resistance to gas flow within the conducting airways. The respiratory system of human, and particularly those with obstructive airway disease, however, is more complex, being characterized by regional variation in time constants and viscoelastic properties.

The term *maximal inspiratory resistance* (Rₘₐₓ) has been applied to the calculation of resistance using P₂ as the postocclusion pressure:

\[ R_{\text{max}} = \frac{(P_{\text{pk}} - P_2)}{V_1} \]

The numerator used in the calculation of Rₘₐₓ includes the total pressure dissipation on airway occlusion, including the contributions of gas redistribution and stress relaxation as well as intrinsic airway resistance. To calculate the pressure component solely caused by airway resistance, termed "minimal airway resistance" (Rₘᵢₙ), the difference between peak pressure (Pₚₖₑᵃₜ) and P₁ is used in the numerator:

\[ R_{\text{min}} = \frac{(P_{\text{pk}} - P_1)}{V_1} \]

Animal studies in which alveolar capsules have been used to quantify alveolar pressure have confirmed that Rₘᵢₙ is caused entirely by the flow resistance of the conducting airways. That includes the resistance imposed by the native airways and the endotracheal tube. The component of total respiratory system resistance caused by gas redistribution and stress relaxation (deltaRrs) is represented by the difference between Rₘₐₓ and Rₘᵢₙ:

\[ \text{deltaRrs} = \frac{(P_1 - P_2)}{V_1} \]
Calculation of inspiratory resistances has been used clinically to help assess the severity and course of airflow obstruction and to evaluate the response to bronchodilators. To calculate $R_{\text{min}}$, $P_1$ must be identified by visual inspection or computer analysis of postocclusion airway pressure. $R_{\text{max}}$ is calculated more conveniently, using the ventilator’s end-inspiratory pause function to measure $P_2$ (plateau pressure). The inspiratory resistance measured at the bedside often represents neither $R_{\text{min}}$ nor $R_{\text{max}}$ because the commonly used pause duration (0.5-1 second) are too long to measure $P_1$ and too short to measure $P_2$. This is of minimal clinical importance, provided that duration of airway occlusion is always similar in making serial comparisons.

Several studies have assessed $R_{\text{max}}$, $R_{\text{min}}$, and delta $R_{\text{rs}}$ in mechanically ventilated patients with COPD. Average values have ranged from 13 to 26 cm H$_2$O/L/s for $R_{\text{max}}$, 8 to 18 cm H$_2$O/L/s for $R_{\text{min}}$, and 4 to 10 cm H$_2$O/L/s for delta $R_{\text{rs}}$. These resistances are considerably higher than those obtained in normal individuals ($R_{\text{max}} = 4-6$, $R_{\text{min}} = 1.5-2.5$, and delta $R_{\text{rs}} = 2-4$ cm H$_2$O/L/s). It should be appreciated that endotracheal tubes can have a significant affect on $R_{\text{max}}$ and $R_{\text{min}}$. The effect of the endotracheal tube on calculations of inspiratory resistance is increased with smaller tube size, higher V1, and in vivo as opposed to in vitro conditions. In one study, the inspiratory resistance of an 8-mm endotracheal tube as determined in vivo by simultaneous measurement of airway pressures at the Y connection between the endotracheal tube and ventilator circuit and in the trachea. The in vivo inspiratory resistance caused by the endotracheal tube was approximately 13 cm H$_2$O/L/s at a V1 of 80 L/minute and was considerably higher than the measured resistance to flow under in vivo as opposed to in vitro conditions also was found in a subsequent investigation. Only a few clinical studies of expiratory resistance in patients with obstructive airway disease have been done. In them, the interrupter technique was used to quantify resistance during passive expiration (Fig. 2). This method employs intermittent brief airway occlusions to allow equilibration of pressure between alveoli and the proximal airway, while expiratory flow is recorded simultaneously. The expiratory resistance at any point during passive exhalation computed as the quotient of the pressure difference preinterruption and postinterruption and the flow immediately before airway occlusion. In one study, patients with COPD who were studied 1 to 9 days after intubation were found to have interrupter-derived expiratory resistance of 17 to 43 cm H$_2$O/L/s at an expiratory flow of 1 L/s (normal = 2.5 cm H$_2$O/L/s). It is likely that expiratory resistance would have been higher if measured soon after commencement of mechanical ventilation because respiratory mechanics generally are most abnormal on the first day of ventilatory support. A second study, involving 10 patients with severe COPD, calculated expiratory resistance at different lung volumes. Mean values for early, middle, and end-exhalation were 36, 66, and 181 cm H$_2$O/L/s, respectively. The ratio of expiratory-to-inspiratory resistance ranged from approximately 2:1 at the higher lung volumes to 10:1 at the lowest lung volumes.

The endotracheal tube influences net resistance to expiratory flow, but its effect is less than during inspiration. Resistive pressure losses caused by the endotracheal tube increase with increasing flow. At the onset of expiration, when elastic recoil pressure and expiratory flow are greatest, the endotracheal tube may impose a significant added resistance. Expiratory flow declines rapidly in patients with severe airflow obstruction, however, and the flow resistive properties of the endotracheal tube are minimal at the very low flow rates present throughout the great majority of expirations. For this reason, endotracheal tube size probably has a relatively minor influence on the overall severity of pulmonary hyperinflation in the setting of severe airflow obstruction.

**Expiratory Flow Limitation and External Positive End-expiratory Pressure**

Normal individuals become flow-limited only with forced expiration. In contrast, expiratory flow limitation is present during relaxed tidal breathing in obstructive airways disease. The presence of expiratory flow limitation may be apparent by the typical concave appearance on
visual inspection of the expiratory flow-volume curve displayed on some ventilators. When a flow-volume curve is not displayed, expiratory flow limitation may be inferred by other methods. At the bedside, flow limitation is suggested by persistent flow at the end of a passive expiration, as documented by the presence of auto-PEEP or measurement of an exhaled volume in excess of machine delivered VT when expiratory time (TE) is prolonged abruptly. Many modern ventilators also display flow graphically, providing a convenient way of detecting end-expiratory flow. One must be careful when conventional scaling is used, however, because with severe airway disease expiratory flow may be below the threshold of detection and it may appear that flow has ceased well before the end of expiration.

It is important to appreciate that dynamic hyperinflation with auto-PEEP and expiratory flow limitation need not always coexist. Patients who are not flow limited may develop significant auto-PEEP if TE is shortened greatly as a result of high

Figure 2. (Figure Not Available) Interrupter technique for measuring expiratory resistance. During passive exhalation a series of brief airway occlusions are performed. The expiratory resistance at any time point during expiration is computed as the occlusion pressure divided by the flow immediately preceding the airway occlusion. (From Gottfried SB, Rossi A, Higgs BD, et al: Noninvasive determination of respiratory system mechanics during mechanical ventilation for acute respiratory failure. Am Rev Respir Dis 131:414-420, 1985, with permission.)

V̇E or prolongation of inspiratory time (T I). Conversely, prolongation of Te may allow some flow limited patients to reach their relaxed lung volume by the onset of the next inspiration.

Another way of showing flow limitation is by applying external PEEP. In patients who are not flow limited, the reduction in driving pressure (elastic recoil pressure minus mouth pressure) from external PEEP leads to a decrease in expiratory flow and to an increase in lung volume and airway pressures. In contrast, application of external PEEP downstream from the flow-limiting segment of a patient with COPD typically does not affect lung volume or elastic recoil pressure, provided that the amount of external PEEP is less than auto-PEEP. One way of showing the independence of expiratory flow on downstream pressure in flow-limited patients is by construction of isovolume pressure-volume curves. The isovolume pressure-volume relationship expresses expiratory flow versus expiratory driving pressure (elastic recoil pressure minus mouth pressure), with measurements made at a constant lung volume. In the absence of flow limitation, expiratory flow decreases as driving pressure is reduced by application of external PEEP. In contrast, with flow limitation, a PEEP-induced reduction in driving pressure does not affect expiratory flow until a critical reduction in driving pressure is reached.

At the bedside, flow limitation may be assessed more conveniently by observing the change in airway pressures in response to a modest amount of external PEEP (e.g., 5-8 cm H₂O). Peak and plateau pressures normally increase by an amount roughly equal to applied PEEP, but in the presence of flow limitation they remain largely unaffected or rise by an amount that is only a small fraction of the applied PEEP. The effect of external PEEP in the setting of flow limitation has been likened to a waterfall, with the waterfall representing the flow-limiting segment and external PEEP the downstream pressure.

Using this analogy, it is apparent that at some point during the application of increasing amounts of external PEEP there will be a reduction in flow and a resultant increase in lung volume. Several studies have examined the effect of varying amounts of external PEEP in COPD. The results of these investigations consistently have shown that application of external PEEP less than auto-PEEP does not produce a significant increase in lung volume. Once external PEEP approximates auto-PEEP, however, lung volume increases. One study applied external PEEP that was 35%, 58%, and 86% of auto-PEEP. The two lower levels had no effect on lung volume, but at the highest level of PEEP, there was a significant increase in lung volume. A more recent study used external PEEP of 5, 10, and 15 cm H₂O and concluded that lung volume did not increase until the external PEEP-to-auto-PEEP ratio exceeded a critical level, above which there was an increase in lung volume and an associated reduction in cardiac index. The critical ratio of external PEEP-to-auto-PEEP was estimated to be approximately 0.75. In the waterfall model, it would seem that external PEEP should have no
effect unless it exceeds auto-PEEP. The fact that lung volume may increase when external PEEP is equal to or slightly less than auto-PEEP may be explained by inhomogeneity, with applied PEEP exceeding local end-expiratory pressure in certain regions of the lung. Based on the available literature, an external PEEP that is less than or equal to 75% of the baseline static auto-PEEP may be used during mechanical ventilation of patients with COPD without fear of worsening pulmonary hyperinflation.

Even though low-level external PEEP may do no harm in COPD, neither does it reduce lung volume. As such, there is no clear rationale for its use in patients with airflow obstruction. During patient-initiated cycles, however, use of external PEEP may enhance effective trigger sensitivity and thereby reduce the inspiratory effort required to initiate inspiration. This effect may improve patient comfort and possibly may expedite weaning in marginal patients.

Anecdotal reports have suggested that external PEEP may reduce lung volumes and airway pressures in acute, fulminant asthma. However, when the effect of PEEP was studied prospectively, it was found that lung volume was increased at a PEEP of 10 and 15 cm H\textsubscript{2}O and the increased lung volume was associated with a reduction in blood pressure. Auto-PEEP was not quantified in that study, and it is possible that a PEEP of 10 to 15 cm H\textsubscript{2}O exceeded the auto-PEEP for most patients, accounting for the adverse effects on lung volume. Alternatively, it is possible that the response to external PEEP could be different in asthma and COPD because of differences in the nature of flow limitation.

Although downstream pressure generally has been manipulated by the use of PEEP, the application of external negative pressure also can be used to show flow limitation. A recent study used a commercial vacuum cleaner attached to the exhalation tubing to create negative downstream pressure during expiration. In the absence of flow limitation, expiratory flow increased significantly when the vacuum was tuned on, but in flow-limited patients, the negative pressure had no effect on expiratory flow. These findings are entirely consistent with the concept of a flow-limiting "choke point" and the waterfall model.

**PULMONARY HYPERINFLATION**

During mechanical ventilation of patients with asthma and COPD, dynamic hyperinflation is initiated when \( V_T \) cannot be exhaled fully during the allotted \( T_E \). The same process of incomplete emptying is repeated with subsequent tidal breaths (Fig. 3 (Figure Not Available) ). An equilibrium is reached quickly, allowing the entire \( V_T \) to be exhaled because the increased elastic recoil pressure and a larger airway caliber at

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**Figure 3. (Figure Not Available) Dynamic hyperinflation (DHI).** A, Lung volume progressively increases until a new equilibrium is reached, at which point the entire tidal volume (\( V_T \)) is exhaled. Lung volume above functional residual capacity (FRC) is increased at end-expiration (\( V_{EE} = V_{DHI} \)) and at end-inspiration (\( V_{EI} \)). (Adapted from Tuxen DV: Permissive hypercapnic ventilation. Am J Respir Crit Care Med 150;870-875, 1994; with permission.) B, The \( V_{EI} \) can be measured by collecting the amount of gas exhaled during a prolonged apnea, and the \( V_{EE} \) (\( V_{DHI} \)), by subtracting \( V_T \) from \( V_{EI} \). (Adapted from Tuxen DV, Lane S: The effects of ventilatory pattern on hyperinflation, airway pressures, and circulation in mechanical ventilation of patients with severe airflow obstruction. Am Rev Respir Dis 136;872-879, 1987, with permission.)

the higher lung volume serve to enhance expiratory flow. Unfortunately, the increase in lung volume that allows \( V_T \) to be exhaled may lead to alveolar overdistention and increased risk of hypotension and barotrauma, two potentially life-threatening complications.

**Ventilatory Determinants of Dynamic Hyperinflation**

Tuxen and associates have used a prolonged apnea, beginning at end-inspiration and ending when no further gas can be exhaled passively, to help define the ventilatory determinants of dynamic hyperinflation in paralyzed patients with severe airflow obstruction. With this method, the total volume of gas exhaled during the 40 to 60 seconds of apnea represents the volume above functional residual capacity (FRC) at end-inspiration (\( V_{EI} \)). The volume above FRC at end-expiration (\( V_{EE} \)) is computed by subtracting \( V_T \) from \( V_{EI} \) (see Fig. 3 (Figure Not Available) ). \( V_{EE} \) represents the increase in lung volume caused by dynamic hyperinflation.
The principal factors that influence the degree of dynamic hyperinflation are expiratory flow, \( V_T \), and \( T_E \). The latter is influenced by cycling frequency and \( V_T \). When the effect of various combinations of \( V_T \) and \( V_V \) were evaluated eight patients with obstructive airway disease (four asthma and four COPD), the most important determinant of the magnitude of dynamic hyperinflation was \( V_T \) (Fig. 4). For a given \( V_V \), the severity of dynamic hyperinflation will be similar regardless of the specific combination of respiratory rate and \( V_T \); however, the end-inspiratory lung volume, of course, will be higher when a higher \( V_T \) and lower respiratory rate are used to achieve a given \( V_V \). Reasonable initial ventilator settings for asthma and COPD would be a \( V_T \) of 8 to 10 mL/kg and a respiratory rate of 12 to 14 breaths/minute. Subsequent adjustments in \( V_V \) should be made on the basis of arterial blood gas measurements and some means of monitoring for risk of complications associated with excessive hyperinflation (discussed subsequently).

Another factor that may influence the severity of dynamic hyperinflation is \( V_V \). Use of a high \( V_V \) shortens \( T_I \) and lengthens \( T_E \), thereby decreasing lung volume. Besides its effect on \( T_E \), another way in which a high \( V_V \) reduces dynamic hyperinflation is by increasing peak pressure because, with a higher peak pressure, a larger fraction of the set \( V_T \) is lost to the ventilator circuit, thereby decreasing effective \( V_T \). When highly compliant ventilator tubing is used, any reduction in dynamic hyperinflation following an increase in \( V_V \) may be related as much to a reduction in effective \( V_T \) as prolongation of \( T_E \).

The inspiratory waveform and the compliance of the ventilator circuit are additional factors that may affect dynamic hyperinflation. At the same maximal \( V_T \), \( T_I \) is shorter and \( T_E \) longer when the inspiratory waveform is square rather than decelerating. In addition, peak pressure will be higher and effective \( V_T \) lower, with a square wave of inspiratory flow. Use of low compliance tubing allows delivery of the same \( V_T \) at a lower set \( V_V \) on the ventilator. As a result, for the same \( V_T \), \( T_I \) will be shorter and \( T_E \) longer. Studies examined the effect of different \( V_V \) on gas exchange and dynamic hyperinflation in the setting of severe airflow obstruction. The authors of one study hypothesized that high \( V_V \) would worsen gas exchange because increased maldistribution of ventilation, but the opposite was observed. When \( V_V \) was increased from 40 to 100 L/minute, the calculated dead space-to-tidal volume (\( V_D/V_T \)) ratio fell by 23% and \( PaO_2 \) increased by 18%. The improvement is gas exchange at the higher \( V_V \) was attributed to longer \( T_E \). In the study by Tuxen and Lane, \( V_T \) profoundly influenced the severity of dynamic hyperinflation when \( V_V \) was very high (26 L/minute). At the lower \( V_V \) that would be more appropriate for patients with severe airflow obstruction, however, \( V_T \) had a relatively minor effect (see Fig. 4). Once \( T_E \) is at least several seconds in duration, flow rates by the end of expiration often are reduced markedly-i.e., the amount of gas exhaled per unit time is very low. Only a small amount of gas, therefore, will be exhaled in the relatively brief extension of \( T_E \) achievable through manipulation of \( V_V \). From a practical standpoint, a wide range of \( V_V \) is acceptable for managing patients with airflow obstruction.

Most ventilators display the inspiratory-to-expiratory (I:E) ratio on a breath-by-breath basis. It is a mistake to be overly focused on the I:E ratio in managing patients with severe airflow obstruction. When manipulating \( V_V \) and respiratory rate, it is \( T_E \), not the I:E ratio per se, that influences dynamic hyperinflation. By using a high \( V_V \), one can achieve an I:E ratio that appears favorable, even though \( T_E \) may be shortened (Table 1 (Table Not Available)).

**Complications**

The two most serious consequences of excessive hyperinflation are hypotension and barotrauma. Hypotension occurs most often immediately after intubation because of a combination of factors, including excessive hyperinflation, sedation, and pre-existing volume obstruction.
Another potential factor may be a lessening of sympathetic tone associated with rapid reductions in PaCO2. In a recent study, hypotension occurred in 25% of emergency intubations and the risk was highest in hypercapneic COPD. Initial management of postintubation hypotension includes aggressive volume resuscitation and an empiric reduction in Ve until the patient can be placed on a mechanical ventilator that allows more precise monitoring. Liberal use of intravenous fluids mitigates the hemodynamic effects of hyperinflation, but it is a mistake to permit excessive hyperinflation and combat the decrease in venous return with massive fluid infusion because that exposes the patient to ongoing risk of barotrauma. Hypotension also may be a manifestation of tension pneumothorax. In fact, the clinical presentation of excessive hyperinflation per se and tension pneumothorax may be remarkably similar in that both processes may produce hemodynamic collapse with increasing airway pressure. As a practical approach, the hemodynamic response to a 30-second to 40-second trial of apnea should be assessed before empiric chest tube insertion to determine whether hypotension will respond favorably to a reduction in lung volume. When chest catheters are required for a pneumothorax, they should be placed carefully and by blunt dissection because the grossly hyperinflated lung may be injured during cavalier insertion.

Assessing Risk of Complications
Based on a review of the available literature, Fiehl and Perret recently concluded that ventilator strategies that place an upper limit on lung volume or airway pressure appear to reduce the frequency of ventilator-related complications in mechanically ventilated patients with severe asthma. It is likely that the same would be true in the setting of severe COPD. Although the principle of avoiding excessive pulmonary hyperinflation is accepted widely, the most appropriate method of monitoring risk of hypotension and barotrauma is uncertain. The most commonly used strategy is to limit peak pressure to 50 cm H2O or less, a strategy that first was described more than a decade ago. When peak pressure is kept below 50 cm H2O, the incidence of ventilator-related complications is low. The primary problem with the use of peak pressure to assess risk of complications in patients with severe airflow obstruction is the profound influence of inspiratory flow resistive pressure on peak pressure. Flow resistive pressure highly depends on the size of the endotracheal tube and the V1, and unless auto-PEEP is generated or relieved, neither factor directly influences alveolar distention. Indeed, two studies involving mechanically ventilated patients with severe asthma reported that a high peak pressure, of itself, is not associated with increased risk of barotrauma or hypotension. Indices that more closely reflect the severity of pulmonary hyperinflation also may be used to monitor for risk of complications. These include the previously described volumetric measurements (Ve and Ve) and the measurement of plateau pressure or auto-PEEP. In an investigation of complications during mechanical ventilation of patients with severe asthma, William et al found Ve to be the best predictor of hypotension and barotrauma. Complications were not observed when the Ve remained less than 1.4 L (Fig. 5) (Figure Not Available). In this study, Ve correlated poorly with the end-inspiratory elastic recoil pressure (plateau pressure), and plateau pressure was not a reliable predictor of complications. The absence of an expected correlation between plateau pressure and Ve was attributed to varying respiratory system compliance but also, in part, could have resulted from airway closure. A major drawback to the routine use of Ve is that maintaining apnea for the 30 to 60 seconds required to complete exhalation,
in all likelihood, will require neuromuscular paralysis (discussed subsequently). Notwithstanding the previously cited results, a plateau pressure-based strategy for managing patients with severe asthma has been recommended. 18-42 Based entirely on theoretic considerations, a ventilator strategy that seeks to keep plateau pressure below 30 cm H\textsubscript{2}O has been recommended. In one series, a plateau pressure-based strategy was employed in the management of a large group of patients with severe asthma, and the incidence of barotrauma was very low. 42 Plateau pressure typically has been measured with a relatively brief (0.4 - 0.5 second) pause. 18-77 This does not provide sufficient time for equilibration of alveolar pressure in different lung units in the setting of severe airflow obstruction. Indeed, a true plateau in pressure may not be reached for several seconds. Although a prolonged airway occlusion may yield the most appropriate estimate of the average alveolar pressure at end-inspiration, the pressure recorded with a shorter pause is closer to the highest regional end-inspiratory alveolar pressure. Whatever pause duration is selected, it is important to maintain consistency in the measurement so that fluctuations in plateau pressure solely caused by variation in the duration of airway occlusion are not interpreted as representing changes in the degree of hyperinflation. Measurement of auto-PEEP provides a useful estimate of the severity of dynamic hyperinflation. Heterogeneity causes the dynamic method of measuring auto-PEEP to underestimate the average end-expiratory alveolar pressure assessed by the static method. Although the dynamic method may be useful for assessing the effect of auto-PEEP on work of breathing, static auto-PEEP is preferable for monitoring dynamic hyperinflation. Several important technical considerations are involved in the measurement of static auto-PEEP. Perhaps of greatest importance is that the patient must be completely relaxed. Tensing of abdominal expiratory muscles at end-expiration may cause measured auto-PEEP to greatly overestimate endexpiratory elastic recoil pressure. 56 It also is crucial that the airway occlusion be maintained for several seconds to avoid gross underestimation of average end-expiratory alveolar pressure. Use of a conventional distal airway occlusion may lead to a slight underestimation of end-expiratory alveolar pressure if a compliant ventilator circuit is used because of the relatively large amount of compressible volume. 34 A final consideration is that auto PEEP measures only the pressure in those lung units that are in communication with the airway at end-expiration. Extensive airway closure characterizes asthma that requires mechanical ventilator support. One study 36 suggested that the predominant component of total pulmonary hyperinflation in severe asthma is gas trapped behind occluded airways, rather than dynamic hyperinflation. Perhaps for that reason, patients occasionally have low measured auto-PEEP even when the chest roentgenogram and plateau pressure suggest considerable hyperinflation (Fig. 6 (Figure Not Available) ). 43 This may occur more often when T is prolonged, perhaps because the latter provides a greater opportunity for airway closure.

CONTROLLED HYPOVENTILATION WITH PERMISSIVE HYPERCAPNIA

One of the primary goals of ventilator management traditionally has been to achieve PaO\textsubscript{2} and PaCO\textsubscript{2} values within the physiologic range. Maintaining adequate oxygenation at an inspired oxygen fraction (FIO\textsubscript{2}) less than or equal to 0.5 in mechanically ventilated patients with airflow obstruction usually is easy to accomplish. Patients with asthma and, to a lesser extent, those with COPD, however, often are profoundly hypercapneic despite a V\textsubscript{E} that is normal or even increased. Hypercapnia at normal to increased V\textsubscript{E} is caused by increased Vd/Vt, and the latter has been shown to correlate positively with the severity of dynamic hyperinflation. 36 Attempts to lower PaCO\textsubscript{2} by further increasing V\textsubscript{E} often are frustrated by an additional increase in Vd/Vt, caused by worsening of pulmonary hyperinflation. Furthermore, the resultant increase in lung volume exposes the patient...
to greater risk of hemodynamic compromise and barotrauma. An alternative strategy for managing hypercapnia is to largely ignore it and focus instead on the prevention of complications caused by alveolar overdistention. \[8\] The technique of controlled hypoventilation with permissive hypercapnia has been used widely in patients with severe asthma and the outcome appears favorable. \[25\] The physiologic effects and potential consequences of permissive hypercapnia were discussed recently, in two authoritative reviews. \[76\] Hypercapnic acidosis generally is well tolerated, at least in patients who have neither intracranial pathology nor marked impairment in cardiac function. The presence of an intracerebral process that might be worsened by increased intracranial pressure is a contraindication to intentional hypoventilation. In the absence of clinical data, it seems reasonable to suggest that severe respiratory acidosis also should be avoided, if possible, when the patient has significant impairment in ventilator function. It is uncertain how low the pH may be allowed to go without incurring significant risk. Keeping pH greater than 7.15 to 7.2 commonly is recommended, but lower values may be acceptable. Buffering agents may be used in an attempt to increase pH, but that may require considerable amounts of buffer. \[25\] A slow infusion of bicarbonate has been used most often and appears safe. \[84\] \[59\] An alternative approach is to use tromethamine, an agent that (unlike sodium bicarbonate) does not produce carbon dioxide in the buffering process. \[9\] \[42\] In most instances, it probably makes little difference which buffer is used or, indeed, whether a buffer is given at all. Many patients with severe asthma are severely hypercapnic during the first few hours of mechanical ventilation but improve significantly during the subsequent 6 to 12 hours. \[46\] In otherwise stable patients, it may be appropriate to forego buffer therapy initially and follow serial blood gas measurements for a few hours to see whether acidosis improves.

**Sedation and Paralysis**

Maintenance of intentional hypoventilation despite the powerful stimulus of a low pH on respiratory drive may be problematic. Maintenance of controlled hypoventilation with permissive hypercapnia commonly has been accomplished with the combined use of sedation and neuromuscular-blocking agents. One of the most important sources of morbidity for asthmatic patients who undergo mechanical ventilation has been the development of residual muscle weakness, attributable to an acute myopathy. \[29\] \[39\] \[44\] Although the cause of the acute myopathy in severe asthma is understood incompletely, an association with the prolonged use of neuromuscular-blocking agents has been reported (Fig. 7) (Figure Not Available). Neuromuscular paralysis may potentiate myotoxicity from corticosteroids, \[19\] \[26\] the latter being a necessary component of the treatment protocol. It would be premature, however, to conclude that avoidance of neuromuscular blockade will eliminate the risk of myopathy. Cases of myopathy in asthmatic patients who received corticosteroids alone have been reported. \[41\] Furthermore, prolonged use of sedation, in doses large enough to suppress intrinsic muscle activity completely, might increase the risk of residual muscle weakness in corticosteroid-treated patients.

**Figure 7.** (Figure Not Available) The relationship between duration of paralysis and diffuse muscle weakness in acute asthma. Weakness was defined by a significant functional limitation and by a need for physical rehabilitation. \(P < 0.001\). (From Leatherman JW, Fleugel W, David W, et al: Diffuse muscle weakness in mechanically ventilated patients with severe asthma. Am J Respir Crit Care Med 153:1686-1690, 1996; with permission.)

Nonetheless, available information suggests that controlled hypoventilation should be accomplished with large doses of sedatives, rather than by paralysis, whenever possible. The sedative regimen used to achieve relaxation is largely a matter of personal preference. A combination of a benzodiazepine and a narcotic often has been used. A newer drug is propofol, a potent alkylphenol that has a short duration of action. One advantage of propofol in acute severe asthma is that some patients improve rather quickly, and propofol's short duration of action allows...
rapid awakening. Another possible advantage is that propofol may possess bronchodilator properties. A recent study found a reduction in $R_{\text{max}}$, $R_{\text{min}}$, and peak pressure following the administration of propofol to mechanically ventilated patients with COPD. Whether a beneficial effect on bronchomotor tone would be seen in patients already receiving bronchodilator therapy is unclear. When used alone or in combination with a narcotic, propofol may prove a useful, albeit costly, agent for ventilatory management of patients with severe airflow obstruction. When neuromuscular-blocking agents are required, the duration should be as brief as possible. It likely makes little difference which neuromuscular-blocking agent is used with regard to risk of myopathy, but vecuronium should not be used in patients with renal failure. If continuous paralysis is required, monitoring with a neuromuscular twitch stimulator is advisable. Use of intermittent paralysis has the advantage of forcing caregivers to repeatedly re-evaluate the need for ongoing paralysis and the adequacy of sedation.

**BRONCHODILATOR AND CORTICOSTEROID THERAPY**

Many studies have evaluated the use of bronchodilators during mechanical ventilation, and the subject was reviewed recently. In nearly all studies, the response to bronchodilator therapy was assessed in patients with COPD. Many of the principal findings may be reasonably extrapolated to patients with asthma. In one of the earlier studies, Gay et al assessed respiratory mechanics by the interrupter technique before and after the administration of nebulized metaproterenol. The beta-agonist lowered expiratory resistance, as evidenced by increased expiratory flow at the same elastic recoil pressure. Because of the effect on airway resistance, there also was a significant reduction in peak and plateau pressures and auto-PEEP. The authors suggested that the response of peak pressure may be a simple and useful method of evaluating bronchodilator responsiveness because it reflects bronchodilator-induced changes in dynamic hyperinflation and inspiratory resistance. Additional studies have shown a positive bronchodilator response to a nebulized beta-agonist during mechanical ventilation.

A major inconvenience is that some ventilators do not have the built-in capability for nebulization. The nebulizer must be placed in-line with the ventilator circuit, and the machine-delivered $V_T$ must be reduced to account for the additional volume during nebulization. Moreover, the nebulizer must be turned off and $V_T$ returned to the original setting before measuring airway occlusion pressures. Failure to interrupt the continuous flow of gas provided by the nebulizer before measuring airway occlusion pressures may lead to gross overestimations of plateau pressure and auto-PEEP. The response to administration of beta2 agonist via a metered-dose inhaler (MDI) also has been evaluated. A response to as few as three puffs of metaproterenol has been shown, but most studies used larger doses. Manthous et al assessed the change in flow resistive pressure (peak minus plateau pressure) after cumulative doses of 5, 15, and 30 puffs of albuterol (Fig. 8). To optimize drug delivery, the drug was delivered via a spacer placed in the inspiratory line fewer than 10 cm proximal to the Y piece. Flow resistive pressure fell by a mean of 4 cm H$_2$O after five puffs and by an additional 2 cm H$_2$O after a total of 15 puffs. The additional 15 puffs (total, 30) did not produce further benefit. Only one patient developed side effects. More recently, the change in respiratory mechanics during 1 hour in seven mechanically ventilated patients with COPD was evaluated following the administration of 10 puffs of albuterol, also given via a spacer in the inspiratory line. This dose of albuterol led to significant reductions in nearly all relevant parameters (including peak and plateau pressures, auto-PEEP, $R_{\text{max}}$, and $R_{\text{min}}$) without causing any change in heart rate or blood pressure. An effect was seen within 5 minutes of administration. Maximal response was reached by 15 minutes and persisted for the 1-hour period of evaluation. Current evidence suggests that use of an MDI is as effective as nebulization, and the former is less costly and more convenient. Although the optimal dose and frequency of administration...
are yet to be determined, it appears that use of a beta2 agonist via an MDI produces significant bronchodilation without side effects in most patients with obstructive airway disease. Dosing every 2 to 4 hours probably is safe and effective for patients with COPD, but hourly dosing may be considered in fulminant asthma. Higher doses may be needed in some cases, and individual titration to effect is appropriate. A reasonable initial approach to bronchodilator therapy of mechanically ventilated patients with asthma or COPD would be to administer 10 puffs of albuterol or equivalent. It is appropriate to adjust the dose and frequency of administration in an individual patient on the basis of the degree and duration of response. Although a variety of parameters may be assessed to determine effectiveness, the change in peak pressure may be as useful clinically as more detailed measurements. Of considerable importance is the method of delivery. Failure to use an optimal mode of delivery may preclude a beneficial response, even when up to 100 puffs are given. It is uncertain whether variation in Vl or inspiratory waveform, or use of an inspiratory pause, will influence the efficacy of bronchodilator therapy. Inhaled ipratropium and aminophylline have been shown to produce a bronchodilator response in mechanically ventilated patients with COPD. It is unclear whether they offer any additional benefit over monotherapy with a beta2 agonist. One study found that the combination of ipratropium and fenoterol was better than either agent alone, but submaximal doses of both agents were used. Again, use of an "n=1" trial to assess therapy in individual patients is appropriate.

Some centers have used an intense bronchodilator regimen for treating mechanically ventilated patients with severe asthma, including the combined use of a beta2 agonist and ipratropium by inhalation and a beta2 agonist and aminophylline intravenously. In nonintubated patients with severe asthma, beta2 agonists have equal or greater efficacy when given by inhalation rather than parenterally, and the inhaled route of delivery produces fewer side effects. Whether that also is true for mechanically ventilated patients is unknown. Given the potential toxicity of intravenous beta2 agonists, however, and the lack of evidence that they are more effective than inhaled agents, their routine use is not recommended. Apart from cardiac arrhythmias and hypokalemia, high doses of P2 agonists frequently produce lactic acidemia, a side effect that may be particularly undesirable when controlled hypoventilation already has resulted in acute respiratory acidosis. As with other side effects, lactic acidemia is more common with intravenous or frequent subcutaneous administration of beta-agonists but may be a rare complication of excessive nebulization. Corticosteroids should be given to all patients with severe asthma. Doses higher than the equivalent of 1 to 2 mg/kg/day of prednisone probably are unnecessary. Corticosteroids also may produce a modest benefit for patients with an acute exacerbation of COPD, but that is less certain. A recent study found a slight, but measurable, effect of corticosteroids on lung mechanics in mechanically ventilated patients with COPD. Empiric use of corticosteroids in acute exacerbations of COPD is reasonable. Given their uncertain benefit and the increased risk associated with prolonged therapy, however, treatment beyond 5 to 7 days may not be warranted.

OUTCOME

Short-term and long-term prognoses for mechanically ventilated patients with asthma and COPD are different, and these two causes of severe airflow obstruction must be considered separately. A recent review of the literature cited a mean in-hospital mortality rate of 13% for asthmatic patients who underwent mechanical ventilation for severe asthma. The mortality in various series ranged from 0% to 38%. Some deaths were attributable to profound cerebral anoxia before intubation, but others were caused by complications that occurred in the ICU, including barotrauma, profound hypotension without barotrauma, ventilator malfunction,
 accidental or premature extubation, and nosocomial infections. A recent review of the use of permissive hypercapnia in severe asthma concluded that this approach may be associated with an improved outcome.\(^2\) Whether because of the use of controlled hypoventilation or other factors, several centers have reported zero mortality among mechanically ventilated patients with asthma.\(^4\)\(^11\)\(^21\) Although the short-term prognosis is good, patients who have required mechanical ventilation for an episode of severe asthma are at significantly increased risk for future life-threatening episodes and should be managed accordingly. The prognosis for patients with COPD exacerbations who require mechanical ventilation is much worse. In a recent review of 11 studies, Weiss and Hudson\(^82\) found an average mortality of 43%. A recent analysis of the Acute Physiology and Chronic Health Evaluation III database revealed that 16% of patients died in the ICU and 32% of patients died before hospital discharge.\(^71\) Fewer than one half of patients survived for 1 year. Another study found that evidence of pulmonary infiltrates on the admission chest roentgenogram was a strong predictor of increased risk of death.\(^64\) The mortality rate in acute exacerbations of COPD recently was reported to be reduced by the early application of noninvasive mask ventilation.\(^10\)\(^12\) The benefit from noninvasive ventilation on mortality, in part, may be derived from the avoidance of endotracheal intubation and mechanical ventilation. If subsequent experience confirms the results of these early studies, the routine use of mask ventilation may lead to a significant reduction in the number of patients with COPD who die during a hospitalization for acute respiratory failure.

References


43. Leatherman JW, Ravenscraft SA: Low measured intrinsic positive end-expiratory pressure in mechanically ventilated patients with severe asthma: Hidden auto-PEEP. Crit Care Med 24:541-546, 1996


75. Tuxen DV: Detrimental effects of positive end-expiratory pressure during controlled mechanical ventilation of patients with severe airflow obstruction. Am Rev Respir Dis 140:5-9, 1989


77. Tuxen DV, Lane S: The effects of ventilatory pattern on hyperinflation, airway pressures, and circulation in mechanical ventilation of patients with severe airflow obstruction. Am Rev Respir Dis 136:872-879, 1987


