Mechanical ventilation is a mainstay of support for patients with respiratory failure. However, morbidity and mortality of patients supported by mechanical ventilators, especially those receiving prolonged support, remain very high. No doubt this reflects in large part the severity of the underlying disease. However, there has been increasing concern over the last several years that iatrogenic problems related to mechanical ventilatory support may be important contributing factors. Two such problems are patient ventilator dyssynchrony and alveolar overdistension.

Patient ventilator dyssynchrony is a phenomenon that occurs when the ventilator is being used to either assist or support a patient effort. When the ventilator’s response is not adequate to meet the flow demands of the spontaneous patient effort, high pressure loads are placed on the patient’s muscles that can substantially increase the oxygen cost of breathing and perhaps perpetuate muscle fatigue and failure (Fig 1). New ventilatory support strategies to better synchronize ventilator gas delivery to patient effort would therefore seem desirable.

Alveolar overdistension is a consequence of the high inflation pressures required by conventional mechanical ventilatory support strategies. While these high baseline and inflation pressures can be effective in recruiting and ventilating abnormal lung units, they also serve to overdistend the remaining normal alveoli (Fig 2). The classic manifestation of alveolar overdistension is lung rupture and extra-alveolar gas. However, less dramatic forms of barotrauma may also include direct alveolar damage which manifests itself as a pathologic picture closely resembling the adult respiratory distress syndrome (ARDS). Of concern is that this alveolar damage may occur at alveolar distending pressures much lower than that required for rupture. New ventilatory support strategies, therefore, to reduce alveolar pressures and consequent distension seem desirable.

The discussion that follows will focus on two strategies that are currently clinically available on modern adult mechanical ventilators and that specifically address the issues of synchrony and alveolar distension: the use of pressure-limited breaths instead of volume-cycled breaths, and the use of inspiratory time as an alternative to applied positive end-expiratory pressure (PEEP).

**Pressure-Limited versus Volume-Cycled Breaths**

In the adult, most positive pressure breaths are delivered with a flow-limited, volume-cycled strategy (Fig 3). If triggered by the machine, this type of breath is often called a volume-controlled breath, and if triggered by the patient, it is often called a volume-assisted breath. Once triggered, breath delivery is given according to a selected flow magnitude and pattern (usually sine, square, or decelerating). Because

**Figure 1.** Schematic depiction of airway and pleural pressure during a single inspiratory and expiratory cycle with a constant tidal volume. Depicted are a volume-cycled controlled (a) and volume-cycled assisted breath (b) designed to provide total support in a patient with abnormal impedances. Volume-assist synchrony is represented by solid pressure curves that are superimposable on the volume control breath after triggering. Volume assist dysynchrony is represented by the dashed curves. The area between the controlled and assisted curves represents work and pressure-time product imposed by the dysynchrony.
breath delivery ends when a volume target has been reached, these breaths are also referred to as volume-cycled. With a flow-limited, volume-cycled breath, pressure is the dependent variable and is the parameter which should be monitored and alarmed. These breaths form the basis of the modes known as volume-controlled ventilation (VCV), volume-assist control ventilation (VACV), intermittent mandatory ventilation (IMV), and synchronized IMV (SIMV).

Pressure-limited breaths are fundamentally different in their design. With these breaths, pressure, rather than flow, is the limiting or governing feature of breath delivery. Flow (and volume) are thus the dependent variables which will rise or fall depending on patient impedances and patient effort since the ventilator adjusts these variables to maintain the selected level of inspiratory pressure. Since the ventilator creates a "square wave" of pressure in the airway, the driving pressure between airway and alveolus progressively decreases as the lung fills. Thus, the flow pattern with pressure-limited breaths tends to be decelerating.

There are two basic types of pressure-limited breaths. The first can either be triggered by the ventilator (controlled) or by the patient (assisted), and the off signal (cycle) is a set inspiratory time. These breaths are commonly referred to as pressure-controlled or pressure-assisted breaths, respectively. The other type of pressure-limited breath is always triggered by the patient, and the off signal (cycle) is when...
the inspiratory flow has decreased to a set level below the initial inspiratory flow. This is referred to as a pressure-supported breath. Ventilatory modes that use pressure-limited breaths with the inspiratory time as the off signal include pressure-control ventilation (PCV), pressure-assist control ventilation (PACV), pressure-limited SIMV, and pressure-limited IMV. Ventilatory modes that use pressure-limited breaths with flow as the off signal include pressure support as a stand alone mode or pressure support interspersed with SIMV/IMV.

**Features of Volume Versus Pressure Breaths**
There are four important features of volume and pressure breaths that can be compared and contrasted: gas mixing (ventilation/perfusion—V/Q matching), assist synchrony, volume guarantees, and barotrauma risks.

**Gas Mixing and V/Q Matching:** There is surprisingly little data comparing these two breath types in terms of gas exchange. While pressure breaths that are coupled with long inspiratory times (see below) have been compared in a number of clinical studies to more conventional volume-cycled techniques, direct comparisons of a pressure-assist control and a volume-assist control for the same tidal volume and inspiratory time are surprisingly few. One can speculate that the rapid initial flows of a pressure breath will fill alveoli quicker and maintain a longer mean inflation pressure. However, only one study has suggested that these effects indeed may improve gas exchange, and thus, more work is needed to confirm this.

**Assist Synchrony:** There are data, both theoretic and clinical, suggesting that the rapid initial flows and the subsequent adjustable flows of the pressure-limited breath respond better to patient effort during patient-triggered breaths than the fixed flows of the flow-limited volume-cycled breath. Several studies have reported that the pressure support mode is more “comfortable,” and indeed, the better arterial Po2 that is sometimes ascribed to the pressure breath may reflect a lower muscle oxygen consumption as a consequence of better patient-ventilator synchrony. A feature that is appearing on some of the newer ventilators is the capability to adjust the initial flows of the pressure breath. Evidence exists that in some patients, the capability to adjust this initial flow may further enhance the patient’s ability to synchronize spontaneous breathing efforts with ventilator support.

**Volume Guarantees:** While the pressure-limited breath guarantees a certain airway pressure, the flow-limited, volume-cycled breath guarantees a tidal volume and minute ventilation (Fig. 3). Patients with unreliable respiratory drives and/or unstable lung mechanics will thus always be guaranteed a certain minute ventilation with volume-based support as opposed to pressure-based support.

**Barotrauma Risk:** There are no studies comparing the incidence of iatrogenic lung injury using either of these breath types. However, from theoretic considerations, it may be that there is really no difference if the same tidal volume and inspiratory time are used. That is because with volume and timing parameters held constant, the maximum alveolar distension using either breath will be identical. Thus, although the peak airway pressures are lower for a pressure breath than a volume breath (because of the decelerating flow pattern), the peak alveolar pressures (which relate more to alveolar distension and lung injury) are comparable. On the other hand, the very rapid initial flows of the pressure breath may have theoretically different effects of regional filling patterns, and thus, the barotrauma risk due to “shearing” may be different using pressure- versus volume-based breaths. However, no data exist to either support or refute this hypothesis.

In summary, pressure breaths offer potential benefits in terms of gas mixing and clearly improve patient ventilator synchrony. On the other hand, the volume breath offers the guaranteed volume. The logical next step in ventilator breath design would appear to be some combination of these two. The most straightforward approach would be a breath design that would allow the clinician to select the variable flows and pressure limit of the pressure breath at the beginning of the breath and thus provide a certain minimal inspiratory flow and inspiratory time such that a volume guarantee exists at the end of the breath. A less direct approach to combining features of pressure- and volume-based breaths would be servo mechanisms that adjust the level of pressure based upon previous breath volume delivery. Both of these approaches are currently under investigation.

**Applications of Volume Versus Pressure-Based Breaths During Total and Partial Ventilatory Support**
Total mechanical ventilatory support can be supplied by VCV, VACV, PCV, PACV, and even pressure support if the pressure support level is high enough (sufficient to give tidal volumes comparable to other modes of 10 to 12 mL/kg). Total mechanical ventilatory support is designed to take virtually all of the load off a patient’s ventilatory muscles while supplying adequate O2 and CO2 transfer. As noted above, there are differences between volume- and pressure-based approaches that may be important. However, comparison of patient outcome using these two basic strategies has not been done. Decisions as to which approach to use therefore must be based on physiologic considerations, clinical assessment, and experience. While volume-based modes have clearly “stood the test of time” in applying reasonable ventilatory support, there are enough theoretic benefits to the pressure-based approaches that they should be considered as an alternative to volume-cycled ventilation for total support, especially if patient-ventilator dysynchrony exists with the volume breaths. As noted above, future approaches to total ventilatory support may utilize positive pressure breaths that have combined features of both pressure and volume. Under these conditions, however, the breath would be set to a substantial tidal volume and the pressure level would be adjusted to assure proper synchrony with the assisted breaths.

Partial mechanical ventilatory support can range from very high levels of support to aggressive reductions in the level of support (weaning). Partial support always requires some patient contribution to the work of breathing which, by definition, means that less ventilatory pressures are being used. Partial support using volume-based modes utilize intermittent volume breaths as IMV or SIMV. Partial support using pressure-based modes are supplied as pressure support. The IMV approaches offer the advantages of a guaranteed volume but pressure support offers the advantage of...
both improved patient synchrony and a lower maximal alveolar distending pressure. The type of work a patient does is also different using these two approaches. With IMV, patient work is designed to be performed only during spontaneous breaths. The work during these types of breaths is characterized by a high pressure-low volume form of work which may be less efficient and less comfortable than the more normal pressure volume configuration of the work that the patient performs with pressure support.\textsuperscript{6,10-13} Very little data exist comparing these different approaches to partial support in terms of ultimate outcome. Thus, the decision to use one versus the other again would be based upon physiologic principles, clinical judgement, and experience.

Monitoring of partial support using volume-based approaches requires assessment both of airway pressures (recall that pressure is the dependent variable) as well as the adequacy of ventilation since the patient is required to do some level of spontaneous breathing. With partial support through pressure support, monitoring of delivered volume is critical since it is the dependent variable. It should be noted, however, that there are two ways to guarantee a certain volume delivery with pressure support. The first is to couple it with IMV. This approach, however, forces clinicians to now deal with two support modes and may disrupt the synchrony advantages. It also requires that the high pressure volume breath be delivered intermittently. An alternative in the future is the combination breath noted above which would put a volume "safety net" under the pressure support.

**Inspiratory Time Versus PEEP**

**Rationale**

Alveolar collapse is a common feature of many forms of respiratory failure. This collapse is a consequence of alveolar flooding, surfactant loss, and increased interstitial stiffening.\textsuperscript{16-18} Recruiting and stabilizing these alveoli is thus a major goal of respiratory support in order to improve VQ matching, reduce shunts, and maintain adequate oxygen content in the arterial blood. Positive end-expiratory pressure has clearly proven itself as a technique to provide alveolar recruitment and stabilization.\textsuperscript{19-21} The concept is that expiratory pressure prevents the alveoli from collapsing during expiration. Gas thus remains in the alveoli throughout the respiratory cycle, and the inspiratory work and alveolar filling characteristics of subsequent breaths are more advantageous. A necessary consequence of applied PEEP, however, is that all inflation pressures go up. Thus, for a constant tidal volume and inspiratory time, a given increase in PEEP often necessitates a comparable increase in maximal alveolar pressures. Because of the concerns noted above regarding alveolar overdistension, it would seem that the ideal level of PEEP is the minimal level which prevents collapse.

In managing patients in respiratory failure, PEEP titration should be done with these principles in mind. Unfortunately, however, respiratory failure is usually a heterogenous disease, and thus, what is a useful level of PEEP in one lung region may result in overdistension in another or be suboptimal in yet another (Fig 2). An alternate strategy to applied PEEP is the use of a longer inspiratory time.\textsuperscript{11,22,23} This should be considered when the level of applied PEEP has reached a level that alveolar overdistension in more normal units is developing (eg, 40 cm H\textsubscript{2}O peak alveolar pressures). The longer inspiratory time permits a longer period of fresh gas exposure to the alveolar capillary and provides a longer mixing time for fresh gas and the airway to mix with that in the alveoli. As long as expiration time is adequate for a return to baseline volume, this longer inspiratory time in itself will thus produce an elevation in mean pressure (and consequent improved oxygenation) without the necessary rise in peak pressure and alveolar distension imposed by applied PEEP. Note, however, that if inspiratory time is lengthened to the point that exhalation to baseline lung volume is not permitted, air trapping will occur creating an "intrinsic" PEEP.\textsuperscript{14,25} This intrinsic PEEP will have several

![Figure 4. Intrinsic PEEP (PEEP) during volume-controlled ventilation with an inspiratory hold. In the upper panel, airway pressure (solid lines) and alveolar pressure (dashed lines) are plotted; in the middle panel, flow is plotted, and in the bottom panel, volume is plotted. Volume controlled breaths are delivered either with (A) or without (B) inspiratory holds. In curves A, expiratory flow = 0 before next inspiration; there is no air trapping and PEEP, \(=0\). In curves B, expiratory flow >0 before next inspiration; there is air trapping in PEEP, >0. Note that PEEP, in volume control ventilation raises peak pressure but keeps delivered volume constant (compare Fig 5). Reprinted with permission.\textsuperscript{6}](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21674/ on 06/26/2017)
effects. First, it will elevate the baseline pressures in the alveoli (just like applied PEEP) but without a concomitant rise in observed airway expiratory pressures. Second, the development of intrinsic PEEP affects the delivery of mechanical ventilatory support (Fig 4 and 5).* Briefly, if one is using volume-cycled ventilation, the development of intrinsic PEEP, while not appearing in the expiratory pressures, will appear as an elevation in peak airway and peak plateau pressures (Fig 4). Conversely with pressure ventilation, the development of intrinsic PEEP will reduce the delivered volumes (Fig 5). With either form of ventilatory support, intrinsic PEEP is characterized by an abrupt termination in an expiratory flow signal before baseline is reached (Fig 4 and 5—flow signal). Third, intrinsic PEEP can produce an inspiratory threshold load which increases patient work to trigger a ventilator's demand system.

In summary, longer inspiratory times have two distinct phases with two distinct mechanisms of action. Longer inspiratory times without air trapping may improve V/Q matching by allowing longer mixing time between conducting airways, alveoli, and capillary. This is accomplished without a consequent increase in peak alveolar pressures or distension. Longer inspiratory times that do produce air trapping can create an “intrinsic PEEP” effect in the lung in the alveoli. This probably has an effect similar to applied PEEP at the alveolar level but is more difficult to monitor and will result in important changes in the pattern of delivered ventilatory support.

Application

A reasonable stepwise approach to oxygenation support that utilizes both pressure breaths and inspiratory time would be as follows:

1) Applied PEEP is given to assure that the bulk of alveoli is being prevented from collapsing. This can be verified through assessment of critical closing pressures from a pressure volume graphic or assessment of compliance. If oxygenation is not adequate, further increases in applied PEEP can be used until peak alveolar pressures are approaching 40 cm H2O.

2) At this point, pressure breaths should be considered as an alternative to volume breaths (if they are not already being used).

3) Inspiratory time can now be lengthened watching the flow graphics and the delivered pressures and volumes as described above to assess for air trapping. Inspiratory times are increased in a gradual fashion monitoring oxygenation goals (see below) and avoiding air trapping.

4) If oxygenation levels are still not reached and inspiratory time has been pushed to the point of air trapping, then one is forced to choose between two alternatives: apply more PEEP, or continue lengthening inspiratory time to produce intrinsic PEEP. Our approach has been to use applied PEEP to carry out this last step rather than resorting to longer inspiratory times and intrinsic PEEP. Our rationale is that there are no data showing that intrinsic PEEP has any advantages over applied PEEP and that extrinsic or applied PEEP is far easier to monitor and is more predictable in terms of its effects on ventilator patient interactions.

The oxygenation goals being strived for are beyond the scope of this discussion, but generally under these desperate situations, an index of oxygen delivery (rather than just the Po2) is appropriate. This is because other factors such as hemoglobin and cardiac output might be manipulated in an attempt to minimize the need for FlO2, ventilatory pressures, or both.

A final point is that as the inspiratory and expiratory ratio starts to exceed 1:1, patients tend to become more uncomfortable. Adequate sedation and/or paralysis is important at this point not only for patient comfort but to reduce unnecessary patient agitation and consequent oxygen consumption, which in turn will lower the mixed venous Po2 and make arterial oxygenation that much more difficult.

Conclusions

Respiratory failure still is associated with a very high

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* Figure 5. PEEP, during pressure-controlled ventilation with long inspiratory time (ti). Variables plotted are similar to Figure 1 except that curves A have short ti and long expiratory time (te) and curves B have long ti and short te. In curves A, expiratory flow = 0 before next inspiration; there is no air trapping and PEEP = 0. In curves B, expiratory flow > 0 before next inspiration; there is air trapping and PEEP, > 0. Note that PEEP, in pressure control ventilation maintains peak pressure but lowers delivered volume (compare Fig 4). Re-printed with permission.
morbidity and mortality. The role of positive pressure mechanical ventilatory support may be an important iatrogenic factor in worsening this outcome. While a number of new ventilatory devices and techniques (eg, high-frequency ventilation, extracorporeal membrane oxygenation, etc) are being developed to address these issues, none is ready for widespread clinical application. Thus, new strategies that utilize features that are currently available on traditional devices to reduce iatrogenic problems would seem to be important to consider. Two such approaches are the use of pressure-limited breaths and the use of longer inspiratory times. First, pressure-limited breaths may improve gas mixing, and they clearly improve patient-ventilator synchrony. These breaths appear reasonable for both total and partial support of a patient, although the lack of a volume guarantee must be considered. The capability to manipulate the initial slope of the pressure breath to improve synchrony and the addition of a volume guarantee to the pressure breath (the combination pressure-volume breath) should broaden the application of the pressure breath. Second, as an alternative to applied PEEP with its consequent necessary elevations in peak alveolar pressure and distension, the use of longer inspiratory time may be an alternative. This strategy has two phases that need to be considered separately: the phase of prolonged alveolar mixing without air trapping and the phase of air trapping and intrinsic PEEP. The development of intrinsic PEEP may offer no benefits over further increases in applied PEEP and can be considerably more difficult to monitor. Clinical studies validating these strategies in terms of outcome are lacking. Nevertheless, physiologic principles and clinical judgment can justify careful applications.

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