Pressure-control ventilation in managing acute respiratory distress syndrome

The search for mechanical ventilation strategies that enhance lung-protection in patients with acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) has focused interest on pressure-regulated modes that prevent high airway pressure (Paw), which is believed to be injurious to the lungs. Pressure-control ventilation (PCV) is the most common pressure-regulated mode, wherein the ventilator actively monitors and adjusts the gas flow to maintain Paw as a square wave during inspiration. This results in a characteristic decreasing ramp flow pattern that may result in improved pulmonary mechanics, gas exchange and patient work of breathing. A literature review of 17 prospective clinical trials of PCV and other pressure-regulated modes in patients with ARDS/ALI has produced mixed results. There is some evidence that pressure-regulated modes may effect modest improvements in respiratory system compliance, oxygenation, dead-space fraction and patient work of breathing. However, nearly all studies were done with a traditional-sized tidal volume which may have influenced the effects of the decreasing ramp flow pattern. Therefore, the extension of these results to the era of low tidal volume ventilation remains uncertain. In the only large, multicentred, randomised, controlled trial of patients with ARDS/ALI, PCV was not shown to have improved morbidity or mortality compared to volume control ventilation.

Acute respiratory distress syndrome (ARDS) is characterised by decreased compliance, pulmonary oxygen transfer dysfunction with elevated dead-space fraction and elevated carbon dioxide production; these require increased minute ventilation to maintain adequate pulmonary gas exchange. Historically, these characteristics prompted clinicians to use high tidal volumes (VT) and airway pressures (Paw) to maintain minute ventilation. However, over the past 30 years it has been established that high-volume, high-pressure mechanical ventilation in the setting of acute lung injury (ALI) exacerbates lung inflammation and directly contributes to mortality. The search for mechanical ventilation strategies that enhance lung-protection has focused interest on pressure-regulated modes, such as pressure control ventilation (PCV), that prevent high Paw, which is believed to be injurious to the lungs. Unfortunately, misconceptions exist regarding what PCV can offer clinicians in the management of ARDS. This review will discuss the theory behind PCV and review the clinical evidence regarding its use in patients with ARDS and ALI. Similar modes such as pressure support ventilation (PSV), volume-assured pressure support ventilation (VAPSV) and pressure-regulated volume control (PRVC) will also be discussed. Because of their inherent complexity, other pressure-regulated modes such as airway pressure-release ventilation (APRV), proportional-assist ventilation (PAV) and adaptive support ventilation (ASV) will be omitted from this review.

PCV is classified as a pressure-regulated mode of ventilation: those in which the ventilator actively monitors and adjusts inspiratory gas flow to maintain Paw as a square wave. Titrating inspiratory flow rate (\( V_i \)) to maintain Paw as a square wave results in a variable, decreasing ramp flow waveform (Figure 1A). Peak \( V_i \) occurs as inspiration commences, so that the flow-resistive properties of the patient-ventilator system can be utilised to create a ‘pressure-step’ that approaches the peak Paw target (\( Paw = V_i \times \text{resistance} \)). Because the initial \( V_i \) may be very high (>100 L/min when a traditional-sized VT is used), lung volume and alveolar pressure rise rapidly in consequence. To maintain Paw as square-wave \( V_i \) then must ‘taper off’ at a pace that is determined by the respiratory system compliance (Cr). A decreasing ramp flow pattern can also be created during volume control ventilation (VCV). The difference is that both the peak \( V_i \) and the rate at which flow tapers-off are fixed and independent of patient effort, Cr or respiratory system resistance (Rrs).

Figure 1. Scalar waveforms of gas flow, tidal volume (Vol), and airway pressure (Paw) during pressure control ventilation under various mechanical conditions. Panel A: Reference condition of relatively high peak flow and rapid tapering-off in the flow waveform. The slope of Paw rise is more rapid than occurs during volume ventilation with a square wave flow waveform. Panel B: Increased resistance is characterised by a low peak flow and a gradually decreasing slope in flow. The high resistance results in a rapid pressure-step to the peak Paw and often produces oscillations in the pressure tracing giving it a jagged appearance. Most importantly, there is an increase in the pressure gradient between peak and plateau Paw. Panel C: Severely decreased compliance is characterised by a pronounced, very rapid tapering-off in gas flow and prolongation of the end-inspiratory plateau. Typically, the rate-rise in Paw to the plateau occurs more rapidly.
PCV is an attractive means of achieving lung-protective ventilation as V\textsubscript{T} is delivered at the lowest possible Paw. However, regulating \dot{V} to limit Paw also limits the work output of the ventilator. As a consequence, an acute deterioration in R\textsubscript{rs} or Crs will decrease V\textsubscript{T} and minute ventilation so that arterial blood gases may deteriorate acutely. Thus, appropriate alarm settings for low minute ventilation, low V\textsubscript{T} and oxygen saturation - along with vigilant monitoring in a critical care setting - are prerequisites for using any pressure-regulated mode. An algorithm for determining the cause of decreased V\textsubscript{T} during PCV is given in Table 1 and is illustrated in Figures 1B and 1C.

A brief description of other modes discussed in this review is required. PSV has the same Paw and gas flow waveforms as PCV; the only difference is the criteria used to commence and terminate inspiration. PSV requires patient effort to trigger inspiration. The ventilator cycles over to expiration when inspiratory flow decreases to a specified threshold. There is neither a mandatory back-up rate nor a set inspiratory time (Ti); thus this mode is contraindicated in patients with insufficient respiratory drive.

VAPS\textsubscript{V} is a form of PSV whereby dual algorithms regulate inspiratory flow to achieve both a target Paw and a minimum V\textsubscript{T}. VAPS\textsubscript{V} constitutes a relatively new form of mechanical ventilation known as ‘dual mode control’. Although the initial flow pattern is the same as PSV, if the ventilator determines that the minimum V\textsubscript{T} target will not be achieved, then the flow pattern changes over to a square

**THEORETICAL BENEFITS**

The theoretical advantages of PCV include improved pulmonary mechanics, gas exchange and patient work of breathing (WOB). For any delivered V\textsubscript{T}, peak Paw is lower during PCV compared to VCV delivered with a square-wave flow pattern. During PCV, the flow-resistive forces are highest in early inspiration (when the elastic forces opposing ventilation are low) and lowest in late inspiration (when the elastic forces are highest). This is why the peak Paw during PCV approaches the end-inspiratory plateau pressure (Pplat) measured during VCV. Therefore, PCV has the ‘effective dynamic compliance’ of the respiratory system (VT + (Peak Paw - End Expiratory Pressure)) is reduced. However, this does not necessarily translate into a reduced risk of barotrauma, or ventilator-induced lung injury. This is because the artificial airway is the major resistance in the patient-ventilator system; monitoring pressure proximal to the artificial airway reveals little about the degree and distribution of stress in the lung parenchyma.

Maximal stress in the lung parenchyma is determined by the end-inspiratory lung volume (V\textsubscript{T} + functional residual capacity) and the elastic/viscoelastic properties of the lung tissue. The maximal inspiratory lung pressure is referred to as ‘P-1’, or the instantaneous drop in Paw at the moment of zero flow; it is used to calculate the dynamic Crs (Figure 2). Unfortunately, P-1 cannot be determined with clinical bedside monitoring. Therefore, the best clinical indicator of maximal lung stress during mechanical ventilation is Pplat, which is used to determine static Crs (V\textsubscript{T} + (Pplat - PEEP)).

The mechanisms by which PCV improves pulmonary gas exchange are increased alveolar residence time (from more rapid volume delivery) and a more even distribution of V\textsubscript{T}, which improves ventilation-perfusion matching. Further-more, PCV also may lessen patient WOB, which in turn may reduce global oxygen consumption and increase mixed venous oxygen tension.
CLINICAL EVIDENCE

Fifteen clinical studies have compared respiratory system mechanics, pulmonary gas exchange, haemodynamics, outcome and work of breathing between VCV and PCV.8,10,16,18,19 or other forms of pressure-regulated ventilation in patients with ARDS/ALI,17,20-25 or those with various forms of acute haemoxymic respiratory failure including ARDS/ALI. Two additional studies prospectively compared features of pressure-regulated ventilation in patients with acute hypoxaemic respiratory failure including ARDS/ALI.26,27

Respiratory system mechanics

When compared to the square-wave flow pattern of VCV, the decreasing ramp flow pattern consistently results in a lower peak Paw,8,10,11,13,21,22,24 and increased effective dynamic compliance.11,21 When VT was held constant and showed no significant differences in either Pplat or static Crs between flow patterns,13,15,19 Lessard,12 who also measured oesophageal pressure, was unable to detect a difference in static lung compliance. In contrast, Al-Saady and Bennett found that the decreasing ramp pattern yielded a significantly lower P1 and Pplat and a higher dynamic and static Crs.10 Rappaport found that static Crs improved more rapidly with PCV compared to VCV (2.86 ±1.75 vs. -1.45 ±0.65 mL/cmH2O/day respectively).14 Yet another larger study failed to show any improvement in Crs or Pplat.19 The two studies that directly compared the decreasing ramp flow pattern of PCV to the decreasing ramp flow pattern of VCV found no significant differences in peak Paw, Pplat or static Crs.12,15

Most studies reported an insignificant but consistent increase in mean Paw of approximately 1 cmH2O with the decreasing ramp flow pattern compared to VCV with a square wave flow pattern.10,11,13,16,21 Only Davis reported a substantially higher mean Paw (3-4 cm H2O) with the decreasing ramp flow pattern,21 which may reflect a bias in Paw measurements peculiar to the Vleolar ventilator.12 The modest increase in mean Paw with the decreasing ramp flow pattern explains why neither clinical nor animal studies reported changes in haemodynamic function.9,11,11,12,21

Gas exchange

PCV may improve pulmonary gas exchange as a result of increased alveolar residence time (from the more rapid volume delivery) or a more even distribution of VT that improves ventilation-perfusion matching.9 Only five studies20,11,13,16,21 have included reports of significant improvements in either PaO2, intrapulmonary shunt or dead-space fraction with the decreasing ramp flow pattern. In one study11 the presentation was non-randomised while in another,21 the increased PaO2 coincided with a substantially higher VT, making attribution to the flow pattern problematic. Interestingly, in two studies, the improvement in pulmonary gas exchange coincided with significant improvements in both dynamic and static Crs (suggesting more even distribution of ventilation and/or lung recruitment).10,15 Nonetheless, the magnitude of improvement in pulmonary gas exchange reported in the positive studies was modest.

Morbidity and mortality

Only one multi-centred, randomised, controlled trial has examined the impact of PCV and VCV on patient outcomes using a lung-protective ventilation strategy.19 Although hospital mortality was significantly greater in patients managed with VCV compared to PCV (69 vs. 49% respectively; p = 0.02), patients at risk for renal failure at study entry, and those with shock as a risk factor for ARDS, were disproportionately randomised to VCV. Multivariate logistic regression analysis failed to identify ventilator mode as an independent risk factor for mortality. Neither intensive care unit nor hospital length of stay was different between treatment groups.

Work of breathing and patient-ventilator synchrony

Patients with severe respiratory failure often exhibit a highly variable respiratory pattern wherein there is considerable breath-to-breath variation in both peak V and Vt demand. This can vex even the most skilled clinician attempting to adjust the ventilator to improve patient synchrony and WOB. Patients often appear more synchronous with PCV because the ventilator automatically titrates V to keep Paw constant throughout inspiration. Therefore, when negative muscle pressure from patient effort is transmitted to the ventilator circuit, causing a transient decrease in Paw, the ventilator responds rapidly with increased gas flow to return Paw to its target.8 Thus, during patient-triggered PCV the peak V, the flow pattern and the Vt are determined partly by the magnitude and duration of patient effort.8,28 In contrast, during patient-triggered VCV, transmission of negative muscle pressure to the circuit causes the ventilator to increase inspiratory valve resistance to prevent VT ‘overshoot’. This results in an increased imposed WOB that is proportional to patient effort.20,29 Evidence from small clinical trials of PCV8 and VAPSV,21,22 carried out with a traditional-sized Vt in patients with ARDS/ALI, suggest WOB and patient effort are reduced compared to the VCV mode. In two studies this was apparently due to increased peak V,3,22 while in the other study the ability to augment Vt probably contributed to the reduced WOB.21 Yet in the era of lung-protective ventilation, when both Vt and end-inspiratory transpulmonary pressure must be curtailed, pressure-regulated modes may not afford sufficient lung-protection. Attempts to titrate the inspiratory pressure level downward to limit Vt delivery may in fact negate the beneficial effects of pressure-regulated modes by reducing peak V. In addition, both lung model20,29 and clinical30 studies demonstrate that limiting the ventilator-delivered VT increases patient WOB independent of peak V. Furthermore, in most previous studies the peak V during VCV was low (45-55 L/min) relative to the levels commonly used in the clinical setting.4,16,22,23 MacIntyre found that when pressure-regulated ventilation was compared to VCV with a high peak (approximately 75 L/min) patient effort was not significantly different.25 These concerns were addressed recently in a study18 comparing PCV and PRVC to VCV with a peak V of 75 L/min in patients ventilated according to the ARDS Network low-Vt protocol.17 Neither PCV nor PRVC offered an advantage in terms of decreased WOB compared to VCV. Furthermore, there was a substantial violation in Vt (1.5-2 mL/kg) in approximately 40% of patients. Pressure-regulated modes generally were ineffective in reducing WOB because inspiratory pressures had to be reduced to constrain Vt delivery, which in turn reduced peak V to approximately 60 L/min.18

During PCV and PRVC asynchrony commonly manifested as prolonged active expiration that extended into
Scalar waveforms of gas flow, tidal volume (VT), airway pressure (Paw) and oesophageal pressure (Pes) demonstrating patient-ventilator asynchrony during lung-protective ventilation with the pressure control mode. Note that the inspiratory gas flow pattern during the first three breaths is an ascending ramp rather than a decreasing ramp. This is a common manifestation of patient-ventilator asynchrony during pressure-regulated lung-protective ventilation. Reproduced from Kallet with permission.

Because patients stiffened their chest wall as inspiration commenced, the ventilator flow rapidly tapered off. However, within the same breath, patients subsequently made inspiratory efforts that paradoxically caused the flow pattern to transform from a descending ramp into an ascending ramp, thus negating the beneficial effects of a decreasing ramp flow pattern on WOB (Figure 3). During PRVC, increased patient effort caused the ventilator-delivered VT to exceed the pre-set target, along with a progressive decrease in peak Paw and peak V. This reflected the ventilator’s attempt to reduce VT towards the target and resulted in a corresponding increase in WOB. Similarly, WOB was increased during VSV in patients with ARDS when patient VT demand exceeded the target VT. Therefore, clinicians must be vigilant when using pressure-regulated modes for lung-protective ventilation as the anticipated benefits may dissipate in the face of patient-ventilator asynchrony.

Another feature of pressure-regulated ventilation is the ability to control the rate rise in Paw to its target plateau. This is referred to as ‘pressure-slope’ or ‘pressure risetime’ (PRT). Although originally developed for PSV, PRT is available on other pressure-regulated modes. At high levels of PS, the V at which the ventilator cycles to expiration (typically 25% of peak V) may be higher than a patient with inspiratory muscle weakness can generate as a result, mechanical inspiration can be terminated prematurely. PRT regulates the rate rise in airway pressure by limiting the rise to peak V. As a consequence T1 increases both by delaying and decreasing peak V, thereby lowering the threshold of VT needed to terminate inspiration. As PRT increases beyond 0.2 sec, the inspiratory flow waveform also changes from a decreasing ramp to a sine wave and ventilator T1 increases markedly. Therefore, high levels of both PRT and PS may lead to air-trapping and asynchrony. Furthermore, patient WOB may increase from decreased peak V and flow waveform mismatching. In patients with ARDS, increased PRT during PSV decreases peak V and increases WOB. Although Ti is not affected when PRT is used during PCV or PRVC, the effects on peak V, flow waveform and WOB are likely to be the same as with PSV. Anecdotally, we have found PRT useful in patients who require a pressure-regulated mode because of a highly variable inspiratory flow demand, but in whom the initial high V induces coughing. Thus, PRT allows clinicians more flexibility to fine-tune the inspiratory flow pattern.

In conclusion, PCV does not appear to improve morbidity or mortality in patients with ARDS/ALI compared to VCV. There is inconsistent clinical evidence suggesting that pressure-regulated modes may modestly improve end-inspiratory lung stress and pulmonary gas exchange function. Yet, the reported beneficial effects of pressure-regulated modes come from studies in which a traditional-sized VT was used. Therefore, the salutary effects of these modes on lung mechanics and gas exchange may not necessarily extend to those of low VT ventilation. Pressure-regulated modes do not reduce WOB better than VCV when allow VT is used, because a lower peak Paw is needed to constrain VT which reduces peak V as well. Yet allowing VT to vary with patient effort during PCV and PRVC may produce occult high VT-high [Author: is the repetition of ‘high’ intended here?] transpulmonary pressure ventilation that in theory may promote ventilator-induced lung injury. This potential problem represents an important aspect of ARDS/ALI management that should be a high priority for future research.

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