



# Controlled Mechanical Ventilation: Modes and Monitoring

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Controlled mechanical ventilation (CMV) occurs when the ventilator controls, during the inspiratory phase, one variable from the equation of motion (Eq. 4.1): either flow ( $\dot{V}$ ) or airway pressure ( $P_{aw}$ ). The reason one can only control one variable (either  $\dot{V}$  or  $P_{aw}$ ) at a time is that all the others are given constants ( $R_{rs}$  and  $C_{rs}$  are intrinsic properties of the respiratory system), derived variables (volume is the integration of flow), or determined by an independent control system (inspiratory and expiratory muscle pressure).

$$P_{aw}(t) = V(t) / C_{rs} + R_{rs} \times \dot{V}(t) + \text{PEEP} - P_{mus}(t) \quad (4.1)$$

where  $V(t)$  is the instantaneous volume above end-expiratory volume, PEEP is the end-expiratory pressure, and  $P_{mus}$  represents the pressure generated by inspiratory and expiratory muscles. During strictly controlled mechanical ventilation,  $P_{mus}$  is zero, and the breathing pattern is monotonous.

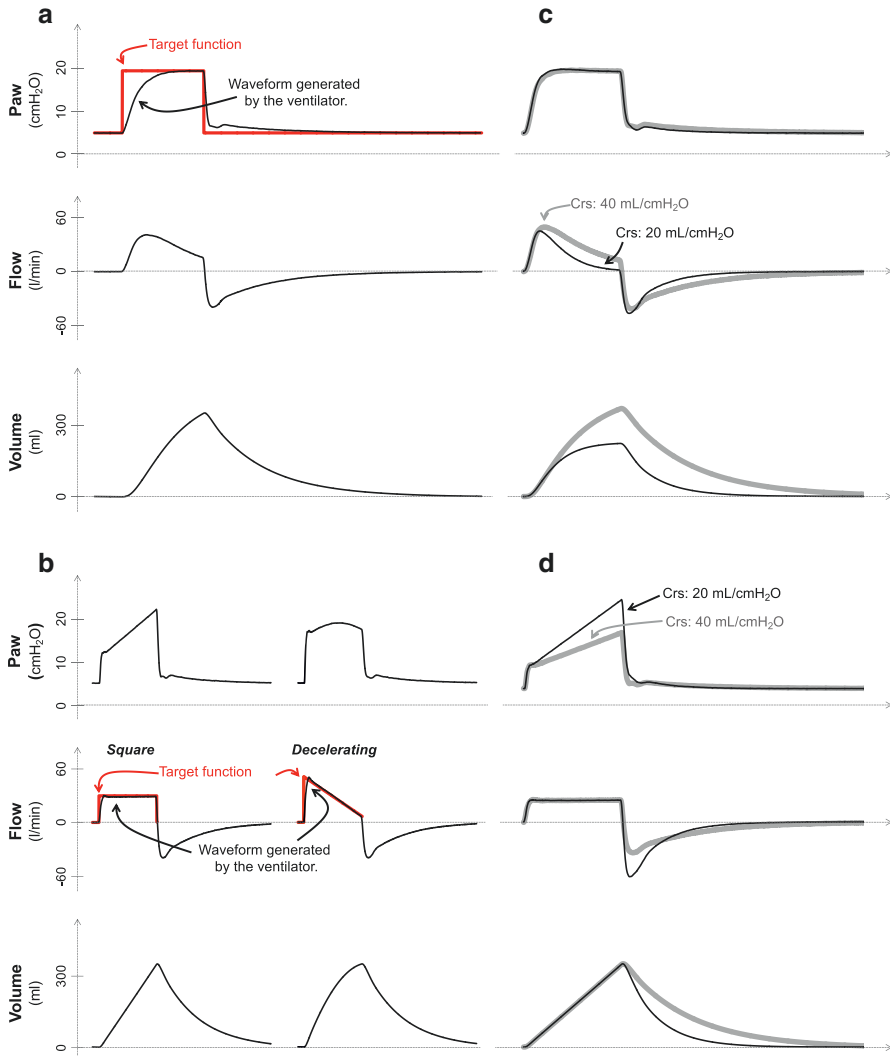
The choice of which variable to control gives rise to the classically known pressure-controlled and volume-controlled modes. The term volume-controlled could alternatively (and more properly) be called flow-controlled mode as flow is controlled to achieve the target volume, but the former term is more commonly used.

According to the choice of ventilation mode, the controlling system receives a different task in the form of a target function defined by the user-adjusted ventilator settings. In pressure-controlled modes, this function consists of a target airway pressure (including a linear ramp with adjustable slopes) towards the inspiratory pressure. This pressure is then maintained during the set inspiratory time after which the pressure should fall as fast as possible to the user-defined PEEP level (Fig. 4.1a). To

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**Fig. 4.1** Airway pressure ( $P_{aw}$ ), flow and volume waveforms behavior during pressure-controlled ventilation (PCV, panel a), and volume-controlled ventilation (VCV, panel b). The line in red represents the target function in each mode. (c) and (d) illustrate the effect of changes in respiratory system compliance ( $C_{rs}$ ) during pressure-controlled and volume-controlled modes, respectively. In PCV (c), the worsened  $C_{rs}$  reduces the delivered tidal volume. In contrast, in VCV (d), tidal volume is similar despite changes in  $C_{rs}$ ; however,  $P_{aw}$  changes inversely to changes in  $C_{rs}$ .

accomplish this task, the ventilator continuously receives inputs from pressure transducers and usually uses a “PID” controller, which defines the inspiratory flow generated by the inspiratory valve according to three estimates of distance from the target pressure: (1) flow is Proportional to the absolute difference in airway pressure from the set airway pressure, (2) flow increases when this absolute distance persists

over time (Integral), and (3) flow also depends on the error rate (Derivative). This is the basis of the statement that flow is free in pressure-controlled modes.

In volume-controlled modes, the PID control is more straightforward because control and target variables are the same. The target function is the flow in a pre-defined shape during inspiration. This way, the controller will determine how much electrical current to send to the proportional flow valves to reach the target flow waveform (Fig. 4.1b). Similar to pressure-controlled modes, the target function is the PEEP itself during expiration.

Although there is no evidence of a better choice of controlled ventilation mode in terms of outcome [1, 2], this decision certainly carries a handful of implications at the bedside, which we will explore in detail in this chapter.

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## 4.1 Pressure-Controlled Ventilation

The mainstay of a pressure-controlled ventilation (PCV) is the application of a pre-defined pressure waveform (most commonly squared or trapezoid) at the airway opening (Fig. 4.1a). This implies that maximum airway pressures are set by the clinicians, a characteristic that can be particularly interesting when limiting pressures is considered a priority for lung protection and for avoidance of hemodynamic instability. For example, during PCV, it is possible to limit plateau and driving pressures irrespective of changes in respiratory system mechanics (Fig. 4.1), although these will affect the delivered tidal volume. Aside from external PEEP and fraction of inspired oxygen (settings common to all modes), only three parameters are set to define the target function: inspiratory pressure (maximum or increment above external PEEP), inspiratory time, either absolute or fractional ( $T_I/T_{TOT}$ ), and mandatory frequency.

By choosing to control the pressure pattern, one must give up control over the flow and be aware of the necessity to closely monitor tidal volume and minute ventilation (Fig. 4.1c), which will inevitably vary according to the impedance of the respiratory system.

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## 4.2 Volume-Controlled Ventilation

This ventilatory mode consists of ventilation with inspiratory airway flows in predefined, user-selected flow waveforms, the most common of which is square (Fig. 4.1b). In this case, airway pressure will vary according to respiratory mechanics (Fig. 4.1d). In several surveys, volume-controlled ventilation (VCV) was the most used ventilatory mode in critical care, although lately pressure-controlled and pressure-support modes have been increasingly more adopted. The main characteristic of VCV is the delivery of fixed tidal volumes, defined by the clinician. Because respiratory rate is also set, minute ventilation is guaranteed.

Apart from external PEEP, the target function is defined by the following settings: tidal volume, inspiratory flow, shape of flow waveform (squared, on some ventilators also sinusoidal or decelerating), and mandatory respiratory rate.

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### 4.3 Pressure-Regulated Volume-Guaranteed Ventilation

Pressure-regulated volume-guaranteed ventilation (PRVG) is a closed-loop mode that offers the possibility of constant tidal volume in a pressure-controlled mode. Measured tidal volume serves as a feedback control variable for breath-by-breath automatic adjustment of pressure control. This ventilatory mode has various names, according to the manufacturer, such as pressure-regulated volume control (PRVC), AutoFlow, adaptive pressure ventilation, and others. Briefly, in the first cycle, the ventilator calculates respiratory system compliance during a VCV cycle. During subsequent breaths, the ventilator delivers the inspiratory pressure necessary to achieve the preset tidal volume based on the compliance calculation. This feature of PRVG is useful to account for ongoing changes in respiratory mechanics. On some ventilators, a high-pressure limit can be set to avoid injurious peak alveolar pressures in patients with low compliance. In the presence of spontaneous effort, tidal volume may increase or decrease frequently, causing the ventilator to often change pressure support, affecting patient comfort and work of breathing.

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## 4.4 Physiological Features of Fully Controlled Modes

### 4.4.1 Lung Protection

In the absence of patient effort, PCV and VCV are comparable in terms of lung protection. Both modes can be set to avoid high values of driving pressures, plateau pressures, tidal volumes, and respiratory rates. In terms of limiting pressures, the settings in PCV can be more straightforward, but tidal volume requires close monitoring including careful settings of ventilator alarms (Fig. 4.1c). Conversely, in VCV, it is important to routinely measure plateau pressures and carefully set pressure alarms (detailed in the monitoring session; Fig. 4.3). A decrease in  $C_{rs}$ , for example, due to atelectasis or mucus plug, can result in higher airway pressures for a given tidal volume (Fig. 4.1d).

There is one important difference between modes in terms of peak airway pressure. Because of the decelerating flow waveform, typical of PCV, peak airway pressures are usually lower as compared with VCV with square-flow waveforms even for the same values of inspiratory time and tidal volume (Fig. 4.1a, b). The mechanism underlying this characteristic is that airway flows peak at the beginning of inspiration in PCV, when the lungs are only starting to inflate. Consequently, resistive pressure ( $P_{res}$ ) decreases as elastic pressure ( $P_{el}$ ) rises in contrast with square-wave volume-controlled modes characterized by constant  $P_{res}$  and increasing  $P_{el}$ . This lower peak airway pressure can be important especially when air leak is a

concern (e.g., laryngeal mask ventilation) [3]. However, it is important to stress that a given tidal volume will lead to the same plateau pressure both in VCV and PCV.

#### 4.4.2 Alveolar Ventilation

After a step change in  $P_{aw}$ , either after triggering or after cycling-off, it takes a while before the alveolar pressure reaches equilibrium. It is possible to estimate the time needed to completely inflate or deflate the lungs using the concept of time constant. Briefly, considering that the respiratory system is adequately represented by one elastic compartment and one resistive element, which together produce monoexponential decays, the time constant can be defined as the product of  $R_{rs}$  and  $C_{rs}$ . After three to four times constants, near complete (95–99%) lung filling or emptying will take place.

This notion is essential for two main reasons involving the use of high respiratory rates. First, it is unusual to obtain complete lung filling at high respiratory rates. In PCV, inspiratory pressures sometimes much higher than alveolar pressures are required to generate enough inspiratory flow to allow for the delivery of tidal volume with a short inspiratory time. Even when accomplished, this goal comes with the risk of delivering too high tidal volume if, for example, airway resistance decreases suddenly, such as after bronchodilators. Correctly setting tidal volume alarms is imperative in this scenario. In VCV, by directly controlling tidal volumes, it can be easier to safely guarantee a short inspiratory time by applying short inspiratory pauses to monitor plateau pressures.

The second reason is to adequately set the ventilator to avoid the occurrence of intrinsic PEEP (detailed in the monitoring session; Fig. 4.3). When expiratory time is too short (less than three time constants), incomplete lung emptying will occur leading to intrinsic PEEP. For example, with a respiratory compliance of 40 mL/cmH<sub>2</sub>O and airway resistance of 20 cmH<sub>2</sub>O L<sup>-1</sup> s<sup>-1</sup>, the time constant will be 0.8 s, which means that the target expiratory time will be above 2.4 s. Here lies an important difference between PCV and VCV. If intrinsic PEEP occurs during VCV, tidal volume will not be affected, since it is controlled by the ventilator, but plateau pressure will rise. During PCV, plateau pressures will still be limited, but tidal volume will decrease. Of note, concerns regarding auto-PEEP or intrinsic PEEP should be minimal when minute volume is low, especially when below 10 L/min [4].

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#### 4.5 Modes Particularities During Inspiratory Effort

Presence of inspiratory effort changes mechanical ventilation substantially, since an independent control system (the respiratory center in the medulla) will now add muscle pressure ( $P_{mus}$ ) to the equation of motion. How the ventilator responds to inspiratory effort is an important difference between pressure and volume-controlled modes, especially regarding delivery of inspiratory flow and changes in transpulmonary pressure.

**Matching Inspiratory Flow Demand** During VCV, inspiratory flow is preset by the healthcare provider. Matching flow demand from the patient can thus be difficult, especially while ventilating patients with high inspiratory drive. Low peak inspiratory flow can increase work of breathing and promote patient-ventilator dyssynchrony (“air hunger”) (Fig. 4.2a).

Conversely, in PCV, the ventilator can respond more freely to different patient efforts (Fig. 4.2b). Patient comfort and synchrony with the ventilator can thus be more easily achieved [5]. If in VCV peak inspiratory flow is carefully adjusted to match patient demand, then this difference between PCV and VCV can be overcome, with little or no difference regarding work of breathing [2].

**Transpulmonary Pressure** Transpulmonary pressure is expressed as the sum of positive pressure applied by the ventilator and the absolute pressure generated by inspiratory muscles ( $P_{\text{mus}}$ ). The presence of inspiratory muscle pressure will impact differently the transpulmonary pressure in PCV vs. VCV.

In PCV, negative pleural pressure swings promoted by the diaphragm signals the ventilator to increase inspiratory flow and tidal volume to match the patients’ demand and keep airway pressure close to the set value (Fig. 4.2b). Transalveolar pressure, in this context, can be higher than the inspiratory pressure set by the clinician, since  $P_{\text{mus}}$  (unmeasured) will be added to the pressure generated by the ventilator, possibly leading to lung injury [6, 7].

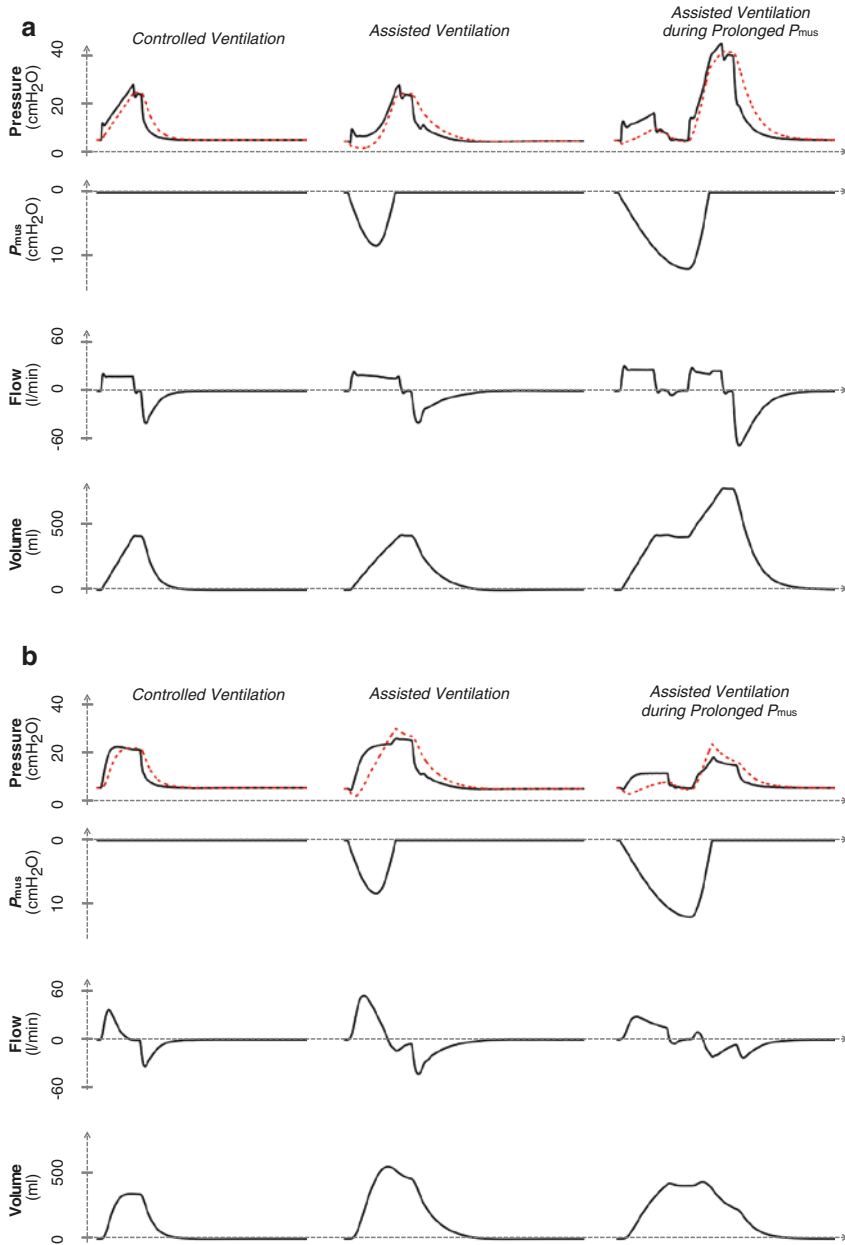
Conversely, one possible advantage of VCV is to maintain constant transpulmonary pressure during inspiratory effort. Because flow is predetermined by the clinician, in the presence of patient effort, airway pressure will decrease, maintaining the preset tidal volume (Fig. 4.2a). This characteristic does not guarantee, however, that there will be no regional increase in transpulmonary pressure. This regional overdistension was demonstrated as intratidal movement of air between different lung regions leading to persistence of injurious patterns of inflation (e.g., pendelluft and tidal recruitment) during VCV [8].

**Breath Stacking** Another important difference between PCV and VCV is revealed when the inspiratory effort is longer than the set inspiratory time. A prolonged inspiratory effort may produce a consecutive ventilatory cycle, defined as double triggering asynchrony. In VCV, double triggering can induce an injurious “stacked” volume, which can be as much as twice the size of the set tidal volume if the respiratory cycles are separated by a short expiratory time. PCV mode can minimize the chance of excessive breath stacking because the delivered inspiratory flow depends on the pressure gradient between the airway and alveoli (Fig. 4.2).

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## 4.6 Monitoring During Controlled Ventilation

Monitoring the mechanical properties of the respiratory system during passive ventilation is helpful to understand the pathophysiology of respiratory failure, set the mechanical ventilator, and minimize ventilator-induced lung injury. There are many



**Fig. 4.2** Airway pressure, alveolar pressure (red dashed lines), muscular pressure ( $P_{mus}$ ), flow and volume waveforms during controlled/assisted volume-controlled ventilation (VCV, *panel a*), and pressure-controlled ventilation (PCV, *panel b*). Note that in VCV, airway pressure decreases during assisted ventilation, with fixed inspiratory flow and volume. The limited flow can be associated with respiratory discomfort and is defined as “air hunger”, which increases the risk of double triggering. In contrast, the assisted-PCV is associated with increased inspiratory flow, combined with higher alveolar pressure as compared to fully controlled ventilation. A  $P_{mus}$  longer than the set inspiratory time may produce double triggering asynchrony (right plot on *panels a* and *b*). Note the difference of “stacked” volume between VCV and PCV for a fixed  $P_{mus}$ ; the true tidal volume delivered was calculated by integrating the flow-time waveform during the consecutive inspiratory cycles

methods to assess respiratory mechanics in static (*occlusion techniques*), quasi-static (*low-flow pressure-volume (P–V) curves*), and dynamic conditions (*stress index*). We refer to other chapters for advanced monitoring systems, such as esophageal manometry and electrical impedance tomography.

#### 4.6.1 Static Measurements of Inspiratory Resistance and Respiratory Compliance

As previously presented, the equation of motion characterizes the mechanical forces required to overcome  $P_{\text{res}}$  and  $P_{\text{el}}$  of the respiratory system (Eq. 4.1). The inspiratory  $P_{\text{res}}$  will remain approximately constant applying a constant flow rate during VCV (Fig. 4.3a). An end-inspiratory occlusion (EIO) maneuver is required to interrupt flow and hold the lung volume at the end of inspiration. The EIO results in a rapid decay in the  $P_{\text{aw}}$ , from peak inspiratory pressure (PIP) to  $P_{\text{I}}$ , representing the pressure dissipated by the flow-dependent resistance (Fig. 4.3a). The rapid drop in  $P_{\text{aw}}$  can be followed by a slow decay until a plateau is reached ( $P_{\text{plat}}$ ). The magnitude of the second decay depends on the viscoelasticity of the system (Fig. 4.3a). Thus, inspiratory  $R_{\text{rs}}$  can be obtained:

$$R_{\text{rs}} = (PIP - P_{\text{plat}}) / \dot{V}_i \quad (4.2)$$

The average  $R_{\text{rs}}$  in healthy adults under controlled ventilation is  $\sim 10 \text{ cmH}_2\text{O L}^{-1} \text{ s}^{-1}$ . Changes in  $R_{\text{rs}}$  may occur during ventilation due to bronchospasm, reduced lung volume, and mucus production, leading to increased airway pressure (if a patient is under VCV) or reduced  $V_{\text{T}}$  (if a patient is under PCV).

The  $C_{\text{rs}}$  typically denotes compliance calculated from two pressure points during quasi-static conditions. An EIO allows the identification of  $P_{\text{plat}}$ , the alveolar pressure at end-inspiration, which represents the elastic end-inspiratory recoil pressure of the respiratory system. An end-expiratory occlusion (EEO) assesses the end-expiratory alveolar pressure (PEEP<sub>tot</sub>) (Fig. 4.3a). Then,  $C_{\text{rs}}$  can be calculated as:

$$C_{\text{rs}} = V_{\text{T}} / (P_{\text{plat}} - \text{PEEP}_{\text{tot}}) \quad (4.3)$$

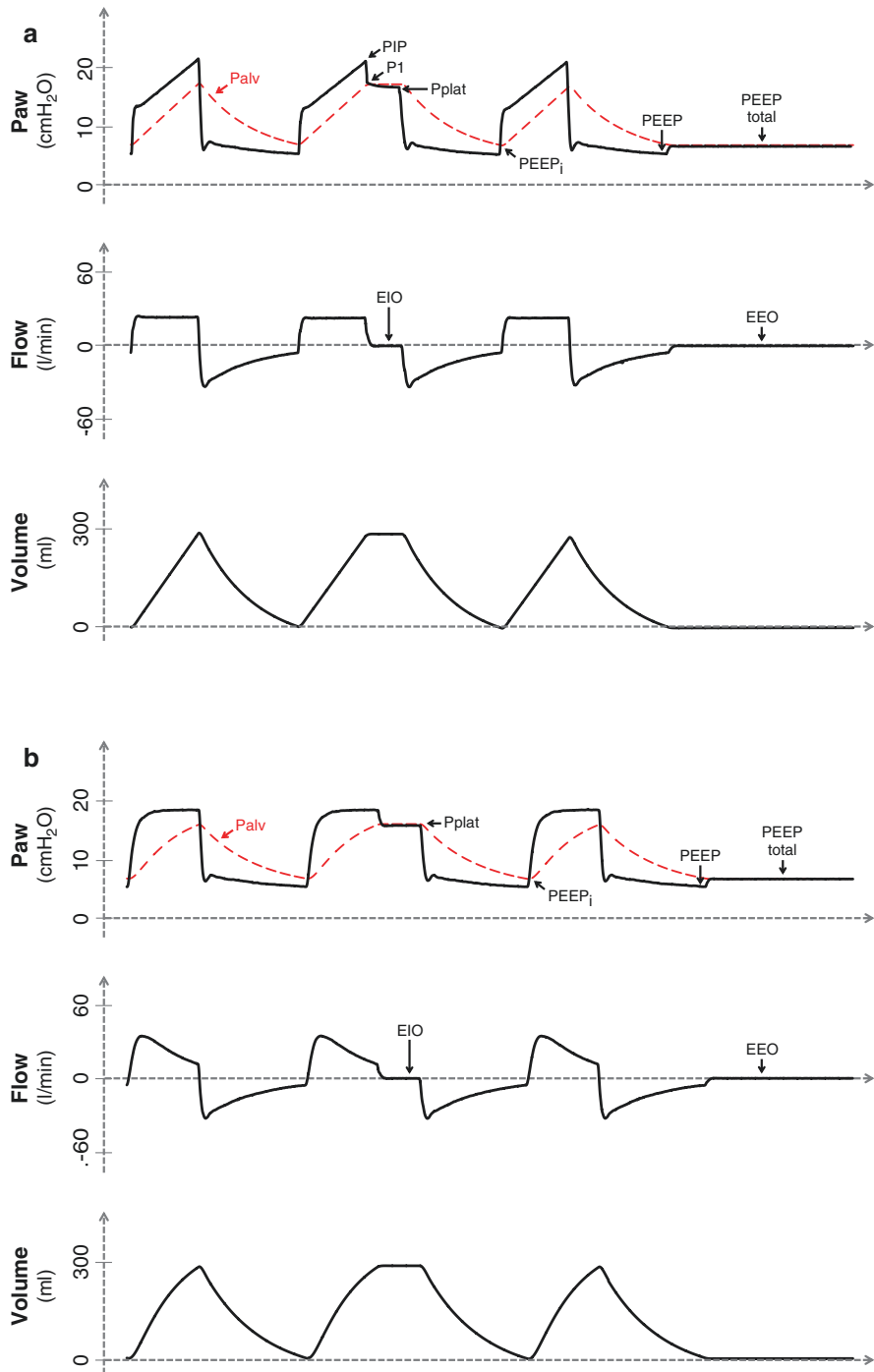
Prolonged EIO ( $>2 \text{ s}$ ) may cause underestimation of  $P_{\text{plat}}$  due to the viscoelastic properties and imperceptible leaks in the circuit. Thus, a shorter EIO ( $\leq 0.5 \text{ s}$ ) is recommended [9].

The measurement of  $C_{\text{rs}}$  during PCV is also allowed by many ventilators through an EIO (Fig. 4.3b). In the absence of an EIO, the inspiratory pressure will be close to  $P_{\text{plat}}$  during PCV only if flow approaches zero at the end of inspiration during PCV.

#### 4.6.2 Low-Flow Pressure-Volume (P–V) Curves

The early use of  $P$ – $V$  curves was performed by connecting supersyringes to the endotracheal tube, with complexity due to apparatus and the risk of lung collapse





**Fig. 4.3** Measurements of static respiratory mechanics during volume-controlled ventilation (VCV, panel a) and pressure-controlled ventilation (PCV, panel b).  $P_{aw}$ , airway pressure,  $P_{alv}$  alveolar pressure,  $P_{plat}$  plateau pressure,  $PEEP$  positive end-expiratory pressure,  $PEEP_i$  intrinsic PEEP,  $EIO$  end-inspiratory occlusion,  $EEO$  end-expiratory occlusion

caused by circuit disconnection. Nowadays, several ventilators offer tools to perform automated  $P-V$  curves (Fig. 4.4a), usually with a constant inspiratory flow  $\leq 5$  L/min after a prolonged expiration. The low inspiratory flow minimizes the resistive pressure, thus allowing a close estimate of the elastic pressure, in a patient sufficiently sedated or even paralyzed.

The  $P-V$  curve may assume a sigmoidal shape in ARDS patients, with an upward concavity at low inflation pressures and a downward concavity at higher inflation pressures (Fig. 4.4a). Physiological studies in ARDS patients suggest risk of lung collapse at pressure levels below the “lower inflection point” (LIP) and excessive alveoli deformation (strain) above the “upper inflection point” (UIP) (Fig. 4.4a). Some studies suggest the use of  $P-V$  curves to set the ventilator in a zone of high compliance, setting PEEP according to the LIP [10, 11]. However, there is no proof of the superiority of the  $P-V$  curve method over other PEEP titration approaches, such as the decremental PEEP trial for maximum  $C_{rs}$ , use of positive end-expiratory transpulmonary pressure, and PEEP adjusted according to inspired oxygen fraction (PEEP/ $F_iO_2$  table).

Recently, the low-flow  $P-V$  curve has been described to identify complete airway closure [12] (Fig. 4.4b). The authors observed airway closure in approximately one-quarter of patients with moderate/severe ARDS under controlled mechanical ventilation. This finding indicates an increased risk of misinterpreting respiratory mechanics when PEEP is not enough to overcome the airway opening pressure.

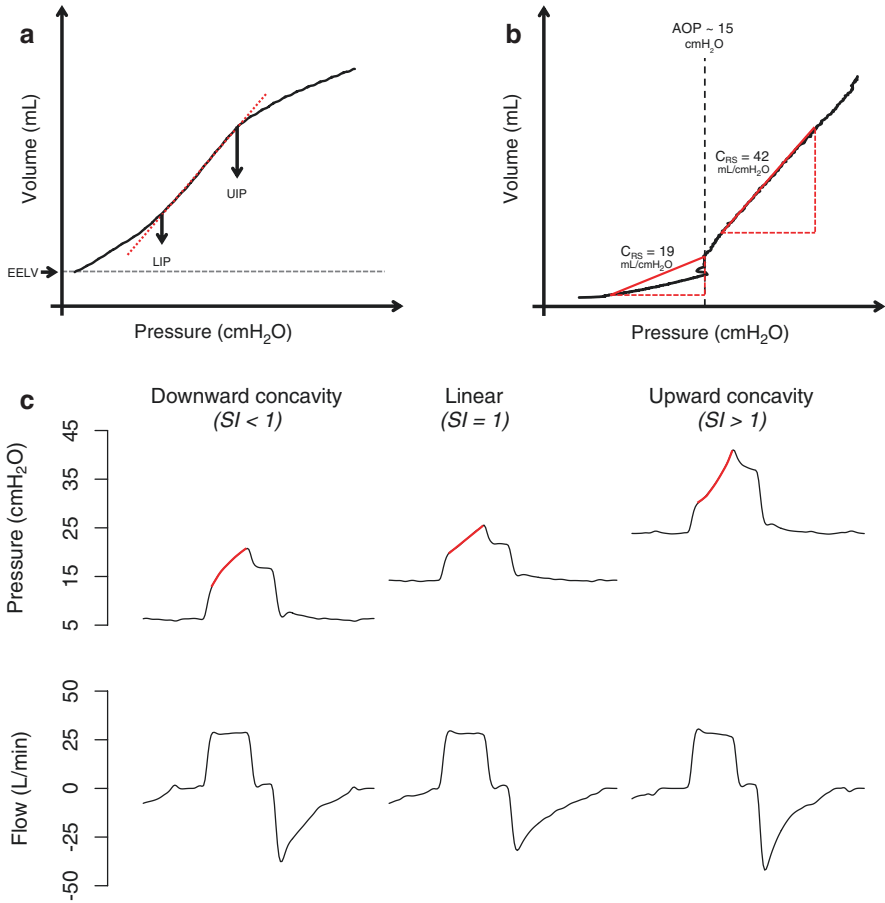
### 4.6.3 Stress Index

The stress index (SI) is a value derived from the airway pressure vs. time curve during a constant inspiratory flow. Assuming that  $R_{rs}$  is constant during inspiration, the slope of the pressure-time signal can identify dynamic changes in  $C_{rs}$  along the increasing lung volume. The SI calculation is based on the following equation applied to  $P_{aw}$  vs. time curve:

$$P_{aw}(t) = a \times t^b + c, \quad (4.4)$$

where  $b$  is the SI parameter, which reflects the shape of the  $P_{aw}$  vs. time curve,  $a$  represents the slope of  $P_{aw}$  vs. time at  $t = 1$  s, and the coefficient  $c$  is the pressure at  $t = 0$  s. For values of coefficient  $b < 1$ , the  $P_{aw}$  vs. time curve will present a downward concavity, indicating that compliance increases with time, whereas compliance decreases with time for values of coefficient  $b > 1$ , producing an upward concavity. Value of the coefficient  $b = 1$  indicates a straight  $P_{aw}$  vs. time relation and a constant compliance (Fig. 4.4c).

In an experimental model of ARDS, lungs ventilated with an SI range between 0.90–1.10 presented inflammatory biomarkers levels similar to those observed in non-ventilated lungs [13]. Although promising as a noninvasive approach to detect injurious lung patterns, SI use was limited in the past due to the necessity of dedicated software. However, a recent study found a good sensitivity and specificity using visual inspection to detect downward and upward concavity [14].



**Fig. 4.4** (a) The pressure-volume curve of a model with acute respiratory distress syndrome (ARDS). The lower inflection point (LIP) and the upper inflection point (UIP) are defined by where the curve first begins to deviate from the maximum compliance line (red dashed line). (b) Low-flow inflation pressure-volume curve in a model with airway closure. Note the extremely low slope at the beginning of the  $P - V$  curve, followed by an abrupt change in compliance above an airway opening pressure (AOP)  $\sim 15$  cmH<sub>2</sub>O. The airway closure phenomenon can lead to an erroneous calculation of respiratory system compliance ( $C_{RS}$ ). (c) Illustration of the dynamic pressure-time curves with a fixed inspiratory flow. Left, the downward concavity (stress index [SI]  $< 1$ ) indicates recruitment during the breath. Center, the linear relationship between pressure and time ( $SI = 1$ ), suggests no recruitment or overdistension. Right, the upward concavity ( $SI > 1$ ) indicates overdistension during the breath

## 4.7 Conclusion

With a good understanding of controlled modes and its implications, PCV and VCV are very similar during passive ventilation. However, if muscle effort occurs, these modes present substantially different features, which can impact patient comfort

and transpulmonary pressure applied onto the lungs. Despite evidence mainly showing clinical equivalence between PCV and VCV during controlled ventilation, ongoing research focusing on patient-ventilator interaction and monitoring of spontaneous breathing during mechanical ventilation could bring new insight regarding differences between these modes.

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## References

1. Esteban A, Alía I, Gordo F, Pablo R, Suarez J, Gonzá Lez G, Blanco JS. Prospective randomized trial comparing pressure-controlled ventilation and volume-controlled ventilation in ARDS. *Chest*. 2000;117:1690–6.
2. Rittayamai N, Katsios CM, Beloncle F, Friedrich JO, Mancebo J, Brochard L. Pressure-controlled vs volume-controlled ventilation in acute respiratory failure: a physiology-based narrative and systematic review. *Chest*. 2018;148:340–55.
3. Natalini G, Facchetti P, Dicembrini MA, Lanza G, Rosano A, Bernardini A. Pressure controlled versus volume controlled ventilation with laryngeal mask airway. *J Clin Anesth*. 2001;13:436–9.
4. Leatherman JW, McArthur C, Shapiro RS. Effect of prolongation of expiratory time on dynamic hyperinflation in mechanically ventilated patients with severe asthma. *Crit Care Med*. 2004;32:1542–5.
5. MacIntyre NR, McConnell R, Cheng KC, Sane A. Patient-ventilator flow dyssynchrony: flow-limited versus pressure-limited breaths. *Crit Care Med*. 1997;25:1671–7.
6. Dreyfuss D, Soler P, Basset G, Saumon G. High inflation pressure pulmonary edema respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. *Am Rev Respir Dis*. 1988;137:1159–64.
7. Morais CCA, Koyama Y, Yoshida T, Plens GM, Gomes S, Lima CLAS, et al. High positive end-expiratory pressure renders spontaneous effort noninjurious. *Am J Respir Crit Care Med*. 2018;197:1285–96.
8. Yoshida T, Nakahashi S, Nakamura MAM, Koyama Y, Roldan R, Torsani V, et al. Volume-controlled ventilation does not prevent injurious inflation during spontaneous effort. *Am J Respir Crit Care Med*. 2017;196:590–601.
9. Henderson WR, Chen L, Amato MBP, Brochard LJ. Fifty years of research in ARDS: respiratory mechanics in acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2017;196:822–33.
10. Dall’ava Santucci J, Armaganidis A, Brunet F, Dhainaut JF. Mechanical effects of PEEP in patients with adult respiratory distress syndrome. *J Appl Physiol*. 1990;68:843–8.
11. Amato MBP, Barbas CSV, Medeiros DM, Magaldi RB, Schettino GPP, Lorenzi-Filho G, et al. Effect of a protective ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med*. 1998;338:347–54.
12. Chen L, Del Sorbo L, Luca Grieco D, Shklar O, Junhasavasdikul D, Telias I, et al. Airway closure in acute respiratory distress syndrome: an underestimated and misinterpreted phenomenon. *Am J Respir Crit Care Med*. 2018;197:132–6.
13. Ranieri VM, Zhang H, Mascia L, Aubin M, Lin CY, Mullen B, et al. Pressure-time curve predicts minimally injurious ventilatory strategy in an isolated rat lung model. *Anesthesiology*. 2000;93:1320–8.
14. Sun XM, Chen GQ, Chen K, Wang YM, Xuan H, Huang HW, et al. Stress index can be accurately and reliably assessed by visually inspecting ventilator waveforms. *Respir Care*. 2018;63:1094–101.