Review

Clinical review: Respiratory mechanics in spontaneous and assisted ventilation

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Published online: 18 April 2005
This article is online at http://ccforum.com/content/9/5/472

Critical Care 2005, **9**:472-484 (DOI 10.1186/cc3516)

Abstract

Pulmonary disease changes the physiology of the lungs, which manifests as changes in respiratory mechanics. Therefore, measurement of respiratory mechanics allows a clinician to monitor closely the course of pulmonary disease. Here we review the principles of respiratory mechanics and their clinical applications. These principles include compliance, elastance, resistance, impedance, flow, and work of breathing. We discuss these principles in normal conditions and in disease states. As the severity of pulmonary disease increases, mechanical ventilation can become necessary. We discuss the use of pressure–volume curves in assisting with poorly compliant lungs while on mechanical ventilation. In addition, we discuss physiologic parameters that assist with ventilator weaning as the disease process abates.

Introduction

In humans ventilation involves movement of the chest wall to produce a pressure gradient that will permit flow and movement of gas. This can be accomplished by the respiratory muscles, by negative pressure ventilation (iron lung), or by positive pressure ventilation (mechanical ventilator). Measurements of respiratory mechanics allow a clinician to monitor closely the course of pulmonary disease. At the bedside, changes in these mechanics can occur abruptly (and prompt immediate action) or they may reveal slow trends in respiratory condition (and prompt initiation or discontinuation of mechanical ventilation). Here we focus on the mechanical measurements that can be used to help make clinical decisions.

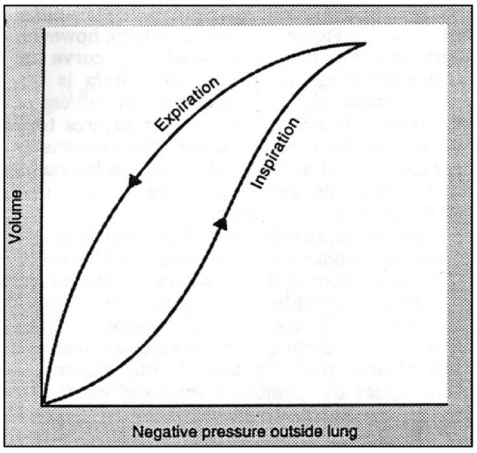
Compliance

In respiratory physiology, lung compliance describes the willingness of the lungs to distend, and elastance the willingness to return to the resting position. Compliance is determined by the following equation: $C = \Delta V/\Delta P$, where C is compliance, ΔV is change in volume, and ΔP is change in pressure. The inverse of compliance is elastance ($E \sim 1/C$). Airway pressure during inflation is influenced by volume, thoracic (lung and chest wall) compliance, and thoracic resistance to flow. Resistance to flow must be eliminated if compliance is to be measured accurately. This is accomplished by measuring pressure and volume during a period of zero flow, termed static measurements. Therefore, compliance is determined by taking static measurements of the distending pressure at different lung volumes and can be done during inflation or deflation [1]. Plotting pressure measurements throughout the respiratory cycle allows a pressure–volume (PV) curve to be constructed (Fig. 1).

The slope of this curve is equal to the compliance. The inspiratory and expiratory curves are separated on the PV curve; this area of separation is termed hysteresis. Hysteresis develops in elastic structures when the volume change from an applied force is sustained for some time after the force is removed [2]. In the lungs, hysteresis results both from the collapse of small airways and from the surface tension at the gas–liquid interface of alveoli that must be overcome to inflate the lungs. The degree of hysteresis is greater when a breath is initiated near the residual volume and less when it is initiated at higher lung volumes [2]. Both the chest wall and the lung influence respiratory compliance. The total thoracic compliance is less than individual compliances of the chest or lung because the two add in parallel (elastances, the inverse, add in series) [3]: $Crs = Ccw \times Cl/(Ccw + Cl)$, where Crs, Ccw, and Cl are the compliances of the respiratory system, chest wall, and lung, respectively (Fig. 2 and Table 1).

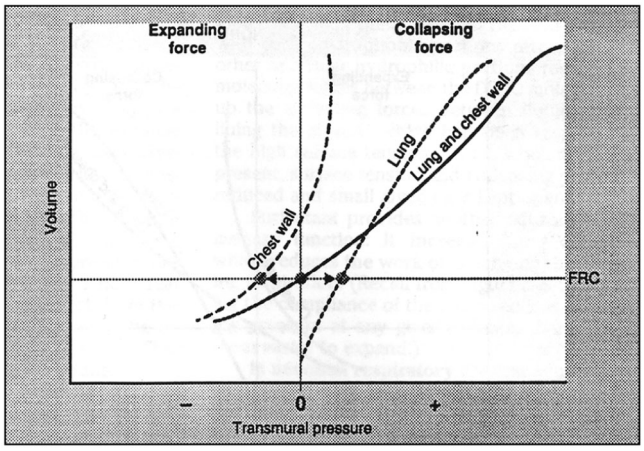
ARDS = acute respiratory distress syndrome; ATC = automatic tube compensation; Ccw - chest wall compliance; Cl = lung compliance; COPD = chronic obstructive pulmonary disease; CPAP = continuous positive airway pressure; Crs = respiratory system compliance; IPL = inspiratory pressure level; LIP = lower inflection point; MIP = maximal inspiratory pressure; NIPPV = noninvasive positive pressure ventilation; Pavg = average inspiratory pressure; Paw = airway pressure; PEEP = positive end expiratory pressure; PEFR = peak expiratory flow rate; Pes = esophageal pressure; Pex = end-expiratory pressure; Ps = inspiratory pressure; PTI = pressure time index; PTP = pressure time product; PV = pressure–volume curve; RSBI = rapid shallow breathing index; SBT = spontaneous breathing trial; UIP = upper inflection point; Vt = tidal volume; WOB = work of breathing.

Figure 1



Pressure–volume curve. Shown is a pressure–volume curve developed from measurements in isolated lung during inflation (inspiration) and deflation (expiration). The slope of each curve is the compliance. The difference in the curves is hysteresis. Reprinted from [3] with permission from Elsevier.

Figure 2



Compliance of the lungs, chest wall, and the combined lung–chest wall system. At the functional residual capacity, the forces of expansion and collapse are in equilibrium. Reprinted from [3] with permission from Elsevier.

Table 1

Causes of decreased intrathoracic compliance

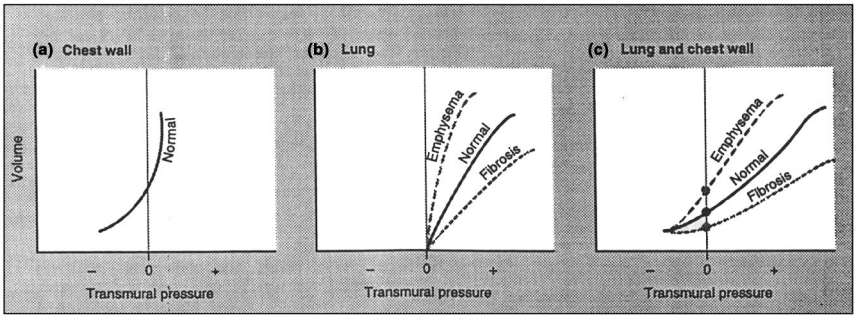
Causes of decreased measured chest wall compliance	Causes of decreased measured lung compliance
Obesity	Tension pneumothorax
Ascites	Mainstem intubation
Neuromuscular weakness (Guillain–Barre, steroid myopathy, etc.)	Dynamic hyperinflation
Flail chest (mediastinal removal)	Pulmonary edema
Kyphoscoliosis	Pulmonary fibrosis
Fibrothorax	Acute respiratory distress syndrome
Pectus excavatum	Langerhans cell histiocytosis
Chest wall tumor	Hypersensitivity pneumonitis
Paralysis	Connective tissue disorders
Scleroderma	Sarcoidosis
	Cryptogenic organizing pneumonitis
	Lymphangitic spread of tumor

Shown are the causes of decreased intrathoracic compliance, partitioned into causes of decreased measured chest wall compliance and causes of decreased measured lung compliance.

Reduced compliance can be caused by a stiff chest wall or lungs, or both. The distinction can be clinically significant. To separate the contribution made by each to total lung compliance, a measure of intrapleural pressure is needed. The most accurate surrogate marker for intrapleural pressure is esophageal pressure, which can be measured by placing an esophageal balloon [1]. However, this is rarely done in clinical practice. Alternatively, changes in central venous pressure can approximate changes in esophageal pressure, but this technique is yet to be verified [1].

Respiratory system compliance is routinely recorded at the bedside of critically ill patients. In mechanically ventilated patients, this is done by measuring end-expiratory alveolar pressure (Pex) and end-inspiratory alveolar pressure (also called peak static or plateau pressure [Ps]), so that the change in volume is the tidal volume (Vt). Alveolar pressure can easily be assessed after occlusion of the airway, because the pressure in the airway equilibrates with alveolar pressure. Pex is the pressure associated with alveolar distention at the end of a breath. In normal individuals this is usually zero when

Figure 3



Compliance in emphysema and fibrosis. Shown are changes in the compliance of the inspiratory limb of the pressure–volume curve with respect to **(a)** chest wall, **(b)** lungs, and **(c)** combined lung-chest wall system in patients with emphysema and fibrosis. The functional residual capacity (FRC), represented on the vertical axis at a transmural pressure of 0, is elevated in emphysema, which can lead to dynamic hyperinflation. Reprinted from [3] with permission from Elsevier.

referenced to atmosphere. However, when positive end-expiratory pressure (PEEP) is applied, Pex is at least as great as PEEP. It may be greater if air trapping occurs, and the associated pressure beyond PEEP is termed auto-PEEP or intrinsic PEEP. The clinician will need to know Ps, Pex, auto-PEEP, and Vt to determine respiratory compliance at the bedside. For example, if the PEEP is 5 cmH_2O, auto-PEEP is 0 cmH_2O, Ps is 25 cmH_2O, and Vt is 0.5 l, then Crs = $\Delta V/\Delta P$ = 0.5 l/(25 – 5) = 0.5/20 = 0.025 l/cmH_2O or 25 ml/cmH_2O. In a normal subject on mechanical ventilation, compliance should be greater than 50–100 ml/cmH_2O [4].

Patients with obstructive lung disease have a prolonged expiratory phase. At baseline, most patients with emphysema have increased compliance (because of decreased elastance of the lungs). If the Vt is not completely exhaled, then a certain amount of air will be 'trapped' in the alveoli. If this continues over several breaths, then it will result in 'stacking' of breaths until a new end-expiratory thoracic volume is achieved. As the volume increases (dynamic hyperinflation), the functional residual capacity will be increased. As a result, tidal breathing will occur at a less compliant portion of the PV curve (Fig. 3).

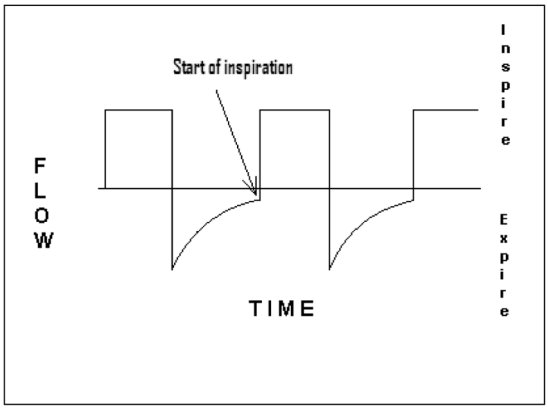
The pressure difference associated with the trapped volume is called auto-PEEP. Caution must be used in a patient who has obstructive lung disease and is on mechanical ventilation. Usually, such patients are treated aggressively for airway inflammation (bronchodilator treatments and corticosteroids), while the respiratory rate is decreased and the expiratory phase of respiration is prolonged. If the functional residual capacity is increased, delivering the same Vt may increase the transalveolar pressure, which can impede venous return (resulting in hypotension) or lead to a pneumothorax. The development of hypotension in a patient with dynamic hyperinflation should prompt the clinician to listen to the lungs and assess the ventilator for auto-PEEP. If auto-PEEP is suspected, then the patient should be disconnected from the ventilator to determine whether the hypotension resolves when delivered breaths are withheld (Fig. 4).

Auto-PEEP can be measured in patients on mechanical ventilators by creating an end-expiratory pause. The end-expiratory pause maneuver allows the pressure transducer of the ventilator to approximate the end-expiratory alveolar pressure, or auto-PEEP. Some ventilators allow the clinician to create and control the expiratory pause, whereas other ventilators perform an end-expiratory pause as an automated function that requires only the push of a button. Measurements of auto-PEEP require a passive patient because patient interaction in breathing will alter the measurements of the pressure transducer. In the intensive care unit, this usually requires sedation and, occasionally, paralysis.

Decreasing the amount of auto-PEEP on mechanical ventilation requires one to decrease the respiratory rate and prolong the expiratory phase of ventilation. Execution of these goals often requires eliminating patient effort through heavy sedation or paralysis. Once patient effort is eliminated, it is important to follow respiratory mechanics closely, including auto-PEEP and compliance. In order to protect the lungs from barotrauma, it is common to permit a certain amount of hypoventilation, termed permissive hypercapnia. Permissive hypercapnia has been proven safe and allows a clinician to use the lowest respiratory rate and Vt possible, thus protecting the lungs while they are impaired.

Patients with auto-PEEP (or intrinsic PEEP) who require mechanical ventilation are often asynchronous with the ventilator. During assisted modes of ventilation, patients with auto-PEEP often have difficulty triggering the ventilator to initiate a breath. The patient must first overcome the auto-PEEP before creating the negative intrapleural pressure required to trigger the ventilator. The patient can be assisted by applying extrinsic PEEP, of a magnitude less than Pex, to the circuit. Now the pressure needed to be generated by the

Figure 4



Ventilator tracing with a square wave, or constant flow, pattern. Note that the machine is triggered to initiate a breath before flow returns to zero (the horizontal axis). This indicates that auto-PEEP (positive end-expiratory pressure) is present and directs the clinician to investigate further.

patient to trigger the ventilator is decreased because the trigger sensitivity of the ventilator is centered around the applied extrinsic PEEP and not atmospheric pressure. Therefore, more patient initiated efforts will be able to trigger the ventilator successfully.

Acute respiratory distress syndrome (ARDS) is a common condition in the intensive care unit and is characterized by low compliance. Typically, the start of inspiration occurs at low volumes (near the residual volume) and requires high pressure to overcome surface tension and inflate the alveoli. The relation between pressure and surface tension is explained by Laplace's Law, which relates pressure to radius in spherical structures: $P = 2T/r$, where P = pressure, T = surface tension, and r = radius. Below we discuss the role of PV curves in patients with ARDS who require mechanical ventilation.

Pressure–volume curves and ventilator management in ARDS

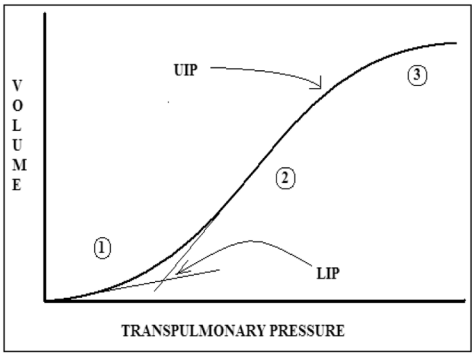
The PV curve of the lung and chest wall is obtained by plotting the corresponding pressure at different Vts. As mentioned previously, the resulting slope is the compliance of the lung and chest wall. In recent years, much interest has centered on using the PV curve to help select the optimal ventilator settings for patients on mechanical ventilation. Patients with ARDS on mechanical ventilation have been the focus of this attention.

There are various ways to measure the PV curve in patients on mechanical ventilation. Each method has advantages and disadvantages [5]. Some methods require specialized equipment that is not available in all intensive care units. With the syringe technique, the patient is removed from the mechanical ventilator and a 2 l syringe is placed on the endotracheal tube. Increments of 50–150 cc of 100% oxygen are delivered, and a transducer measures the corresponding airway pressure at each volume [2]. These values are then plotted and connected to form the PV curve. An alternative approach is to use the multiple occlusion technique. With this method, the patient remains on the ventilator. The plateau pressure is measured at different Vts (ranging from 200 cc to 1300 cc) and plotted to form the PV curve. It is important to allow several breaths at a standard volume between measurements to obtain the most accurate result. A recent study [5] showed that the multiple occlusion technique and the syringe technique yield similar measurements. A third approach is the continuous low-flow technique. Maintaining a low inspiratory flow rate on the mechanical ventilator (less than 10 l/min) minimizes resistance, permitting estimation of the PV curve [2]. All methods used to obtain a PV curve generally require a passive patient for accurate results. The risks associated with sedation and paralysis (which may be needed) should be considered before proceeding to create a PV curve.

The PV curve will change with time and with differences in pressure [5]. In ARDS, the PV curve will change as the disease progresses or resolves [6]. In the early (exudative) stage, the PV curve generally exhibits low compliance and a well demarcated lower inflection point (LIP). As the disease progresses (fibrotic stage), the compliance remains low but the LIP is obscured [2]. ARDS is also associated with a rapidly changing clinical course. The shape of a PV curve may change over several hours in the same patient. Therefore, up-to-date measurements are needed before ventilator settings are manipulated, if one is relying upon the PV curve. Traditionally, the PV curve has been calculated with zero end-expiratory pressure [7-9]. When calculated with different levels of PEEP, the PV curve will be altered [8,9]. In addition, the ventilator mode and level of ventilation that a patient is on before calculation of a PV curve can affect the shape of the curve [9]. These drawbacks make it difficult to know whether PV curves may be relied upon for bedside use (Fig. 5).

The inspiratory phase of the PV curve consists of three sections. The first section occurs at a low volume, and is nonlinear and relatively flat (low compliance). As the volume increases, the second section of the curve is linear and has a steeper slope (higher compliance). The third section of the curve is again nonlinear and flat (return to low compliance). The junction between the first and second portion of the curve is called the LIP. The LIP can be calculated by intersecting the lines from the first and second portions of the curve. Alternatively, the LIP can be calculated by measuring the steepest point of the second section and then marking the LIP as the point of a 20% decrease in slope from this steepest point. Studies assessing interobserver reliability have varied. Some have found good interobserver variability, whereas others have found significant variability [2,5,7]. The junction of the second and third portions of the curve is

Figure 5



The inspiratory limb of the pressure–volume curve (dark line) divided into three sections. Section 1 (low compliance) and section 2 (high compliance) are separated by the lower inflection point (LIP). Section 2 (high compliance) and section 3 (low compliance) are separated by the upper inflection point (UIP). In this example, the LIP is marked at the point of crossing of the greatest slope in section 2 and the lowest slope of section 1. The UIP is marked at the point of 20% decrease from the greatest slope of section 2 (a calculated value).

called the upper inflection point (UIP). The UIP can be measured in the same way as the LIP (except the UIP would represent a 20% increase from the point of the greatest slope). Studies have generally found that there is good interobserver agreement and good agreement between methods for measuring UIP [5,10].

The LIP and UIP are points that represent changes in compliance. In the past, the LIP was thought to represent the end of alveolar recruitment. The opening of an alveolus during inspiration was thought to cause shear stress that would be harmful to the lung. Therefore, by setting the amount of PEEP above the LIP, the level of shear stress could be decreased [11,12]. The UIP was thought to represent the start of alveolar overdistension. It was thought that if the airway pressure exceeded the UIP, then harmful alveolar stretch and overdistension would occur [11,12]. In keeping the level of PEEP above the LIP and the plateau pressure below the UIP, the patient would receive Vts at the most compliant part of the PV curve. By following the PV curve over time, the ventilator settings could be individually tailored to provide the maximal benefit and the minimal damage to the patient with ARDS requiring mechanical ventilation.

In 1999, Amato and coworkers [11] reported the results of a prospective, randomized, controlled trial using the PV curve as a guide to ventilation. The level of PEEP was maintained at 2 cmH_2O above the LIP in the experimental group, with a plateau pressure of 20 cmH_2O or less. When compared with 'conventional ventilation' (use of lower PEEP, higher Vts, and higher plateau pressures), there was a significant difference in mortality at 28 days (38% versus 71%) and a significant difference in the rate of weaning favoring the experimental group. This study supported the clinical practice of setting the PEEP at 2 cmH_2O above the LIP. However, because the plateau pressure was also manipulated, it is difficult to attribute the mortality difference to PEEP. Moreover, the mortality rate in the control group was higher than expected, because other studies conducted in ARDS patients have consistently found mortality rates around 40% in control arms [13].

It is now apparent that alveoli are recruited throughout the inspiratory limb of the PV curve (not just below the LIP, as was previously assumed) [14,15]. We now believe that the LIP represents a level of airway pressure that leads to increased recruitment of alveoli. This increased recruitment is sustained throughout the second portion of the PV curve and is reflected by a steep slope, indicating increased compliance. The UIP, in turn, represents a point of decreased alveolar recruitment. Recruitment of alveoli on inspiration begins in the nondependent portion of the lungs and slowly spreads to the dependent portion of the lungs [16]. Areas of atelectasis may require inspiratory pressures above 40 cmH_2O before alveoli will be recruited [16]. Clearly, in this model of the PV curve, setting the PEEP above the LIP will not reduce shear stress by starting inspiration after alveolar recruitment.

The model of continuous recruitment also dissociates the LIP from PEEP [16]. Previously, when the LIP was thought to represent the completion of alveolar recruitment, the PEEP that corresponded to the LIP was thought to sustain alveolar recruitment and prevent alveolar shear stress. However, because alveoli are continually recruited along the inspiratory limb of the PV curve, the 'optimal PEEP' may be difficult to determine from the inspiratory limb. Moreover, PEEP is an expiratory phenomenon, and it corresponds to pressures on the expiratory curve rather than the inspiratory curve [17]. Because hysteresis exists between the inspiratory and expiratory limbs, it is difficult to estimate the effect that PEEP will have on the inspiratory curve [17,18].

Clinical studies attempting to improve outcomes in ARDS by varying levels of PEEP have had disappointing results. In 2004 the ARDS Network investigators [19] reported a prospective study comparing the effects of lower PEEP (mean 8–9 cmH_2O) with those of higher PEEP (mean 13–15 cmH_2O). The results did not reveal a significant difference in clinical outcomes (mortality, time of ICU stay, time on mechanical ventilator) between the two groups. In that study, the LIP was not used to guide the 'high PEEP' group as had been done in the study conducted by Amato and coworkers. A weakness of the study was that the level of PEEP used in the 'high PEEP' group was changed during the study, potentially altering the outcome [20].

Clinical research has proven that large Vts are detrimental in ARDS. In 2000, findings were reported by the ARDS Network investigators [21]. In that prospective, randomized,

controlled trial, low Vts (yielding plateau pressures <30 cmH_2O) were compared with higher Vts (plateau pressures up to 50 cmH_2O). The results showed a significant decrease in mortality (from 37% to 31%) when the lung protective strategy (low Vt of 6 ml/kg predicted body weight) was used. That study did not use PEEP as part of the ventilator strategy for lung protection. However, the assumption is that, by limiting Vt, fewer patients will reach a plateau pressure greater than the UIP. Therefore, alveolar overdistension and excessive stretch will be minimized. Intuitively, one might assume that the largest benefit would be in the subset of patients with the poorest compliance. However, the mortality difference was independent of respiratory system compliance, leading the investigators to attribute the benefit to other factors (such as stretch). However, it is not clear that the UIP can be used to set plateau pressure and therefore avoid harmful alveolar stretch. It has been shown that alterations in alveolar recruitment will change the UIP [14,22]. This supports the idea that the UIP represents a decrease in alveolar recruitment. Therefore, the UIP would not be expected to predict reliably an alveolar phenomena unrelated to recruitment (such as stretch or overdistension).

At present, we do not recommend routine use of the inspiratory PV curve in patients with ARDS. Measurements can be time consuming and, as evident from the above discussion, meaningful interpretation is difficult. Instead of setting PEEP values just above the LIP, we currently recommend following the nomogram used by the ARDS Network [21]. Recently, more attention has been given to the expiratory limb of the PV curve. As mentioned above, PEEP is an expiratory measurement, and the appropriate setting of PEEP may be estimated by a point on the expiratory curve. Holzapfel and coworkers [23] recently showed that, when manipulating PEEP according to the inflection point on the deflation limb of the PV curve, intrapulmonary shunting was maximally reduced (when compared with the LIP). Although further studies are needed to define the role of the expiratory curve in ARDS, the rationale and small clinical trials appear promising.

Flow and resistance

Flow (Q) is the movement of air. Flow is dependent on a pressure gradient (ΔP) and is inversely related to the resistance to flow (R). This relationship is described in the following equation: $Q = \Delta P/R$. In the lungs, two types of flow are present – laminar flow and turbulent flow. In general, turbulent flow is present in large airways and major bifurcations, whereas laminar flow is present in the more distant airways. The type of flow present in an airway is influenced by the rate of flow (V), the airway radius (r), the density of gas (p), and the viscosity of gas (η). Reynold's number is a calculation of the above variables used to determine whether flow will be turbulent or laminar. Reynold's number $= 2Vrp/\eta$, and values greater than 2300 generally indicate that flow will have a turbulent component. Flow with a Reynold's number greater than 4000 is completely turbulent [24].

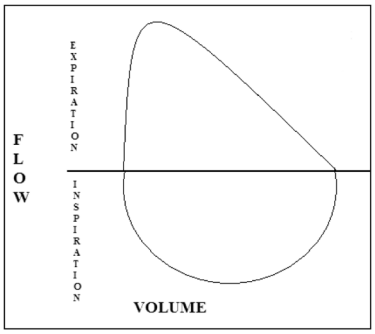
In airways governed by laminar flow, resistance is related to the radius (r), airway length (l), and gas viscosity (η) through Poiseuille's Law ($R = 8\eta l/\pi r4$). This equation highlights the strong relation of the radius on resistance (i.e. doubling the radius decreases the resistance 16-fold). When flow is turbulent (in large airways), the equation for flow must also incorporate a frictional factor (f). The modification of Poiseuille's equation for turbulent flow is as follows: $R = Vfl\eta/\pi^2r^5$ [25].

At each division of the airways, the branches of the lungs lie in parallel. With resistances in parallel, the total resistance (Rt) is less than the individual resistances ($1/Rt = 1/R1 + 1/R2 + 1/R3 + \ldots$). Because of their large number and parallel arrangement, the bronchioles are not the primary site of greatest resistance. In a spontaneous breathing, normal person, the medium-sized bronchi are the site of greatest resistance [3]. The flow–volume loop demonstrates airflow at different points in the respiratory cycle. A normal flow–volume loop is shown in Fig. 6.

In a normal individual maximal inspiratory flow is limited only by muscle strength and total lung and chest wall compliance. Resistance to flow is minimal and does not limit inspiration. Maximal expiratory flow is initially limited only by expiratory muscle strength (when the airway radius is large and resistance is minimal). However, as the airway lumen decreases, resistance to flow will increase and flow is limited by resistance. The accurate measurement of airway resistance during spontaneous breathing requires placement of an esophageal balloon to estimate pleural pressure [1]. This allows for the determination of the pressure gradient (transpulmonary pressure equals pleural minus airway pressure) at any given lung volume. Through extrapolating flows at the same volume from a flow–volume loop, an isovolume flow–pressure curve can be established (Fig. 7). By manipulating the pressure gradient at different lung volumes (through increasing pleural pressure), it has been shown that maximal flow is limited once a volume-specific pleural pressure is achieved. Several physiologic theories have been put forward in an attempt to explain this expiratory flow limitation [26].

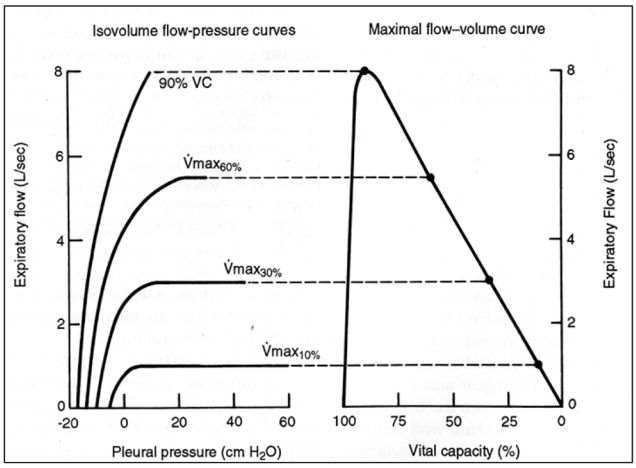
The wave speed theory of flow limitation is derived from fluid mechanics. When airflow approaches the speed of wave propagation within the airway wall, flow will be limited. According to this model, the cross-sectional area of the airway, the compliance of the airway, and the resistance upstream from the flow limiting segment all contribute to flow limitation. This theory has been well validated during expiration, when vital capacity is between 0% and 75% of the total lung capacity [26]. At a vital capacity greater than 75% of total lung capacity, it has been difficult to limit flow by increasing pleural pressure in normal individuals [27]. Therefore, traditional teaching indicated that early expiration is primarily limited by effort dependent muscle strength [27].

Figure 6



Flow–volume loop. A flow–volume loop is shown, with exhalation above the horizontal axis and inspiration below.

Figure 7



The maximal flow–volume curve. The isovolume flow–pressure curve (left) is created from measurements of pleural pressure and expiratory flow at different volumes of forced expiration. These measurements can be extrapolated to show a maximal flow–volume curve (right). Note that, at a volume specific pleural pressure, the maximal expiratory flow will be limited. VC, vital capacity. Reprinted from [1] with permission from Elsevier.

However, a recent model in normal individuals showed that peak expiratory flow was limited by mechanical properties of the lung (in accordance with the wave speed mechanism), and not by muscle strength [26]. As peak flow normally occurs at around 80% of total lung capacity, the wave speed theory can be used to explain expiratory flow limitation from a vital capacity of 80% and less [26].

Patients with asthma and chronic bronchitis have airway inflammation, which decreases the radius of the airway. By decreasing the radius, the resistance to flow is increased (in accordance with Poiseuille's Law). This is most prominent during expiration, when the increase in resistance leads to decreased flow and 'air trapping'. The peak expiratory flow rate (PEFR) is a common bedside measure of expiratory flow in patients with asthma. With good patient effort, limitations in PEFR are likely caused by the mechanical properties of the airways (such as decreased cross-sectional area). Assuming that a patient is able to generate a similar pressure gradient on subsequent measures of PEFR, differences in flow would reflect differences in airway resistance, and differences in airway resistance correlate with inflammation and disease severity. In fact, peak flow has correlated well with airway hyperresponsiveness, and diurnal variation in peak flows correlate well with diurnal variation in symptoms [28]. In addition, peak flow levels of less than 100 l/min have been associated with need for hospitalization and oral steroid therapy [29]. PEFR is frequently used at home by asthmatic persons in order to provide an objective measure of disease activity [30,31].

Heliox is a combination of helium and oxygen, and is available as 60%, 70%, or 80% helium. The decreased density of helium can decrease the total density of the gas by 300% (with 80% helium). Because airway resistance is directly influenced by density (Poiseuille's Law), there has been much interest in using heliox to reduce resistance during acute exacerbations of asthma. Unfortunately, a recent meta-analysis conducted by the Cochrane Airway Group [32] failed to find significant benefit from the existing studies. Observational data and case reports suggest that heliox assists patients with vocal cord dysfunction, a disorder characterized by increased resistance to expiratory flow at the level of the vocal cords. It may also be useful with other types of upper airway obstruction.

Inspiratory resistance can easily be approximated in patients requiring mechanical ventilation. The pressure gradient for flow is constant throughout a constant flow breath. Once this pressure gradient is established, inspiratory resistance can be measured at any point in the respiratory cycle, provided the airway pressure and the pressure distending the alveoli and chest wall are known. The pressure gradient that drives flow is easily determined near the end of inspiration, subtracting end-inspiratory plateau pressure (peak static or plateau pressure) from peak airway pressure (peak dynamic pressure). Therefore, inspiratory resistance equals peak dynamic pressure minus plateau pressure, divided by flow ($Ri = [Pd - Ps]/V$). In a normal individual inspiratory resistance rarely exceeds 15 cmH_2O/l per s [4]. In mechanically ventilated patients, a sudden increase in peak pressures without an increase in plateau pressure signifies a sudden increase in resistance. A cause for the increased resistance should immediately be sought, because the most common causes (problem with ventilator circuit, mucous in the airway, or bronchospasm) can be readily treated.

The size of the endotracheal tube can be critical in determining the cause of elevated resistance [25]. Because flow in

the trachea is turbulent, the resistance is inversely proportional to the radius of the trachea to the fifth power. Because most endotracheal tubes are significantly smaller than the trachea, resistance to flow is significantly increased [25]. To maintain flow, the pressure gradient must be appropriately increased. With traditional modes of weaning from mechanical ventilation (pressure support), a level of pressure support is maintained to overcome the resistance in the endotracheal tube. Automatic tube compensation (ATC) is a method of reducing the work needed to overcome the increased resistance of the endotracheal tube [33]. ATC is a flow triggered mode that varies pressure levels throughout the respiratory cycle. Studies have found that the increased work of breathing caused by high endotracheal tube resistance is decreased with ATC when compared with pressure support [33,34].

Least squares fit method

As described above, traditional methods for measuring respiratory mechanics require ventilator manipulation. Maneuvers such as inspiratory pause, expiratory pause, and airway occlusion have been used to measure variables such as compliance, resistance, and auto-PEEP. More advanced ventilators have built-in pressure transducers and pneumotachographs to permit continuous measurement of pressure and flow. By incorporating these data into mathematical models, such as the least squares fit method, measurements of respiratory mechanics can potentially be monitored continuously and without ventilator manipulation. Through constant knowledge of flow, pressure, and volume (obtained through the integration of flow), other variables (compliance, resistance, and auto-PEEP) can be resolved.

Small series have compared the least squares fit method with traditional methods, and have tielded promising findings. The least squares fit method correlates well with traditional methods of measuring compliance, resistance, and auto-PEEP [35,36], but it is not in widespread use at present. The technology for computing continuous measurements and computing by the least squares fit method is not readily available in most intensive care units. A potential weakness of the least squares fit method is that data are presented for a block of time, usually a single breath. If the start of inspiration or the end of exhalation are not measured correctly by the ventilator, the measurements will be incorrect [36]. Although this does not present a major problem in paralyzed patients, interaction between patient and ventilator can skew the mechanical measurements. Also, the mathematics of 'fitting' nonlinear patient breaths into linear mathematical models will always create some degree of error. At this time the least squares fit method of calculating respiratory mechanics is intriguing, and further work will help to define its role in the intensive care unit.

Work of breathing and impedance

Impedance to airflow includes the resistance to airflow as well as the force required to overcome the elasticity of the lungs and chest wall. The inertia of the airway is also part of impedance, but its contribution is negligible in respiratory physiology. Impedance can be estimated through measurements of the work of breathing (WOB).

Work is defined as the product of pressure and volume ($W = P \times V$). In respiratory physiology, WOB describes the energy required as flow begins to perform the task of ventilation. The calculation of WOB is usually associated with inspiratory effort, because expiration is generally a passive process. However, in patients with air trapping or acute respiratory failure, expiration can be an active process and can require significant work. As the WOB increases, increased demand is imposed on the respiratory muscles. The respiratory muscles of patients in acute respiratory distress will use an increasing percentage of the cardiac output (which can induce ischemia in patients with coronary artery disease). As the demand increases, the respiratory muscles will eventually fatigue. Bellemare and Grassino [37] first described the diaphragmatic threshold for fatigue as the product of inspiratory time and the change in transdiaphragmatic pressure with inspiration. When the diaphragmatic threshold for fatigue exceeded 0.15, the task of ventilation could not be performed for longer than 45 min. As the diaphragm fatigues, the accessory muscles of respiration are recruited, and the respiratory rate is increased. When fatigue leads to inadequate ventilation, carbon dioxide levels in the blood increase and indicate a need for mechanical ventilation.

Usually, the goal of mechanical ventilation is to provide the vital organs with adequate oxygenation and ventilation while decreasing the WOB. As the underlying disease process resolves, the ventilator work is decreased and the patient's WOB is increased until the patient is able to approximate the WOB needed when extubated. From the above discussion, it should be apparent that estimating the WOB in patients breathing spontaneously and on mechanical ventilation can be clinically important. WOB can be determined through analysis of a PV plot, where work is the area under the curve. Therefore, integrating the PV plot yields WOB. In such a plot, pressure represents the sum of the transpulmonary pressure gradient and the chest wall pressure gradient.

In a spontaneously breathing patient, transpulmonary pressure can be measured by placing an esophageal balloon, because esophageal pressure (Pes) estimates pleural pressure. However, there is no direct method for measuring the chest wall pressure gradient. Three estimates of the chest wall gradient have been used to assess the WOB indirectly [1]. First, the chest wall gradient can be estimated using computer analysis. The equation of motion ($P = V/C + [Q \times R]$) is the basis of computer analysis for pulmonary mechanics [38]. When modified for the chest wall, resistive forces ($Q \times R$) can be eliminated, and the equation describes the elastic forces of the chest wall ($Pcw = Vt/2Ccw$) or work (product of average inflation pressure and Vt): $W = Vt^2/2Ccw$ [1].

Second, the chest wall pressure gradient can be estimated by delivering a known volume to a passive patient and measuring the change in esophageal pressure. By adding this pressure to that of a spontaneous breath of the same volume and integrating the area, The WOB can be estimated (Fig. 8). In a patient receiving mechanical ventilation, the WOB can be measured directly. In a passive individual (resulting from heavy sedation or paralysis), the WOB can be determined by measuring the average inspiratory pressure (Pavg) and multiplying it by the volume. Several methods of determining average inspiratory pressure can be used.

During spontaneous breathing or while the patient is receiving mechanically delivered breaths, the equation of motion can be modified to determine the Pavg: Pavg = (Vt/ti × R) + (Vt/2C) + Pex, where ti = inspiratory time. In this modification, Pex is the end-expiratory pressure. Therefore, Pavg will indicate the pressure needed to overcome frictional forces, elastic forces, and impedance, as well as the pressure resulting from hyperinflation.

During mechanical ventilation in a passive patient, Pavg and WOB can be determined by integrating the airway pressure (Paw)–volume plot, with Pavg determined by dividing the area by Vt. Alternatively, airway pressure at mid-inspiratory time or mid-volume can be used to estimate Pavg. This is the easiest method, but it is not the most accurate, and during constant flow inflation the Paw–time tracing can be used to determine Pavg. This tracing can be obtained at the bedside by transducing Paw using a hemodynamic pressure monitor [1]. Finally, Pavg can be determined from commonly recorded airway pressures – peak inspiratory pressure (Pd), Ps, and Pex – during constant flow inflation. In this case, Pavg = Pd – (Ps – Pex)/2 (Fig. 9) [1].

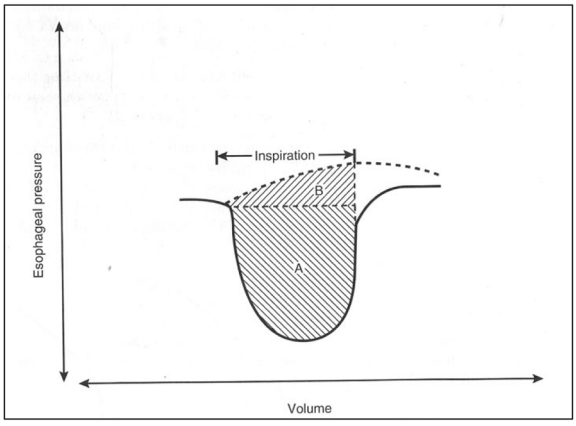
In most circumstances, the mechanically ventilated patient will perform part of the WOB, while the ventilator will provide the remainder. To estimate the WOB done by the patient, measurements must be taken when the patient is active (participating in ventilation) and when they are passive (the ventilator does all of the work while the patient is heavily sedated or paralyzed). During volume modes of ventilation, the Paw–volume plot can be integrated to estimate the work. By measuring the difference in the WOB between patient-active and patient-passive breaths, the patient's WOB on a volume assist mode can be determined. Alternatively, an esophageal balloon can be placed to measure pleural pressure accurately. After a Pes–volume plot is constructed, the difference between active and passive breaths can determine patient's WOB. Although esophageal balloon placement yields more accurate results, it is rarely done in clinical practice.

Determination of the WOB in patients on pressure modes of ventilation is more complicated [1]. If the patient is passive, measurements can be made as explained above. However, if the patient is participating in the WOB (pressure support mode), the initial effort produces a negative transthoracic pressure (pleural pressure). When the machine is triggered, positive pressure is applied and the transthoracic pressure increases. Therefore, the change in pressure from a PV plot on the ventilator will not accurately reflect the total change in pressure. The airway pressure from the ventilator can be used to estimate muscular effort and calculate the WOB, but this is difficult. Alternatively, an esophageal balloon can be placed and the integral of Pes and flow can be used to calculate the lung's WOB. The equation of motion must then be used to estimate the work performed by the chest wall, and the thoracic WOB can then be determined.

In different individuals with the same WOB, the respiratory efficiency (WOB/oxygen consumption of respiratory muscles) can have wide variation [39]. This variation can be understood by noting that the calculation of work requires a change in volume. In respiratory physiology, energy can be expended during the isometric phase of respiration. The pressure time product (PTP) is the product of the average inspiratory pressure (starting from the onset of effort) and the duration of inspiration: PTP = Pavg × Ti. The PTP was developed to account for energy expenditures during the dynamic and isometric phases of respiration. Therefore, the PTP will more directly measure the total energy (in addition to the total work) of breathing [1,39].

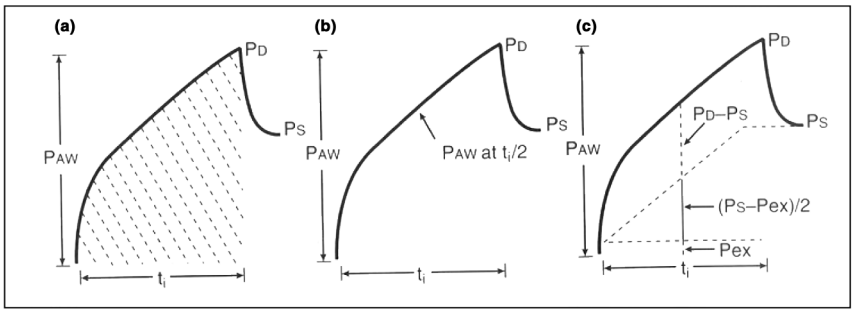
Traditionally, the PTP has been measured as the time integral of the difference between the esophageal pressure tracing and the recoil pressure of the chest wall [40]. However, this

Figure 8



Calculating the work of breathing during spontaneous ventilation using an esophageal balloon. Area A represents the work to move air into and out of the lungs. Area B represents the work to expand the chest wall and is calculated from a pressure–volume curve in a passive patient receiving a mechanically generated breath. The sum of A and B represents the total work of breathing, and it can be determined through integration of the product of esophageal pressure and flow. Reprinted from [1] with permission from Elsevier.

Figure 9



Calculation of work per liter of ventilation (Pavg) in a passive patient on constant-flow mechanical ventilation. Pavg can be calculated by three methods. **(a)** Dividing the integral of the airway pressure (Paw) by the inspiratory time (Ti). **(b)** Recording the airway pressure at the mid-inspiratory time (Ti/2). **(c)** Calculating Pd – (Ps – Pex)/2, where Pd = peak inspiratory pressure, Ps = estimate of end-inspiratory pressure, and Pex = estimate of end-expiratory pressure. Reprinted from [1] with permission from Elsevier.

method may not account for energy expenditure needed to overcome the load on inspiratory muscles at the beginning of inspiration in patients with dynamic hyperinflation [40]. The traditional measurement may also fail to account for the energy needed to stop active expiration [40]. Determination of 'upper bound PTP' and 'lower bound PTP' have enabled calculations of PTP throughout the respiratory cycle so that total energy expenditure can be approximated (Fig. 10).

The pressure time index (PTI) expands on the PTP. It is determined by the following equation [1,41]: PTI = (Pavg/MIP) × (Ti/Ttot), where MIP is the maximal inspiratory pressure that can be generated by an individual, Ti is the duration of inspiration, and Ttot is the duration of the respiratory cycle. By including the measurements used in the PTP, the PTI also yields a more reliable estimate (compared with WOB) of the total energy expended in respiration. Addition of the MIP to the calculation of PTI permits determination of the respiratory effort as related to respiratory strength. MIP can easily be calculated at the bedside of a mechanically ventilated patient with the use of a one-way valve [1]. Inclusion of the Ttot in the PTI permits the duration of energy expenditure in the respiratory cycle to be compared with the duration of rest. The PTI, much like the diaphragmatic threshold for fatigue of Bellemare and Grassino [37], has been used to predict the likelihood of subsequent respiratory fatigue and the need for intubation [41,42]. Conversely, it has been applied to prediction of successful discontinuance of mechanical ventilation in patients weaning from mechanical ventilation [43,44]. A weakness of the PTI in determining success of extubation is that it does not incorporate the respiratory rate. A common reaction of patients in respiratory failure is to increase the respiratory rate and to decrease Vt in order to decrease the subjective sensation of dyspnea. In such patients, the PTI would decrease as the Vt decreased.

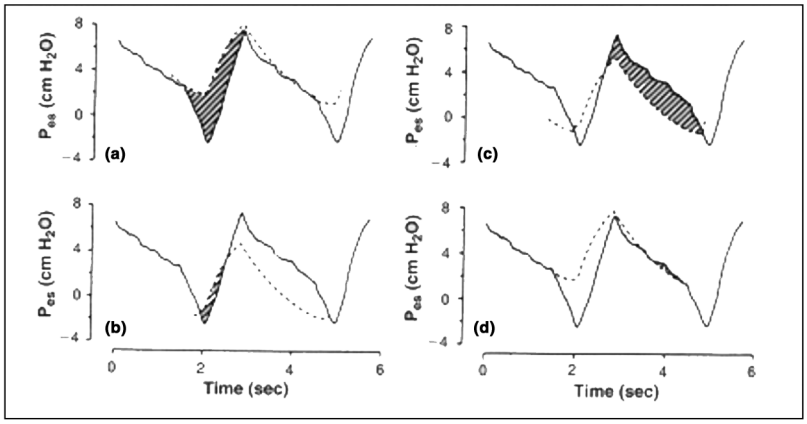
Quantifications of the inspiratory WOB have also been applied to prediction of weaning success. Unfortunately, these calculations, like the PTI, have not proven to be highly predictive, limiting their use at the bedside. Other measures that are simpler to determine have proven to be more useful and are discussed in the following part of the review.

Discontinuation of mechanical ventilation

As stated above, successful discontinuation of mechanical ventilation will depend on close assessment of the patient's respiratory mechanics while on the ventilator. In addition to assessing the mechanics, there are many other considerations. First, it is important to recall the indication for mechanical ventilation and intubation. Some indications (e.g. altered mental status, upper gastrointestinal bleed threatening airway safety, inability to handle secretions, recurrent aspiration, hemoptysis) may be accompanied by normal respiratory mechanics, but mechanical ventilation may be necessary until the indication for intubation has been addressed. For example, a patient with severe alteration in mental status requiring intubation for airway protection should have improved mental status, require suctioning less than every 2 hours, be able to follow basic commands, and have a cough and gag reflex before extubation. However, in patients intubated for respiratory failure, assessment of respiratory mechanics before extubation can help to predict the success of extubation.

Weaning trials are recommended for patients with prolonged intubation or cardiopulmonary causes for intubation [45]. In general, a weaning trial involves reducing the work performed by the ventilator while monitoring for evidence of fatigue or altered gas exchange. There are several different ways to perform a weaning trial. Pressure support ventilation is a mode of ventilation characterized by patient triggered ventilation with both an inspiratory pressure level (IPL) and PEEP. The IPL and PEEP are gradually decreased to minimal levels before extubation. Although exceptions occur, the IPL should usually be less than 12 cmH_2O and the PEEP should be less than 7 cmH_2O before extubation is attempted.

Figure 10



Energy expenditure determined by the pressure time product (PTP) in a patient on pressure support ventilation. In all graphs, the continuous line is esophageal pressure (Pes) and the interrupted line represents the estimated recoil pressure of the chest wall (Pescw). **(a)** Pressure tracings have been superimposed so that Pescw is equal to Pes at the onset of the first inspiratory effort, and the integrated difference (hatched area) represents the upper bound PTPinsp. **(b)** Pressure tracings have been superimposed so that Pescw is equal to Pes at the first moment of transition from expiratory to inspiratory flow, and the integrated difference (hatched area) represents lower bound PTPinsp. **(c)** Pressure tracings are superimposed so that Pescw is equal to Pes at the second moment of transition from expiratory to inspiratory flow, and the integrated difference (hatched area) represents upper bound expiratory PTP (PTPexp). **(d)** Pressure tracings have been superimposed so that Pescw is equal to Pes at the onset of the second inspiratory effort, and the integrated difference (hatched area) represents lower bound PTPexp. With permission from Jubran *et al*. [56].

Usually, the IPL is under 7 cmH_2O, with PEEP below 5 cmH_2O. Intermittent mandatory ventilation is a mode that provides fully supported, volume controlled breaths with unsupported, patient triggered breaths. The respiratory rate of the supported breaths is gradually decreased to permit the patient to increase their WOB gradually. In general, respiratory rates less than 4/min tolerated for 2 hours yield a favorable prognosis on extubation [46].

Several methods of weaning further reduce the WOB and are termed spontaneous breathing trials (SBTs). With a continuous positive ariway pressure (CPAP) trial, an intubated patient is allowed to breathe spontaneously while receiving CPAP. As the patient is still connected to the ventilator, mechanics can easily be measured. The size of the endotracheal tube will influence the level of CPAP required to overcome the resistance of the tube. It is our experience that, in patients with heart failure and an endotracheal tube above 7.0 mm in diameter, a 30 min trial of CPAP at 0 cmH_2O may help to determine whether a patient will develop pulmonary edema requiring reintubation following extubation. At our institution, with the use of impedance cardiography, we found that patients who fail a CPAP trial at 0 cmH_2O have a significant decrease in cardiac output compared with patients who passed the SBT [47]. In a trach collar trial, a patient with a tracheostomy is removed from the ventilator to breathe with supplemental oxygen. A T-piece trial involves placing a 'T' shaped tube, connected to an oxygen source, over the endotracheal tube so that the patient may breathe spontaneously for a set amount of time.

In 1995, Esteban and coworkers [48] investigated different strategies for weaning patients with respiratory distress. The four weaning strategies compared were pressure support, intermittent mandatory ventilation, a once daily SBT, and intermittent SBTs (more than two per day). With a once daily SBT, the rate of successful weaning was superior to the rates with pressure support ventilation and intermittent mandatory ventilation, and equivalent to the rate with multiple daily trials. Most intensive care units have adopted this strategy for difficult-to-wean patients.

When a patient is on a SBT, there are several mechanical variables that can help to determine whether extubation is appropriate or will likely result in reintubation. The rapid shallow breathing index (RSBI) has been widely used to help to predict subsequent respiratory failure in patients weaning from mechanical ventilation. Measured as the respiratory rate divided by the Vt in liters (RSBI = RR/Vt), it has been shown to correlate well with the WOB and the PTI in mechanically ventilated patients [49]. The extreme ease of its calculation has made this measurement popular. The RSBI should be calculated during an unassisted breathing trial. In patients under 70 years of age, a RSBI below 105 during a weaning trial yields an 80% positive predictive value for successful extubation [49]. In patients older than 70 years, a RSBI under 130 during a weaning trial still yields a positive predictive value of 80% for successful extubation [43].

Alternatively, the time to recovery of minute ventilation following a trial of weaning from mechanical ventilation has been used as a predictor of successful extubation. Minute

ventilation equals the respiratory rate multiplied by the Vt ($Ve = RR \times Vt$). During a SBT, the minute ventilation will commonly increase as the patient attempts to manage the increased workload. When the SBT has concluded and the ventilator work is increased, the minute ventilation will gradually return to its baseline. The rate of return to baseline of minute ventilation is thought to estimate the respiratory reserve, and it has been found to help with prediction of successful extubation. In a recent study, the minute ventilation recovery time was found to be significantly shorter in patients who were successfully extubated than in those who required repeat intubation ($P < 0.01$) [50].

In addition to these measures of respiratory mechanics, several determinants of respiratory muscle strength have been developed. The negative inspiratory force is a marker of the force that a patient can generate against an occluded valve. Generally, this requires 1 s of inspiratory effort against the occluded valve, and the most negative of three measurements is the negative inspiratory force. A negative force that is weaker than -30 cmH_2O (0 to -30 cmH_2O) implies respiratory muscle weakness and difficult extubation [4,51]. The P100, or P0.1, is a measure of inspiratory occlusion pressure. Generally, the inspiratory arm of the ventilator is occluded during expiration for 100 ms, and five measurements of pressure are determined by a pressure transducer over a 60–90 s period. The average of these measures is the P0.1. Several groups have found that the P0.1 is a successful independent predictor of ventilator weaning, with values greater than 4.5 cmH_2O associated with a poorer rate of extubation [4,51,52].

It is known that prolonged intubation leads to increased complications, including pneumonia and muscle weakness. Much attention has been given to the use of noninvasive positive pressure ventilation (NIPPV) following extubation. In several conditions (immunosuppression with bilateral pulmonary infiltrates, chronic obstrcutive pulmonary dosease [COPD], cardiogenic pulmonary edema, and recovery from thoracic surgery), there is good evidence for use of NIPPV to prevent intubation [53]. In patients with COPD who were recently extubated, the application of NIPPV resulted in decreased need for reintubation. However, Esteban and coworkers [54] recently found that, in patients developing acute respiratory failure shortly after extubation, the application of NIPPV did not result in improved outcomes. That study enrolled few patients with COPD. Moreover, delays in reintubation following NIPPV were correlated with increased mortality. Therefore, although it is reasonable to attempt NIPPV following extubation, such patients must be carefully monitored. If no improvement is seen within 2 hours and the patient's wishes are to be intubated if necessary, then reintubation should be performed to minimize the chance of a poor outcome [55].

Conclusion

Monitoring of respiratory mechanics is done widely in pulmonary medicine and in intensive care units. Measurements are readily available at the bedside and can be used to assist with diagnosis and treatment of various illnesses. Measurement of respiratory mechanics is most widely done in patients receiving mechanical ventilation. In mechanically ventilated patients, measurements of mechanics can provide information about the severity of disease, the response to treatment, and the safety of ventilator discontinuation. Mechanics have also become a treatment modality, because measuring plateau pressures and making appropriate ventilator adjustments can lead to improved outcomes in selected patients receiving mechanical ventilation. We anticipate that, as technology improves and the measurement of mechanics moves toward automation and ventilator algorithms, the use of respiratory mechanics at the bedside will increase further.

Competing interests

The author(s) declare that they have no competing interests.

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