Assessing Respiratory System Mechanical Function

Ruben D. Restrepo, MD, RT[a,b,*],
Diana M. Serrato, MSc, RT[a,b], Rodrigo Adasme, PT, MSc, RT[c]

KEYWORDS

• Lung compliance • Esophageal pressure • Impedance • Lung injury • Respiratory mechanics
• Ventilator graphics

KEY POINTS

- Assessment of the respiratory system mechanical function in critically ill patients can detect early signs of abnormalities that could affect patient outcomes.
- The patient-ventilator interaction can be evaluated through noninvasive and invasive methods.
- A wide range of measurements and calculations of respiratory mechanics are available to optimize the selection of ventilatory modalities and specific ventilator parameters.
- All ventilatory strategies should be directed to minimize the patient's work of breathing and minimize lung injury.

INTRODUCTION

The assessment of the respiratory mechanical function during mechanical ventilatory support refers to the evaluation of respiratory system physiology and ventilator performance through a variety of methods with the ultimate goal of understanding the interactions between applied pressures and flows inside the respiratory system.[1] Early detection of abnormalities in this interaction is critical because it could affect the patient's outcomes. In the critical care setting, it has become increasingly important to recognize whether the respiratory function has improved or deteriorated, whether the ventilator settings match the patient's demand, and whether the selection of ventilator parameters follows a lung-protective strategy. Respiratory measurements include several single and combined parameters but also a long list of derived values. In order to obtain these values and identify abnormalities in the respiratory mechanical function, a variety of monitoring methods are currently available to clinicians. Ventilator graphics, esophageal pressure, intra-abdominal pressure, and electric impedance tomography are some of the best-known monitoring tools to obtain measurements and adequately evaluate the respiratory system mechanical function.

Almost 16 years after the National Institutes of Health Acute respiratory Distress Syndrome (ARDS) Network (ARDSnet) reported the benefits of lower tidal volumes (VTs) on survival rates for

Disclosure: The authors have nothing to disclose.
[a] Department of Respiratory Care, The University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, MC 6248, San Antonio, TX 78229, USA; [b] Department of Respiratory Care, Universidad Santiago de Cali, Calle 5#62-00, Cali, Colombia 760035; [c] Universidad Catolica de Chile, 328 Avenida Libertador Bernardo O' Higgins, Santiago de Chile, Chile
* Corresponding author.
E-mail address: restrepor@uthscsa.edu

Clin Chest Med 37 (2016) 615–632
http://dx.doi.org/10.1016/j.ccm.2016.07.003

mechanically ventilated patients with ARDS, much research has been focused on methods that evaluate the effects of other respiratory parameters in the overall management of patients undergoing mechanical ventilation.[2,3] Evaluations of positive end-expiratory pressure (PEEP), synchrony, flow delivery, breath cycling, triggering, alveolar stress, and alveolar distension, among others, have become routine in the critical care setting. It must be remembered that mechanical ventilation is a supportive therapy and as such it should be carefully monitored to minimize complications.

This article reviews some of the basic and advanced methods to assess the respiratory system mechanical function as well as the most current evidence that supports their use in the critical care setting.

VENTILATOR GRAPHICAL DISPLAYS

Modern ventilators continuously measure pressure, flow, and volume in the ventilator circuit and can display a variety of waveforms. Common scalar displays provide a representation of pressure, flow, and volume against time, whereas loops show 2 parameters plotted against each other. These displays constitute the fastest and most readily available tools to evaluate respiratory system mechanical function.[4,5]

Common Scalar Displays

Pressure-time displays

Airway pressure (P_{aw}) is displayed on the ventilator screen as a function of time. The shape of the P_{aw} waveform is influenced by inspiratory flow, respiratory system mechanics, and the presence of patient's inspiratory effort. Delivery of flow using a square versus decelerating pattern also provides a different configuration to the pressure-versus-time waveform (Fig. 1).

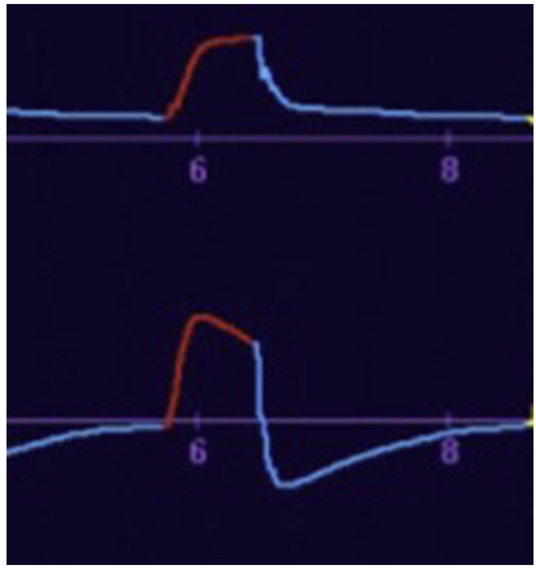

Fig. 1. Pressure and flow curves showing the typical appearance of a pressure-limited ventilation in which the inspiratory flow pattern is decelerating.

Alveolar versus airway pressure Because peak inspiratory pressure (P_{peak}) is always be greater than alveolar pressure (P_{alv}) during inspiration because of the presence of flow and airway resistance, P_{alv} is estimated with an end-inspiratory pause (EIP) maneuver. Applying an EIP for 0.5 to 2 seconds during passive breathing allows pressure equilibration throughout the system while flow decreases to zero. Under these static conditions, a plateau pressure (P_{plat}) measured at the proximal airway approximates the P_{alv} (Fig. 2).

During pressure control ventilation P_{plat} is equal to the applied inspiratory pressure if flow is zero at the end of the set inspiratory time. An EIP can also be applied during pressure control ventilation to measure P_{plat} in passive patients. Special consideration needs to be given to the fact that P_{plat} can be greatly affected by low chest wall compliance (C_{CW}) so it should be used as a surrogate for P_{alv} only when C_{CW} is normal.

Limiting P_{alv} (P_{plat}) to 30 cm H_2O seems to decrease the risk of alveolar overdistension and ventilator-induced lung injury.[6] However, some clinicians have argued that there may not be a

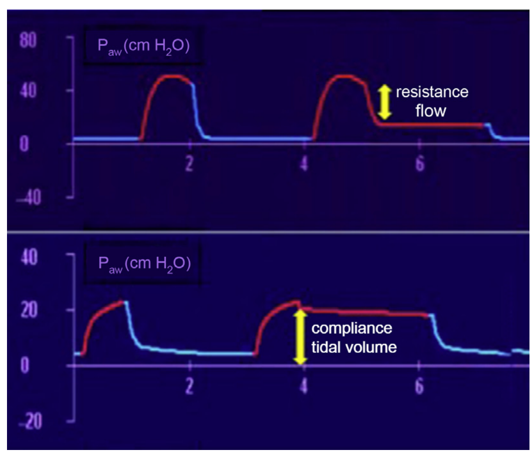

Fig. 2. Pressure-time scalars showing the effect of an EIP. With a period of no flow, the pressure equilibrates to the P_{plat}. P_{plat} represents the peak alveolar pressure. The gradient between the peak inspiratory pressure (PIP) and P_{plat} is determined by resistance and flow. The gradient between P_{plat} and PEEP is determined by VT and respiratory system compliance.

safe P_{alv} (P_{plat}) and thus targeting a P_{plat} as low as possible may be a better lung-protective strategy.[7,8]

Al-Rawas and colleagues[9] recently described the use of the expiratory time constant (T_E; the time for approximately 63% of the expiration to occur) during a passive deflation for determinations of P_{plat}, respiratory system compliance, and total resistance. This method avoids the need to apply an EIP, allows continuous and automatic surveillance of P_{plat}, and permits real-time assessments of pulmonary mechanics even in spontaneously breathing modes such as pressure support (Fig. 3).[9]

Auto–positive end-expiratory pressure Any condition that causes incomplete emptying of the lungs leads to increased end-expiratory volumes (air trapping, dynamic hyperinflation) and alveolar pressures greater than the preset PEEP level (auto-PEEP, inadvertent PEEP, intrinsic PEEP, or occult PEEP). Auto-PEEP in passive patients can be estimated from the pressure-time tracing by applying an end-expiratory pause for 0.5 to 2 seconds (Fig. 4).[10]

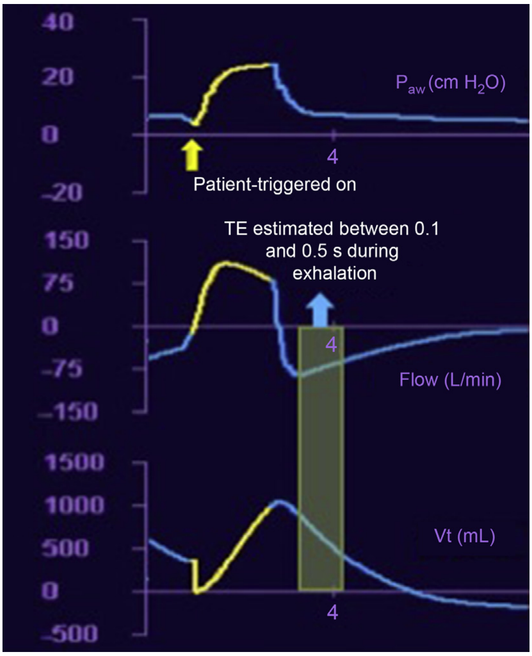

Fig. 3. Pressure, flow, and volume scalars for determination of T_E constant. In the first breath a patient is ventilated with pressure support ventilation at 25 cm H_2O and positive PEEP at 5 cm H_2O. The T_E constant was estimated during passive exhalation between 0.10 and 0.50 seconds using exhaled flow rate and VT scalar.

During volume assist control ventilation, auto-PEEP increases P_{alv} throughout the ventilator cycle; during pressure-targeted ventilation, auto-PEEP decreases the alveolar pressure gradient for inspiration (driving pressure) and thus reduces the VT. An important effect of auto-PEEP is that it produces a gradient between P_{alv} and circuit pressure, which must be overcome by the patient's effort to trigger a ventilator breath. If severe enough, auto-PEEP is associated with asynchrony because of missed triggered patient breaths. This condition is most common in patients with obstructive airway disease who require long T_E.[11,12]

Patient-Ventilator flow synchrony During volume assist control ventilation, the configuration of the pressure-time curve provides important information about patient-ventilator synchrony. In Fig. 5, the patient's increased inspiratory effort coupled with an inadequate delivery of flow by the ventilator results in a scooped contour on the airway pressure curve during inspiration.[13]

Patient-ventilator trigger synchrony Assisted breaths are commonly triggered by either a circuit pressure or continuous flow change produced by patient effort. On modern systems, both types of triggers are effective and respond promptly to patient effort.[14] Trigger sensitivity should be set as sensitive as possible without producing autotriggering. An insensitive trigger setting may cause no ventilator response to an effort (missed breath or missed trigger) or else force the patient to create an enormous amount of inspiratory effort that can be displayed on the pressure-time curve as an excessive negative deflection at the beginning of each breath (Fig. 6). Trigger dyssynchronies cause excessive and wasted diaphragmatic energy expenditure.

Patient-ventilator cycle synchrony Inspiratory muscle relaxation and recruitment of expiratory muscles such as the transversus abdominis signals the initiation of the exhalation phase. If termination (cycling) of the mechanical breath occurs after this point (delayed cycling) the attempt to cycle causes an increase in P_{aw} at the end of inspiration (Fig. 7).[13,15]

In contrast, if ventilator breath cycling occurs before the patient inspiratory effort has ceased (premature cycling), a decrease in P_{aw} may be noted at the beginning of the ventilator's expiratory phase and sometimes a second breath is triggered.

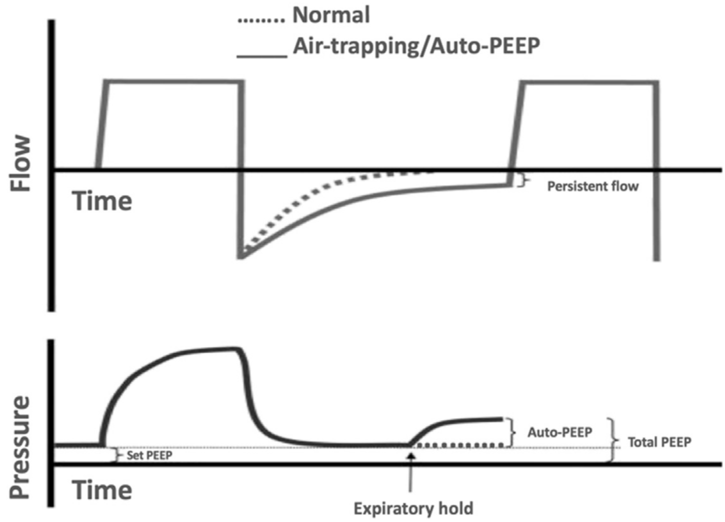

Fig. 4. Flow-time scalar (*top*) indicating persistency of expiratory flow at the end of the breath, indicating air trapping. The end-expiratory alveolar pressure is obtained after applying an end-expiratory pause. The difference between the pressure measured during this maneuver (total PEEP) and the level of PEEP selected by the operator is the amount of auto-PEEP. The pressure-time scalar (*bottom*) displays the end-expiratory alveolar pressure obtained after applying an end-expiratory pause.

Flow-time curve

A unique feature of the flow-time curve compared with the pressure or volume scalar displays is that it provides as much information above as below the baseline.[16] By convention, inspiratory flow is positive. It is either preset (volume assist control ventilation) or variable (pressure-targeted ventilation) Expiratory flow is negative and always passive (Fig. 8).

As previously discussed, any condition that causes incomplete emptying of the lungs leads to auto-PEEP. Under these conditions, the characteristic feature on the flow-versus-time scalar display is the failure of the expiratory tracing to return to baseline (zero flow) before the next mechanical breath (Fig. 9) The 2 most common causes of this phenomenon are increased airway resistance (R_{aw}) or insufficient T_E.[18]

The presence of intermittent notching in the expiratory flow tracing may occur in the presence of missed trigger efforts (see flow tracing in Fig. 8).

Volume-time curve

Because most modern ventilators compensate for circuit compression, the VT displayed on the volume-versus-time curve closely resembles the volume output from the ventilator. The presence of air leak can be easily identified when the expiratory tracing of the curve does not return to baseline before the next breath delivery. In most cases, it gives the appearance of a check mark as the volume tracing resets to zero when an inspiration begins (Fig. 10) The use of the volume-time curves may be particularly important in quantifying air leaks after chest tube placement or to titrate cuff inflation.[19]

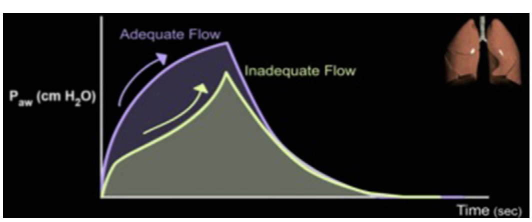

Fig. 5. Effect of asynchrony on the P_{aw} waveform during volume control ventilation. The arrows indicate a decrease in P_{aw} caused by the fixed flow from the ventilator and the increased patient effort.

Loops

Flow-volume loops

Most ventilators display flow-volume loops with inspiratory flow above baseline and expiratory flow below baseline. In obstructed airway disease

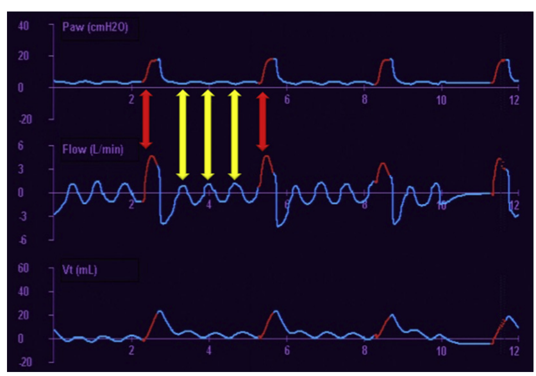

Fig. 6. Pressure-time and flow-time scalars indicating the presence of 3 missed triggered breaths (*yellow arrows*). There are P_{aw} decreases ($\geq$0.5 cm H_2O) simultaneous to flow decrease and not followed by an assisted breath (*red arrows*).

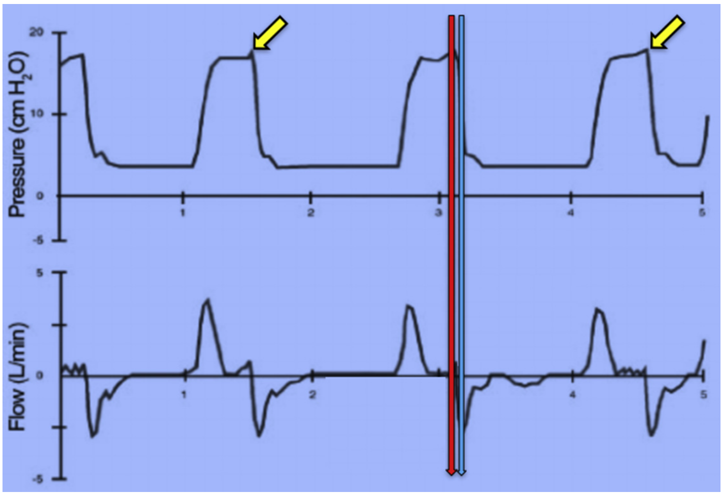

Fig. 7. Pressure-time scalar (*top*) showing a bump toward the end of the inspiratory tracing (*yellow arrow*) indicating the patient's attempt to exhale before preset cycling of the mechanical breath. The flow-time scalar[10] (*bottom*) shows patient's cycling into exhalation (*red arrow*) before the mechanical breath cycling (*blue arrow*).

there is a decrease in the peak expiratory flow and a scooped-out pattern. The flow-volume loop can be a useful tool to evaluate bronchodilator response (Fig. 11).

The presence of a saw-tooth pattern on both the inspiratory and expiratory flow-volume curves suggests excessive secretions or presence of condensate in the ventilator circuit (Fig. 12).[20]

Pressure-volume loops

Pressure-volume (P-V) plots can be dynamic (flow present) or static (multiple measurements under no-flow conditions with increasing discrete small changes in volumes). On some ventilators, a static curve can be approximated with a slow-flow inspiration/expiration, which minimizes the flow-related pressures.

The slope of the static curve is a reflection of the respiratory system compliance (C_{RS}). An inflection point is a point on a curve at which the sign of the curvature (ie, the concavity) changes. Lower and upper inflection points on a P-V loop have been regarded as points of interest to detect cyclic derecruitment and overdistension, respectively (Fig. 13, Fig. 14).[21,22] Importantly, derecruitment is probably better assessed on the deflation rather than the inflation limb of the P-V curve.

Using inflection points on the static or slow-flow P-V loop in patients with acute lung injury and ARDS has been proposed as a way to set lung-protective VT and PEEP settings.[23,24] However, 2 important limitations of this approach are that measurement of the P-V curves often requires sedation and sometimes the use of muscle relaxants, and that chest wall mechanics affect the shape of the loop.[25,26] Furthermore, because of the heterogeneity of lung injury, reducing the mechanical properties of the respiratory system to a single schematic approach is overly simplistic. Because alveolar recruitment occurs along the entire P-V loop, the lower inflection point should not be considered a discrete point reflecting global alveolar opening and closure and thus may not reflect the ideal PEEP setting. Similarly, the upper inflection point, classically thought to be the beginning of overdistension, likely also reflects the end of recruitment.[27]

The dynamic P-V loop can be extremely useful in identifying flow asynchrony. Inadequate flow is indicated by the presence of concavity along the inspiratory limb (Fig. 15). Addition of pressure

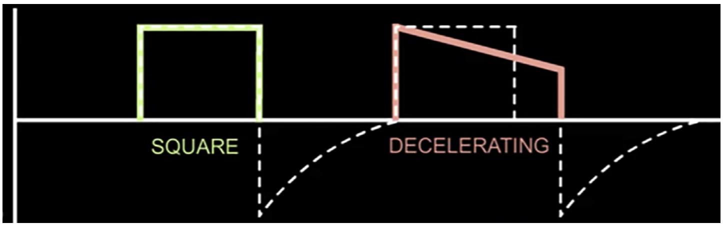

Fig. 8. Typical flow-time scalar configuration of a constant square-flow pattern (*left*)[17] and a decelerating flow pattern (*right*).

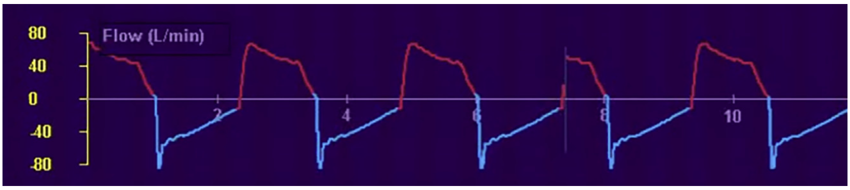

Fig. 9. Flow-time curve showing inability of the expiratory tracing to return to baseline (zero flow) before the next mechanical breath.

support or increase in the inspiratory flow can correct this abnormality and the normal convexity of the inspiratory limb should be restored.

The dynamic P-V loop of a patient on volume assist control ventilation with severe airway obstruction shows an abnormal widening of the curve on the X axis, reflecting the need for high flow-related inflation pressure (Fig. 16).

COMMON DERIVED MEASUREMENTS FROM STANDARD MEASUREMENTS OF PRESSURE, FLOW, AND VOLUME

Compliance (Elastance)

Compliance is defined as the change in lung volume (ΔV) per unit change in pressure (dP). Elastance is the inverse of compliance. Compliance usually refers to a static measurement (ie, no flow is occurring) and thus is determined solely by the elastic properties of the system. Compliance can be calculated for the entire respiratory system ($C_{RS} = \Delta V/P_{plat}$-PEEP); for the lungs alone [$C_L = \Delta V/(P_{plat}$-PEEP – $\Delta P_{es})$]; and for the chest wall ($C_{CW} = \Delta V$/dPes), where dPes is change in Pes over the volume change. A C_{RS} of 50 to 100 mL/cm H_2O is considered normal in mechanically ventilated patients.

Titration of PEEP is routinely used in critically ill patients undergoing mechanical ventilation. The C_{RS} has been a popular mechanics-based method to evaluate the PEEP level. The underlying concept is to use C_{RS} as a surrogate for C_L to detect derecruitment and overdistention, which are situations associated with reduced C_L. A protective lung approach that applies PEEP to obtain the highest C_{RS} has been associated with less organ dysfunction and a trend to lower mortality.[28,29] Importantly, C_{RS} can be used as a surrogate for C_L only when C_{CW} is near normal (100–200 mL/cm H_2O). In situations with low C_{CW} (eg, thoracic deformities, chest wall edema, morbid obesity, abdominal compartment syndrome,[30–32] chest wall trauma, ascites, and chest wall burns), C_{RS} becomes a poor surrogate for C_L and P_{es} measurements to quantify the effects of C_{CW} must be used for accurate assessments of C_L.

Airway Resistance

Airway resistance (R_{aw}) is the frictional opposition offered by the airways to flow and by the tissues to being displaced during both phases of the breathing cycle. During inspiration R_{aw} can be estimated using the following equation: RI = (PIP − P_{plat})/$\dot{V}$i, whereas RE can be estimated as follows: RE = (P_{plat} − PEEP)/$\dot{V}$e, where $\dot{V}i$ and $\dot{V}e$ are inspiratory and expiratory flow respectively.[33]

The main factors affecting airway resistance are viscosity and density of the gas mixture; length and lumen radius of artificial and patient airways; and ventilator flow rate and flow pattern. These factors are mathematically related to airway resistance in the Poiseuille law and determine whether airflow becomes laminar or turbulent.[34] Although normal R_{aw} ranges from approximately 0.5 to 2.5 cm H_2O/L/s, a healthy adult intubated with an 8.0-mm endotracheal tube would have an R_{aw} that could range from 4 to 10 cm H_2O/L/s. The most common causes of increased R_{aw} are the presence of airway secretions, bronchospasm, and obstruction of the endotracheal tube.

Time Constant

The time constant, the product of C_{RS} and R_{aw}, is defined as the time necessary to complete 63% of

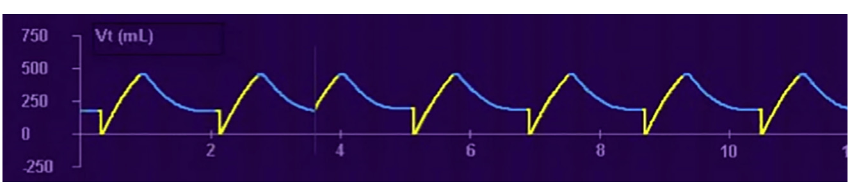

Fig. 10. Volume-time scalar shows the expiratory tracing of the curve (*blue tracing*) not returning to baseline. It gives the appearance of a check mark on delivery of the next breath (*yellow tracing*).

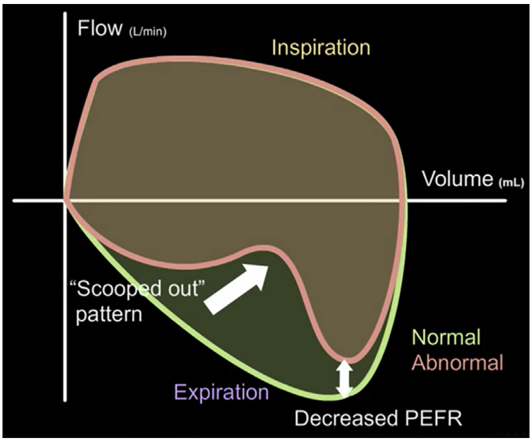

Fig. 11. Flow-volume curve showing the scooped-out pattern of obstructive disease (*red shaded area*) and the pattern associated with either normal airways or positive response to bronchodilation. PEFR, peak expiratory flow rate.

the total change in lung volume following a tidal breath or in response to a pressure step. From this definition, it takes approximately 3 time constants to complete 95% of the lung volume change. Lung units with a higher resistance and/or compliance have longer time constants and require more time to fill and to empty. These units are thus more prone to air trapping and intrinsic PEEP. In mechanically ventilated patient, there are 2 more flow-resistive elements that contribute to the time constant: the artificial airway and the ventilator tubing.[35]

ESOPHAGEAL PRESSURE MONITORING

Esophageal pressure measurements approximate pleural pressure (P_{pl}) and can be used to calculate chest wall mechanics and transpulmonary pressure (P_{tp}; $P_{tp} = P_{aw} - P_{pl}$). Obesity, increased abdominal pressure, scoliosis, spondylitis, fibrothorax, and pleural effusion alter chest wall mechanics and can significantly affect P_{tp} and measured P_{aw}.[36,37] In contrast, negative pleural pressure generated by spontaneous patient efforts also need to be considered in calculating P_{tp}. Because P_{tp} is the pressure that stretches the lung, it is possible that the inability to accurately assess the P_{tp} may explain the lack of efficacy observed in some clinical trials of ventilator management.[38]

Mechanical ventilation has been guided by P_{tp} calculations from esophageal pressure monitoring in studies in patients with acute lung injury. The general goals are to limit end-inspiratory P_{tp} to less than 30 cm H_2O and prevent a negative P_{tp} during expiration (ie, PEEP is set to counterbalance the alveolar collapsing effects of a stiff chest wall).[39] Adjustments of PEEP according to measurements of P_{es} have resulted in significantly greater oxygenation and compliance than those protocols following the ARDSnet low PEEP table.[40] The Esophageal Pressure-Guided Ventilation 2 Trial (EPVent2) has been designed to test the primary hypothesis that adjusting ventilator pressure to achieve positive pressure-time product (PTP) values will result in improved mortality and ventilator-free days in patients with moderate to severe ARDS.[41] At present, because not every patient with ARDS has chest wall involvement, routine measurement of esophageal pressure for the setting of PEEP is not recommended. However, it is likely beneficial in patients with reduced C_{CW} or perhaps with vigorous inspiratory efforts during assisted breaths.

Routine application of esophageal manometry has been considered a challenge to intensivists.[40,42–44] The most important limitations for widespread use of this technique include technical issues, the need for background physiologic knowledge, and the fact that very few studies

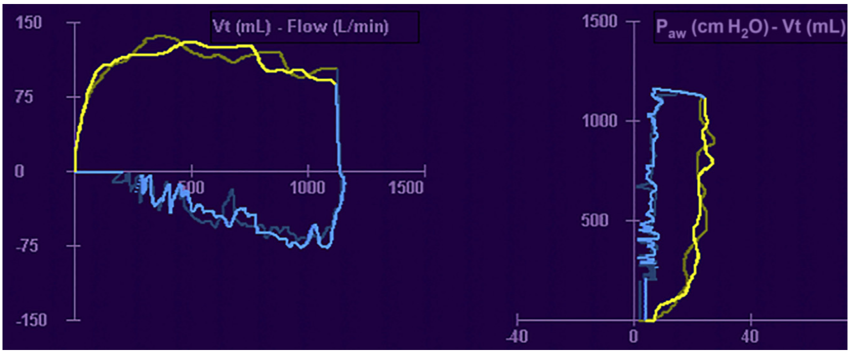

Fig. 12. Saw-tooth pattern on flow-volume and pressure-volume loops representing secretions in the airway.

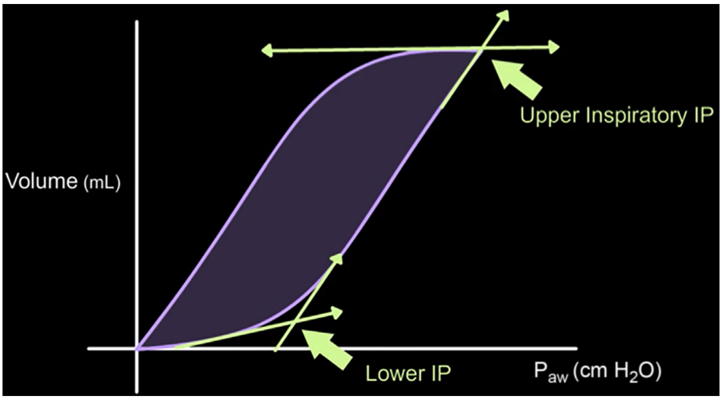

Fig. 13. P-V loop showing the lower inflection point (IP) and upper IP.

have assessed a direct influence of this measurement on patients' outcomes.[45] In addition, the recording of P_{es} in the supine position and in inhomogeneous parenchymal lung disease is affected by important factors that include the elastance and weight of the lung, the elastance and weight of the rib cage, the weight of the mediastinal organs (the weight of the heart can bias the P_{es} by as much as 5 cm H_2O),[46] the elastance and weight of the diaphragm and abdomen, the elastance of the esophageal wall, and the elastance of the esophageal balloon (if filled with too much air).[47] It is important to remember that esophageal pressure monitoring estimates P_{pl} at midthorax and that P_{pl} is more negative in the nondependent thorax and more positive in the dependent thorax.[48–51]

P_{es} monitoring can also be useful in assessing patient muscle energy expenditure through measurements of patient muscle work (work equals the integral of pressure and volume) or PTP(integral of pressure and time) during either assisted or unassisted breathing (see discussion on loads later).

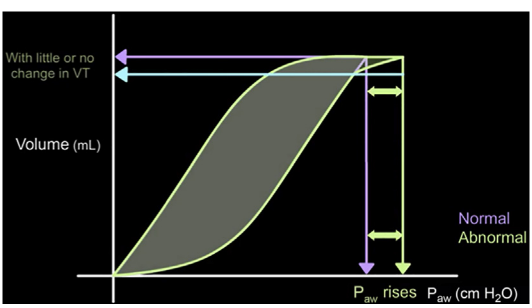

Fig. 14. P-V loop shows increase in P_{aw} without significant change in volume, suggesting the presence of overdistension.

In addition, P_{es} can be used to measure the threshold-triggering load imposed by auto-PEEP, which is obtained by measuring the P_{es} decrease that occurs before P_{aw} decreases during patient efforts. Using this approach, applying circuit PEEP up to 70% to 80% of this measured auto-PEEP can effectively reduce the triggering load without overdistending the lungs.

STRESS INDEX

The stress index (SI), a parameter derived from the shape of the pressure-time curve, can identify injurious mechanical ventilation. It defines the slope of the airway opening pressure during a period of constant flow.[7,52,53] Mathematically, the SI is the coefficient b of a power equation ($P = a \times T_I^b + c$), which describes the shape of the curve (Fig. 17). A linear increase in pressure (SI = 1) suggests adequate alveolar recruitment (minimal derecruitment) and absence of overdistention. If compliance worsens at end inspiration from overdistention, an upward concavity (SI>1) on the pressure-time curve appears. In contrast, if there is derecruitment at end expiration and rerecruitment with inspiration, a progressive improvement in compliance occurs and produces a downward concavity (SI<1), which suggests a potential for additional recruitment.[7,54,55]

It has been advocated that adjusting VT and PEEP to a noninjurious SI (0.95–1.05) can reduce lung injury compared with simply limiting P_{plat} to less than 30 cm H_2O and VT to 6 mL/kg ideal body weight (IBW).[55,56] A recent comparison by Terragni and colleagues[7] of the accuracy of P_{plat} and SI to identify morphologic indices of injurious ventilation using computed tomography revealed that a P_{plat} of greater than 25 cm H_2O and an SI of greater than 1.05 best identified morphologic

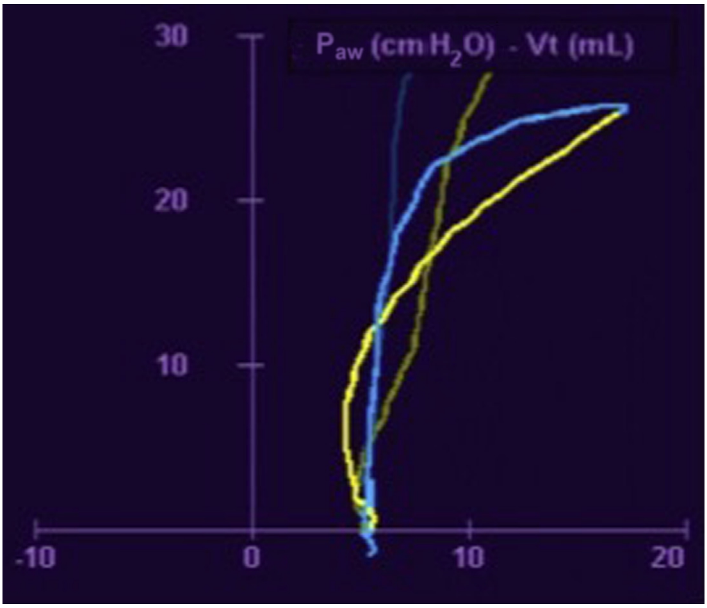

Fig. 15. P-V curve indicating exaggerated patient effort caused by flow starvation, which gives the concave pattern of the inspiratory limb (*yellow tracing*).

markers of injurious ventilation compared with a P_{plat} greater than 30 cm H_2O.[54,57,58]

LUNG STRESS AND STRAIN

Stress and strain are engineering concepts that have been used to describe mechanical aspects of lung stretch. When positive P_{aw} is applied to the lungs, alveoli are exposed to stress forces (end-inspiratory stretch) and undergo a physical deformation known as strain (tidal stretch).[59,60]

Although the P_{plat} and the VT/IBW ratio have been used as the most important targets to limit lung injury during positive pressure ventilation, they are often inadequate surrogates for regional stress and strain[56] because Plat is a P_{aw} measurement, not a P_{tp} measurement; also, regional strain is heavily affected by regional lung mechanics and regional resting lung volumes.[59–61]

Regional stress and strain is also important when adjacent alveoli are exposed to a certain P_{aw} and one of them loses elasticity. Under these conditions, the strain and stress increase in the normal alveoli almost 5-fold.[60,62,63] This phenomenon has been described as a stress raiser. It has been advocated that reducing P_{plat} may minimize these stress increasers.[60] Using recruitment maneuvers and the addition of PEEP may also add benefit by ether correcting or diminishing inhomogeneities (reducing stress increasers).[64,65]

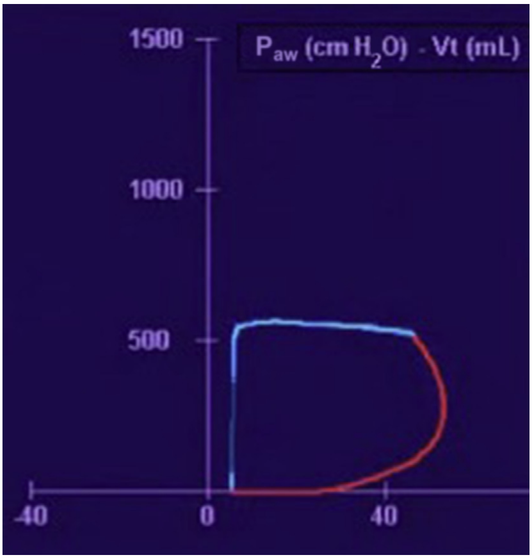

Fig. 16. Abnormal widening of the P-V loop showing air trapping. The expiratory phase[18] shows how, despite the decrease in P_{aw}, the volume remains high for a large proportion of the phase before it decreases to zero before the initiation of a new breath.

INTRA-ABDOMINAL AND TRANSDIAPHRAGMATIC PRESSURES

The diaphragm is the obvious link between the thoracic and abdominal compartments. Any condition that increases the intra-abdominal pressure (P_{abd}) shifts the diaphragm upward and decreases C_{CW}. Under these conditions, the P-V loop typically shifts to the right, making the lower inflection point increase.

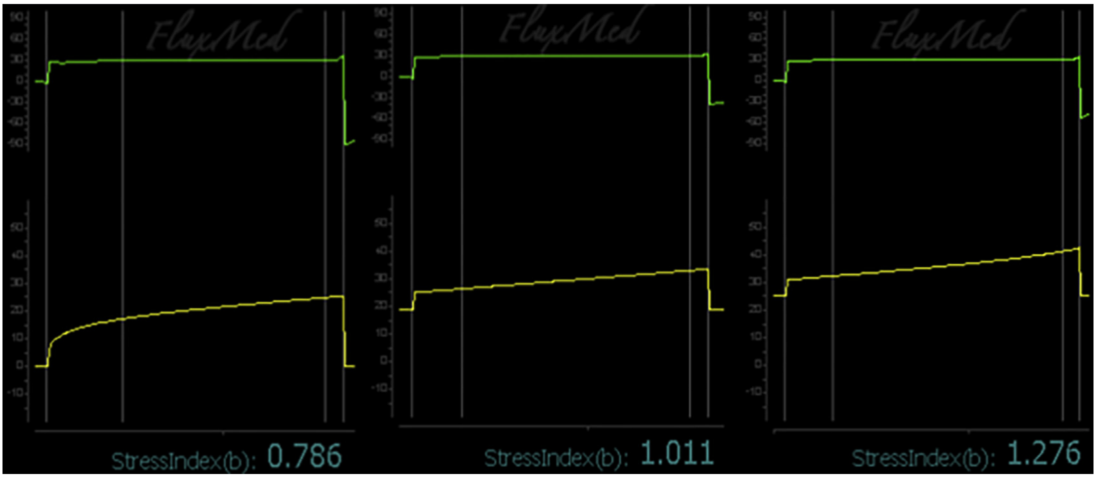

Fig. 17. During the period of constant flow (*green curve*) of a pressure-time curve the presence of a straight line on the opening pressure (SI = 1) suggests the absence of tidal variations in elastance. The presence of a downward concavity (SI<1) suggests decrease in elastance, whereas an upward concavity (SI>1) suggests increase in elastance. (*Courtesy of* SilverSwiss Technology; Available at: http://www.mbmed.com/index.html.)

Normal P_{abd} is 5 mm Hg and increases during inhalation because of the downward displacement of the diaphragm. Although measurement of intraperitoneal pressure is the accepted standard for determination of intra-abdominal pressure, it is not practical. Therefore, the most common method used is via bladder access. The transducer is zeroed at the midaxillary line in the supine position and the P_{abd} should be measured during exhalation, avoiding any abdominal muscle contraction.

Because P_{abd} may be affected by the intrathoracic pressure, P_{peak}, P_{plat}, and mean P_{aw} have been used by some surgeons as surrogate estimates of P_{abd} during abdominal closure.[66,67] However, P_{es} has been found to have an inconsistent correlation with baseline P_{abd} and thus P_{abd} may have a limited value in guiding the management of mechanically ventilated patients.[68]

The transdiaphragmatic pressure (P_{di}; $P_{di} = P_{abd} - P_{es}$) has been routinely used to determine diaphragmatic strength in response to phrenic nerve stimulation. The length-tension relationship of the diaphragm can be studied by measuring twitch P_{di} over the range of lung volume.[69] Conceptually, P_{di} measurements can be used to improve patient-ventilator synchrony using P_{di}-driven P_{aw} and flow.[70,71]

RESPIRATORY MUSCLE LOADS: PRESSURE-TIME PRODUCT AND WORK OF BREATHING

Mechanical loads associated with breathing can be expressed by either the PTP or the work of breathing (WOB). PTP is the integral of pressure over time and WOB is the integral of pressure over volume. Although both load measurements correlate with energy demands, PTP is more closely correlated and, as described later for pressure-time indices, can be coupled with breath timing measurements to predict fatigue.[72–74]

According to the simplified equation of motion, the pressure requirement for a given VT is calculated as: VT = triggering pressure (valve sensitivity/responsiveness + auto-PEEP) + (elastance × VT) + (flow × resistance) (Fig. 18).

During unassisted breathing, this pressure requirement is the difference between Pes and the passive recoil pressure of the chest wall. During controlled mechanical ventilation, this pressure requirement is the applied P_{aw}. When this Pes or P_{aw} is integrated over time it is the PTP and when integrated over volume it is the WOB for the patient and ventilator respectively. In mechanically ventilated patients, when PTP and WOB calculations using only P_{aw} measurements (ventilator loads) are done during both a controlled and an assisted breath with similar flows and volumes, the difference in PTP or WOB between the two breath types reflects the patient loads during the assisted breaths.[72,75]

Importantly, the PTP and WOB both include the elastance and resistive loads in the equation of motion but, unlike WOB, PTP also includes the isometric load imposed by the assist triggering process.[76–79] This process includes how much time and pressure it takes for the patient's effort to be recognized by the ventilator (sensitivity) and how much time it takes the ventilator to pressurize the patient after the inspiratory effort is recognized (responsiveness) (Fig. 19).

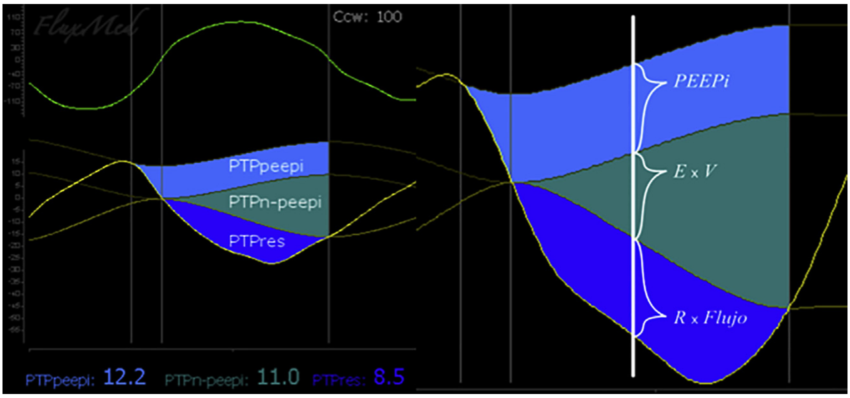

Fig. 18. PTP tracing with the 3 levels of pressure expenditure. PTPn-peepi, PTP not associated with auto-PEEP; PTPpeepi, PTP associated with auto-PEEP; PTPres, PTP associated with resistive forces. (*Courtesy of* SilverSwiss Technology; Available at: http://www.mbmed.com/index.html.)

PTP is expressed in terms of centimeters of H_2O per second with normal values of 5 cm H_2O/s. WOB is properly expressed in units of joules (J) but is often evaluated or reported in terms of joules per liter of volume change with normal values of 0.3 to 0.7 J/L. It is important to realize that using joules per liter eliminates the volume term from the WOB calculation and thus WOB per liter becomes simply a measurement of the mean pressure required for a given volume and flow.

On modern mechanical ventilators, the PTP is graphically displayed by the standard pressure-time scalar displays using either P_{aw} or Pes as described earlier (ventilator and patient PTP respectively). Using a P-V loop can display the WOB performed in a so-called Campbell diagram (Fig. 20). Diagrams of increasing complexity based on the Campbell diagram depict the physiologic elastic and resistive WOB for the lungs and chest wall under normal and abnormal conditions. A modification of the Campbell diagram includes an additional area depicting the imposed WOB from resistive loads imposed on the respiratory muscles by the endotracheal tube, breathing circuit, and the ventilator's demand-flow system during spontaneous breathing.[80]

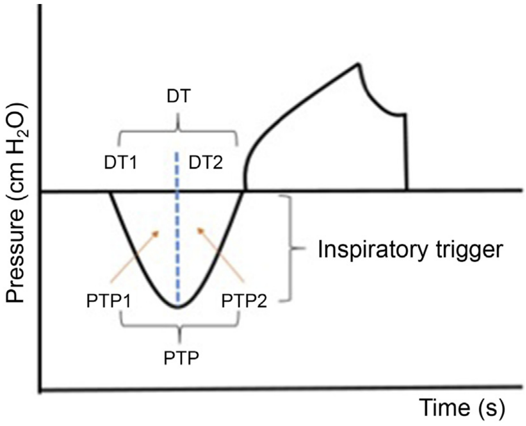

Fig. 19. PTP in a mechanical ventilator. Delayed time (DT) is before and after the threshold of the inspiratory trigger is reached. PTP is before and after the threshold is reached. The pressurization time or pressurization rate is the time from threshold is reached until PIP is reached.

It has been suggested that measuring the power of breathing (WOB per minute) may be a better assessment of respiratory muscle load[81,82] because it is not limited to a single breath. It could be useful in setting pressure support levels to unload the respiratory muscles.[81,83] Normal power of breathing is 4 to 8 J/min.[84] Other tools to assess loads include the diaphragmatic electromyogram and ultrasonography.[85]

Although[86,87] it is not clear whether measuring loads during mechanical ventilation improves patient outcomes, it has been shown that increased physiologic and/or imposed loading during spontaneous or assisted breathing can cause harm to respiratory muscles. Excessive loading increases oxygen consumption, damages myofibrils, and results in the development of fatigue and hypercapnia.

TENSION-TIME INDEX AND PRESSURE-TIME INDEX

Bellemare and Grassino[88] described the tension-time index (TTI) in 1982 as a tool to predict

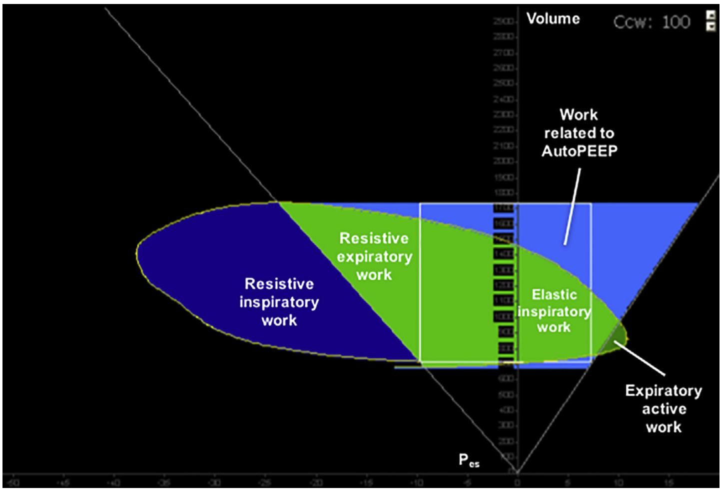

Fig. 20. Campbell diagram showing all the components of the WOB. (*Courtesy of* SilverSwiss Technology; Available at: http://www.mbmed.com/index.html.)

diaphragmatic fatigue. TTI is calculated as follows: TTI = $(Pdi/Pdi_{max}) \times (Ti/Ttot)$; where Pdi_{max} is the maximum Pdi, and *Ti/Ttot* is the inspiratory time divided by total time, known as duty cycle or contraction duration. The cutoff point of TTI is greater than 0.15 to predict respiratory muscle fatigue. Because P_{es} and P_{abd} are not routinely performed in the intensive care unit (ICU), a good proxy is the use of the pressure-time index (PTI), calculated in spontaneous ventilated patients as PTI= $(P_{breath}/P_{imax}) \times (Ti/Ttot)$, where P_{breath} is the patient-generated pressure required for a given VT and P_{imax} is the maximum patient-generated pressure against a closed shutter.[89] The cutoff value is the same, but it requires patient collaboration and a technique to occlude the airway. The result can predict respiratory fatigue in respiratory muscles, but data to support its use and benefits are limited. In a pediatric study by Harikumar and colleagues[90] the sensitivity of the PTI was 100% to predict extubation failures if greater than 0.15.

DRIVING PRESSURE

Recent interest has arisen in airway driving pressure (DP), which is the pressure required to deliver a given VT into a respiratory system with a given compliance (P_{plat} − PEEP) (**Fig. 21**). Because driving pressure is the ratio between VT and respiratory system compliance (VT/C_{RS}), in essence DP allows scaling of the VT to the functional size of the lung (often reduced by lung injury) rather than to an ideal lung size derived from IBW. VT targets progressively less than 6 mL/kg IBW would thus occur as functional lung size and compliance decrease. Conceptually, lung stress and regional lung strain should be reduced with this approach, especially if P_{tp} rather than P_{aw} is used. A target DP of less than 15 to 18 cm H_2O has been proposed based on retrospective analyses of large ventilator management trials.[91–93]

Amato and colleagues[91] recently showed that DP was a powerful stratified risk predictor of lung injury and that its decrease was strongly

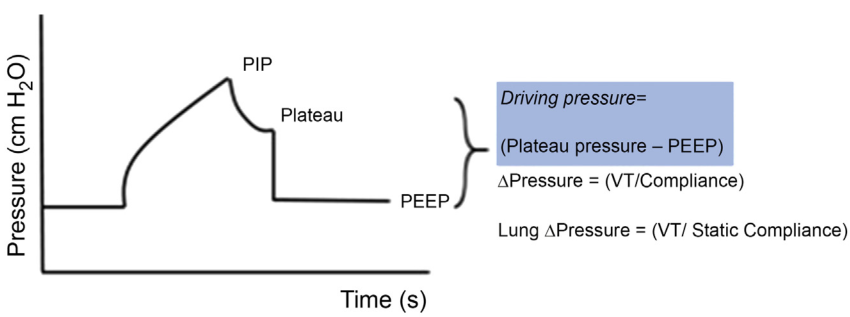

Fig. 21. DP is the difference between P_{plat} and PEEP, and is a correlate of the ratio between VT and the compliance of the respiratory system.

Fig. 22. Placement of the thoracic belt with 16 electrodes at the sixth intercostal space for measurement of pulmonary impedance.

associated with increased survival even in patients with protective P_{plat} (<30 cm H_2O) and a normal VT of 5 to 7 mL/kg. An increase in 1 standard deviation in DP (≈7 cm H_2O) was associated with increase mortality (RR [relative risk], 1.41; 95% confidence interval, 1.31–1.51; *P*<.001). Some other studies have confirmed these findings.[94–96]

ELECTRICAL IMPEDANCE TOMOGRAPHY

Electrical impedance tomography (EIT) is a noninvasive, radiation-free, bedside monitoring tool that allows real-time imaging of ventilation. It provides a continuous view of the regional pulmonary volume dynamics by using analyses of thoracic impedance derived from 16 or 32 skin electrodes placed around the chest.[97]

The display is of a visual slice of the lung similar to the one seen in a coronal cut of a chest tomographic image (computed tomography). The belt containing the electrodes is generally placed at the sixth intercostal space (**Fig. 22**).

EIT is considered safe and easy to use. Furthermore, EIT has shown a good correlation with findings obtained by computed tomography, nitrogen washout, PET, and single-photon emission computed tomography.[98–103]

The changes in the trend of impedance can be reflected in the changes of end-expiratory lung impedance. Therefore, EIT can determine changes in end-expiratory lung volume and VT associated with PEEP titration[100,104–107] (**Fig. 23**), postural changes, and prone position,[108] as well as recruitment maneuvers[109] and nonconventional modes of ventilation such as P_{aw} release ventilation and high-frequency oscillatory ventilation.[110]

Pulmonary edema is common in the injured lung. Its assessment has been considered a key factor in monitoring and guidance of therapy in critically ill patients. Trepte and colleagues[111] recently developed a novel approach to assess extravascular lung water in an animal model by making use of the functional imaging capabilities of EIT. A lateral body rotation was used to measure a new metric, the lung water ratio EIT, which reflected total extravascular lung water. The lung water ratio EIT was compared with postmortem gravimetric lung water analysis and transcardiopulmonary thermodilution measurements. There was a significant correlation between extravascular lung water as measured by postmortem gravimetric analysis and EIT (*r* = 0.80; *P*<.05).

It is important to remember that the clinical usability and plausibility of EIT measurements depend on proper belt position, proper impedance visualization, monitor calibration, and correct analysis and data interpretation.[101] Moreover, EIT only provides information on a transverse slice of the lung.[112–116]

SUMMARY

The assessment of respiratory system mechanics provides critical information in the ICU. This assessment involves a series of methods and tools

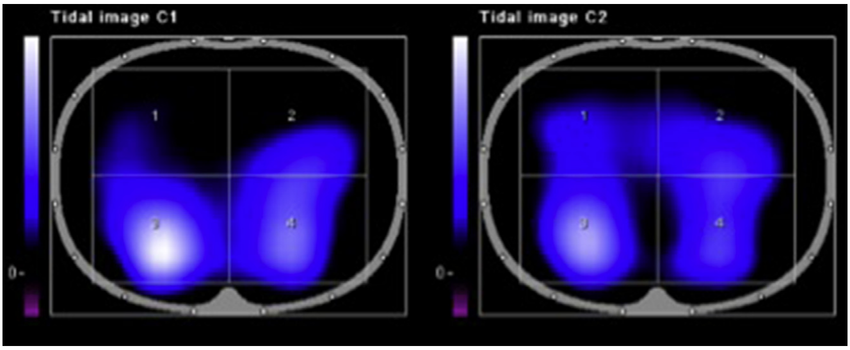

Fig. 23. EIT divided into 4 regions of interest (ROIs). The noticeable improvement in the impedance (ventilation) of the ventral regions (ROIs 1 and 2) follow an increase in PEEP. The areas in white show the maximum ventilation.

that require skills and experience. A solid understanding of respiratory physiology is the first step to selecting the best and most feasible strategy to optimize the management of patients in the critical care setting, particularly those receiving mechanical ventilation.

REFERENCES

1. Lucangelo U, Bernabe F, Blanch L. Lung mechanics at the bedside: make it simple. Curr Opin Crit Care 2007;13(1):64–72.
2. Kallet RH, Katz JA. Respiratory system mechanics in acute respiratory distress syndrome. Respir Care Clin North Am 2003;9(3):297–319.
3. Terragni PP, Rosboch GL, Lisi A, et al. How respiratory system mechanics may help in minimising ventilator-induced lung injury in ARDS patients. Eur Respir J Suppl 2003;42:15s–21s.
4. Lucangelo U, Bernabe F, Blanch L. Respiratory mechanics derived from signals in the ventilator circuit. Respir Care 2005;50(1):55–65 [discussion: 65–7].
5. Dhand R. Ventilator graphics and respiratory mechanics in the patient with obstructive lung disease. Respir Care 2005;50(2):246–61 [discussion: 259–61].
6. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342(18):1301–8.
7. Terragni PP, Filippini C, Slutsky AS, et al. Accuracy of plateau pressure and stress index to identify injurious ventilation in patients with acute respiratory distress syndrome. Anesthesiology 2013;119(4):880–9.
8. Terragni PP, Rosboch G, Tealdi A, et al. Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. Am J Respir Crit Care Med 2007;175(2):160–6.
9. Al-Rawas N, Banner MJ, Euliano NR, et al. Expiratory time constant for determinations of plateau pressure, respiratory system compliance, and total resistance. Crit Care 2013;17(1):R23.
10. Rocha LA, Aleixo A, Allen G, et al. Specimen collection: an essential tool. Science 2014;344(6186):814–5.
11. Marini JJ. Dynamic hyperinflation and auto-positive end-expiratory pressure: lessons learned over 30 years. Am J Respir Crit Care Med 2011;184(7):756–62.
12. Blanch L, Bernabe F, Lucangelo U. Measurement of air trapping, intrinsic positive end-expiratory pressure, and dynamic hyperinflation in mechanically ventilated patients. Respir Care 2005;50(1):110–23 [discussion: 123–4].
13. Nilsestuen JO, Hargett KD. Using ventilator graphics to identify patient-ventilator asynchrony. Respir Care 2005;50(2):202–34 [discussion: 232–4].
14. Takeuchi M, Williams P, Hess D, et al. Continuous positive airway pressure in new-generation mechanical ventilators: a lung model study. Anesthesiology 2002;96(1):162–72.
15. Tobin MJ. Advances in mechanical ventilation. N Engl J Med 2001;344(26):1986–96.
16. Sanborn WG. Monitoring respiratory mechanics during mechanical ventilation: where do the signals come from? Respir Care 2005;50(1):28–52 [discussion: 52–4].
17. Gabopoulou Z, Mavrommati P, Chatzieleftheriou A, et al. Epidural catheter entrapment caused by a double knot after combined spinal-epidural anesthesia. Reg Anesth Pain Med 2005;30(6):588–9.
18. Bluemke DA. Coronary computed tomographic angiography and incidental pulmonary nodules. Circulation 2014;130(8):634–7.
19. Bolzan DW, Gomes WJ, Faresin SM, et al. Volume-time curve: an alternative for endotracheal tube cuff management. Respir Care 2012;57(12):2039–44.
20. Jubran A, Tobin MJ. Use of flow-volume curves in detecting secretions in ventilator-dependent patients. Am J Respir Crit Care Med 1994;150(3):766–9.
21. Harris RS. Pressure-volume curves of the respiratory system. Respir Care 2005;50(1):78–98 [discussion: 98–9].
22. Albaiceta GM, Blanch L, Lucangelo U. Static pressure-volume curves of the respiratory system: were they just a passing fad? Curr Opin Crit Care 2008;14(1):80–6.
23. Chiumello D, Carlesso E, Aliverti A, et al. Effects of volume shift on the pressure-volume curve of the respiratory system in ALI/ARDS patients. Minerva Anestesiol 2007;73(3):109–18.
24. Blanch L, Lopez-Aguilar J, Villagra A. Bedside evaluation of pressure-volume curves in patients with acute respiratory distress syndrome. Curr Opin Crit Care 2007;13(3):332–7.
25. Villar J, Kacmarek RM, Perez-Mendez L, et al. A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. Crit Care Med 2006;34(5):1311–8.
26. Harris RS, Hess DR, Venegas JG. An objective analysis of the pressure-volume curve in the acute respiratory distress syndrome. Am J Respir Crit Care Med 2000;161(2 Pt 1):432–9.
27. Maggiore SM, Richard JC, Brochard L. What has been learnt from P/V curves in patients with acute lung injury/acute respiratory distress syndrome. Eur Respir J Suppl 2003;42:22s–6s.

28. Pintado MC, de Pablo R, Trascasa M, et al. Individualized PEEP setting in subjects with ARDS: a randomized controlled pilot study. Respir Care 2013;58(9):1416–23.
29. Costa EL, Slutsky AS, Amato MB. Driving pressure as a key ventilation variable. N Engl J Med 2015;372(21):2072.
30. Hecker A, Hecker B, Hecker M, et al. Acute abdominal compartment syndrome: current diagnostic and therapeutic options. Langenbecks Arch Surg 2016;401(1):15–24.
31. Cortes-Puentes GA, Keenan JC, Adams AB, et al. Impact of chest wall modifications and lung injury on the correspondence between airway and transpulmonary driving pressures. Crit Care Med 2015;43(8):e287–95.
32. Brazzale DJ, Pretto JJ, Schachter LM. Optimizing respiratory function assessments to elucidate the impact of obesity on respiratory health. Respirology 2015;20(5):715–21.
33. Koch B, Friedrich N, Volzke H, et al. Static lung volumes and airway resistance reference values in healthy adults. Respirology 2013;18(1):170–8.
34. Kaminsky DA. What does airway resistance tell us about lung function? Respir Care 2012;57(1):85–96 [discussion: 96–9].
35. Guttmann J, Eberhard L, Fabry B, et al. Time constant/volume relationship of passive expiration in mechanically ventilated ARDS patients. Eur Respir J 1995;8(1):114–20.
36. Akoumianaki E, Maggiore SM, Valenza F, et al. The application of esophageal pressure measurement in patients with respiratory failure. Am J Respir Crit Care Med 2014;189(5):520–31.
37. Cherniack RM, Farhi LE, Armstrong BW, et al. A comparison of esophageal and intrapleural pressure in man. J Appl Physiol 1955;8(2):203–11.
38. Huang Y, Tang R, Chen Q, et al. How much esophageal pressure-guided end-expiratory transpulmonary pressure is sufficient to maintain lung recruitment in lavage-induced lung injury? J Trauma Acute Care Surg 2016;80(2):302–7.
39. Sarge T, Loring SH, Yitsak-Sade M, et al. Raising positive end-expiratory pressures in ARDS to achieve a positive transpulmonary pressure does not cause hemodynamic compromise. Intensive Care Med 2014;40(1):126–8.
40. Talmor D, Sarge T, Malhotra A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med 2008;359(20):2095–104.
41. Fish E, Novack V, Banner-Goodspeed VM, et al. The Esophageal Pressure-Guided Ventilation 2 (EPVent2) trial protocol: a multicentre, randomised clinical trial of mechanical ventilation guided by transpulmonary pressure. BMJ Open 2014;4(9):e006356.
42. Sarge T, Talmor D. Targeting transpulmonary pressure to prevent ventilator induced lung injury. Minerva Anestesiol 2009;75(5):293–9.
43. Cortes GA, Marini JJ. Two steps forward in bedside monitoring of lung mechanics: transpulmonary pressure and lung volume. Crit Care 2013;17(2):219.
44. Chiumello D, Cressoni M, Colombo A, et al. The assessment of transpulmonary pressure in mechanically ventilated ARDS patients. Intensive Care Med 2014;40(11):1670–8.
45. Grasso S, Cassano S. Measuring (and interpreting) the esophageal pressure: a challenge for the intensivist. Minerva Anestesiol 2015;81(8):827–9.
46. Loring SH, O'Donnell CR, Behazin N, et al. Esophageal pressures in acute lung injury: do they represent artifact or useful information about transpulmonary pressure, chest wall mechanics, and lung stress? J Appl Physiol (1985) 2010;108(3):515–22.
47. Hedenstierna G. Esophageal pressure: benefit and limitations. Minerva Anestesiol 2012;78(8):959–66.
48. Hess DR. Respiratory mechanics in mechanically ventilated patients. Respir Care 2014;59(11):1773–94.
49. Garnero A, Hodgson C, Arnal JM. Transpulmonary pressure cannot be determined without esophageal pressure in ARDS patients. Minerva Anestesiol 2016;82(1):121–2.
50. Beitler JR, Guerin C, Ayzac L, et al. PEEP titration during prone positioning for acute respiratory distress syndrome. Crit Care 2015;19:436.
51. Chiumello D, Cressoni M, Carlesso E, et al. Bedside selection of positive end-expiratory pressure in mild, moderate, and severe acute respiratory distress syndrome. Crit Care Med 2014;42(2):252–64.
52. Grasso S, Stripoli T, De Michele M, et al. ARDSnet ventilatory protocol and alveolar hyperinflation: role of positive end-expiratory pressure. Am J Respir Crit Care Med 2007;176(8):761–7.
53. Ranieri VM, Zhang H, Mascia L, et al. Pressure-time curve predicts minimally injurious ventilatory strategy in an isolated rat lung model. Anesthesiology 2000;93(5):1320–8.
54. Terragni P, Bussone G, Mascia L. Dynamic airway pressure-time curve profile (stress index): a systematic review. Minerva Anestesiol 2016;82(1):58–68.
55. Ferrando C, Suarez-Sipmann F, Gutierrez A, et al. Adjusting tidal volume to stress index in an open lung condition optimizes ventilation and prevents overdistension in an experimental model of lung injury and reduced chest wall compliance. Crit Care 2015;19:9.
56. Kucher N, Tapson VF, Goldhaber SZ, et al. Risk factors associated with symptomatic pulmonary

embolism in a large cohort of deep vein thrombosis patients. Thromb Haemost 2005;93(3):494–8.
57. Pan C, Tang R, Xie J, et al. Stress index for positive end-expiratory pressure titration in prone position: a piglet study. Acta Anaesthesiol Scand 2015;59(9):1170–8.
58. Blankman P, Hasan D, Bikker IG, et al. Lung stress and strain calculations in mechanically ventilated patients in the intensive care unit. Acta Anaesthesiol Scand 2016;60(1):69–78.
59. Chiumello D, Carlesso E, Cadringher P, et al. Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 2008;178(4):346–55.
60. Gattinoni L, Carlesso E, Caironi P. Stress and strain within the lung. Curr Opin Crit Care 2012;18(1):42–7.
61. Garcia-Prieto E, Lopez-Aguilar J, Parra-Ruiz D, et al. Impact of recruitment on static and dynamic lung strain in acute respiratory distress syndrome. Anesthesiology 2016;124(2):443–52.
62. Mead J, Takishima T, Leith D. Stress distribution in lungs: a model of pulmonary elasticity. J Appl Physiol 1970;28(5):596–608.
63. Kollisch-Singule M, Emr B, Smith B, et al. Airway pressure release ventilation reduces conducting airway micro-strain in lung injury. J Am Coll Surg 2014;219(5):968–76.
64. Protti A, Votta E, Gattinoni L. Which is the most important strain in the pathogenesis of ventilator-induced lung injury: dynamic or static? Curr Opin Crit Care 2014;20(1):33–8.
65. Wellman TJ, Winkler T, Costa EL, et al. Effect of local tidal lung strain on inflammation in normal and lipopolysaccharide-exposed sheep*. Crit Care Med 2014;42(7):e491–500.
66. Bunnell A, Cheatham ML. Airway pressures as surrogate estimates of intra-abdominal pressure. Am Surg 2015;81(1):81–5.
67. Gonzalez L, Rodriguez R, Mencia S, et al. Utility of monitoring intra-abdominal pressure in critically ill children. An Pediatr (Barc) 2012;77(4):254–60 [in Spanish].
68. Sindi A, Piraino T, Alhazzani W, et al. The correlation between esophageal and abdominal pressures in mechanically ventilated patients undergoing laparoscopic surgery. Respir Care 2014;59(4):491–6.
69. Hamnegard CH, Wragg S, Mills G, et al. The effect of lung volume on transdiaphragmatic pressure. Eur Respir J 1995;8(9):1532–6.
70. Sharshar T, Desmarais G, Louis B, et al. Transdiaphragmatic pressure control of airway pressure support in healthy subjects. Am J Respir Crit Care Med 2003;168(7):760–9.
71. Kimura T, Takezawa J, Nishiwaki K, et al. Determination of the optimal pressure support level evaluated by measuring transdiaphragmatic pressure. Chest 1991;100(1):112–7.
72. Grinnan DC, Truwit JD. Clinical review: respiratory mechanics in spontaneous and assisted ventilation. Crit Care 2005;9(5):472–84.
73. Jabour ER, Rabil DM, Truwit JD, et al. Evaluation of a new weaning index based on ventilatory endurance and the efficiency of gas exchange. Am Rev Respir Dis 1991;144(3 Pt 1):531–7.
74. Bellani G, Patroniti N, Weismann D, et al. Measurement of pressure-time product during spontaneous assisted breathing by rapid interrupter technique. Anesthesiology 2007;106(3):484–90.
75. Jubran A, Tobin MJ. Monitoring during mechanical ventilation. Clin Chest Med 1996;17(3):453–73.
76. Murata S, Yokoyama K, Sakamoto Y, et al. Effects of inspiratory rise time on triggering work load during pressure-support ventilation: a lung model study. Respir Care 2010;55(7):878–84.
77. Villar J, Blanco J, Kacmarek RM. Current incidence and outcome of the acute respiratory distress syndrome. Curr Opin Crit Care 2016;22(1):1–6.
78. Briel M, Meade M, Mercat A, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA 2010;303(9):865–73.
79. Grasso S, Fanelli V, Cafarelli A, et al. Effects of high versus low positive end-expiratory pressures in acute respiratory distress syndrome. Am J Respir Crit Care Med 2005;171(9):1002–8.
80. Banner MJ, Jaeger MJ, Kirby RR. Components of the work of breathing and implications for monitoring ventilator-dependent patients. Crit Care Med 1994;22(3):515–23.
81. Banner MJ, Euliano NR, Brennan V, et al. Power of breathing determined noninvasively with use of an artificial neural network in patients with respiratory failure. Crit Care Med 2006;34(4):1052–9.
82. Freiermuth D, Poblete B, Singer M, et al. Difficult diagnosis of malignant hyperthermia during laparoscopic surgery. Eur J Anaesthesiol 2013;30(10):635–8.
83. Ozcan MS, Bonett SW, Martin AD, et al. Abnormally increased power of breathing as a complication of closed endotracheal suction catheter systems. Respir Care 2006;51(4):423–5.
84. Banner MJ, Euliano NR, Martin AD, et al. Noninvasive work of breathing improves prediction of post-extubation outcome. Intensive Care Med 2012;38(2):248–55.
85. Bellani G, Pesenti A. Assessing effort and work of breathing. Curr Opin Crit Care 2014;20(3):352–8.
86. Unroe M, MacIntyre N. Evolving approaches to assessing and monitoring patient-ventilator interactions. Curr Opin Crit Care 2010;16(3):261–8.

87. Yoshida T, Uchiyama A, Matsuura N, et al. Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: high transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury. Crit Care Med 2012;40(5):1578–85.
88. Bellemare F, Grassino A. Effect of pressure and timing of contraction on human diaphragm fatigue. J Appl Physiol Respir Environ Exerc Physiol 1982;53(5):1190–5.
89. Ramonatxo M, Boulard P, Prefaut C. Validation of a noninvasive tension-time index of inspiratory muscles. J Appl Physiol (1985) 1995;78(2):646–53.
90. Harikumar G, Egberongbe Y, Nadel S, et al. Tension-time index as a predictor of extubation outcome in ventilated children. Am J Respir Crit Care Med 2009;180(10):982–8.
91. Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 2015;372(8):747–55.
92. Gattinoni L, Pelosi P, Suter PM, et al. Acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease. Different syndromes? Am J Respir Crit Care Med 1998;158(1):3–11.
93. Chiumello D, Guerin C. Understanding the setting of PEEP from esophageal pressure in patients with ARDS. Intensive Care Med 2015;41(8):1465–7.
94. Kacmarek RM, Villar J, Sulemanji D, et al. Open lung approach for the acute respiratory distress syndrome: a pilot, randomized controlled trial. Crit Care Med 2016;44(1):32–42.
95. Borges JB, Hedenstierna G, Larsson A, et al. Altering the mechanical scenario to decrease the driving pressure. Crit Care 2015;19:342.
96. Protti A, Andreis DT, Monti M, et al. Lung stress and strain during mechanical ventilation: any difference between statics and dynamics? Crit Care Med 2013;41(4):1046–55.
97. Gong B, Krueger-Ziolek S, Moeller K, et al. Electrical impedance tomography: functional lung imaging on its way to clinical practice? Expert Rev Respir Med 2015;9(6):721–37.
98. Frerichs I, Becher T, Weiler N. Electrical impedance tomography imaging of the cardiopulmonary system. Curr Opin Crit Care 2014;20(3):323–32.
99. Becher TH, Bui S, Zick G, et al. Assessment of respiratory system compliance with electrical impedance tomography using a positive end-expiratory pressure wave maneuver during pressure support ventilation: a pilot clinical study. Crit Care 2014;18(6):679.
100. Wrigge H, Zinserling J, Muders T, et al. Electrical impedance tomography compared with thoracic computed tomography during a slow inflation maneuver in experimental models of lung injury. Crit Care Med 2008;36(3):903–9.
101. Riera J, Riu PJ, Casan P, et al. Electrical impedance tomography in acute lung injury. Med Intensiva 2011;35(8):509–17 [in Spanish].
102. Mellenthin MM, Mueller JL, Bueno de Camargo ED, et al. The ACE1 thoracic Electrical Impedance Tomography system for ventilation and perfusion. Conf Proc IEEE Eng Med Biol Soc 2015;2015:4073–6.
103. Barber DC. Quantification in impedance imaging. Clin Phys Physiol Meas 1990;11(Suppl A):45–56.
104. Bikker IG, Leonhardt S, Bakker J, et al. Lung volume calculated from electrical impedance tomography in ICU patients at different PEEP levels. Intensive Care Med 2009;35(8):1362–7.
105. Lowhagen K, Lundin S, Stenqvist O. Regional intratidal gas distribution in acute lung injury and acute respiratory distress syndrome–assessed by electric impedance tomography. Minerva Anestesiol 2010;76(12):1024–35.
106. Cinnella G, Grasso S, Raimondo P, et al. Physiological effects of the open lung approach in patients with early, mild, diffuse acute respiratory distress syndrome: an electrical impedance tomography study. Anesthesiology 2015;123(5):1113–21.
107. Becher T, Kott M, Schadler D, et al. Influence of tidal volume on ventilation inhomogeneity assessed by electrical impedance tomography during controlled mechanical ventilation. Physiol Meas 2015;36(6):1137–46.
108. Kotani T, Tanabe H, Yusa H, et al. Electrical impedance tomography-guided prone positioning in a patient with acute cor pulmonale associated with severe acute respiratory distress syndrome. J Anesth 2015;30(1):161–5.
109. Rosa RG, Rutzen W, Madeira L, et al. Use of thoracic electrical impedance tomography as an auxiliary tool for alveolar recruitment maneuvers in acute respiratory distress syndrome: case report and brief literature review. Rev Bras Ter Intensiva 2015;27(4):406–11.
110. Wolf GK, Grychtol B, Frerichs I, et al. Regional lung volume changes in children with acute respiratory distress syndrome during a derecruitment maneuver. Crit Care Med 2007;35(8):1972–8.
111. Trepte CJ, Phillips CR, Sola J, et al. Electrical impedance tomography (EIT) for quantification of pulmonary edema in acute lung injury. Crit Care 2016;20(1):18.
112. Karsten J, Stueber T, Voigt N, et al. Influence of different electrode belt positions on electrical impedance tomography imaging of regional ventilation: a prospective observational study. Crit Care 2016;20(1):3.

113. Chiumello D, Marino A, Brioni M, et al. Lung recruitment assessed by respiratory mechanics and by CT Scan: what is the relationship? Am J Respir Crit Care Med 2016;193(11):1254–63.
114. Casserly B, McCool FD, Saunders J, et al. End-expiratory volume and oxygenation: targeting PEEP in ARDS patients. Lung 2016;194(1):35–41.
115. Gattinoni L, Pesenti A, Caspani ML, et al. The role of total static lung compliance in the management of severe ARDS unresponsive to conventional treatment. Intensive Care Med 1984;10(3):121–6.
116. Davis GM, Coates AL, Papageorgiou A, et al. Direct measurement of static chest wall compliance in animal and human neonates. J Appl Physiol (1985) 1988;65(3):1093–8.