Lung Volume Measurement and Ventilation Distribution During Invasive Mechanical Ventilation

Thomas Piraino

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Lung volume measurement performed during invasive mechanical ventilation can be used to determine functional residual capacity, changes in end-expiratory lung volume with the application of PEEP, and lung strain. However, many bedside measurements provide useful information without the use of specialized equipment. Ventilation distribution through the lung has traditionally been assessed with computed tomography, but more recently electrical impedance tomography has brought the ability to monitor this at the bedside, and without exposure to radiation. This review will describe techniques to measure lung volumes in the ICU and the relationship between lung strain, stress, and other measurements. This review will also discuss monitoring ventilation distribution at the bedside and the clinical assessment of regional compliance that this technology provides. *Key words: lung volume measurement; electrical impedance tomography; mechanical ventilation.* [Respir Care 2020;65(6):760–771. © 2020 Daedalus Enterprises]

Introduction

The measurement of lung volume is required to diagnose a variety of conditions in out-patient clinics, but its utility during mechanical ventilation is less common and is not considered routine practice. Lung volume measurements can be used to determine the safety of mechanical ventilation, but simpler methods exist (eg, plateau pressure).

Ventilation distribution is traditionally determined with computed tomography (CT) and is not considered a routine measurement during mechanical ventilation. Electrical impedance tomography (EIT) is a noninvasive and radiation-free imaging technique that uses a minimum of 16 leads positioned around the thorax. EIT provides breath-by-breath dynamic imaging of ventilation distribution through measuring impedance changes across lung regions. The availability of EIT at the bedside has generated a growing interest in the information provided and how it can used to adjust ventilator settings.

Mr Piraino is affiliated with St. Michael's Hospital, Toronto, Ontario, Canada.

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Correspondence: Thomas Piraino RRT FCSRT FAARC, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario M5B 1W8, Canada. E-mail: thomaspiraino@gmail.com.

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Lung Volume Measurements During Mechanical Ventilation

Lung volume measurements, such as inspiratory capacity, vital capacity, or even expiratory reserve volume, can be measured using simple spirometry measurements, whereas measurements of total lung capacity and functional residual capacity (FRC) require more sophisticated methods. Although these methods are routinely performed in pulmonary function labs to diagnose various lung diseases, their use in the ICU is far less common.

The gold standard for measuring lung volumes in outpatient clinics is by using a device commonly referred to as a body box. This method employs Boyle's law to determine changes in volume relative to pressure. For obvious reasons (ie, size and shape), the body box is not an option for measuring lung volumes in patients undergoing invasive mechanical ventilation. Although there exists no true gold standard for measuring lung volumes in invasively ventilated patients, CT has become the standard comparison because it is not affected by lung pathology and it likely reflects the most accurate measure of end-expiratory lung volume (EELV). However, this technique typically requires patient transport and exposure to radiation. Bedside methods for measuring absolute lung volume include inert gas (eg, helium) dilution and the nitrogen washin/washout technique. Although these methods are limited by lung pathology (ie, only areas with ventilation distribution and gas exchange will be measured), they can be done at the bedside without patient transport or radiation exposure.

Computed Tomography

CT has become a standard for measuring lung volume in critically ill patients. However, it is a significant source of radiation to patients as it uses beams of x-ray electrodes aimed at detectors in a circular arrangement that the patient is passed through. The device rotates around the patient to create a slice along the transverse plane, and an image is generated based on the attenuation of the x-ray beam caused by differences in tissue density. The result is a 2-dimensional axial image composed of multiple pixels. The movement of the patient through the CT scanner allows for a 3-dimensional pixel called a voxel to be rendered. The degree of attenuation caused by air or tissue is given a value called a Hounsfield unit, which represents the density of the tissue within an arbitrary scale; the range of this scale is from −1,000 to 1,000, with water being 0 and air being −1,000.[1] Today's CT scanners can image an entire thorax in a single breath, and computer software can reconstruct the image to provide an accurate volume measurement for both gas and tissue. To calculate lung volume, the following equation is used:

$$\text{gas volume} = \left(\frac{\text{CT number}}{-1,000}\right) \times \text{voxel volume}.$$

Although CT can accurately measure lung volume related to inflation, it does not determine the presence of air compared to ventilated regions. Therefore, the presence of lung volume does not automatically imply efficiency of gas exchange, particularly in patients with hyperinflation due to severe airway disease or COPD.[2] The more common use of CT in the literature related to invasive mechanical ventilation is in the area of lung recruitment, lung stress, and lung strain. However, even if the need to transport patients could be eliminated by the use of a portable CT scanner, there remains the issue of radiation exposure. This has resulted in the evaluation of other noninvasive, nonradiologic methods for measuring lung volume at the bedside.

Inert Gas Dilution (Helium-Dilution Method)

Lung volume measurements using inert gas dilution is based on the equilibration between the lungs and a known volume of the inert gas. The inert gas dilution method that has been used for many years in spontaneously breathing patients for lung volume assessment is the helium-dilution method. The common helium-dilution technique used in spontaneously breathing patients has been modified for use during invasive mechanical ventilation. In 2004, Patroniti et al[3] conducted a study in 21 subjects with mild-to-moderate ARDS to test the accuracy and precision of a simplified bedside helium-dilution method compared to CT. The subjects were sedated, paralyzed, and placed on a CPAP level equal to the clinically set PEEP level for the duration of the CT scan to keep EELV constant. The EELV determined from the CT ($EELV_{CT}$) was calculated using the equation discussed in the previous section. After restarting ventilation for a 5-min stabilization period, an end-expiratory pause was performed, the endotracheal tube was clamped, and the subject was disconnected from the ventilator. A bag with 1.5 L of gas containing 13.44% helium in oxygen was connected, the clamp was released, and 10 breaths were delivered with the bag to dilute the bag mixture with the gas from the subject's lungs. The bag was then clamped and separated from the patient, and the ventilator was connected and ventilation resumed. The gas was analyzed with a calibrated heliometer, and EELV determined with this method ($EELV_{He}$) was calculated with the following equation:

$$EELV_{He} = \left(V_b \times \left(\frac{C_i}{C_f}\right)\right) - V_b$$

where V_b is the initial volume of gas in the bag, C_i is the initial concentration of helium, and C_f is the final concentration of helium.

Table 1. Methods of lung volume measurement compared to computed tomography

Method	Bias (% Difference)	Limits of Agreement	Considerations
Helium dilution[a]	32.5 ± 202.8 mL (4.8)	−373 to 438 mL	ARDS patients only
Helium dilution[b]	−136 ± 133 mL (16)	−3 to −269 mL	Excluded COPD patients
Nitrogen washin/washout[b]	94 ± 143 mL (15)	−50 to −236 mL	Excluded COPD patients

[a] From Reference 3.
[b] From Reference 2.

After another 5 min of ventilation (ie, a stabilization period), the helium dilution measurement was performed again to test the precision of multiple measurements. There was a linear correlation between $EELV_{CT}$ and $EELV_{He}$: $EELV_{He} = 208 + 0.858 \times EELV_{CT}$ ($r = 0.941$, $P < .001$). However, $EELV_{CT}$ was overestimated at low lung volumes and underestimated at high volumes. The bias between these methods was 32.5 ± 202.8 mL (4.75 ± 15.9%) with a 95% CI limit of agreement of −373 and 438 mL and an absolute percent difference of 14.6 ± 10.1%. The large limits of agreement could be explained by a number of factors, including the loss of PEEP when subjects were connected to the helium-dilution bag, and also because $EELV_{He}$ represents ventilated regions only, whereas $EELV_{CT}$ would represent regions that are aerated but may not be ventilated (and contributing to gas exchange). Despite the large limits of agreements, the authors suggest that this is within clinically acceptable limits (Table 1).[3]

The assessment of multiple $EELV_{He}$ measurements had a bias of −24 ± 83 mL (−2.1 ± 9.6%), and the 95% CI limits of agreement between the measurements was −191 mL and 141 mL, with an absolute difference of 6.3 ± 7.4%. This supports the reproducibility of this type of helium-dilution method. Finally, the authors acknowledge the fact that patients require disconnection from the ventilator and may experience a significant loss of PEEP; however, they stated there were no significant effects on respiratory or hemodynamic stability.[3]

Nitrogen Washin/Washout

Another technique for measuring lung volumes at the bedside is the nitrogen (N_2) washin/washout method. This technique is based on the principle that the volume of N_2 in the lung is based on the fraction of N_2 multiplied by the EELV. Because F_{IO_2} is inversely related to the fraction of N_2 in a volume of alveolar gas, the relationship to EELV can be written as $EELV = \Delta N_2/\Delta F_{IO_2}$, where ΔN_2 is the change in N_2 content (in mL) after a stabilization period of ΔF_{IO_2}. The line of ventilators from GE Healthcare (Madison, Wisconsin) allow bedside measurement of lung volume using the N_2 washin/washout method. However, rather than measuring the concentration of N_2, the ventilator estimates it by measuring the concentrations of CO_2 and O_2. Chiumello et al[2] compared the N_2 washin/washout technique to both the helium-dilution method and the CT method in 30 subjects admitted to the ICU; they did not exclusively enroll patients with ARDS as in the previously mentioned helium-dilution study. The authors reported that the N_2 washin/washout technique also had excellent correlation with the CT method ($r^2 = 0.89$) with a bias of 94 ± 143 mL (15 ± 18%, $P < .001$) and limits of agreement of −50 mL to −236 mL). The average overestimation was also acceptable (less than the manufacturer's accuracy limit of 20%). Table 1 provides a comparison of methods and their limits of agreement with lung volumes measured with CT. The authors also compared repeated measurements of the N_2 washin/washout, which exhibited excellent reproducibility between 2 measurements of 48 ± 165 mL, which was not statistically different than having no difference between measurements ($P = .12$).

Similar to the previously mentioned study on the helium-dilution method,[3] the authors also reported excellent correlation between EELV with the helium-dilution method and EELV measured with CT ($r^2 = 0.91$). There was a negative bias of −136 ± 133 mL (16 ± 13%) with limits of agreement of −3 mL to −269 mL. A possible explanation for the different results from the previous helium-dilution study[3] is the inclusion of only subjects with ARDS. Patients with ARDS typically have lower lung volumes, as opposed to patients with normal lung compliance who have higher lung volumes. Thus the 10 breaths used with this method may not have been sufficient to allow sufficient gas equilibration. Additionally, the differences between N_2 washin/washout and helium-dilution values could also be due to the number of breaths used. The N_2 washin/washout technique uses 20 breaths for equilibration compared to the 10 breaths used in the helium-dilution method.

Electrical Impedance Tomography to Estimate EELV

In addition to measuring ventilation distribution through the lung, which will be discussed later, EIT devices also provide additional tools for measuring changes in end-expiratory lung impedance (ΔEELI), both globally and to selected regions of interest. Impedance changes during tidal breathing (tidal variation) represent changes in tidal volume, and

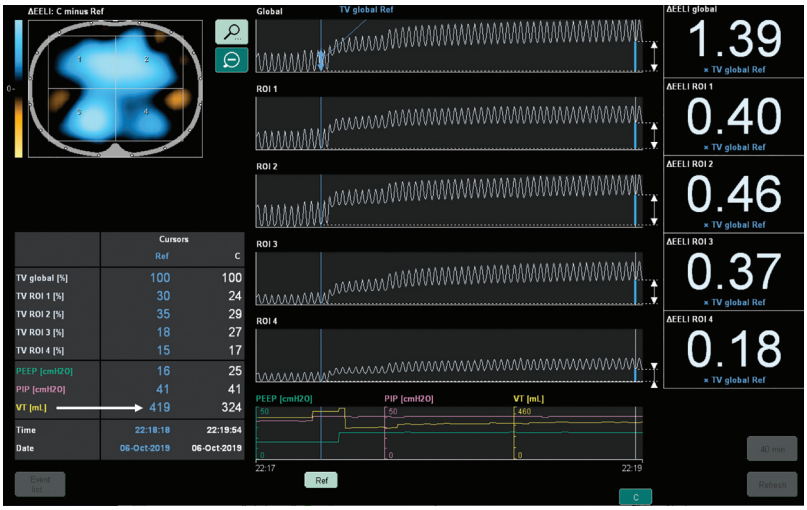

Fig. 1. End-expiratory lung volume (EELV) can be estimated by using the reference tidal volume (white arrow) and multiplying it by the global change in end-expiratory lung impedance (ΔEELI) of 1.39. Additionally, ΔEELI of each region can be used to estimate the change in EELV for each region of interest. Although the change volume correlates with other methods of lung volume measurements, the limits of agreement are not considered to be clinically acceptable.

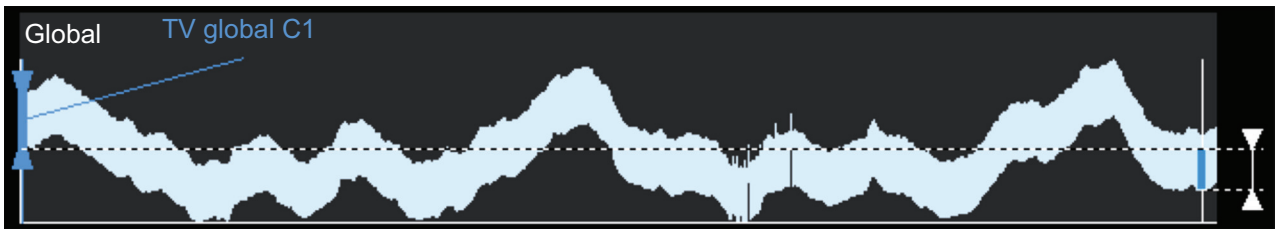

Fig. 2. The effect of a pulsating bed mattress on the end-expiratory lung impedance trend.

this tidal variation value, measured in arbitrary units called ΔZ, is used as a reference value to estimate change in EELV. By comparing ΔEELI to the height of a reference tidal breath, the volume of change is inferred (Fig. 1).

A number of studies have compared changes in EELV estimated by ΔEELI to helium dilution and N_2 washin/washout, but not to CT.[4-7] All of these studies found good or excellent correlation between EIT estimates of EELV and other methods, but these studies have not considered the limits of agreement to be clinically acceptable for estimating actual volume change.

A differentiating factor between ΔEELI measurements and other bedside methods is that EIT captures a field or region around the area where the EIT belt is placed. Although this region is larger than the belt width, it may not represent all regions being ventilated with the N_2 washin/washout or helium-dilution techniques. However, ΔEELI is not affected by ventilation changes and can measure ΔEELI in lung regions that may not be ventilating well, making it potentially similar to CT scans. A proper study comparing EELV changes estimated by EIT to CT would be useful because it is unknown whether the values are closer to those found with a CT scan than the other methods.

The ΔEELI has been used as a method to set optimal PEEP in patients with ARDS. Eronia et al[8] enrolled 16 patients with hypoxemic respiratory failure of noncardiogenic origin into a study to assess the use of EIT to set a PEEP level that maintains alveolar recruitment after a recruitment maneuver. Overall, they found the method to be safe despite noting that it required the use of higher PEEP. The method also resulted in lower driving pressure and an increase in oxygenation. In addition, although it was feasible in most subjects, there were 2 subjects with unstable EELI trends, which precluded any analysis.

There are limitations to measuring ΔEELI with EIT. The stability of the EELI trend is largely affected by external pressure and aggressive fluid balance shifts. Certain ICU bed mattresses with pulsating pressure can greatly influence the stability of the EELI trend over time (Fig. 2). Fluid removal with either dialysis or simply a bolus of furosemide can also affect impedance measurements, causing an increase in EELI that suggests an improvement in EELV without any changes in respiratory system mechanics or distribution of ventilation. Administering a fluid bolus can also cause a downward shift in EELI that suggests a loss in

EELV, again without any changes in respiratory system mechanics or distribution of ventilation.[9]

Why Measure Lung Volumes During Invasive Ventilation?

An increase in PEEP will always increase EELV, and respiratory-system compliance can predict the amount of volume it would increase. For example, if your compliance is 50 mL/cm H_2O, an increase of 10 cm H_2O would increase EELV by 500 mL (50 mL × 10 cm H_2O). If EELV is measured and found to increase more than expected, increasing PEEP has recruited alveolar units. Patients who exhibit recruitment when PEEP is increased are considered PEEP responders, and higher PEEP is likely more beneficial. However, PEEP and EELV contribute to lung strain.

Strain refers to the deformation, or change, in the shape of a structure compared to its resting condition.[10] Lung strain is defined as the change in volume relative to FRC, and lung volume measurements are used to measure FRC in mechanically ventilated patients.[10] For the calculation of lung strain, values of FRC are obtained at zero end-expiratory pressure: lung strain = ΔV/FRC, where ΔV refers to the change in volume during inspiration. The concept of lung strain becomes complicated and less intuitive with the application of PEEP. As already stated, the application of PEEP always increases EELV. However, some consider the impact of PEEP-induced EELV to be in the numerator of the strain equation,[10] which would increase strain: lung strain = (ΔV + EELV)/FRC, whereas other authors appear to group EELV (from PEEP) and FRC in the denominator: lung strain = ΔV/(FRC + EELV).[7,11]

The difference in concepts are likely due to the fact that both are possible, but both rely heavily on the recruitment potential of the lung. A ventilated patient with significant atelectasis would have low FRC but may be highly recruitable, hence an increase in PEEP (increasing EELV) would likely improve the resting state and decrease strain (EELV in the denominator). A ventilated patient with consolidated lung regions or with pleural effusions may not be overly recruitable and the application of PEEP (increasing EELV) would likely increase strain (EELV in the numerator). If we consider recruitable volume (V_{rec}) when increasing PEEP, lung strain is likely a compromise:

$$\text{Lung strain} = \frac{\Delta V + (EELV - V_{rec})}{FRC + V_{rec}}.$$

Lung volume measurements are feasible and safe, but whether they add clinical value or guide clinicians to make better clinical decisions to manage their ventilated patients compared to other more common measurements is still unknown.

Do We Need to Measure Lung Strain?

Lung stress is considered to be the internal distribution of counterforce in a given area that reacts to an external load.[10] In clinical terms, lung stress refers to the distending pressure within the lung, and the counterforce (external load) is the chest wall. Therefore, the stress on the lung is the transpulmonary pressure. Lung stress is directly related to lung strain: stress = k × strain, where k is the specific lung elastance (~13.5 cm H_2O in humans).[10] Although stress can be estimated with transpulmonary pressure measurements (with esophageal balloon), these measurements are still not common practice in the majority of ICUs.[12]

Simple bedside assessments can assist clinicians in determining whether they are potentially increasing stress or strain to the patient's lungs. For example, both lung stress and strain have a linear relationship with plateau pressure.[10,13] Maintaining a plateau pressure < 25 cm H_2O in most patients (< 30 cm H_2O in patients with ARDS) would limit lung strain to < 2 (considered detrimental) and lung stress to 22–24 cm H_2O (considered the upper limit of stress).[10]

A bedside maneuver for assessing recruitability has also been described.[14] Just as lung volume measurements to measure EELV after a PEEP change can suggest recruitment if the ΔEELV is greater than expected, this simplified maneuver involves decreasing PEEP by 10 cm H_2O in a single-breath and observing the exhaled volume during the transition from higher to lower PEEP. The expected loss (exhaled tidal volume + predicted loss from PEEP change based on respiratory-system compliance at low PEEP) is subtracted from the exhaled volume. The excess loss is used to determine the recruitment-to-inflation ratio (Fig. 3).[15] Validation of the recruitment-to-inflation ratio using lung recruitment measurements (multiple P-V curve method) was published recently.[15] An online calculator is also available at (https://crec.coemv.ca, *Accessed April 3, 2020*).

In patients with ARDS, oxygenation by itself may not be a good indicator of patient outcome.[16] However, in a secondary analysis of the Lung Open Ventilation Study (LOVS), a positive oxygenation response to PEEP change was associated with a lower probability of death.[17,18] The authors noted that an improvement in oxygenation after PEEP change was associated with reduced mortality in a multivariate logistic regression analysis (adjusted odds ratio 0.80, 95% CI 0.72–0.89, for every 25 mm Hg increase in P_{aO_2}/F_{IO_2}).[18]

Although driving pressure (plateau pressure − PEEP) > 15 cm H_2O has been shown to be associated with higher mortality in subjects with ARDS,[19] the best limit has not been tested in a prospective randomized trial.[20] Despite the lack of prospective data, making changes to ventilator settings that maintain or even lower driving pressure may not

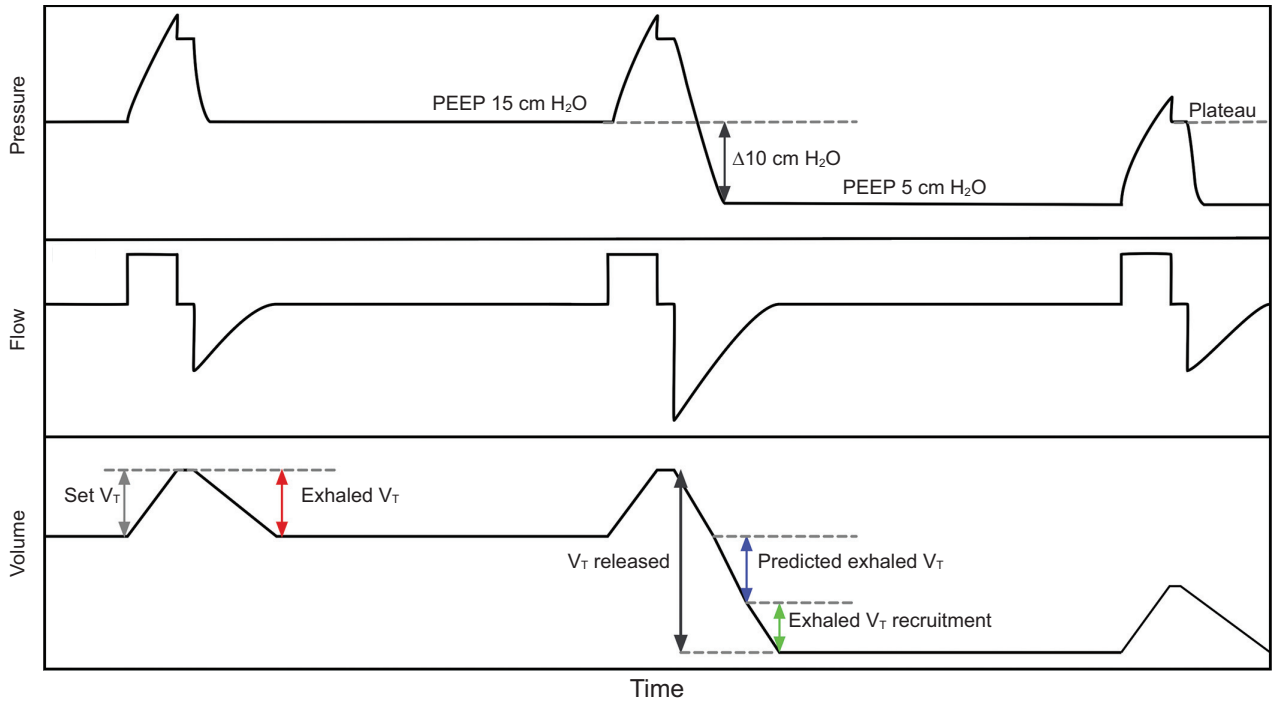

Fig. 3. The recruitment-to-inflation ratio is a ratio between compliance of recruited lung (on high PEEP) compared to respiratory-system compliance (on low PEEP). It uses continuous mandatory ventilation (ie, a passive patient) and a 10 cm H_2O drop in PEEP (from high to low). Compliance of the recruited lung (due to the higher PEEP) is determined by first subtracting the exhaled volume at high PEEP and the predicted loss of volume (predicted based on respiratory-system compliance) from the exhaled volume released during the PEEP drop, then dividing the remaining volume (ie, recruitment) by the drop in pressure (10 cm H_2O). Respiratory system compliance is determined by the set tidal volume (V_T) divided by plateau pressure – PEEP at the lower PEEP level. The compliance of the recruited lung is divided by the compliance of the respiratory system to determine the ratio. A ratio of $\geq$ 0.5 indicates recruitment potential (the higher the value above 0.5, the greater the recruitment potential), suggesting higher PEEP recruits lung units. The presence of airway closure should first be assessed before performing the maneuver. Video demonstrations of both maneuvers and an online calculator are available at (https://crec.coemv.ca, *Accessed April 3, 2020*).

have the same impact on lung stress or strain compared to changes that result in a significant increase in driving pressure (an increase is likely more injurious). However, the lowest driving pressure, or best compliance, does not always indicate that ventilation is the safest.[21] In fact, the best compliance may not reflect the optimal balance between overdistention and collapse assessed with EIT.[22,23]

More complex concepts have recently been introduced regarding the amount of mechanical power applied to the lung during positive-pressure ventilation.[24] The total energy of mechanical ventilation is composed of multiple components including tidal volume, PEEP, driving pressure (ie, compliance), flow, and breathing frequency. Considering that PEEP, plateau pressure, and tidal volume should be set individually, when these elements are excessive, or when the breathing rate is considerably high, all elements factor into potential for injury and should be minimized whenever possible. However, when faced with the dilemma of reducing the pressure applied to the lung or respiratory rate, pressures applied to the lung (ie, plateau pressure or driving pressure) have consistently been associated with mortality and should take priority. Consider permissive hypercapnia to help with lowering breathing frequency.

In summary, limiting plateau pressure, assessing recruitability using a single-breath decremental PEEP maneuver (ie, recruitment-to-inflation ratio), observing the oxygenation response when increasing PEEP, monitoring driving pressure, and allowing permissive hypercapnia are simple strategies that can assist in clinical decisions for mechanically ventilated patients, particularly those with ARDS. However, lung strain and transpulmonary pressure measurements (lung stress) may be helpful in the personalization of mechanical ventilation when ventilating a patient at or above the limits of recommended pressures is required yet may be safe. Patients with very high baseline pleural pressure or a stiff chest wall may benefit from measurements of lung stress and strain to confirm the safety of ventilator settings.

Ventilation Distribution

Ventilation distribution is traditionally determined with CT. In 1995, Gattinoni and colleagues[25] described the

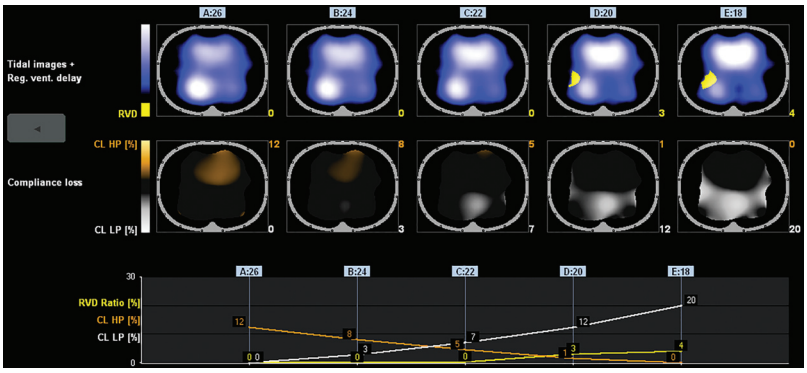

Fig. 4. The Costa approach refers to the plotting of regional compliance after performing a stepwise PEEP trial. Loss of regional compliance at high levels of PEEP is plotted against compliance loss at low levels of PEEP.

response to PEEP in 8 subjects with ARDS in terms of regional distribution, particularly in the ventral, middle, and dorsal lung regions. The authors described the importance of plateau pressure as the opening pressure of the lung, and PEEP as the pressure that can maintain opened and recruited alveolar units. However, if the plateau pressure reached does not recruit dorsal regions of the lung, the result is overdistention (and poor perfusion) to the ventral regions of the lungs, with a lack of distribution to the dorsal lung regions. When the lung is open and PEEP maintains recruitment, tidal volume distribution during inspiration is maintained closer to a 1:1 ratio between the ventral and dorsal lung regions when considering a caudal-cranial view. Until recently, the ability to view distribution changes throughout the lung at the bedside was not considered possible.

The use of EIT monitoring has made the assessment of ventilation distribution at the bedside a reality. Considering that lung recruitability plays an important role in the appropriate setting of PEEP and the resulting lung stress and strain, the ability to visually assess ventilation distribution changes, as they happen, at the bedside is a giant step forward in bedside monitoring. Similarities between ventilation distribution and lung CT have also been assessed. In 2004, Victorino et al[26] performed a validation study of regional lung ventilation measured with EIT compared to CT. They found that changes in air content measured with CT highly predicted regional changes in impedance ($r^2 = .93$), which means that impedance changes occurring during ventilation measured with EIT explain ventilation changes observed in CT (93% of its variance). Right-to-left differences in ventilation distribution show a bias of 0% and limits of agreement of −10% to 10% ($P = .31$). Although CT and EIT detected similar imbalances between the ventral and dorsal distribution, with good matching within each case, EIT showed a marginally larger imbalance between the ventral and dorsal distribution ($P = .04$).

In addition to regional ventilation changes, regional compliance changes can also be determined with EIT. Considering that tidal variation represents tidal volume delivery, compliance changes can be calculated according to changes in tidal variation and the applied ventilation pressure. Instead of mL/cm H_2O, EIT measures percent changes in ΔZ/cm H_2O. EIT software is now available on devices to compare changes in regional compliance during PEEP titration, including an approach often referred to as the Costa approach, named after the first author of the study that described this method.[22] This regional compliance analysis compares compliance changes that occur in the transition from a higher level of PEEP to a lower level of PEEP and displays areas with poor compliance at high and low PEEP levels. Compliance loss at high levels of PEEP suggest areas of overdistention, and compliance loss at low levels of PEEP suggest collapse (Fig. 4). One limitation is that each maximum and minimum level of PEEP represents the point of zero change; this does not actually mean there is no collapse or overdistention at the upper and lower limits of the PEEP trial, rather it is simply the reference point for change. Coincidentally, the balance between overdistention and collapse determined by EIT does not imply best respiratory-system compliance.[22,23]

Although a spontaneous breathing trial and ventilator liberation remains the goal for every invasively ventilated patient, the level of spontaneous effort is important. Very low inspiratory effort can result in prolonged time on the ventilator, as does excessive inspiratory effort.[27] Spontaneous breathing is also a controversial topic for patients with ARDS.[28] Additionally, excessive inspiratory effort has been described as a potential mechanism for self-inflicted lung injury.[28,29] One of the potential mechanisms driving the potential for injury is the regional strain that can occur in the lung due to high inspiratory effort.[30] In an animal model of lung injury, Yoshida et al[31] demonstrated that, despite controlling tidal volume (ie, using volume-controlled ventilation), inspiratory effort can cause a pendelluft effect where volume is pulled from the ventral regions into the dorsal regions, which results in excess strain in the dorsal region. This can be seen visually by monitoring the percentage of tidal volume delivered to the region.

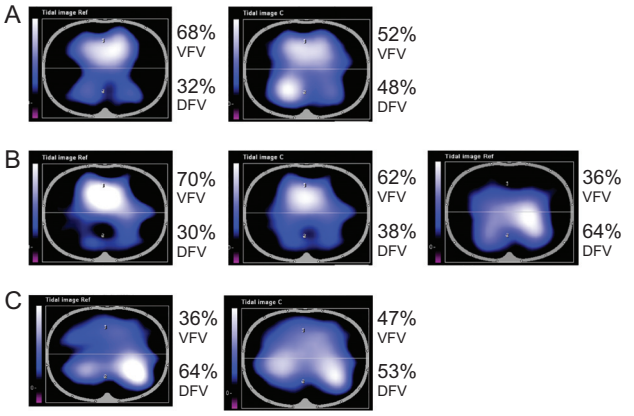

Fig. 5. A: Dorsal fraction of ventilation (DFV) increasing in a PEEP responder. B: DFV in a nonresponder before and after PEEP titration and after being placed in the prone position. C: DFV when PEEP is excessive and after reduction. There is minimal response to PEEP with significant loss of regional compliance in the ventral regions. VFV = ventral fraction of ventilation.

The regions of interest monitored with EIT are normally customizable, but common configurations are available on EIT devices. These configurations include regions such as 4 even horizontal slices (layers), quadrants, left and right separation, and ventral and dorsal separation. The distribution of tidal variation is normally given as a percentage of the global tidal variation (representing tidal volume). However, the correlation between tidal volume and tidal variation depend upon proper belt placement.[32] Ideally, the EIT belt should be placed between the fourth and fifth intercostal space; in female patients, the belt is normally placed above the breast tissue. With proper belt placement, one of the simplest approaches to monitoring distribution of ventilation is the ventral/dorsal configuration. During spontaneous breathing, excessive support can lower patient drive and the resulting effect can be poor distribution to the dorsal regions compared to ventral regions. In a paper by Mauri and colleagues,[33] as pressure support decreased, patient effort increased, resulting in an increase in dorsal region ventilation. Proper monitoring of patient effort is important when implementing such a strategy to avoid excessive patient effort that could lead to prolonged mechanical ventilation.[34]

Monitoring of the ventral/dorsal distribution can provide information regarding the need to attempt an increase in PEEP, but it can also serve as an incentive to decrease PEEP.[35] When the dorsal fraction of ventilation is low (ie, $< 50\%$), increasing PEEP should be attempted and monitored for improved distribution and regional compliance changes. Patients who respond well to increases in PEEP should exhibit a shift from ventral to dorsal regions (Fig. 5A). When patients with severe ARDS fail to show an acceptable increase in the dorsal fraction of ventilation (and oxygenation), EIT can be used to monitor the response to prone positioning (Fig. 5B). When PEEP is excessive, ventilation distribution is reduced in the ventral regions and becomes predominant in the dorsal regions (dorsal fraction of ventilation $> 50\%$); when this occurs in the supine position, PEEP can likely be decreased (Fig. 5C). It is unclear whether PEEP should be reduced in proned patients with a dorsal fraction of ventilation $> 50\%$, as this may be due to collapsed ventral regions (due to gravity), not overdistended regions as it would imply in the supine position.

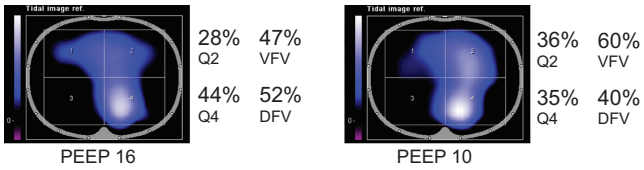

Fig. 6. When only 3 quadrants are being ventilated, the global dorsal fraction of ventilation (DFV) should not be used. In this example, the left lung (right side of the image) should be balanced between ventral and dorsal regions. VFV = ventral fraction of ventilation.

Although the global ventral/dorsal view is one of the more simplistic approaches when using EIT, a major limitation is when only 3 quadrants are participating in ventilation. In this case, it is better to consider the regional ventral/dorsal distribution only on the side (left or right) where the lung is participating most to ventilation. In Figure 6, quadrants 2 and 4 (Q2 and Q4) are not balanced at higher PEEP despite the dorsal fraction of ventilation being 52%. When PEEP is lowered, the dorsal fraction is now only 40%, but Q2 and Q4 are better balanced (36% and 35%, respectively).

Whether the clinical use of EIT results in better patient outcomes has yet to be determined. Clinical experience is growing, but widespread use has not been established. Additionally, there is still no consensus on which parameters should be used to adjust ventilator settings such as PEEP. The ability to monitor the distribution of ventilation and regional compliance offers information that has never been available before at the bedside, making EIT a very exciting and promising bedside monitoring tool for research and, more importantly, clinical practice.

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Discussion

Lamberti: Most of the discussion was on ARDS. How about in obstructive airways disease where measurement of end-expiratory lung volume can be very helpful but it's difficult. Is there any evidence in the literature in regard to the obstructive airways disease patient who's ventilated?

Piraino: I did not gravitate towards non-ARDS patients because I knew I was talking about distribution of ventilation with electrical impedance tomography (EIT) as well, and I have not seen anything published specific to a COPD population. I imagine it would be useful to look at EELV (EELI), but the management of a patient with very bad obstructive pulmonary disease involves so much more than end-expiratory lung volume. I think the bigger issues are often making sure you have appropriate expiratory time, minimizing air-trapping, etc. Trying to estimate EELV wouldn't be of much interest, but minimizing it by controlling respiratory rate or inspiratory time would have value. It would be difficult to lower EELV without reducing respiratory rate.

MacIntyre: Jim [Lamberti], you raise an interesting point. The question always comes up in obstructive lung disease, adding PEEP to facilitate the triggering process. In other words, to balance the autoPEEP that's present in the lung. The theory is to add enough PEEP that you balance the autoPEEP but not so much PEEP that you end up over-distending lung regions. It seems to me that EIT might be a very nice tool, and if you're doing the right thing the FRC will not increase. There's a potential role there.

Piraino: I agree, I think the distribution of ventilation may be more informative than the end-expiratory lung volume, at least with PEEP adjustment because you may not reduce EELI, but distribution of ventilation would likely change if triggering became more effective. But I didn't find anything published on the subject.

MacIntyre: I don't have a lot of experience with EIT. It uses a single band of electrodes around the chest. How much of the lung does this detect?

Piraino: The band itself is a few inches, however it captures a field. It's not just a single slice. For the measurement of EELV it wouldn't represent all the regions where nitrogen wash-in wash-out is measuring, which is everything being ventilated essentially, but the band itself does capture anywhere between 10 and 18 cm of the lung (I've seen both ranges mentioned in my readings). You can't specifically say it's 'this lobar' region, but within the area. The captured region really is more than half the height of an average adult lung.

Blanch: What you have shown in the patient in prone position is anecdotal or usually happens when you are turning patients with ARDS from supine to prone?

Piraino: What we've seen with EIT and proning patients is that most of the patients do exactly what you would expect them to do, you'd expect to change the distribution towards the dorsal regions. Where we've used it more clinically is when we are considering the need for proning with a patient. If we increase PEEP and we see that we are able to redistribute tidal volume at safe pressures, we may wait to see what the oxygenation response is. Having said that, I have seen patients where we prone and do not get that response. I gave you some examples of, 'wow look at that distribution change' but we have proned patients where they only open up on one side, for example. Even after proning their left side, for example, is still not open. This is a patient who may be more complicated, you may prone them because it's the right thing to do in terms of the evidence but in terms of their lack of response it may be reflected in what you see visually. The patient I showed in the example responded nicely and we were able to reduce F_{IO_2} by 0.2 over the next couple of hours. In some patients we are not able to reduce any settings, they're still relatively hypoxemic but you can see with EIT that they haven't opened up the same and some patients take way longer. This example was very quick, there's another example we saw with Tai [Pham] where within an hour aeration was completely redistributed. I've seen patients where it doesn't happen until 16 hours of proning and you don't see volume distribution that impressive.

Pham: The patient he mentioned was even more impressive than that, because the patient showed in your presentation, aeration was redistributed, so you had loss of ventilation in the ventral region and gain in the dorsal region. But there are some patients who only gain when they are proned, which means you have reopened lung homogeneously aerated as opposed to separation between aerated and non-aerated lung.

Scott: I have a question about EIT, as I don't have any experience with it. Is there any risk of skin breakdown from the band when you are placing a patient in the prone position?

Piraino: The manufacturer recommends you take it off every 24 hours. We did have a learning experience with proning. One of the issues with proning is that the belt we use has 4 grommets you push through a hole so, depending upon how tight the band is, you may have more or less leftover holes to attach the belt, and those holes when you prone somebody, if you don't put something underneath, what can happen is they can develop blisters

in the area or the holes. The blisters subside and there was no evidence of tissue injury, but we learned from our experience and we now ensure that we put gauze or padding under there and haven't had that issue since. We generally try to take it off every 24 hours just for skin protection.

Scott: Can you move the location of the EIT slightly up and down to mitigate this issue?

Piraino: There are data looking at the various positions from armpit (as high as you can go) to diaphragm.[1] They found the optimal position is around the 4th or 5th intercostal. So, if you are between the 4th and 5th intercostal and you moved it up or down one belt-width, when you look at the article there isn't a huge change when you move one step up or down. If you went from the maximum to lowest position you'd see a huge change in what the image looks like, but in the areas above and below to my eye were very similar in their examples. Clinically we sometimes can't get it to stay at 4 or 5. In female patients for example, it goes over breast tissue and may slide up slightly. If you can move it, even move it one belt-width, the recommendation for taking it off, is more related to its position on the back. You may move it during nursing care, but you don't know that it's staying the same place after moving back and then repositioning. I think the idea is to remove it, assess the skin, provide any skin care and if there are no issues it could be reapplied.

Schmidt: I'd like to frame what sounds like an impossible situation, but I'm hoping somebody has clever ideas. It relates to ARDS and the setting of PEEP. Depending on the tool we're using to look at PEEP level we can prioritize recruitment or over-distension or compliance or dead space or the homogeneity of ventilation and as you've shown in some of your diagrams these don't always line up. I think even the figures that get published usually the investigator chooses the perfect example of where things did or didn't line up. In light of depending on what lens we're using we see different things, how can we make progress in determining how to customize PEEP for the individual patient?

Piraino: I think using the tools we have is good. You bring up the primary point as to why nobody can agree on how to set PEEP. Someone will say, they use dead space fraction (V_D/V_T) because they've had good results overall and that's their preferred method. If you look at the literature you may get a similar response using respiratory system compliance, which you're right, in many patients they don't align and this adds to the complexity of what is ARDS. PEEP titration may go well for one patient using V_D/V_T, but if they have a pulmonary embolism, it may not be very valuable. There are a number of factors that can affect the utility of each tool you can use. I don't know that anybody will actually agree on the best way to set it.

Goligher: I think Greg's [Schmidt] question and the point behind it is very well taken. To me, what we need to do is to establish what aspect of this problem has the greatest impact on lung injury. Is avoiding derecruitment more important than avoiding over-distension? Personally my read of the literature is that over-distension is the major driver of lung injury and that's really what we should try to minimize as much as possible. What's compelling about using EIT at the bedside is there often does seem to be a PEEP level at which you can substantially minimize over-distension while also achieving 80–90% of the recruitment that can be attained – you can actually visualize that. We're running a trial now in Toronto that uses an EIT titration procedure to identify some version of optimal PEEP and then randomize subjects to that or to PEEP based on the EXPRESS trial. We're using biological measures of lung injury as a very short-term surrogate for how the lung responds to different levels of PEEP. To clarify this issue we need to randomize subjects to the PEEP level at which we can see that recruitment is relatively maximized versus the PEEP level at which over-distension is relatively minimized and progressively work out which of these mechanisms really drive lung injury. A lot of the PEEP trials to date have been predicated on the notion that atelectrauma is a really important mechanistic driver of lung injury. Personally, I'm skeptical of that hypothesis.

Schmidt: I like that response and it runs counter to the implication of the Franchineau paper[2] on ECMO subjects and best PEEP based on balancing derecruitment and over-distention as if those are equivalent insults. It may be that they are, and it visually is attractive to see the minimization of both, but as you suggest these may not be equivalent insults so it may be a misleading idea to think of best being the balancing of two things that may be different.

Piraino: The other challenge that will be facing EIT moving forward is which method of PEEP selection you use with EIT. There's the Costa approach,[3] which I find interesting, but my personal preference at the bedside is simply balancing the distribution of ventilation in all regions as much as possible whether it's a ventral-dorsal balance, or if I'm just using the regions that are important like the left and right. That's something that can be done in real time. The analysis of the Costa approach is that you push a button and you can go back and analyze the data that's just been captured and trending and most of the time I get a very similar result as to where I should set the PEEP

within a couple cm H_2O. But it's a very simplistic approach, but you bring up a good point there have patients where we've set the PEEP not at that point but slightly above or slightly below based on other parameters like what is their driving pressure, what is their Pplat. I think using just one method will be limited, using many can be limited when they don't agree, but when you have things like Pplat that we know nobody's arguing that the higher the Pplat the more injurious it could possibly be. But using all values in conjunction with what you're seeing has guided me. If the Costa approach suggests a PEEP setting, but if my Pplat is 35 and I decrease PEEP 2 cm H_2O and Pplat is now 30, I'll likely keep it there.

Goligher: You gave a nice presentation on the concept of strain and you employed a helpful teaching approach that I hope you highlight in your paper because it's a very difficult concept to explain to trainees. I think it's really important. One of the issues that needs to be better understood in enhancing our thinking on PEEP is the relative importance of global strain which is tidal volume plus an increase in end-expiratory lung volume vs dynamic tidal strain, and which of those is more important driver of lung injury. I'd be interested to know what everybody else here thinks, in the literature it seems that the dynamic strain is probably far more important than global PEEP or static strain. The interesting twist or complexity being that the more you lower the tidal volume the less recruiting the lung impacts on dynamic strain. And so even this issue of how much should you optimize the PEEP, increase it to recruit the lung at the cost of increasing global strain, probably depends on how low you're going with your tidal volume. I think that's an aspect of mechanics that hasn't been well appreciated – the influence of tidal volume on the optimal balance of dynamic and global strain.

Piraino: Again, to add even more complexity, the local strain represented by pendelluft.[5] You've lowered tidal volume you may think you've lowered tidal global strain but in fact it may be dependent on the patient's interactions with the ventilator. You may have a result showing biomarkers that are increasing which doesn't make sense if you're thinking that you've lowered global strain but it could just be localized based on that.

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