Critical Decisions

Enhancing patient-specific care in the critically ill

Continuing Education for Dietititians (CPE) and Respiratory Therapists (CRCE)

Monitoring FRC in Ventilated Patients

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Functional Residual Capacity (FRC) is a measurement of the reservoir of air that keeps lungs oxygenated after a normal exhalation. In mechanically ventilated patients, FRC measures actual lung volume. Although FRC is a vital indicator of acute lung pathology, until recently, FRC could not be measured directly—only estimated through indirect methods. Today's technological advances that enable direct measurement should eliminate the barriers that previously existed in routinely using this parameter in clinical decision-making. Serial FRC measurements provide valuable information regarding disease progression/resolution, optimization of PEEP, and prevention of ventilator-induced lung injury. Clinicians need to be aware that many factors besides disease pathology affect FRC, including prone positioning, recruitment maneuvers, suctioning, and weaning. Direct FRC monitoring is an underutilized tool that can help manage many ventilated patients with developing or resolving acute respiratory illnesses.

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Ventilated patients exhibit decreased functional residual capacity (FRC)—or, more appropriately, aerated end-expiratory lung volume (EELV) during sedation, while resting in recumbent positions, and when lung pathologies such as pneumonia, cardiogenic edema, abdominal distention, acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) are present. Thus, monitoring FRC in these patient populations has potential diagnostic and therapeutic value, as PEEP is routinely applied to restore lost lung volume. Conversely, FRC rises to supra-normal (and heretofore unmeasured) values in the setting of severe airflow obstruction with gas trapping, and treatments are often applied aggressively to reduce the resulting hyperinflation.

FRC monitoring appears to represent an emerging advance in the scientific management of many ventilated patients with developing or resolving acute respiratory illnesses.

Nearly two decades ago, Hedenstierna advocated FRC monitoring in ventilated patients.[1] However, for many years, FRC monitoring was not clinically feasible in the acute care setting. Indirect methods suffered from inaccuracies, technical difficulties, reproducibility problems, or cumbersome logistics that made such methods impractical for clinical use, especially when serial measurements were needed to trend therapeutic response.[2-4] Reliable, near-continuous FRC monitoring in ventilated patients has recently become an option, as ventilator circuitry now contains integrated means for measuring FRC. Thus, after more than 30 years of published reports regarding the technical feasibility of FRC monitoring, its direct measurement is now possible in clinical practice without interrupting care or using extraneous equipment.[3] This technological advance provides respiratory therapists with an additional tool for monitoring a parameter that can aid in the management of acute cardiorespiratory illness.

Rationale for Monitoring FRC

Investigations into FRC monitoring have assessed and quantified the effect of PEEP on FRC, verifying that increases in applied PEEP invariably increase FRC according to a pressure-volume (P-V) relationship of the respiratory system.[5-7] Bikker et al. reported FRC values in patients with normal lungs, primary lung disease, and secondary lung disease at PEEP levels of 5, 10, and 15 cm H_2O.[5] Each cohort demonstrated increased mean FRC in proportion to PEEP incre-

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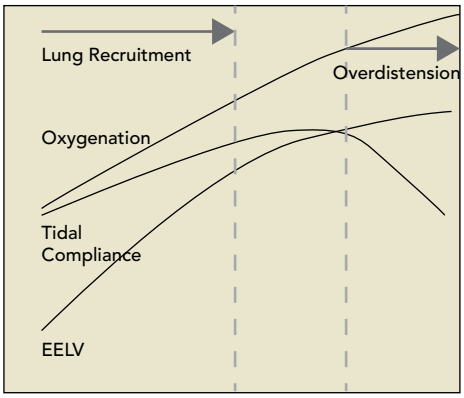
ments. Conversely, in an animal model study of ARDS, Lambermont et al. found consistent reductions in FRC as PEEP was decremented.[8]

Quantifying the association between FRC and PEEP elucidates the functional pressure-volume (P-V) relationship. It is important to consider the P-V curve in association with measured FRC because FRC changes due to PEEP admix volumes result from changes in the number of recruited, functioning lung units, as well as expansion of already-open lung units. PEEP is usually adjusted to increase FRC with the aim of achieving adequate arterial oxygenation.

To obtain a full understanding of FRC in the context of lung disease, FRC monitoring must also be considered in conjunction with oxygenation and tidal compliance data. Compliance relates inversely to the stiffness of the lungs and/or chest wall, but compliance does not necessarily track lung volume. Increases of FRC caused by PEEP adjustments may be due to beneficial lung recruitment that parallels increases in tidal compliance and oxygenation.[8,9] Above a specific level of PEEP, however, (10 cm H_2O in a study of lung recruitment in anesthetized patients),[9] further PEEP increases may simply cause over-distension, indicated by a decrease in compliance (Figure 1).[8-10] Also, risk of lung damage develops in most patients if the selected combination of PEEP and tidal volume causes plateau pressure to exceed approximately 30 cm H_2O.[11] Additionally, elevated airway pressures present the risk of impeding cardiovascular performance and decreasing oxygen delivery.[12] Oxygenation adequacy or simple measurements of FRC may be insensitive to these risks.[9,13] However, in one study of a lung volume recruitment procedure, increases in FRC were maintained if PEEP = 10 cm H_2O was maintained post-procedure.[9]

Figure 1. When PEEP is increased, recruitment is reflected in increases of EELV, oxygenation and tidal compliance. While overdistention causes compliance to decline, EELV and (with rare exception) oxygenation continue to rise and are therefore relatively insensitive indicators of that change.



Studies of the Relationship between FRC, compliance and PEEP

Lung-injury model studies have investigated the relationship between FRC and compliance.[8,14] In a porcine oleic-acid-injury study, Rylander et al. found FRC to be a more sensitive indicator of PEEP-induced aeration and recruitment than compliance.[14] They recommended monitoring both FRC and PaO_2. In another animal study, Lambermont et al. found that both FRC and compliance identified an optimal level of PEEP, where FRC is associated with best compliance and lowest deadspace/tidal volume ratio (VD/VT).[8] They also concluded that FRC and PaO_2 were insensitive to over-distension. In the Bikker et al. study of normal, primary, and secondary lung-injury patients, FRC and compliance correlated well only in secondary lung disease.[5] However, even though compliance and oxygenation have established thresholds for concern and are commonly monitored indicators of lung dysfunction, FRC as yet has neither.

Lung stress and strain

A recent (2008) study that monitored lung-injury risk recommended limiting the exposure of the lung to excessive stress/strain.[15] FRC monitoring may help determine lung stress and may be integral to assessing lung strain. Stress has been defined as transpulmonary pressure (Ptp). At end-expiration, Ptp should be sufficient to avoid lung opening/closing injury (low-pressure stress), and Ptp at end-inspiration should limit the risk of high-pressure stress by limiting Ptp to < 30 cm H_2O. In a study by Talmor et al. examining low-pressure stress risk, patients randomized to receive adequate PEEP to achieve a positive Ptp at end-exhalation exhibited improved oxygenation and greater compliance compared to patients with a negative Ptp.[16] While FRC assessment was not performed in the Talmor study, a critical measure would have been the FRC required to maintain a positive Ptp.

Strain is commonly equated with tissue "stretch." A proposed assessment of lung strain is V_T/FRC; a strain ratio > 2 is considered excessive.[15] To control strain, tidal volume reduction is a clinician-controllable tactic in ventilator patient care management, but the crucial FRC denominator of the global strain equation usually remains unknown. With current techniques, FRC can be measured to calculate strain. A prospective ventilator management strategy that includes monitoring of stress and strain has not been evaluated but should theoretically include FRC monitoring.

Factors that Affect FRC

Supine positioning has a significant effect on FRC—on average, reducing FRC by about 25% compared to sitting upright.[17-19] In a study of obese ventilated patients (vulnerable to FRC reduction), the reduction in FRC when supine and under anesthesia was 51%.[20] Prone positioning can increase FRC in some, but not all, patients with lung injury. Lateral positions have intermediate detrimental effects on FRC compared to sitting and supine postures. Several studies have evaluated how FRC is affected by common procedures or ventilator management strategies.

A study of eight ARDS patients evaluated the effect of endotracheal suctioning on oxygenation and FRC. FRC was restored by post-suctioning lung recruitment but not by PEEP alone.[21] In a study of postoperative cardiac surgery patients, FRC was reduced for up to 15 minutes after endotracheal suctioning. Patients with the greatest reductions in FRC from suctioning should benefit most from recruitment maneuvers.[22] Pleural effusions have space-occupying effects on FRC and cause significant reductions in compliance. In an animal model study of pleural effusion, moderate PEEP completely restored FRC and compliance.[23]

Due to native variability in ventilation during common activities, FRC monitoring is typically more reliable in sedated patients receiving mechanical ventilation than in patients spontaneous breathing. This alludes to the value of FRC monitoring during weaning, which Heinze et al.[24] studied in patients receiving partial ventilatory support during a weaning protocol. These investigators found that FRC could be reliably measured during partial support and that FRC decreased as ventilatory support was reduced. Thus, FRC monitoring during weaning could serve as a guide toward extubation success. Zinserling et al. reported FRC values obtained during six partial-support ventilator modes as breaths were triggered by spontaneous efforts. FRC values were judged to be acceptable with low variability. Variability was greatest during airway pressure release ventilation.[25]

Collectively, this points to the utility of measuring FRC. However, a paucity of data exists for examining the clinical potential of serial FRC monitoring.

History of Indirect Methods for Serial FRC Determinations

Numerous methods of monitoring FRC have been evaluated in test lungs, volunteers, and ventilated patients. These include imaging studies, body plethysmography (BP), gas dilution, and gas washin/washout.[4,26] Most of these methods are considered impractical for clinical monitoring, for reasons outlined in the following paragraphs.

Analyses of lung volumes from images have been performed by planimetry of X-rays, electrical impedance tomography (EIT) and computerized tomography (CT). Planimetry involves tracing and quantifying areas from a series of standard X-rays (planimetry) to estimate lung volumes. This process can provide accurate thoracic gas volume estimates; however, the method's labor intensity and the need for multiple X-rays prohibit its clinical use.[26]

Body plethysmography, first described by DuBois[27] in 1956, estimates FRC by enclosing a patient in an airtight box and measuring pressure changes within the box while the patient attempts to breathe against an occluded valve. This technique is clearly impractical for ventilator patients.

Both X-ray and BP studies produce estimates of FRC that include non-ventilating lung units—a true FRC that is often greater than estimates based on ventilation. However, the additional volume may include sequestered gas that is not participating in gas exchange.

Electrical impedance tomography (EIT) produces medium-resolution video imaging that functionally localizes ventilation quite well, and volumes can be crudely estimated. However, the limited width of the region around the EIT bands leads to inaccuracies in estimates of total lung volume.[28]

Computed tomography (CT) studies are the gold standard for FRC determinations in research studies[29] but are clearly impractical for serial FRC measurements clinically. Image density analysis by CT involves the summation of voxels (volume units) according to the amount of gas in each voxel to obtain a total FRC. Transporting patients repeatedly to radiography and the risk of cumulative radiation exposure limit the use of serial CT imaging for this purpose. CT studies remain a primary diagnostic tool for evaluating the location and extent of lung injury, but they are not used routinely for FRC determinations.

Development of Current Methodology for Serial FRC Testing

As early as 1800, a gas dilution method for quantifying FRC was described using hydrogen.[30] In more modern times to the present day, the gas dilution method used for research in ventilated patients involves disconnecting the ventilator and providing manual ventilation (a fixed volume and concentration of helium) until the helium is uniformly distributed between the lungs and bag—usually ≈ 10 breaths.[31-35] The proportion of helium remaining after mixing provides a direct dilution estimate of FRC. A study comparing this technique to other techniques has verified its accuracy.[28] Because this method requires an interruption of care to connect the helium, there is a risk of lung de-recruitment; and the manual breaths may change the FRC if their pattern does not closely replicate that of the mechanical ventilator. In 10 ARDS patients, Patroniti et al. found that FRC values determined via helium dilution measured after ventilator disconnection did not reproduce resting FRC but instead corresponded to the previously applied PEEP.[35] Therefore, when determining a P-V curve from no PEEP, the P-V curve will be shifted by the previous PEEP setting.

A method for estimating FRC from the washin/washout rate of a "tracking" gas was first described by Durig in 1903[36] and then by Darling in 1940.[37] Generally, as a fixed fraction of inspired gas is changed (added to or washed from the lungs) during ventilation, the rate of equilibration to the new concentration is inversely related to FRC. This method has used changing concentrations of sulfur hexafluoride (SF6), oxygen (O_2) and nitrogen (N_2), although the limited availability of SF6 and difficulties creating accurate sensors for it kept it from being adopted for clinical use.[38,39] In 1993, Fretschner et al. measured FRC via an integrated nitrogen washin/out method in a test lung model and in ventilated patients when FlO_2 was changed by 0.3. The method involved intrabreath signal synchronization of flow and FlO_2. This innovation represented a unique method of carefully determining FRC without ventilator disconnection, but its error range approached 20%.[40]

All the more recent versions of this method use gas concentration sensors that sample gas from the ventilator circuitry to calculate FRC without interrupting ventilation. Rapidly responding sensors, precise solenoid control and software synchronization of signals during ventilation have improved this inline FRC measurement technique.

Overcoming the Challenges of Signal Synchronization

Flow and gas concentration data must be linked to achieve signal synchronization. That

challenge has been solved in two ways: modeling flow viscosity and measuring only end-tidal gas concentrations/volumes without intrabreath synchronization. Both approaches have been verified as accurate in clinical studies.

The LUFU system (Draeger Medical; Luebeck, Germany) synchronizes flow and FlO_2 signals while adjusting for gas viscosity.[41,42] Several studies using LUFU have verified its accuracy and have investigated the role of FRC monitoring in ventilated patients[22,24,41-44] A simplified method using end-inspiratory/end-expiratory sensing of O_2 and CO_2 to estimate N_2 washout has been tested and verified as accurate.[45,46] By each method, an FlO_2 change of only 0.1 generates accurate FRC estimates,[45,47] allowing safe measurements in patients who require very high FlO_2.

A new technology, the Engstrom Carestation (GE Healthcare Madison, WI), directly measures the end expiratory lung volume by slightly altering the delivered FlO2 level for short periods of time using the volumetric O_2 and CO_2 measurement capability. Chiumello et. al. compared this method with gold standard Computer Tomography (CT) studies and found that it correlates well (at all lung volumes) and may be easily used in clinical practice.[29]

Reference Values

Traditionally, FRC has been measured in the pulmonary function testing (PFT) laboratory and compared to predicted values based on height, age and gender.[3] In the outpatient setting, an elevated FRC compared to its predicted value helps categorize an obstructive lung disease component, while decreased FRC quantifies a restrictive impairment. But in ventilated patients, FRC reductions caused by lung pathology, supine positioning, and/or sedation trump the usual gender/age/height determinants for predicting FRC. In these cases, expected values for FRC are much less than outpatient nomogram predictions.

Measured FRC in the acutely ill has been consistently below predicted values for height, age and gender even when PEEP is applied to increase FRC. Bikker et al. reported FRCs of 66%, 42% and 35% of predicted sitting FRC at PEEP = 5 cm H_2O for normal, primary, and secondary lung disease patients.[5] In 22 patients with ALI, FRC was 48% of predicted FRC and only 42% of predicted FRC in 26 acute ARDS patients.[15] Delamonmica et al. measured a mean FRC of 31% of predicted in ARDS patients.[48]

Clearly, FRC in ventilated patients cannot be compared to FRC predicted values determined from PFT nomograms. In addition, definitions of acute respiratory failure, ALI and ARDS are not standardized; so FRC reduction is likely another assessment of the extent of lung injury. In patients with ALI or ARDS only, an FRC of < 1.0 L can be expected with no PEEP. If PEEP is applied (≈ 5 cm H_2O) the FRC marginally exceeds 1 L. Severe ARDS can be expected to have FRC as low as 0.5 L.[27,34] Importantly, measured FRC may or may not reflect airspaces that are interfaced to a perfused alveolar membrane; therefore, as previously discussed, gas exchange and compliance should be monitored in conjunction with FRC. Earlier studies (Table 1 at http://www.critical-decisions.org/table.html)tend to report higher FRC values in patients with respiratory failure—probably without ALI or ARDS.

Due to all these circumstances, reference values have not been established for ventilated patients. However, numerous studies have reported FRC values in normal, respiratory failure, and lung-injured patients (Table 1).

Obtaining Valid FRC volumes

While FRC can be quantified without interruption of care (other than minor changes in FlO_2), there are prerequisites for obtaining accurate values. Accurate FRC measurement requires a stable metabolic baseline that is not changing due to voluntary activities like movements, efforts to communicate, coughing, or sighing. Unfortunately, FRC naturally varies in spontaneously breathing patients. While sedation reduces breath-to-breath variability, sedation has the potential to lower FRC. While varying FRC can be a problem, software algorithms can detect variability to gain confidence in the measure of FRC in the stable, spontaneously breathing patient.

From the purely technical side, there must be no circuitry leaks during the 3–5 minute washin/washout period—a minor restriction for closed-circuit ventilated patients. A quality control assessment for circuit integrity is to review the differences between washin-washout values; they should be minimal. FRC estimates should be elevated in COPD patients and less consistent between repeated measurements, as large FRC volumes require more washin/washout time, and airways may be variably communicating.

Future Studies

Several aspects of FRC monitoring remain to be studied. The effect of disease on FRC has been reported,[5] but FRC monitoring during disease progression or resolution has not been prospectively assessed—a goal recommended in 1993.[1] Generally, altered FRC can be expected after bronchodilator use, certain position changes, or increases in mean airway pressure; but studies have not specifically determined how those circumstances alter FRC. FRC will be elevated in COPD patients where retained thoracic gas volume is imprecisely monitored by pressure (autoPEEP). FRC monitoring would quantify the volume effect of autoPEEP; however, studies of FRC determinations in COPD patients are lacking.

Clinical experience finds oxygenation to be markedly affected by position changes in certain patients. These hypoxemic episodes must be due to position-dependent ventilation/perfusion changes related to abrupt FRC reductions or regional perfusion changes; however, the cause usually remains undetermined. Changes in ventilator strategy include inversion of I:E., high-frequency ventilation, or VT/f adjustments to affect change in FRC; however, studies confirming the therapeutic value of these interventions and their relationship to FRC have not been conducted.

Conclusion

To summarize, several potential applications for FRC monitoring were proposed in 1993, with the primary goals being to track disease progression and the effect of PEEP in ALI/ARDS patients. As yet, serial FRC monitoring has not been evaluated as a metric for tracking disease progression/resolution, nor has FRC been measured during high-frequency oscillation or prospectively after adjustments in mean airway pressure. Nonetheless, monitoring of FRC during PEEP adjustments to optimize lung recruitment can be justified by recent studies that complement traditional indices of oxygenation and tidal compliance. Expanding a protective-lung ventilation strategy to include stress and strain assessments in lung-injury patients includes the use of FRC monitoring. Prone positioning, recruitment maneuvers, suctioning, and weaning affect FRC; and all these considerations are important in daily practice. Technical constraints that previously limited the routine clinical use of FRC monitoring in mechanically ventilated patients have recently been overcome. For these reasons, FRC monitoring appears to represent an emerging advance in the scientific management of many ventilated patients with developing or resolving acute respiratory illnesses.

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Panel Discussion: The Utility of Functional Residual Capacity

Moderator: John Marini, MD
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Measuring absolute resting gas volume (functional residual capacity, FRC) is a fundamental component of measuring lung mechanics in the pulmonary function laboratory, where it facilitates the separation of restrictive from obstructive disease and allows for better interpretation of DLCO as an indicator of parenchymal gas exchanging efficiency. For insight into the place of FRC determinations in the acute care of ventilated patients, we assembled a panel of experts who have extensive clinical experience and strong interests in lung mechanics, applied physiology and mechanical ventilation. The discussion follows.

1. For what conditions would the ability to measure FRC be especially helpful?

Haas: Measuring end-expiratory lung volume (EELV) may prove helpful in any condition that affects FRC, but it might be most helpful in ARDS patients. Many therapies, such as PEEP, recruitment maneuvers, and prone positioning, attempt to improve ARDS hypoxemia by recruiting collapsed lung units and increasing FRC. FRC monitoring may also be helpful in assessing the stress-strain relationship of the lung. This may be important for determining the risk for ventilator-induced lung injury (VILI).[1,2]

Blanch: Measuring FRC would be clinically valuable for patients with bilateral pulmonary infiltrates, specifically, to determine the amount of gas in their lungs at end-expiration. I consider FRC when pressure at end-expiration is atmospheric. I consider EELV when there is PEEP in the system. At this point EELV is the sum of FRC and the increase in lung volume induced by PEEP. Therefore, the measurement of EELV is of particular importance immediately after intubation and to interpret changes in lung volume induced by PEEP. Patients with ALI/ARDS have a wide variability in FRC (and EELV) despite being ventilated with a similar tidal volume.[3]

Measuring end-expiratory lung volume (EELV) may prove helpful in any condition that affects FRC, but it might be most helpful in ARDS patients.

- Haas -

Culver: In hypoxemic respiratory failure (e.g. ALI, ARDS), improvements in oxygenation are most likely a direct result of maintaining an adequate aerated alveolar volume, particularly at end-exhalation to avoid small-airway closure and alveolar collapse. In a spontaneously breathing person with normal lungs and chest wall, this point corresponds to the relaxed functional residual capacity (FRC) determined by the balance of the opposing recoil of lungs and chest wall. In a mechanically-ventilated patient, other factors intervene and may vary, even on a breath-to-breath basis; so the terms dynamic FRC (dFRC) or end-expiratory lung volume (EELV) are commonly used. In recognition that some of this volume represents lack of gas exchange behind closed airways, the EELV measured by gas-dilution or washout techniques may be called the accessible pulmonary gas volume (APGV). This would be expected to correlate best with gas exchange.

Gommers: FRC measurements would be especially helpful for all patients who receive PEEP during mechanical ventilation, but especially patients with severe hypoxemia and high levels of PEEP. It would also be helpful for patients who are operated laparoscopically or have surgery high in the abdomen, such as liver surgery.

2. What factors should be considered before making the measurement of FRC?

Kallet: The newer clinical measurements are based upon some variation of the so-called oxygen washout technique, which relies upon the assumption that the amount of O_2 stored in the blood has not changed significantly during the measurement.[4] Therefore, either hemodynamic instability or a sudden change in oxygen consumption (as when the patient is agitated) could affect the accuracy or reproducibility of the measurement. Therefore, I think it is important that measurements be made after achieving a reasonable steady state following an adjustment in either PEEP or vasopressors.

Haas: The conditions required for a good study depend on the method used to measure FRC but, in general a passive patient with a stable ventilatory, cardiovascular and metabolic state is ideal. Each method of FRC measurement has particular technical factors that must be taken into consideration in addition to specific patient factors related to the limitations of that technique.

Blanch: In principle, FRC is a static measurement. Using the closed dilution technique, the patient breathes a known concentration of helium mixed with oxygen and the helium concentration in the expired breath after an equilibrium period is used to calculate FRC. This method is mainly used for research and the patient must be well-adapted to mechani-

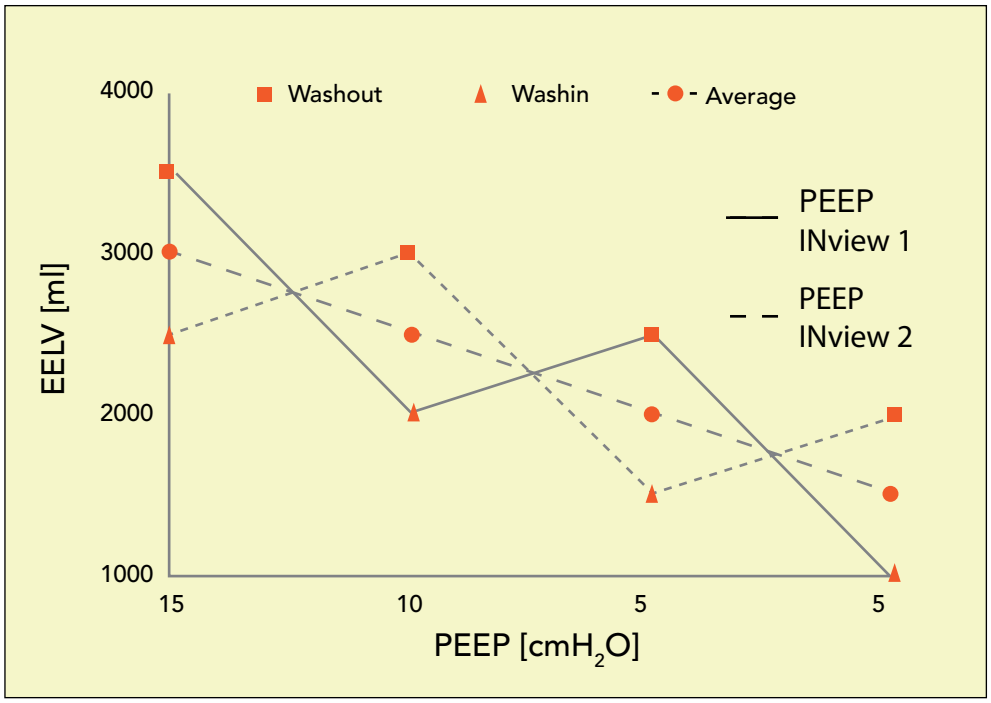

Figure 1.

cal ventilation to achieve a reliable and reproducible FRC measurement. (This requires sufficient sedation and analgesia, or even paralysis if required). Using the oxygen washin/washout technique, FlO_2 should be ≤ 80% to perform an accurate measurement of EELV.

Culver: Whereas a blood gas measurement might be used to assess an acute deterioration, I think measurement of FRC is most likely to be helpful in guiding ongoing management or planned changes in ventilator parameters. Thus, the patient should be in a fairly steady state at least 10 minutes after any ventilator changes, in the position they will be maintained. The measurement will be less consistent if there are irregularities in the ventilatory pattern, such as coughing or closely cycled stacked breaths.

Gommers: As Bruce indicates, make sure you establish a steady state for at least 10 minutes after connecting the patient to the ventilator, because the calculations need a stable VCO_2 baseline for at least 10 minutes prior to the measurements. Figure 1 shows the importance of a stable VCO_2, a major factor in the algorithm. This steady state should be even longer when the lung condition is changed. For example, after a recruitment maneuver, the lung and gas exchange need to adapt to the recruited lung volume. A steady state of 15—30 minutes would then be advised. Also, if a prolonged recruitment maneuver is used with increased tidal volumes, an additional amount of CO_2 will be exhaled. Because the VCO_2 will be increased during this period, a new baseline will need to be established. The energy expenditure (EE) (Fig. 1) and respiratory quotient (RQ) are calculated from the same variables as the FRC, so a stable RQ and EE indicate a stable situation for FRC measurements. Checking a number of readily available parameters before measurements will give valuable information on whether the measurements are feasible:

Ventilatory frequency: the maximum for FRC measurements is 35/min according to the FRC Appliguide (GE Healthcare; Madison, USA); however, if possible a frequency below 25/min is advisable. Because the sampled gas arrives at the analyzer with a time delay over 100 milliseconds and needs constant integration with the measured airway flow, higher frequencies increasingly reduce accuracy. This time delay is also not constant, but depends on the gas mixture (e.g. FlO_2) and pressure.

Ventilatory inhomogeneity: this can be evaluated using ventilatory waveforms, and the capnogram can also be very useful. If there is a severe upslope in phase 3 of the capnogram, there will be a difference in the time constants of individual alveoli. Especially in patients with COPD, theoretically the washout time will be too short for reliable measurements, because slower alveoli will not have enough time for a full washout for the new nitrogen concentration. As a result, the measured values will be underestimated, but they can still be used to show a trend.

Regularity of the breathing pattern: FRC cannot be measured during very irregular breathing, because there will not be a steady state before measurements and gas and flow integration will be difficult. This is especially true if there is also a severe upslope in phase 3 of the capnogram, which causes a constant difference in end tidal gas concentrations. However, with a regular breathing pattern, FRC can be measured with precision both in controlled and partial support modes.

Air leaks: major air leaks (e.g. chest drains, cuff leak) will influence the amount of nitrogen inhaled and exhaled used by the Engström algorithm to calculate FRC.

3. Do you think FRC would be helpful in tracking the progression of disease and/or the response to treatment?

Kallet: Absolutely! There are two crucial aspects to FRC in the management of patients with ARDS. First, in the recumbent position, FRC is nearly the same as alveolar volume, a major determinant of PaO_2.[5] Second, "specific compliance" (the lung's elastic properties relative to resting lung volume) is probably the most relevant measure of lung mechanics and may be the most important determinant of ventilator-induced lung injury.[6] Because lung injury in ARDS is heterogenous, effective lung recruitment often comes at the price of regional overdistention. Therefore, it is difficult to determine the optimal balance between these two considerations in a syndrome characterized by its unique presentation in individual patients.[7]

Haas: It definitely would be interesting to monitor FRC if it was easy and accurate. FRC monitoring has not moved to bedside clini-

cal practice, primarily for technical reasons. We are just now getting systems that can integrate with the ventilator and measure FRC in an automated manner so that monitoring can be done in a semicontinuous manner, rather than intermittently. Clinical studies are needed to determine the value of FRC monitoring. It appears that the washin-washout method and the CO_2-rebreathing method are the most promising techniques for ICU monitoring.[4,8-12]

FRC may be helpful in monitoring the progression of many disease processes that affect FRC, especially ARDS. FRC is reduced postoperatively due to pain, decreased chest wall recoil, increased abdominal pressure, and atelectasis formation. The reduction is more pronounced with obesity. Although the reduced FRC can be partially restored by using PEEP or by increasing the patient's head of bed, these techniques may not be as effective in obese patients.[13]

Blanch: Yes. If we agree that the magnitude of lung deformation or strain (i.e. ratio between tidal and end-expiratory lung volumes) is key for explaining the origin of VALI, then lower EELV and higher strain could be associated with increased lung injury. Moreover, some authors have hypothesized that certain values for these parameters could define a threshold for ventilator induced injury to occur.[1,14-16]

Culver: I expect there would be changes in FRC as lung or chest wall compliance change over the course of an illness. However, I don't see this as an end in itself, but only as part of the means toward the desired end of the ability to spontaneously maintain adequate gas exchange. So I would see little utility of FRC measurement in an improving patient, but the data might help in understanding the pathophysiology of a progressive deterioration or failure to improve.

4. Can FRC be used to adjust PEEP?

Kallet: Yes! The most practical utility of measuring FRC is to access the mechanical effects of recruitment either by PEEP titration, prone positioning, recruitment maneuvers

Because lung injury in ARDS is heterogenous, effective lung recruitment often comes at the price of regional overdistention.

- Kallet -

or some combination of all three. Because of the complexity of both hemodynamic and pulmonary mechanical responses to PEEP titration in ARDS, FRC must be integrated with other measurements. Both PaO_2 and FRC may increase beyond the point that both lung compliance and cardiac output decrease, and physiologic dead space fraction increases—these being classical signs of lung overdistention.[7] Remember that PEEP not only indirectly recruits collapsed alveoli by raising inspiratory pulmonary pressure, but also further expands poorly and normally inflated alveoli.[17] In addition, the effect of PEEP on lung overdistention is a function of tidal volume magnitude.[18] Therefore, measuring FRC during PEEP titration in ARDS is important but of limited value without detailed consideration to other variables such as tidal volume, specific compliance, dead space fraction and CO_2 excretion.

Haas: In general the FRC measurement by a gas dilution or washout technique can detect lung recruitment during PEEP titration, but it cannot detect overdistension; so it must be used in combination with another measure of respiratory mechanics, such as dynamic compliance. (Bikker 2008) On the other hand, electrical impedance tomography (EIT) can provide information on EELV as well as differentiate between recruitment and overdistension.[19,20]

To minimize overdistension and potential for VILI, it is suggested that higher PEEP levels be used with patients demonstrating recruitment potential and lower PEEP levels for those demonstrating minimal recruitment potential. A challenge is how to identify potential responders. Dellamonica and colleagues compared methods of assessing PEEP-induced strain and lung recruitment, which included FRC measurements via the washout/washin method.[21] They found that the ratio of the change in EELV between PEEP levels to the FRC level at ambient pressure (change in EELV/FRC) differentiated high from low recruiters.

Blanch: The surfactant system, alveolar interdependence, collateral ventilation, extracellular matrix, and mechanical properties of the chest wall work together to avoid alveolar collapse. These mechanisms guarantee a minimal resting volume (FRC/EELV) at end-expiration and a large number of alveoli to distribute each tidal volume. The net result is that healthy lungs present minimal changes in their structure during ventilation and only minor variations in alveolar size and shape. Ventilatory parameters can influence lung deformation and alveolar instability. PEEP could definitely decrease alveolar instability when the net effect is recruitment, and hence increase FRC/EELV. PEEP can increase lung overdistension in patients with severe lung injury with lower lung compliance and late ARDS. In these circumstances, PEEP will increase plateau pressure with no recruitment and EELV remains lower. Excessive tissue deformation can also explain why healthy lungs ventilated with high VT and moderate pressures develop lung injury. VT promotes a time-dependent increase in alveolar instability that could lead to lung damage. In this situation, FRC/EELV measurements cannot be useful to determine immediate lung damage. In summary, at similar VT and concomitantly tracking changes in plateau pressure or compliance, the measurement of EELV is important to adjust PEEP to maximize recruitment. See the figures in Albaiceta et al.[22]

Culver: Even with esophageal pressure monitoring, the calculated transpulmonary

pressure can give only a rough guide to lung volume due to uncertainties around the abnormal lung compliance, the correlation of esophageal pressure to locally effective pleural pressure, and the degree of air trapping. The ability to readily and repeatably measure FRC as APGV could be quite helpful in guiding the application of PEEP to provide an adequate alveolar volume for gas exchange, and to assess the response to recruitment efforts. However, a lung volume measurement that appears adequate may include both collapsed and over-distended alveoli, so FRC measurement is not sufficient to avoid the risk of barotrauma-volutrauma.

Gommers: Yes. A possible method of identifying optimal PEEP could be the measurement of FRC. It has been shown that FRC is decreased by 25% in healthy volunteers after changing from sitting to supine position during spontaneous breathing. In critically ill patients receiving mechanical ventilation, the level of PEEP determines FRC and therefore it is better to speak of EELV. Application of higher levels of PEEP leads to increased EELV values as a result of recruitment or further distention of already ventilated alveoli. To differentiate between recruitment and distention, EELV changes should be combined with dynamic compliance values or dead space measurements.

5. How variable is FRC in an otherwise stable patient? Should more than one measurement be made at a given time point?

Kallet: With the oxygen washout technique there can be a considerable degree of variability between measurements. For example, in a recent study the coefficient of repeatability was approximately 13% or 300 mL.[12] Given that this test/retest variability represents 17—50% of the average reported FRC measured in patients with ARDS (600-1800 mL)[23], I would not feel comfortable relying upon a single measurement of FRC to assess my therapeutic interventions.

Haas: If diagnostic procedures are easy, quick and safe to perform, you can average 2 or 3 measurements, so it is reasonable that 2 FRC measurements would be desirable until research shows that an individual study is adequate. Several studies have reported the difference between repeated FRC measurements in patients to be 5—10%.[12, 24-26]

In PEEP INview, only one washout or washin FRC measurement is used at each PEEP step and without averaging the values.

- Gommers -

Blanch: Olegard and colleagues studied a modified nitrogen washin/washout technique based on standard monitors using inspiratory and end-tidal gas concentration values for functional residual capacity (FRC) measurements in patients with acute respiratory failure (ARF).[24] They showed good precision of FRC measurements with standard monitors using a change in FlO_2 of only 0.1. Measurements can be performed with equal precision up to an FlO_2 of 1.0. Today, the washin/washout technique is built into ventilators and it seems that the technique is reproducible with only a few measurements.

Culver: Variability in FRC measurements will reflect both the reproducibility of the test itself and true short-term changes in EELV. I would expect the latter to be small in a sedated patient on a volume control or a stable assist-control ventilator mode with no position change preceding the measurement. More variability would be expected when spontaneous efforts are present, as in an IMV or pressure-cycled mode. Breath-breath stability of exhaled tidal volume may be an indicator of a stable FRC. In the pulmonary function lab, it is typical to average three plethysmographic measurements of FRC, though gas dilution measurement are usually not repeated due to the time required. It would be prudent for any ICU to do repeated measurements until the consistency of the measurement in their hands is established.

Gommers: In contrast to a single measurement that provides the average of both a washout and washin, the PEEP INview® (GE Healthcare) only performs a washout or a washin at each PEEP step (one measurement). During a PEEP trial, the washout either over- or underestimates the average with the washin exhibiting the opposite behavior. This behavior depends on a number of physiological principles (e.g. transfer of nitrogen between blood and alveoli), but is eliminated by averaging a washin and washout. In PEEP INview, only one washout or washin FRC measurement is used at each PEEP step and without averaging the values.

6. How influential is position in the FRC?

Kallet: To my knowledge, the effects of body position on FRC have only been measured in normal subjects between the sitting and supine positions, wherein FRC is uniformly diminished by 25%.[27] Because bodily position changes in critically-ill patients are much less drastic (e.g., from 20˚ to 30° semi-Fowlers to the supine position), it's difficult to estimate the magnitude of change in FRC. That being said, in the context of making crucial ventilator adjustments in a patient with severe ARDS, I would want to keep the patient in the same position during all measurements, just to remove the possibility of confounding influence. In terms of the effects on FRC due to positioning a patient from side to side, I would be concerned about the compressive effects of the heart, or an enlarged liver on lung recruitment/de-recruitment and FRC measurements as body position was changed. That would actually be a very interesting and clinically useful study!

Blanch: FRC is influenced by age, position and height. Whereas V/Q mismatch improves from supine to prone it seems that total vol-

ume changes (FRC or EELV) are similar in patients with ALI/ARDS. Richard and colleagues demonstrated that vertical positioning is a simple technique that may improve oxygenation and lung recruitment in ARDS patients.[28] Although FRC or EELV was not measured in that study, the authors found that the volume at 20 cmH_2O of airway pressure measured on the PV curve from PEEP increased using the vertical position only in responders (233±146 vs. -8±9 mL in nonresponders); this change was well correlated to oxygenation change. This article highlights the importance of lung recruitment in EELV variations in patients with ARDS.

Culver: In normal individuals, there is a well-documented decrement in FRC with a change from upright posture (standing or sitting) to supine.With obesity or increased abdominal pressure, the change may be more marked, but it may also be attenuated when the FRC is already very reduced in the sitting position. The normal positional change raises the question as to whether to target the normal sitting FRC, widely available from PFT prediction equations, or the expected reduced value expected in a recumbent position.

7. Does FRC measurement have value in the spontaneously breathing patient?

Kallet: That is a hard question to answer. First, there is the issue of measurement reliability under circumstances when the breathing pattern is poorly controlled. In normal subjects, when measurements are repeated under well-controlled laboratory conditions, the mean difference is typically only 1% to 2%.[7] But those are decidedly not the circumstances under which clinical measurements are made in patients with ARF. Furthermore, the validity of the test is based upon the assumption that inspired and expired volumes are essentially equal, so that performing FRC measurements when the breathing pattern is unstable presents a particularly vexing problem. Second, it is not apparent to me that measuring FRC in this situation is clinically useful. If the patient's clinical condition is deteriorating, then they should be ventilated with a full support mode such as volume- or pressure-assist control and sedated appropriately. If they are recovering sufficiently to allow spontaneous breathing trials, I don't think that information about the FRC is important in terms of management decisions.

In normal individuals, there is a well-documented decrement in FRC with a change from upright posture (standing or sitting) to supine.

- Culver -

Haas: FRC monitoring may be particularly helpful when applying modes of mechanical ventilation that encourage spontaneous breathing, especially APRV, which is used with ARDS patients. In general, FRC monitoring systems designed to be used with ventilators are validated on spontaneous breathing individuals with no lung disease,[4,7] but those systems may not be accurate when there is considerable variability in tidal volume and respiratory rate, particular at low volumes and fast rates.

Blanch: Patients with ARDS ventilated with modes that allow spontaneous breathing (e.g., APRV, BIPAP) seem to improve ventilation to dorsal lung areas and FRC/EELV improves as a result. In ARDS patients with quiet breathing, historic data seem to support reproducibility on those measurements.[29] In patients with very active breathing who do not interact well with the ventilator, FRC measurements are not reproducible.

Culver: In the ICU, the main utility of FRC measurement would be to guide therapy directed at changing the FRC so, in a patient receiving no ventilator support this would be limited to position change. If CPAP or biilevel NPPV is being used to support oxygenation, then the same considerations apply as for PEEP adjustments.

Summary

There appears to be strong agreement among the expert panelists that accurate knowledge of the end-tidal resting volume of the lungs would provide information to the clinician that cannot be easily inferred from the airway pressure and tidal flow and volume data alone. Although the latter continue to be of unquestioned value and have served well for more than a half century, FRC is a complementary "missing piece" that completes the bedside pulmonary function battery. Moreover, for some applications, FRC offers unique information that conceptually is closer than traditional spirometric indicators to the actual clinical questions that confront the practitioner. Diagnostically, these include determinations of the nature, severity, and progression of disease. Therapeutically, tracking FRC may allow the clinician to determine the effects of attempted interventions; e.g., re-positioning, recruiting maneuvers, PEEP selection, and relief of hyperinflation. Limitations of current washout technology do not allow its application to every clinical setting. At present, FRC determinations is a new tool for care of the acutely ill whose appropriate application to clinical practice awaits more widespread deployment and utilization in the context of everyday ICU care.

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