

REVIEW ARTICLE

Alveolar recruitment in acute lung injury

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Alveolar recruitment is one of the primary goals of respiratory care for acute lung injury. It is aimed at improving pulmonary gas exchange and, even more important, at protecting the lungs from ventilator-induced trauma. This review addresses the concept of alveolar recruitment for lung protection in acute lung injury. It provides reasons for why atelectasis and atelectrauma should be avoided; it analyses current and future approaches on how to achieve and preserve alveolar recruitment; and it discusses the possibilities of detecting alveolar recruitment and derecruitment. The latter is of particular clinical relevance because interventions aimed at lung recruitment are often undertaken without simultaneous verification of their effectiveness.

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Atelectasis describes the state of absent air in alveoli being attributable to their prolonged collapse. By contrast, *atelectrauma* describes alveolar damage being a result of transient and repeated closure and reopening of alveoli during the respiratory cycle. *Alveolar recruitment* refers to the opening of collapsed alveoli, *derecruitment* to the collapse of open alveoli. The term *ongoing recruitment* describes the state of sustained alveolar recruitment, preventing derecruitment. From a mechanistic point of view, ongoing recruitment is thus the opposite of atelectasis.

It is a commonly held view among intensivists that ongoing alveolar recruitment, with the aim of avoiding atelectasis and atelectrauma, is beneficial in patients with acute lung injury (ALI). This view is based on the results of experimental studies that demonstrated reduced pulmonary oedema and atelectrauma once the lungs are fully recruited at end-expiration.^{20 87 125} As atelectrauma may cause local and systemic inflammation, bacterial translocation, and gross barotrauma,²⁰ ongoing alveolar recruitment should be of clinical benefit.

However, extrapolation of experimental data to the bedside is hindered because alveoli in experimentally injured lungs are relatively easy to recruit and those in patients' lungs are not. Not surprisingly then, while few clinicians dispute the benefit of alveolar recruitment in general, they debate the optimal means of achieving and maintaining it in clinical practice. The debate centres around how to adjust PEEP, whether or not to use recruitment manoeuvres, on the value of placing the patient in the prone position, and, most important, on the 'price', in terms of airway pressure, that

should be paid to recruit the lungs. Accordingly, it is the aim of this review to discuss recent experimental and clinical data on alveolar recruitment in ALI, and to assess the feasibility of transferring experimental concepts into clinical practice.

Reasons for recruitment

More than 30 yr ago, theoretical calculations suggested that alveolar structures are subjected to high shear forces when closed alveoli are adjacent to open ones.⁷⁷ Even at a comparatively low inflation pressure of 30 cm H₂O, shear forces are comparable to a mechanical stress caused by a pressure of 140 cm H₂O.⁷⁷ These calculations implied that, in order to reduce mechanical stress on the alveolar wall, alveoli should be fully recruited (e.g. by PEEP). An early experimental study, showing that PEEP protects against pulmonary oedema caused by high peak airway pressure, received little attention.¹²⁵ However, by the early 1990s high PEEP and recruitment manoeuvres were advocated in clinical practice to open closed alveoli.⁶¹ This therapeutic strategy primarily aimed at lung protection rather than at improvement of oxygenation. Shortly thereafter, the protective effect of PEEP was confirmed experimentally.⁸⁷

In clinical practice the question arises, whether it is in fact possible and advisable to open all closed alveoli. In the experimental setting, the lungs are rendered susceptible to atelectasis by various interventions (e.g. surfactant removal with a detergent,¹¹² instillation of hydrochloric acid,⁷⁹ or infusion of endotoxin⁴ or oleic acid¹⁵). In such experimental

models, alveolar recruitment by PEEP reduced the tidal change of alveolar volume, lung trauma, inflammation,¹¹³ and the influx of neutrophils.⁸⁵ However, all of these models lack the structural alterations seen in lung tissue. For example, the later stages of Acute Respiratory Distress Syndrome (ARDS) in humans is associated with depletion of cellular material within the alveoli and with fibrosis.⁵ These structural alterations in human lung injury render some if not all lung areas more difficult to recruit than in experimental lung injury, which mimics more the early stages of ARDS. Thus, the view that the recruited lung is a good lung is almost exclusively based on findings in the experimentally injured lung. In human ARDS, however, there is no conclusive evidence as to whether recruitment is always beneficial, and if so, what 'price', in terms of airway pressure, is acceptable for opening up closed alveoli.

In this context, it is important to clarify whether it is atelectasis *per se* or atelectrauma that is deleterious. There are no clinical and only few experimental data to answer this question. In human ARDS, three types of alveoli can be distinguished:³³ (i) Alveoli, which are open throughout the respiratory cycle. These alveoli are predominantly located in the non-dependent lung areas and are especially prone to overdistension. (ii) Alveoli, which are filled with detritus and other cellular material. They are difficult if not impossible to recruit even with very high pressure. (iii) Alveoli, which are closed, at least at end-expiration. They can be recruited but are susceptible to atelectrauma. In isolated lung preparations, atelectasis caused less activation of TNF- α , MIP-2, and IL-6 than atelectrauma.¹⁸ Referring to a previous provocative editorial,⁶¹ the investigators concluded with some irony 'Close the lungs and keep them closed.'¹⁸ Although the clinical relevance of these experimental findings is unclear, they, nevertheless, tend to support the belief of many clinicians that 'full recruitment at any price' is not worth achieving.

In addition to this clinical argument against the use of high airway pressures for opening up closed alveoli, the entire pathophysiological concept of collapse has recently been questioned.^{73 74} Most scientists and clinicians believe that atelectasis and atelectrauma are caused by collapse as a result of the weight of the heart and the diseased lung itself, and because of abdominal pressure. If the commonly held view of collapse were true, collapse and reopening would be traumatic, and should, therefore, be avoided. However, recent experimental findings suggested that alveoli are not collapsed but filled with fluid and foam.^{51 73 74} If the fluid and foam hypothesis were correct, the lungs would be injured by overdistension of aerated alveoli rather than by repeated opening of closed ones.⁵¹

At present, this controversy is not settled. Both hypotheses are not mutually exclusive. Collapse and fluid- or foam-filled alveoli could co-exist in the same lung in different regions.

Taking into account both, the results of experimental studies and the arguments against the concept of collapse,

aiming at ongoing alveolar recruitment in human ALI seems reasonable. Preliminary data suggest that repeated collapse and reopening (atelectrauma) is worse than atelectasis.

Current and future clinical concepts for achieving alveolar recruitment

Two clinical trials convincingly showed that the ventilatory strategy can influence survival in patients with ALI and ARDS.^{3 120} While one of them¹²⁰ was criticized,^{23 86} and other trials failed to demonstrate differences in outcome,^{10 11 115} there is general agreement that ventilatory management affects outcome in patients with ARDS or ALI. Today, low tidal volumes are part of protective ventilation to avoid alveolar overdistension. However, while avoiding overdistension, this strategy may cause derecruitment.¹⁰⁷ Consequently, when attempting to further improve survival, measures to counterbalance derecruitment are becoming increasingly important.⁶⁹

PEEP

In the context of alveolar recruitment, PEEP is of special interest. The American ARDS Net study compared ventilatory strategies using high (13.2 \pm 3.5 cm H₂O) and low (8.3 \pm 3.2 cm H₂O) PEEP.¹²¹ This trial was stopped prematurely because high PEEP failed to improve outcome. Several factors may have contributed to the negative result. First, in both groups arterial oxygenation was used to guide the level of PEEP. However, as arterial oxygenation varies with systemic haemodynamics in ARDS,¹⁹ it does not necessarily reflect alveolar recruitment and is, therefore, not the appropriate means of selecting the level of PEEP required for optimal lung protection. Second, although PEEP was statistically different between both groups ($P < 0.001$), it was relatively low in both groups (8.3 \pm 3.2 and 13.2 \pm 3.5 cm H₂O). In a previous study which showed benefit from PEEP, and other measures,³ PEEP levels were higher (around 16 cm H₂O). In the American Network study,¹²¹ PEEP was probably high enough to improve oxygenation but too low to protect the lung.

Third, the trial was stopped prematurely. Therefore, from a methodological and statistical point of view, the study does not exclude a beneficial effect of PEEP.

Considering all the limitations, this ARDS Network trial does not provide conclusive evidence for or against a protective effect of an appropriately chosen level of PEEP. The experimentally based rationale for the use of 'high' PEEP to protect the lungs remains valid, as there is no conclusive evidence to the contrary.

Recruitment manoeuvres

Recruitment manoeuvres have been repeatedly proposed for alveolar recruitment and lung protection.^{8 9 15 27 40 54 63 98 123} As yet, no prospective randomized trial has demonstrated

any benefit of recruitment manoeuvres on survival of patients with ARDS.⁴⁸ Thus, we can only discuss its pathophysiological rationale. In general, despite the existence of detailed recommendations,⁵⁴ there is no consensus on the optimal performance of such recruitment manoeuvres. Their effectiveness depends on the experimental model used,¹²³ which questions the applicability of the general concept to clinical practice. In addition, it is unlikely that the side-effects of short-term very high airway pressure (e.g. temporary overdistension) were detected.^{89 15 27 40 63 98 123} Furthermore, experimental evidence suggests that alveoli may collapse within seconds after recruitment manoeuvres if not stabilized with sufficient PEEP.^{91–93} On the other hand, a clinical study revealed a longer ‘memory’ of lung tissue for recruitment.⁶⁵

In order to put the findings into proper perspective, it is important to recall that the PEEP level necessary for alveolar stabilization after a recruitment manoeuvre is comparable to that required for alveolar recruitment by PEEP alone (without preceding recruitment manoeuvres).⁸¹ In agreement with this finding, recruitment manoeuvres are less effective at higher baseline PEEP levels,²⁶ and insufficient to keep the lung constantly open at lower ones.^{40 44} Not unexpectedly, recruitment manoeuvres are only effective in the early stages of ARDS (before fibrosis) where recruitment may still be possible.⁴⁰ However, even in early ARDS, recruitment is not sustained after such a manoeuvre.⁹⁶

In conclusion, recruitment manoeuvres may often not be necessary, and at times may even be detrimental. Experimental evidence supporting the use of recruitment manoeuvres is much less robust than that for high PEEP. At present, they cannot be considered standard practice in ARDS or ALI.⁴⁸

Positioning

Prone positioning improves oxygenation in about two-thirds of patients with ALI or ARDS.³⁹ The mechanisms responsible for this improvement are incompletely understood. Prone positioning affects the distribution of both perfusion and ventilation in a complex way. The change in perfusion is partially caused by gravity and the change in ventilation is partially because of recruitment as a result of reduced compression of lung tissue by the heart in the prone position.²

Such recruitment would be expected to result in lung protection and, subsequently, in improved outcome. However, the only multi-centre trial that investigated this aspect of prone positioning failed to detect any benefit on survival.³⁹ The negative result may, however, be related to limitations in study design: (i) Patients in the ‘prone’ group were turned for only around 7 h per day for a total of 10 days and this may have simply been too short a period.⁷⁶ (ii) The study protocol was not always followed. Several patients were not turned prone because of lack of staff. Other patients, who had been randomized to the supine group, were turned prone because of severe hypoxaemia.

Thus, this trial neither proves nor disproves the effectiveness of the prone position. In conclusion, the prone position improves oxygenation in the majority of patients and leads to alveolar recruitment, which should result in lung protection and better outcome. At present, both seem likely, but remain unproven.

Future ventilatory strategies

The measures discussed thus far are related to conventional mechanical ventilation. However, mechanical ventilation is artificial and unphysiological. In addition to causing substantial elevation of the intrathoracic and intrapulmonary pressures, mechanical ventilation delivers uniform breaths. Such uniformity of breaths occurs not only during controlled mechanical ventilation but also during ventilator assisted spontaneous breathing.^{84 127} Mechanical ventilation is monomorphic but normal respiration is polymorphous, with continuously changing tidal volume, flow rate, and respiratory rate.²⁵ Based on the physiological argument that life-support systems should mimic noisy patterns,¹¹⁶ and in an attempt to mimic spontaneous breath-to-breath variability, the concepts of polymorphous ventilation¹²⁶ and of fractal ventilation^{7 64} have been introduced. Both of these biologically variable patterns are conceptually similar and are based on the idea of a mechanical memory effect. Alveolar recruitment achieved by large tidal volumes exceeds the derecruitment by small tidal volumes with the net effect of recruitment, resulting in improved compliance and oxygenation.^{116 117} Biologically variable ventilation seems to be superior, with respect to oxygenation, shunt, and airway pressures, to controlled mechanical ventilation, even when periodic sighs⁸⁸ or repetitive recruitment manoeuvres³² are added to the latter. Polymorphous ventilation could be a means of maintaining alveolar recruitment without increasing mean airway pressure. Although this is a promising concept of ventilatory support, it has not yet been evaluated clinically.⁹⁰

Detection of alveolar recruitment and derecruitment

Ideally, each therapeutic intervention aiming at alveolar recruitment should be evaluated for its effectiveness. Unfortunately, and in contrast to other therapeutic interventions in critical care, such as the application of vasopressors, this is difficult to achieve because, at present, there is no method for direct measurement of alveolar recruitment. We have critically evaluated the quality, validity, and practical usefulness of several indicators of alveolar recruitment.

These indicators can be grouped into four categories:

- (i) indicators of lung function, such as pulmonary gas exchange;
- (ii) imaging techniques, such as computed tomography, inductive plethysmography;

- (iii) static and dynamic respiratory mechanics;
- (iv) measurement of intrapulmonary gas volume.

Pulmonary gas exchange

In clinical practice, ventilator settings are often adjusted to achieve predetermined arterial blood gas tensions. This approach is adequate with respect to oxygenation and carbon dioxide removal. After a change in ventilator settings or other intervention, it is tempting to conclude that an improvement in arterial oxygenation reflects alveolar recruitment. While recruitment may, indeed, be the cause for improved oxygenation, an increase in the arterial partial pressure of oxygen may simply reflect the consequences of a change in ventilator settings on haemodynamics.¹⁹ An increase in intrathoracic pressure, resulting from, for example, an increase in PEEP, may reduce venous return to the right atrium. The subsequent reduction in right ventricular end-diastolic volume leading to a substantial decrease in cardiac output is well accepted. In contrast, that a decrease in cardiac output may improve the effectiveness of hypoxic pulmonary vasoconstriction is less frequently taken into consideration. Improved arterial oxygenation may thus be the result of improved hypoxic pulmonary vasoconstriction after a decrease in venous return rather than a result of alveolar recruitment.¹⁹ This often neglected physiological mechanism is of practical relevance and may explain, why ventilatory strategies based on blood gas analysis have failed to improve outcome.¹²¹

Computed tomography

As arterial oxygenation does not appear to identify a protective PEEP level or to necessarily reflect alveolar recruitment, it seems logical to assess the latter directly. Currently, the method of choice is computed tomography. Its use has greatly contributed to our understanding of alveolar recruitment in ARDS,^{34 36–38 70 71 103 109} and has allowed differentiation between the pulmonary and extra-pulmonary forms of ARDS.^{35 67} These findings may^{35 98} or may not¹⁰⁴ be relevant for alveolar recruitment by PEEP and other measures. Some argue that in ARDS of pulmonary origin alveolar recruitment seems to be more difficult^{35 98} and to require higher PEEP levels¹⁰⁹ than in non-pulmonary ARDS. In non-pulmonary ARDS, greater structural inhomogeneity predisposes to overdistension of already open alveoli by high airway pressures, including PEEP. Consequently, distinguishing pulmonary from non-pulmonary ARDS may help to decide whether PEEP should be rather high (pulmonary ARDS) or low (non-pulmonary ARDS). Computed tomography may therefore be useful for the initial titration of PEEP.¹⁰⁸ However, ongoing changes in lung morphology, patient positioning, and other variables will require continuous re-assessment of the optimal PEEP level. Therefore, while computed tomography is of unquestionable value in the assessment of the patient with ARDS in

general, as far as defining an appropriate ventilatory strategy is concerned, its value is limited to the initial identification of an appropriate PEEP level.

Inductive plethysmography

The practical limitations of computed tomography led to the search for other methods that would image the lung directly in a tomogram. Amongst these methods, inductive plethysmography (or electrical impedance tomography) is the most attractive one. It is a radiation-free, non-invasive imaging technique, which allows bedside assessment of regional lung ventilation,¹² and most fascinating, dynamic evaluation of lung status within each breath.^{17 59 60 68 94 95} Repetitive passage of small alternating electrical currents via a multiple electrode array placed circumferentially on the chest results in potential differences on the body surface. The voltage pattern is analysed and transformed into a *two-dimensional* tomogram. As an increase in regional pulmonary air content is accompanied by an increase in local electrical impedance and vice versa, the tomogram can be interpreted as reflecting pulmonary gas distribution. Electrical impedance tomography is characterized by high temporal resolution but relatively low spatial resolution. Although inductive plethysmography has been considerably improved over the past years,²⁹ interpretation of the plethysmography signal remains difficult. At present, this methodology is used in the clinical setting only as a research tool in the monitoring of regional lung ventilation.^{16 28 30} However, future incorporation of inductive plethysmography into commercially available ventilators or monitoring devices may contribute to more effective monitoring of alveolar recruitment.

Respiratory mechanics

Respiratory mechanics are recorded in an attempt to define the optimal tidal volume and its position on the pressure–volume axis of the lung by defining the correct level of PEEP (Fig. 1). The square within the figure depicts the *recruitment area* where the lung is neither subjected to overdistension nor to atelectrauma. This area can change over time (Fig. 1, dotted square). It is presently unclear whether it is at all possible to define the recruitment area where ventilator-induced trauma is minimal. Nevertheless, the general purpose of recording respiratory mechanics in ALI is to reduce alveolar trauma by avoiding both overdistension and atelectrauma.

Static respiratory mechanics

Traditionally, assessment of respiratory mechanics is based on (quasi-)static measurements. As the word *static* implies, the lungs' movements need to be interrupted during data acquisition in an attempt to distinguish between the respiratory system's elastic and resistive components of impedance. The simplest static measurement is that of the so called two-point compliance, which is obtained by dividing the

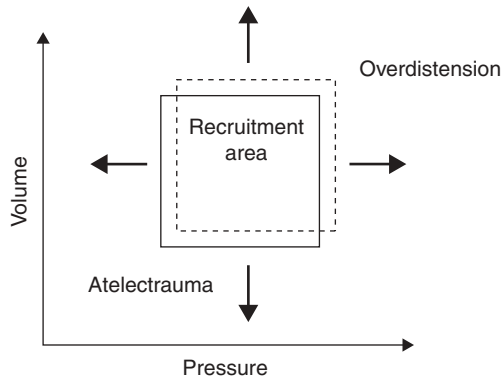


Fig 1 The diagram shows the *recruitment area* (area outlined by solid line) in which both overdistension and atelectrauma should be avoided. Defining this area is difficult but the ultimate goal of performing respiratory mechanics in ALI. The recruitment area may change over time (area outlined by dotted line).

volume difference by the pressure difference over a breath after end-inspiratory and end-expiratory hold manoeuvres. Because simple static compliance provides little if any information about the lungs' condition and the effects of ventilator settings, many authors favour the recording of the static pressure–volume curve.^{45 57 75 78 97 99 100 105 111 124} Usually, only the inspiratory part of the pressure–volume curve is recorded, with the expiratory phase is either not recorded or neglected (Fig. 2A, left). The typical sigmoid curve has two points with maximal curvature, which are called lower (LIP) and upper inflection points (UIP). LIP and UIP of the inspiratory curve are used to select the level of PEEP and the peak airway pressure, respectively. They represent the borders of the recruitment area (Fig. 2A, right).

This approach has several shortcomings: (i) Recording of the curve is complicated technically. Several (semi-)automatic devices have been suggested to overcome this limitation.^{55 102 119} However, none of them has gained widespread acceptance in clinical practice. (ii) Construction of the pressure–volume curve requires assessment of the entire volume range from functional residual capacity (FRC) to total lung volume. This may expose the patient to the risks of both derecruitment⁴⁶ and overdistension. (iii) The inspiratory part of the pressure–volume curve is greatly modified by recruitment.^{49 50 52} The LIP may thus not represent the end of recruitment but rather its beginning.⁴⁹ Consequently, the assumed recruitment area is moved to the right (Fig. 2B, right). Furthermore, as PEEP is an expiratory variable, it is inappropriate to use the LIP of the inspiratory pressure–volume curve for selecting PEEP. For this very reason, some authors favour the use of the expiratory part of the static pressure–volume curve (Fig. 2C).¹⁵⁰ The point of maximum curvature (PMC) is now marked on the expiratory part of the curve, resulting in a different recruitment area. While this appears logical, it does not resolve the most important objection to the use of static respiratory mechanics for setting the ventilator: (iv) The lungs are never in a static condition,

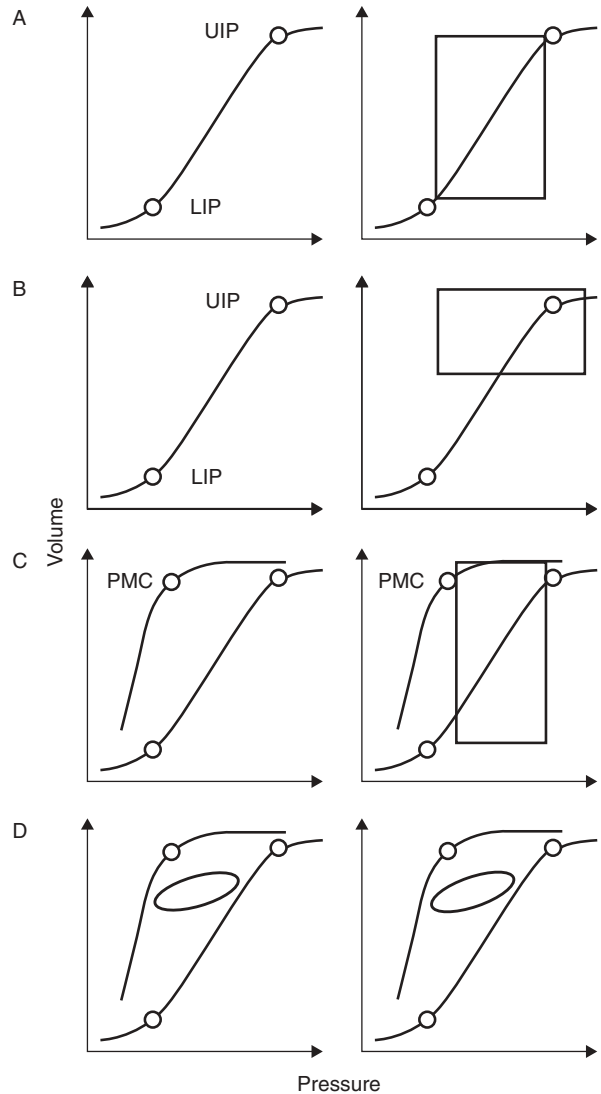


Fig 2 The different concepts of recording respiratory mechanics are shown. The right-hand side curves in all panels depict the static inspiratory pressure–volume curves. The left-hand side curves in panels (C) and (D) depict the static expiratory pressure–volume curve. The rectangles in the right-hand side panels (A–C) depict the recruitment area. (A) Traditional approach to static respiratory mechanics: the static inspiratory pressure–volume curve usually contains a LIP and UIP. These are traditionally interpreted as defining the margins of the recruitment area. (B) Static respiratory mechanics incorporating a new interpretation of LIP: the inspiratory part of the pressure–volume curve is greatly modified by recruitment and the LIP may not represent the end of recruitment but rather its beginning.^{49 50 52} After this consideration, the recruitment area is moved to the right. (C) Static respiratory mechanics focusing on expiration and derecruitment: the expiratory curve has a characteristic PMC where volume loss starts. Following this approach, PEEP should be set at PMC. (D) Dynamic intratidal respiratory mechanics: the loops inside the inspiratory and expiratory static pressure–volume curves represent the actual tidal breath where data for calculation of respiratory mechanics are obtained. With this approach, tidal ventilation rather than the entire lung volume range is monitored.

either normally or in intensive care. Basing the prediction of the lungs' dynamic behaviour on static measurements seems highly questionable,¹¹⁴ in the way one would never produce a cardiac arrest in order to measure the performance

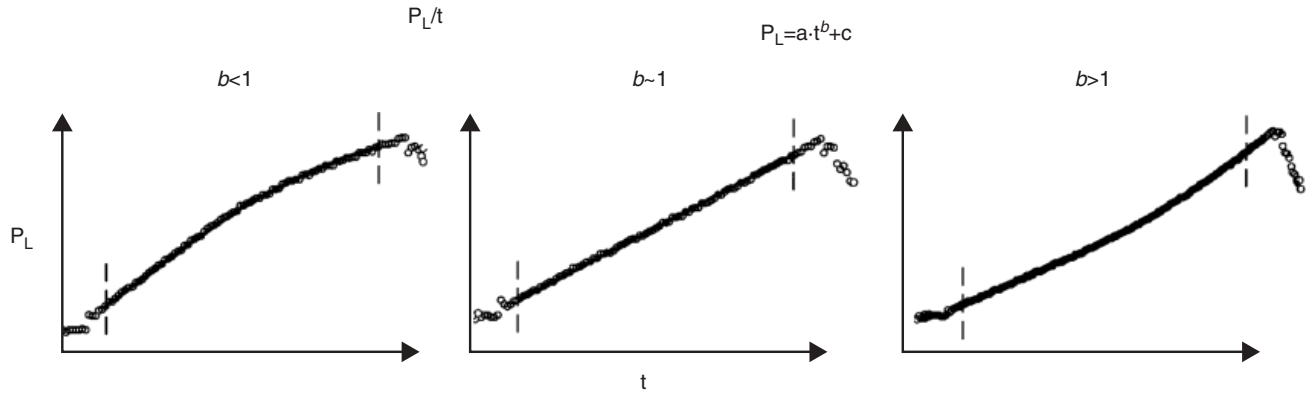


Fig 3 Determination of the stress index. Lung pressure (P_L) is recorded over time (t) during constant flow inflation. The pressure–time relationship is then described by a power equation. The coefficients a , b , and c are constants. However, only b is of interest here, because it describes the shape of the pressure–time relationship. If $b < 1$, its concavity is downward indicating intratidal recruitment and derecruitment with the potential for atelectrauma. If $b > 1$, concavity of the pressure–time relationship is upward indicating alveolar overdistension. If $b = 1$, pressure–time relationship is linear indicating neither intratidal recruitment nor overdistension. Modified from Ranieri *et al.*,¹⁰⁶ with permission.

of the heart.⁵³ Because of the limitations of *static* respiratory measurements, *dynamic* measurements are receiving increasing attention.^{58 62 66 72 101}

Dynamic respiratory mechanics

At present, dynamic respiratory mechanics can be studied by several methods: (i) The *dynostat algorithm* is a method for breath-by-breath analysis of the alveolar pressure–volume curve.⁵⁵ It does not measure resistance but merely assumes identity of inspiratory and expiratory resistance at each iso-volume. (ii) The modulated *low flow technique method* includes measurement of resistance.¹¹⁸ By sinusoidal modulation of the gas flow, the resistive pressure component can be separated from the elastic one. The method has recently been amended by an expiratory flow modulation manoeuvre.⁶ (iii) The *stress-index* records the pressure–time curve during a constant flow single breath at normal tidal volume (Fig. 3).¹⁰⁶ The shape of the pressure–time curve reflects predominantly the change of compliance within this breath and is described mathematically using a simple formula that yields a coefficient b . A coefficient of $b < 1$ indicates downward concavity, that is, increasing compliance with increasing volume. If $b > 1$, concavity is upward, indicating decreasing compliance. Constant compliance can be assumed if $b = 1$, when the pressure–time curve is linear. The stress index assumes that resistance is constant (i.e. independent of volume). This, however, cannot be taken for granted.⁸³ Despite this methodological limitation, the stress-index presents a considerable improvement as it focuses on the actual tidal volume. This actual tidal breath (depicted as a schematic pressure–volume loop in Fig. 2D) is positioned between the static inspiratory and expiratory pressure–volume curves. Both represent extreme, artificial lung conditions, which are of minor practical relevance. Dynamic recordings are therefore more relevant for setting the ventilator than data obtained by the previously mentioned methods.

It has recently been shown that pulmonary inflammation could be reduced when the ventilator setting was based on the stress index.⁸⁹ (iv) The *slice-method* also analyses the intratidal change of compliance and resistance.⁴² It is based on standard multiple linear regression,¹²² and, therefore, does not require a respiratory manoeuvre. Standard multiple regression is used to obtain (whole breath) compliance and resistance in modern ventilators and respiratory monitoring devices. In addition to standard multiple linear regression, the slice-method takes into account dynamic intrinsic PEEP²¹ and the flow-dependent resistance of the tracheal tube.^{41 43} However, the most relevant modification lies in subdividing the tidal volume into six volume slices before applying the regression analysis. Thus, by obtaining several values of compliance and resistance per breath, volume-dependency of both parameters is derived. The derivation of the compliance–volume diagram from the pressure–volume recording is shown in Figure 4 for two different PEEP levels in an experimental setting. The number of six slices is not obligatory to the method but rather constitutes a compromise between adequate volume resolution and acceptable noise caused by cardiogenic oscillations. It should be kept in mind that the course of compliance is recorded only within the actual tidal breath. The intratidal compliance–volume curve (compare Fig. 4B) is thus part of the larger (unrecorded) total lung compliance–volume curve. Depending on end-expiratory and end-inspiratory volume, several shapes of intratidal compliance could occur (Fig. 5). Compliance could be constant (Fig. 5A), decreasing (Fig. 5C and D), increasing (Fig. 5E and F), or both increasing and decreasing (Fig. 5B). Thus, the shape of the compliance-curve provides information on whether ventilation takes place at rather high or low lung volume. Unlike other techniques, the ventilator settings and pattern need not be changed for analysis. In patients, the slice-method has been used to assess the appropriateness of ventilator settings and the effects of its changes.^{65 80} In

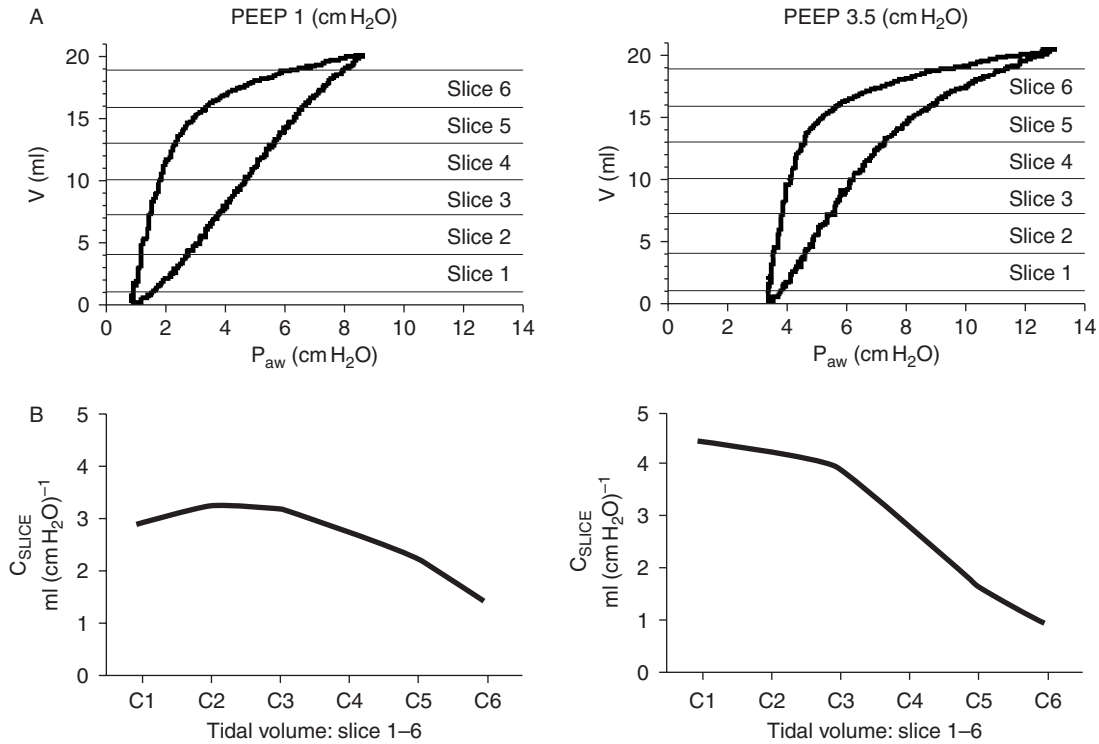


Fig 4 (A) Pressure–volume (P_{aw} , airway pressure) recordings at two PEEP levels in isolated perfused rabbit lungs. The pressure–volume loop is subdivided into six *slices* of equal volume (after removing the upper and lower 5% of the loop). Subsequently, in each slice multiple linear regression is performed yielding six values of compliance (B) and resistance (not shown) per tidal volume. In the left lower panel (ventilation with PEEP 1 cm H₂O), the shape of the intratidal compliance–curve indicates intratidal recruitment and derecruitment with the potential for atelectrauma. By contrast, in the right lower panel (ventilation with PEEP 3.5 cm H₂O) the intratidal compliance–volume curve is decreasing throughout the entire tidal volume indicating ongoing alveolar recruitment in the isolated lung. Modified from Hermle *et al.*,⁴⁷ with permission.

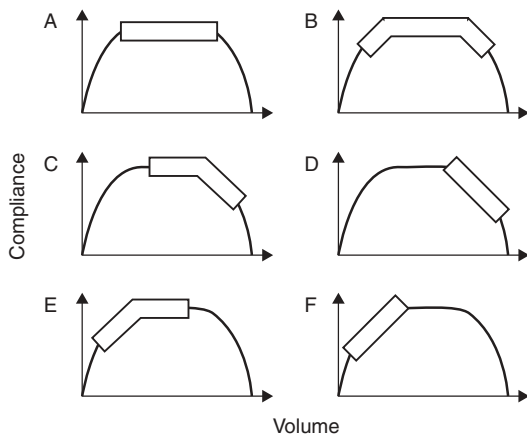


Fig 5 Trapeziform total lung compliance–volume curve with potential shapes of intratidal compliance–volume curve (indicated by the outlined, differently shaped areas): The intratidal compliance–volume curve is part of the larger (unrecorded) total lung compliance–volume curve. The shape of the intratidal compliance–volume curve indirectly indicates whether ventilation takes place at high or low lung volumes. A constant compliance (A) indicates ventilation at medium lung volume. When a decreasing compliance is observed (C and D), the tidal volume is delivered at rather high lung volume with the inherent risk of overdistension. When the compliance–volume curve is increasing (E and F), the tidal volume is delivered at low lung volume with the risk of atelectrauma. A combination of increasing and decreasing compliance, potentially associated with both overdistension and atelectrauma is depicted in panel (B). Modified from Mols *et al.*,⁸⁰ with kind permission of Springer Science and Business Media.

isolated lungs, it was used to assess alveolar recruitment,⁸² to establish a new ventilatory strategy,⁴⁷ and to study the effects of ventilator settings on inflammation.⁵⁶

It should be noted that both the stress index and the slice-method focus on the actual tidal volume (Fig. 2D). In contrast to static approaches, the recruitment area cannot be directly determined. The change of respiratory mechanics within the breath provides information as to whether or not ventilation actually takes place within the recruitment area. The outer static curve is not ‘seen’ by these methods, and the recruitment area could be defined only by manipulation of PEEP and peak airway pressure. On the other hand, ventilator settings could be constantly monitored for lung protection without the need for a special manoeuvre. After several encouraging studies,^{47,80,82,89} both methods are awaiting their introduction into routine clinical practice.

Intrapulmonary gas volume

As discussed above, respiratory mechanics are rather complex and there is no consensus as to which approach is best suited to find the least traumatic ventilator settings in ALI. Alternatively, the intrapulmonary gas volume can be determined. The measurement of FRC provides information about the amount of lung tissue involved in gas exchange. FRC is defined as the intrapulmonary gas volume at the end of a normal expiration.¹³ The rationale of

FRC-determination is based on the assumption that the higher the FRC the more alveoli are recruited.¹¹⁰ However, as FRC does not allow differentiation between normal aeration and overdistension, it does not provide information as to whether or not tidal ventilation occurs in the recruitment area (Fig. 1). Nevertheless, determination of FRC is very useful when combined with respiratory mechanics. Determination of FRC is not as simple as expected and is not a routine monitoring tool. The 'gold standard' of FRC determination in the intensive care setting is the wash-in/wash-out of a tracer gas in a multiple breath procedure. The intrapulmonary nitrogen volume is completely replaced (washed out) over several breaths by the tracer gas. Hence these methods are better known as nitrogen wash-out. FRC determination using nitrogen wash-out works as long as the intrapulmonary gas volume is freely accessible. As this condition is not necessarily met for the whole lung, as a result of trapped air, the volume determined by nitrogen wash-out has been called 'accessible pulmonary (gas) volume' instead of FRC.¹³ The accuracy of FRC determination critically depends on methodological sophistication such as corrections for changes in gas viscosity or sampling delay time compensation,^{14,22} which gains special importance during partial ventilatory support.¹²⁸ Simpler bedside methods for FRC determination using the oxygen wash-out technique have been introduced.^{24,31} Although an easily available bedside method to determine FRC could be of clinical value with respect to monitoring of alveolar recruitment, especially when combined with respiratory mechanical data, FRC measurements have not been evaluated for their usefulness in clinical practice, because of the aforementioned difficulties.

Conclusions

A large amount of experimental data suggests that alveolar recruitment is beneficial in ALI and ARDS. However, there is no single clinical study that clearly proves the effectiveness of alveolar recruitment for lung protection and survival. While there is no consensus on what constitutes the best level of PEEP for lung protection, it may be higher than that needed for improving or maintaining arterial oxygenation. In the context of this problem, there is growing evidence that PEEP and other ventilatory variables need to be adjusted individually at the bedside. Although arterial oxygenation is the most easily obtained respiratory variable, it is not suited for this purpose because it is affected by haemodynamic changes. In the near future, lung morphology obtained by bedside methods and respiratory mechanics, especially when based on dynamic recording, may enhance our ability to monitor alveolar recruitment, adjust PEEP, and guide the use of other recruitment measures.

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