Can we estimate transpulmonary pressure without an esophageal balloon?—yes

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Abstract: A protective ventilation strategy is based on separation of lung and chest wall mechanics and determination of transpulmonary pressure. So far, this has required esophageal pressure measurement, which is cumbersome, rarely used clinically and associated with lack of consensus on the interpretation of measurements. We have developed an alternative method based on a positive end expiratory pressure (PEEP) step procedure where the PEEP-induced change in end-expiratory lung volume is determined by the ventilator pneumotachograph. In pigs, lung healthy patients and acute lung injury (ALI) patients, it has been verified that the determinants of the change in end-expiratory lung volume following a PEEP change are the size of the PEEP step and the elastic properties of the lung, ΔPEEP × Clung. As a consequence, lung compliance can be calculated as the change in end-expiratory lung volume divided by the change in PEEP and esophageal pressure measurements are not needed. When lung compliance is determined in this way, transpulmonary driving pressure can be calculated on a breath-by-breath basis. As the end-expiratory transpulmonary pressure increases as much as PEEP is increased, it is also possible to determine the end-inspiratory transpulmonary pressure at any PEEP level. Thus, the most crucial factors of ventilator induced lung injury can be determined by a simple PEEP step procedure. The measurement procedure can be repeated with short intervals, which makes it possible to follow the course of the lung disease closely. By the PEEP step procedure we may also obtain information (decision support) on the mechanical consequences of changes in PEEP and tidal volume performed to improve oxygenation and/or carbon dioxide removal.

Keywords: Lung compliance; positive end expiratory pressure (PEEP); end-expiratory lung volume change; transpulmonary pressure; esophageal pressure

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The lack of scientific consensus concerning positive end expiratory pressure (PEEP) setting is visualized by the numerous methods proposed for identifying optimal PEEP, such as decremental PEEP trial (1), best dynamic compliance trial (2) and center of ventilation (COV), regional ventilation delay (RVD index), global inhomogeneity (GI index), and intratidal gas distribution by electric impedance tomography (3). Selection of PEEP and tidal volume from airway pressure and total respiratory system compliance may be suboptimal, and lead to too high PEEP levels in some patients, such as patients with direct, pulmonary ARDS while in a patient with extrapulmonary acute respiratory distress syndrome (ARDS), where the chest wall influences respiratory mechanics, set PEEP will be to low (4). It is therefore obvious that lung and chest wall mechanics should be separated and transpulmonary pressure should be determined to provide a rational basis for selection of PEEP and tidal volume (5-10). However, the standard method to determine lung and chest wall mechanics using esophageal pressure measurements is technically complicated and difficult to interpret (8,11-13). This has led to a slow clinical introduction (8). We have developed a new, simple method based on a PEEP step

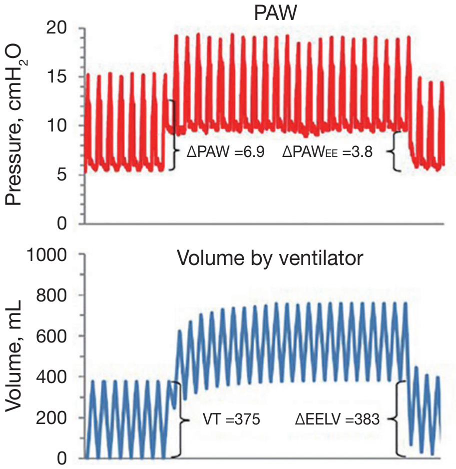

Figure 1 Airway pressure and lung volume in a patient with healthy lungs (15). Airway driving pressure (ΔPAW) at baseline PEEP was ≈6.9 cmH_2O with a tidal volume of ≈375 mL. A PEEP-increase of only 3.8 cmH_2O resulted in a successive increase in end-expiratory lung volume, EELV, with 383 mL.

maneuver to determine lung elastance and transpulmonary pressure (14-16).

Physiological background

Tidal esophageal pressure variations or changes in absolute esophageal pressure?

Esophageal pressure measurements have up to now been the only way of separating lung and chest wall mechanics, but there is no consensus on how to interpret absolute esophageal pressure. Thus, absolute esophageal pressure (PES) at FRC is accepted by some researchers as directly representative of absolute pleural pressure, in spite of the fact that PES is positive at FRC (11,13,17-22), while text books on respiratory physiology and several studies show that pleural pressure quite contrary, is negative, approximately 5–10 cmH_2O (23-32). Such fundamental differences in the view on absolute esophageal pressure have made us refrain from using absolute esophageal pressure for the analysis of the elastic properties of the lung. Instead only tidal variations in esophageal pressure (ΔPES), shown to have a good correlation with tidal pleural pressure variations (27,33), are used for calculation of chest wall and lung elastance and changes in end-expiratory transpulmonary and pleural pressure above FRC/ZEEP (for details on calculations, see Appendix).

Tidal and PEEP inflation

There are differences in the mechanic behaviors of the lung and chest wall when the lungs are inflated by a tidal volume compared to when they are inflated with an increase in PEEP. An increase in PEEP leads to a multi-breath inflation of the lung first described by Katz and coworkers in 1981 (34). They found that only about 70% of the total change in end-expiratory lung volume occurred during the first breath after PEEP. This was confirmed in a study on lung healthy patients (15). During several breaths after the initial breath there is a continuous increase in end-expiratory lung volume despite a constant end-expiratory airway pressure (PEEP). This is shown in a recording from a lung healthy patient (15) (*Figure 1*). In this patient the respiratory system elastance calculated as the increase in airway pressure divided by tidal volume was much higher than the change in PEEP divided by the increase in end-expiratory lung volume (6.9/0.375=18.4 cmH_2O/L compared to 3.8/0.383 =9.9 cmH_2O/L).

The determinants of the change in end-expiratory lung volume following a PEEP increase

The difference in tidal and end-expiratory respiratory system elastance is observed both in lung healthy and ARDS patients (*Figure 2*). The form of the line connecting the end-expiratory airway pressure/volume (P/V) points is not a random phenomenon. It is obvious that it does not follow the respiratory system P/V-curves, which indicates that the increase in lung volume does not depend on respiratory system elastance. What factors do determine the change in lung volume after an increase of PEEP?

In a porcine study and a study on patients with acute respiratory failure it was shown that the change in lung volume after an increase of PEEP is dependent on the size of the PEEP-change and the elastance of the lung (14,16,36). Elastance of the lung was calculated using tidal changes in airway and esophageal pressures in these studies. The finding that the change in lung volume was dependent on lung elastance was further confirmed by analysis of data in three published studies. In two studies PEEP steps of 0-5-0-10-0-15 were performed on patients with healthy lungs, moderate and severe ARDS (37) and in patients with pulmonary and extrapulmonary ARDS (4). The change in end-expiratory

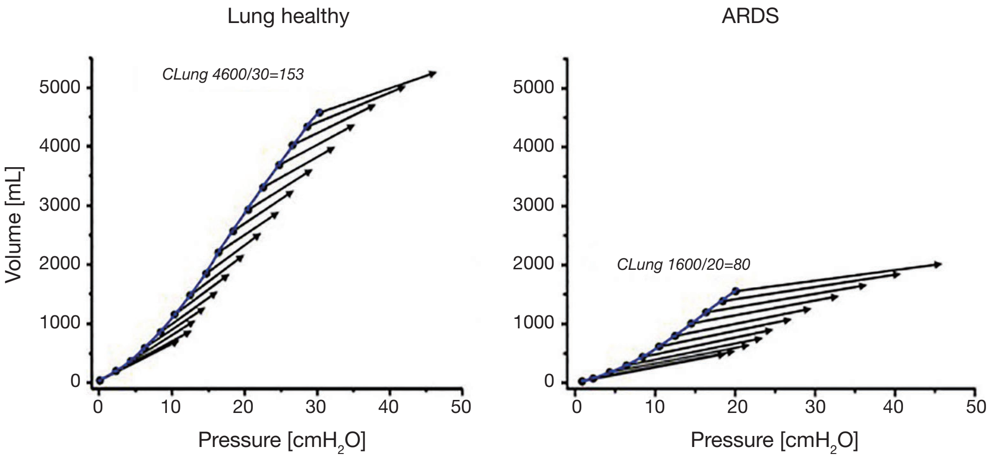

Figure 2 PEEP inflation in lung healthy (left panel) and in ARDS patient (right panel) (with permission from Stahl *et al. Acta Anaesthesiol Scand*) (35). PEEP was increased in steps of 2 cmH$_2$O until end-expiratory airway pressure reached 45–50 cmH$_2$O. Black arrows: Airway (respiratory system) P/V curves. The blue line connecting the end-expiratory airway P/V points does not follow the respiratory system PV-curve. Note that the inspiratory capacity at end-inspiration of the highest PEEP level is 4,600 mL at an end-expiratory airway pressure of 30 cmH$_2$O in lung healthy patients, but only 1,600 mL at an end-expiratory airway pressure of 20, a "baby lung" in the ARDS patient. PEEP, positive end expiratory pressure; ARDS, acute respiratory distress syndrome.

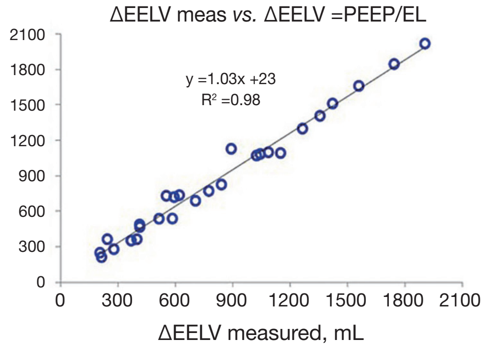

Figure 3 Correlation between increase in measured lung volume (ΔEELV) and ΔEELV calculated from the change in PEEP divided by lung elastance, ΔPAWEE/EL (ΔPAWEE × CL) based on mean data from Pelosi *et al.* (37), Gattinoni *et al.* (4) and Garnero *et al.* (38). PEEP, positive end expiratory pressure.

lung volume was measured during a prolonged expiration to zero in PEEP. In the study on mixed ARDS patients, PEEP steps of 5 cmH$_2$O were performed (from 5 to 40 cmH$_2$O and back again) and changes in end-expiratory lung volume was measured as the cumulative difference in inspiratory and expiratory tidal volume between two steady state PEEP levels. The measured change in end-expiratory lung volume was closely correlated to the change in PEEP divided by lung elastance (*Figure 3*).

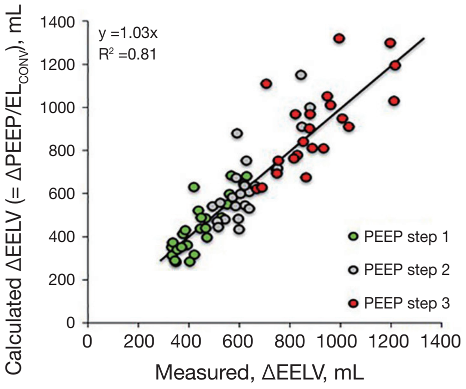

Figure 4 Correlation between measured increase in EELV and ΔEELV calculated as ΔPEEP/EL following an increase of PEEP, based on pooled data of three different sizes of PEEP steps (≈5, ≈7 and ≈9 cmH$_2$O, indicated by different colors in the figure. Modified from (15) (with permission from Persson *et al.*/*Br J Anaesth*). PEEP, positive end expiratory pressure.

Measurements on lung healthy patients in a recently published study confirmed that lung elastance calculated from tidal changes in airway and esophageal pressures and the size of the PEEP-change determines the total change in end-expiratory lung volume after an increase of PEEP (*Figure 4*). The increase in end-expiratory lung volume after the first breath following an increase of PEEP was on the

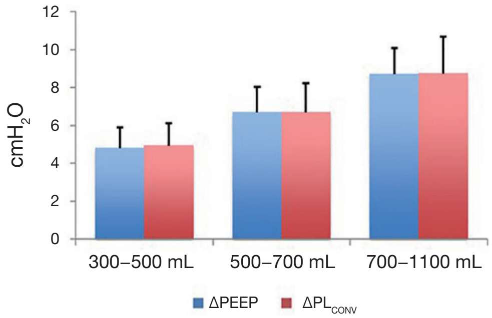

Figure 5 Change in PEEP (ΔPEEP) compared to transpulmonary driving pressure (ΔPL$_{CONV}$) for a tidal volume equal to the PEEP-induced change in end-expiratory lung volume (VT= ΔEELV). Values divided into three groups according to the size of the PEEP-induced change in end-expiratory lung volume and corresponding tidal volume. Bars in diagram represents mean values presented with standard deviation [with permission from Persson *et al.*/*Br J Anaesth* (15)].

other hand dependent on the size of the PEEP change and respiratory system elastance (36).

Regarding the change in end-expiratory lung volume following an increase of PEEP we can so far conclude that:

(I) PEEP needs to be increased less than the airway driving pressure to induce an inflation of the lungs of the same size as the tidal volume.

(II) The change in EELV is determined by the change in PEEP divided by the elastance of the lung.

As a consequence, lung elastance can be determined by a PEEP step maneuver if the change in lung volume (ΔEELV) is measured as:

EL = ΔPEEP/ΔEELV

This may seem as a surprise, as a part of ΔEELV, the difference between ΔEELV and the "minimally predicted volume", calculated as respiratory system compliance times ΔPEEP, has been claimed to be a measure of recruited volume (RecV) (39). However, it was later shown that RecV was twice as high in lung healthy patients with almost no alveolar collapse, as in ARDS patients with substantial collapse (35), which indicated that recruited volume mainly is a measure of a slow fraction of inflation of already aerated lung tissue, and not recruitment of collapsed alveoli.

The increase in end-expiratory transpulmonary pressure following a PEEP increase

In an elastic structure such as the lung, the transpulmonary pressure will increase in relation to the inflated volume and the elastic properties of the lung, V × EL = PL. The mode of inflation, tidal or PEEP inflation, is irrelevant and as a consequence, the static steady state transpulmonary pressure at a certain lung volume is the same irrespective of if this volume has been reached by a tidal or a PEEP-induced inflation. Thus, in the same way as the transpulmonary driving pressure is calculated as the tidal volume times lung elastance, the increase in end-expiratory transpulmonary pressure in response to PEEP inflation can be calculated as the increase in end-expiratory lung volume times lung elastance. Such calculations were applied in a study on lung healthy patients where lung elastance was calculated using tidal changes in airway and esophageal pressures. Three different sizes of PEEP-changes were performed (4.8, 6.9 and 9.2 cmH$_2$O) and the corresponding increase in end-expiratory transpulmonary pressure was 5.0, 7.0 and 9.4 cmH$_2$O (15). At each of these PEEP steps a tidal volume was set to be equal to the change in end-expiratory lung volume and the transpulmonary driving pressure, of these tidal volumes were equal to the change in PEEP (*Figure 5*). In the studies by Pelosi *et al.*, Gattinoni *et al.* and Garnero *et al.* described above, where PEEP steps of 5 cmH$_2$O up to a level of 40 (!) cmH$_2$O were used in patient with lung elastance ranging from 10 (lung healthy) to 25 cmH$_2$O/L (severe ARDS), end-expiratory transpulmonary pressure increased 5.1 cmH$_2$O when PEEP was increased by 5 cmH$_2$O.

Since the transpulmonary pressure increases as much as the PEEP-increase, the lung P/V curve of a PEEP trial will coincide with the end-expiratory airway P/V curve, as shown in a PEEP trial in patients with acute lung injury (14) (*Figure 6*).

Thus, by performing a PEEP step maneuvers the lung pressure-volume curve can be plotted without using esophageal pressure measurements.

The role of the chest wall during tidal volume and PEEP inflation

The chest wall will contribute to the mechanic behavior of the respiratory system in different ways during tidal volume and PEEP inflation. The end-expiratory transpulmonary pressure increases as much as PEEP, which indicates that the calculated end-expiratory pleural pressure does not increase. This is not really a surprising finding as the recoil of the lung is balanced by the expanding force of the rib cage, creating a negative pleural pressure of −5 to −10 cmH$_2$O at end-expiration at functional residual capacity

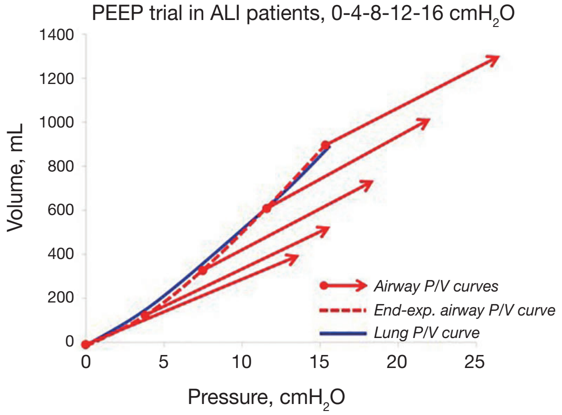

Figure 6 PEEP trial with PEEP steps 0-4-8-12-16 cmH$_2$O in patients with acute lung injury (ALI) (14). Note the close agreement between the lung P/V curve (calculated using esophageal pressure measurements) and the end-expiratory airway P/V curve. PEEP, positive end expiratory pressure.

(23-28,40). The chest wall is striving outwards until it reaches a resting volume at 70–80% of total lung capacity that is around 3 L above FRC (25,41-43). In the volume range between FRC and the chest wall resting volume, end-expiratory pleural pressure is negative irrespective of the pressure inside the lung. During mechanical ventilation, the thoracic cage, the diaphragm, the abdomen and its wall interact to form a "chest wall complex". During inflation the diameter of the caudal rim of the rib cage is increased, the diaphragm is tensed and the diaphragmatic dome is displaced in caudal direction. The driving pressure of the chest wall complex during tidal inspiration is mainly related to the force needed to displace the abdominal weight by the push from the lung when inflated (33,44,45) and not to overcome any elastic recoiling force of the chest wall. As a consequence, the chest wall complex reacts to lung inflation as a weight (the abdomen) that is displaced, rather than an elastic entity that is inflated (44,46). The elastance of the chest wall during tidal inflation is therefore unchanged even when PEEP is increased (47). During tidal expiration the initial flow is high because of the recoil of the lung, but as expiration proceeds, the rib cage counteracts the recoil of the lung and will cause a termination of expiratory flow (48). Thus, the effect of these opposing forces keeps the end-expiratory pleural pressure negative and the chest wall complex off-loaded from the lung. When lung volume is increased by application of PEEP, the lung is inflated with a constant pressure until the new pressure volume equilibrium is reached. The force to inflate the lung and displace the weight of the abdomen (44,49,50) is exerted during the inspirations of the breaths involved in establishing this new equilibrium. The increase in lung volume is caused by the rib cage spring out force braking and eventually stopping the expirations and thereby detaining a part of the expiration. As a consequence, the end-expiratory pleural pressure remains negative at the new P/V equilibrium as long as the end-expiratory exterior lung volume (irrespective of pressure inside the lung) is below the resting volume of the rib cage, schematically shown in *Figure 7*.

The difference between tidal chest wall elastance and end-expiratory chest wall elastance was confirmed in the study on lung healthy patients during anesthesia (15) (*Figure 8*).

The PEEP step measurement procedure

Lung elastance and consequently transpulmonary pressure can be determined without esophageal pressure measurements by a PEEP step procedure as described recently (15) (*Figure 9*). For optimal results a number of important requirements must be met:

(I) Volume control ventilation mode with at least 10% end-inspiratory pause;
(II) The change in lung volume (ΔEELV) preferably determined by "The modified cumulative expiratory tidal volume difference from baseline" method (15,54);
(III) Tidal volume should be set close to the PEEP step induced change in ΔEELV;
(IV) No spontaneous breathing;
(V) No intrinsic PEEP present.

When this procedure was tested on lung healthy patients during anesthesia in a recent study PEEP steps of ≈5, ≈7, and ≈9 cmH$_2$O were applied (15). Lung elastance calculated from tidal changes in airway and esophageal pressures was almost equal to end-expiratory airway elastance (*Figure 10*).

By performing a PEEP step maneuver lung elastance may be calculated as ΔPEEP/ΔEELV and as a consequence, transpulmonary pressure can be determined as (ΔPEEP/ΔEELV) × VT. A Bland & Altman analysis (55) of the transpulmonary driving pressure derived from esophageal pressure (ΔPL_{PES}) measurements and derived from a PEEP step procedure (ΔPL_{PSM}) in lung healthy patients showed a bias of 0.1 cmH$_2$O and limits of

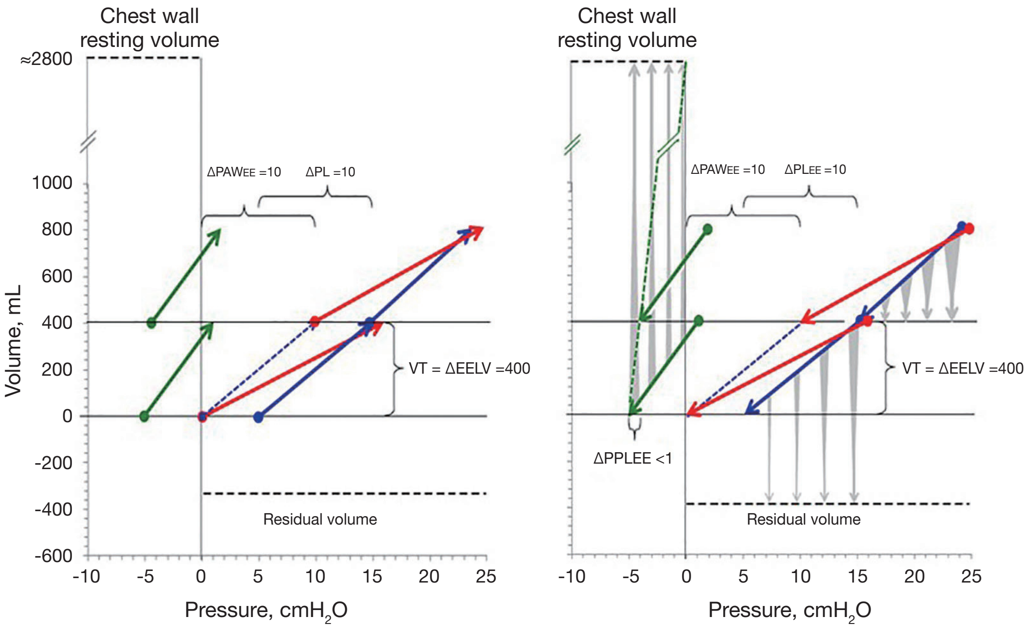

Figure 7 Schematic airway (red), lung (blue) and chest wall (green) P/V curves at ZEEP and at PEEP 10 cmH$_2$O. Left panel: inspiration. Right panel: expiration. The grey vertical up-arrows in the expiratory panel symbolize rib cage spring out force and down-arrows symbolize lung elastic recoil. The dashed green line indicates the end-expiratory chest wall P/V curve compiled from Rahn and coworkers 1946, West 1985 and Nunn 1993 (50-52). The end-expiratory chest wall elastance is equal to the end-expiratory pleural pressure difference (ΔPPL$_{EE}$) between FRC (–5 cmH$_2$O) and the chest wall resting volume, where end-expiratory pleural pressure is zero, divided by the volume between FRC and the chest wall resting volume ≈2.8 liter, 5/2.8=1.8 cmH$_2$O/L. The transpulmonary driving pressure (10 cmH$_2$O) of the tidal volume, which is equal to ΔEELV is equal to the change in end-expiratory airway pressure (ΔPEEP =10 cmH$_2$O). The lung P/V slope is identical to the end-expiratory airway P/V slope as demonstrated by the blue dashed line (the lung P/V curve parallel shifted to the left to start from zero). The difference between the end-inspiratory airway pressure from FRC/ZEEP and the end-expiratory airway pressure at 10 cmH$_2$O PEEP is equal to the pressure needed to displace the chest wall complex, the tidal pleural pressure variation (ΔPPL) (14,16,53). PEEP, positive end expiratory pressure.

agreement of –2.2 to 2.4 cmH$_2$O (*Figure 11*).

It is worth commenting the measurement precision in the PEEP step method. The PEEP step procedure is dependent on measurement of the difference in end-expiratory airway pressure between two PEEP levels and determination of the change in end-expiratory lung volume (ΔEELV). The PEEP level is maintained by the ventilator with extreme precision and consequently, ΔPEEP is a very reliable measurement. It has been argued that ΔEELV should be measured as the difference between EELV measured at the high and low PEEP level by the nitrogen washin/washout method (56), but this method has a variability of ±10%, which in a patient with in a case with an EELV of 1,500 mL at the low PEEP and 1,800 mL at the high PEEP level, i.e., a ΔEELV of 300 mL, the EELV at the low PEEP can be between 1,350 and 1,650 mL. EELV at the high PEEP level can be between 1,620 and 1,980 mL. As a consequence ΔEELV can be between 630 and –30 mL, which is an unacceptable span. Consequently, ΔEELV should instead be determined by the cumulative tidal volume difference method (54), modified as described by Persson *et al.* 2018 (15), which in principle is a direct measurement of ΔEELV as inspiratory tidal volume is maintained constant even when PEEP is changed. Thus, ΔEELV measured by the modified cumulative difference in expiratory tidal volume of the breaths involved in establishing a new PEEP/EELV equilibrium, compared to baseline expiratory tidal volume, has a variability of below ±5%, i.e., a true ΔEELV of 300 mL can be measured as 285–315 mL.

Estimation of the lung P/V curve

Tidal chest wall elastance at baseline PEEP, can be

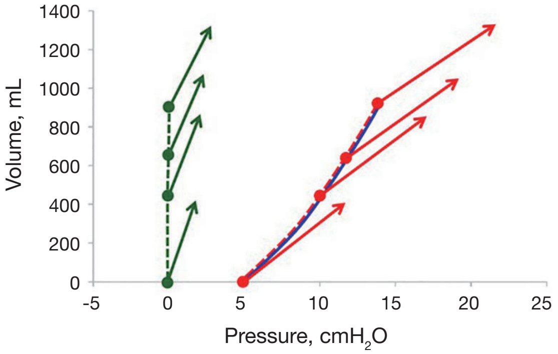

Figure 8 PEEP levels of 5 (baseline), ≈10, ≈12, and ≈14 cmH$_2$O in lung healthy patients during anesthesia (15). Red arrows: Tidal airway (respiratory system) P/V curves. Green arrows: Tidal chest wall P/V curves. The difference between the starting point of the chest wall P/V-curves at different PEEP compared to the first one at baseline PEEP is calculated as the difference between change in PEEP and change in end-expiratory transpulmonary pressure (= calculated change in end-expiratory pleural pressure). Red dash line: end-expiratory airway (respiratory system) P/V curve. Blue line: lung P/V curve. Green dash line: end-expiratory chest wall P/V curve. Note that as end-expiratory respiratory system and lung elastance is equal. The end-expiratory chest wall elastance is zero, i.e., the inverse, end-expiratory chest wall compliance is infinite, as an indication that the chest wall complex yields completely to PEEP inflation. PEEP, positive end expiratory pressure.

determined as the difference in respiratory system elastance (ΔPAW/VT) and lung elastance (ΔPEEP/ΔEELV). As the tidal variations in esophageal pressure is related to the force needed to displace the weight of the abdomen (44,49,50), not the inflation of an elastic structure, chest wall elastance does not change when increasing PEEP, as the weight remains constant. Consequently, tidal chest wall elastance is almost constant during increasing PEEP levels (4,14,16,18,37,38,47,57). As a consequence, the end-inspiratory transpulmonary pressure at the high PEEP level of the procedure can be estimated as end-inspiratory airway plateau pressure minus tidal chest wall elastance times the tidal volume. Applying this on the PEEP step procedure makes it possible to obtain an estimated lung P/V curve from end-expiration at baseline PEEP to end-inspiration at the high PEEP. This constitutes a substantial part of the clinically useful lung P/V curve, when applying protective ventilation. The tidal transpulmonary P/V curve is positioned on this lung P/V curve. In a clinical situation, when deficient oxygenation requires changes in PEEP and/or tidal volume, the consequences of such on both transpulmonary driving pressure and end-tidal transpulmonary plateau pressure can be predicted with a fair precision (*Figure 12*) and the estimated lung P/V curve can be used as a clinical decision support.

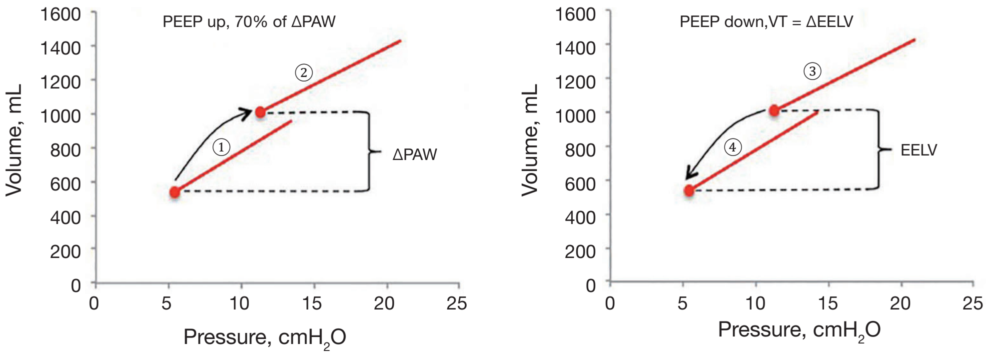

Figure 9 PEEP step procedure [with permission from Persson *et al./Br J Anaesth* (15)]: 1. baseline ventilation and PEEP; 2. increased PEEP ≈0.7× airway driving pressure (ΔPAW) at baseline. Determine the increase in end-expiratory lung volume (ΔEELVup) during 60–90 seconds at the new PEEP level; 3. change PEEP back to baseline level after 120 seconds. Determine the decrease in lung volume (ΔEELVdown) during 60–90 seconds; 4. set tidal volume (VT) as mean of ΔEELVup and ΔEELVdown. Calculate lung elastance as change in PEEP divided by mean change in end-expiratory lung volume (EL = ΔPEEP/ΔEELV) and transpulmonary driving pressure as lung elastance multiplied by tidal volume (ΔPL = EL × VT). PEEP, positive end expiratory pressure.

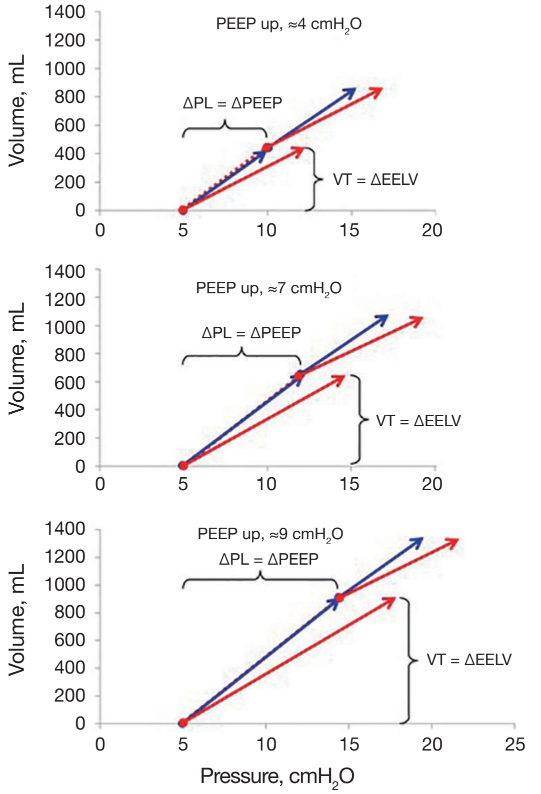

Figure 10 Lung P/V curves (blue arrows) and airway (respiratory system) P/V curves (red arrows) in lung healthy patients during anesthesia (15). Transpulmonary driving pressure of a tidal volume equal to ΔEELV is equal to the change in end-expiratory airway pressure (ΔPEEP) [with permission from Persson *et al.*/*Br J Anaesth* (15)].

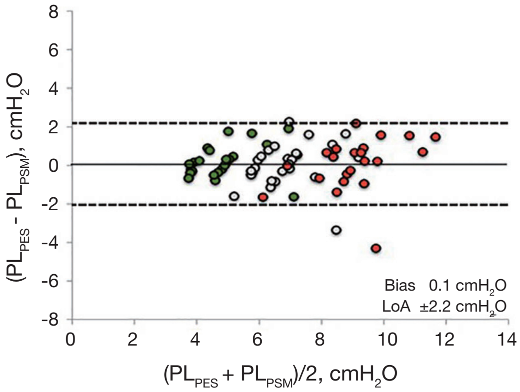

Figure 11 Bland & Altman analysis (51) of the transpulmonary driving pressure derived from esophageal pressure (ΔPL_{PES}) measurements and transpulmonary driving pressure derived from a PEEP step procedure (ΔPL_{PSM}) based on pooled data of lung healthy patients during anesthesia of three different sizes of PEEP steps (≈5, ≈7 and ≈9 cmH$_2$O, indicated by different colors in the figure (15). [With permission from Persson *et al.*/*Br J Anaesth* (15)]. PEEP, positive end expiratory pressure.

Summary of the PEEP step method

(I) The change in EELV after an increase of PEEP is dependent of the size of the PEEP change and the elastance of the lung.

(II) The change in end-expiratory transpulmonary pressure is equal to the change in PEEP because of the chest wall spring out force.

(III) Lung elastance may as a consequence be calculated by a PEEP step maneuver where the change in EELV is measured and then used for calculations of transpulmonary driving pressure.

(IV) There is good correlation between calculations of transpulmonary driving pressure with the PEEP step method and the conventional method using esophageal pressure measurements.

(V) The PEEP step method is based on calculations from changes in PEEP and differences between inspiratory and expiratory tidal volumes, which all are measured with high precision.

(VI) With a PEEP step maneuver it is possible to plot the lung P/V-curve which in turn may be used as a decision support when aiming for lung protective ventilation.

When choosing between the conventional esophageal pressure method and the PEEP step procedure, it seems likely that the PEEP step procedure will result in measurements with high precision. As it is a simple, non-invasive procedure, it would probably be preferable in many situations. The procedure can be repeated to keep close track on the evolution of lung mechanics. Also, the PEEP step procedure offers a possibility for decision support that should be valuable in a clinical setting when a protective ventilation strategy is implemented.

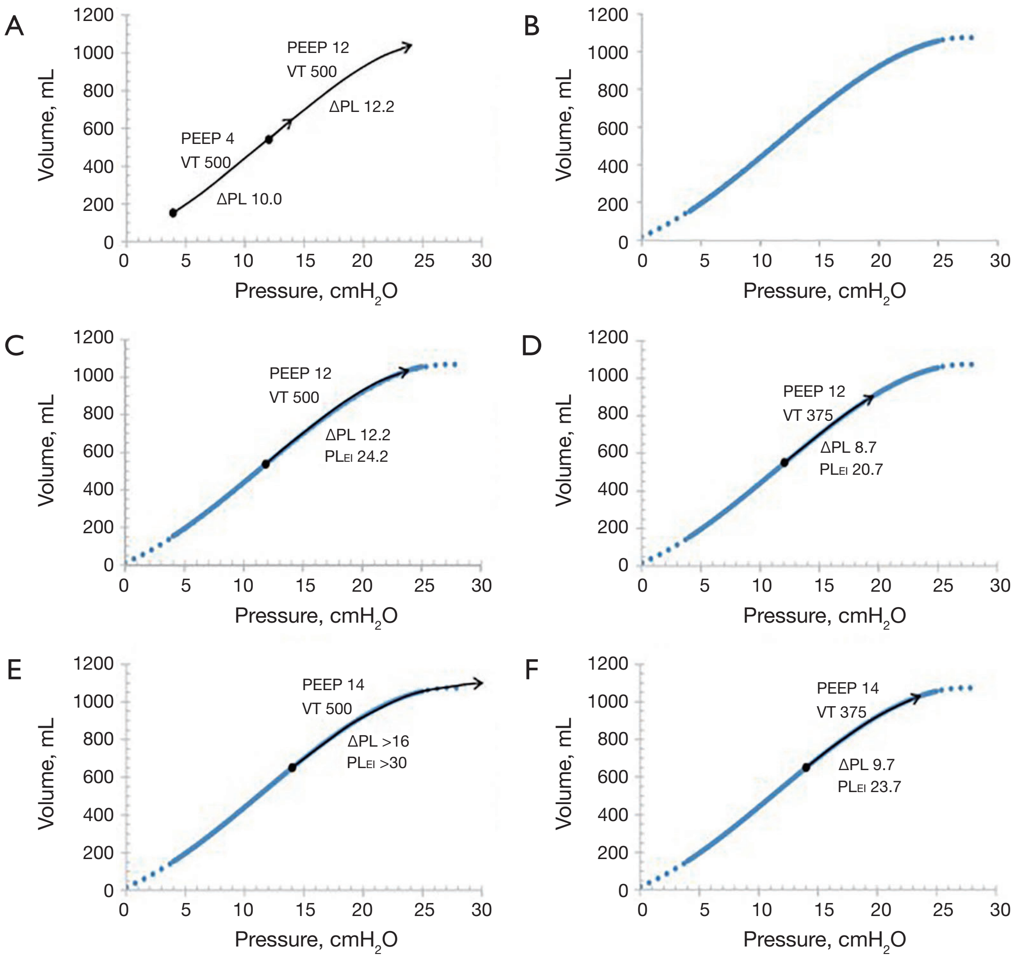

Figure 12 A PEEP step procedure is used to establish the lung P/V curve from baseline PEEP level, to end-expiration at the high PEEP level. The curve is extrapolated to ZEEP (A,B). On this lung P/V curve (blue line), tidal lung P/V curve moves as PEEP and/or tidal volume is changed as visualized in panel C, D, E, and F. PEEP, end-expiratory airway pressure; VT, tidal volume; ΔPL, transpulmonary driving pressure; PL$_{EI}$, end-inspiratory transpulmonary pressure. (A) PEEP step procedure lung P/V curve at baseline PEEP of 4 cmH$_2$O and at the high PEEP level of 12 cmH$_2$O; (B) lung P/V curve (blue line) from end-expiration at baseline PEEP to end-inspiration at the high PEEP level established by the PEEP step procedure of panel A. Dotted blue line: extrapolation of curve to FRC/ZEEP and to an end-inspiratory transpulmonary pressure of 28 cmH$_2$O; (C) black arrow indicates tidal lung PV curve at PEEP 12 cmH$_2$O and a tidal volume of 500 mL; (D) effect of decreasing tidal volume from 500 to 375 mL at PEEP 12 cmH$_2$O. Transpulmonary driving pressure decreases by ≈30% and end-inspiratory transpulmonary pressure decreases below upper limit for protective level of 24 cmH$_2$O (58); (E) if inadequate oxygenation requires an increase of PEEP, an increase from 12 to 14 cmH$_2$O, without reducing the tidal volume, is enough to cause a dangerous increase in both ΔPL (>16 cmH$_2$O) and absolute end-inspiratory transpulmonary pressure, PL$_{EI}$ (>30 cmH$_2$O); (F) a reduction of tidal volume from 500 to 375 mL reduces both ΔPL and PL$_{EI}$ to still high levels, but below upper limits. PEEP, positive end expiratory pressure.

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None.

Footnote

Conflicts of Interest: S Lundin and O Stenqvist are shareholders in The Lung Barometry Sweden AB. P Persson has no conflicts of interest to declare.

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Supplementary

Appendix

Standard mechanics

$\Delta \mathrm{PAW}$	Tidal variation in airway (respiratory system) pressure
$\Delta \mathrm{PES}$	Tidal variation in esophageal (chest wall) pressure
$\Delta \mathrm{PL} = (\Delta \mathrm{PAW} - \Delta \mathrm{PES})$	Tidal variation in transpulmonary (lung) pressure
$\Delta \mathrm{PEEP} = \Delta \mathrm{PAWEE}$	Change in end-expiratory airway (respiratory system) pressure
VT	Tidal volume
$\mathrm{ERS} = \Delta \mathrm{PAW}/\mathrm{VT}$	Respiratory system elastance
$\mathrm{ECW} = \Delta \mathrm{PES}/\mathrm{VT}$	Chest wall elastance
$\mathrm{EL} = (\Delta \mathrm{PAW} - \Delta \mathrm{PES})/\mathrm{VT}$	Lung elastance
$\Delta \mathrm{EELV} = \Delta \mathrm{PEEP}/\mathrm{EL}$	Change in end-expiratory lung volume caused by change in PEEP

End-expiratory mechanics

$\Delta \mathrm{PLEE} = \mathrm{EL} \times \Delta \mathrm{EELV}$	Change in end-expiratory transpulmonary pressure
$\Delta \mathrm{PPLEE} = \Delta \mathrm{PAWEE} - \Delta \mathrm{PLEE}$	Change in end-expiratory pleural pressure
$\mathrm{ERSEE} = \Delta \mathrm{PAWEE}/\Delta \mathrm{EELV}$	End-expiratory respiratory system elastance
$\mathrm{ELEE} = \Delta \mathrm{PLEE}/\Delta \mathrm{EELV}$	End-expiratory lung elastance
$\mathrm{ECWEE} = (\Delta \mathrm{PAWEE} - \Delta \mathrm{PLEE})/\Delta \mathrm{EELV}$	End-expiratory chest wall elastance

PEEP step method mechanics

$\mathrm{EL}_{\mathrm{PSM}} = \Delta \mathrm{PAWEE}/\Delta \mathrm{EELV}$	Lung elastance
$\mathrm{ECW}_{\mathrm{PSM}} = \mathrm{ERS} - \mathrm{ELPSM}$	Chest wall elastance
$\Delta \mathrm{PL}_{\mathrm{PSM}} = \mathrm{EL}_{\mathrm{PSM}} \times \mathrm{VT}$	Transpulmonary driving pressure of baseline PEEP
$\Delta \mathrm{PL}_{\mathrm{PSMHIPEEP}} = \Delta \mathrm{PAW}_{\mathrm{HIPEEP}} - \mathrm{ECW}_{\mathrm{PSM}} \times \mathrm{VT}$	Transpulmonary driving pressure of high PEEP level
$\mathrm{PLEI}_{\mathrm{PSMHIPEEP}} = \mathrm{PAWEE}_{\mathrm{HIPEE}}\mathrm{P} + \Delta \mathrm{PL}_{\mathrm{PSMHIPEEP}}$	End-inspiratory transpulmonary pressure of high PEEP level