COMPARISON OF END-EXPIRATORY LUNG VOLUME MEASUREMENT BY ELECTRICAL IMPEDANCE TOMOGRAPHY AND NITROGEN WASHOUT METHOD IN PIGS

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Abstract

End-expiratory lung volume (EELV) can be determined using several methods that allow clinically accurate measurements, but it is difficult to apply these methods to the patient's bedside. Electrical impedance tomography (EIT) is offered as another method for measuring EELV. The aim of the study is to compare changes in EELV measured by nitrogen washout method with changes of EELV calculated from the change in end-expiratory lung impedance (EELI) measured by EIT and to determine whether changes in EELV calculated from changes in chest impedance can be used as one of the parameters for EIT data analysis and description. The prospective interventional animal study was performed on ten pigs. The animals received total intravenous anesthesia with muscle relaxation. Mechanical lung ventilation was conducted in the volume-controlled mode. 16-electrode EIT system was used for data acquisition. End-expiratory lung volume was measured by a modified nitrogen wash-in/wash-out technique developed by Olegard et al. The study protocol consisted of the baseline phase, two incremental PEEP steps, two decremental PEEP steps and from normal saline i. v. administration. For each animal, a reference frame (baseline frame) was selected from the initial baseline phase and was used for the reconstruction of EIT images and impedance waveforms. For each breath cycle, tidal variation image was calculated as a difference between the end-inspiratory and the previous end-expiratory EIT image. An equivalent end-expiratory volume change ($\Delta EELV_{equiv}$) was calculated from EELI. The values of $\Delta EELV_{equiv}$ were compared with reference EELV data measured by a modified nitrogen wash-in/wash-out technique ($\Delta EELV_{meas}$). The measured and the estimated changes in EELV were statistically compared and correlation between ΔEELVequiv and $\Delta EELV_{meas}$ was calculated. Statistically significant difference between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ was observed only in administration of normal saline bolus. Pearson's correlation coefficients were 0.29 for increase in PEEP, 0.45 for decrease in PEEP and -0.1 during administration of normal saline bolus. The study showed that during changes in PEEP in the porcine model, there was no linear relationship between $\Delta EELV_{equiv}$ and ΔEELVmeas. Although there was no linear relationship between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ with changes in PEEP, no statistically significant difference was demonstrated between these two methods, which justifies the use of $\Delta EELV_{equiv}$ as a parameter suitable for description and evaluation of EIT data.

Keywords

electrical impedance tomography, end-expiratory lung volume, fluid balance, mechanical ventilation, monitoring

Introduction

In practice, the volume of air in the lungs after expiration is described by two parameters—functional residual capacity (FRC) and end-expiratory lung volume (EELV). While FRC is used for spontaneous ventilation, the EELV parameter is used for mechanical ventilation, where positive end-expiratory pressure (PEEP) is used [1]. PEEP affects lung volume after expiration. Lung volumes, especially FRC, are decreased in acute respiratory distress syndrome (ARDS) [2]. As PEEP provides lung recruitment and increases lung volumes, EELV can be used for optimization of mechanical ventilation mode and parameters [3, 4].

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EELV can be determined using several methods that allow clinically accurate measurements, but it is often very difficult to apply these methods effectively to the patient's bedside. The most widely used current methods for detecting EELV include spirometry, computed tomography, gas dilution methods, and whole-body plethysmography. Electrical impedance tomography (EIT) is offered as another method for measuring EELV. EIT is based on the application of weak alternating electric currents with a frequency of about 100 kHz and the subsequent measurement of the electrical impedance of tissues [5].

A number of studies have been published in the last twenty years on the issue of determining EELV using the EIT, but the results of these studies are inconsistent. Changes in end-expiratory pulmonary impedance (EELI), which are used to determine EELV, are induced by changes in PEEP in these studies.

Hinz et al. described dependence between EELV and EELI changes and argue that it can be used to estimate EELV changes across PEEP changes [6]. This work is followed by a study of Bikker et al. The authors argue that across different subjects, i.e., patients with varying degrees of lung damage due to disease, there is no simple linear relationship that can be used to estimate lung volume from electrical chest impedance [7]. Similarly, Markhorst et al. argue that changes in electrical impedance reflect changes in lung volumes, but across different values of EELV (and thus PEEP) there is an overestimation or underestimation and it is therefore not possible to apply linear dependence and apply it to different patients [8].

The aim of the study is to compare end-expiratory lung volume measured by nitrogen washout method with end-expiratory lung volume calculated from the change in end-expiratory lung impedance measured by electrical impedance tomography and to determine whether changes in end-expiratory lung volume calculated from changes in chest impedance can be used as one of the parameters for EIT data analysis and description.

Methods

The prospective interventional animal study was performed in the accredited animal laboratory of the Department of Physiology, First Faculty of Medicine, Charles University in Prague, in accordance with Act No. 246/1992 Coll., on the protection of animals against cruelty that incorporates the relevant legislation of the European Community. The study was approved by the Institutional Animal Care and Use Committee of the First Faculty of Medicine, Charles University in Prague. This study follows the study of Sobota et al. [9]. The groups of laboratory animals from both studies partially overlap; however, different parameters were evaluated and the studies define completely different objectives.

Animal preparation and monitoring

Ten crossbred (Landrace × Large White) female pigs (Sus scrofa domestica) 3–4 months old with an average body weight of 47.5 kg (43–51 kg range) were involved in the study.

The animals received total intravenous anesthesia with muscle relaxation. Mechanical lung ventilation was conducted using an Engström Carestation (GE Healthcare, Madison, WI, USA) ventilator in the volume-controlled mode. The pre-set and measured ventilatory parameters are described in Table 1.

*Table 1: Ventilatory parameters during the study protocol. Data are presented as median and interquartile range (Q1-Q3). * Preset parameter.*

Parameter	Baseline values (Phase 1)	End values (Phase 6)
Expiratory volume (mL)	463 (441–489)	466 (440–492)
Respiratory rate* (breaths/min)	20 (20–22)	20 (20–22)
Inspiratory to expiratory time ratio*	0.5	0.5
Fraction of inspired oxygen* (%)	30 (25–34)	30 (25–34)
End-tidal carbon dioxide concentration (mmHg)	43 (43–44)	42 (41–44)
Peripheral capillary oxygen saturation (%)	98 (97–100)	99 (97–100)
Minute ventilation (L/min)	9.3 (8.9–9.5)	9.3 (8.9–9.5)
Peak airway pressure (cmH_2O)	24 (23–27)	26 (24–26)
Positive end-expiratory pressure* (cmH_2O)	5	5
Compliance (mL/cmH_2O)	31 (29–35)	31 (27–33)

EIT system PulmoVista 500 (Dräger Medical, Lübeck, Germany) was used for data acquisition. An electrode belt of size "S" (chest circumference from 70 to 85 cm) was attached to the animal chest, cranially to the level of diaphragm at PEEP of 5 cmH_2O. In most of the subjects, this position corresponded with the 6th intercostal space. Correct placement of the electrode belt was verified by chest X-ray. The frequency of the applied alternating current was set to 110 kHz and the EIT images were acquired with a frame rate of 50 Hz.

End-expiratory lung volume was measured by a modified nitrogen wash-in/wash-out technique developed by Olegard et al. [10] The nitrogen concentration in the exhaled and inhaled air is not measured directly, but is determined from the concentration of oxygen and carbon dioxide at the end

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of expirium. The FRC INview module of the Engström Carestation ventilator was used to measure EELV. The applied change of FiO_2 for the wash-in/wash-out measurement of EELV was 10 %.

Study protocol

After preparation, instrumentation and myo-relaxation of an animal, calibration of the EIT system was performed and data acquisition was initiated. Recording of ventilatory data was initiated as well. A steady phase in a duration of approximately 30 minutes was introduced.

The study protocol consisted of six phases and is described schematically in Fig. 1.

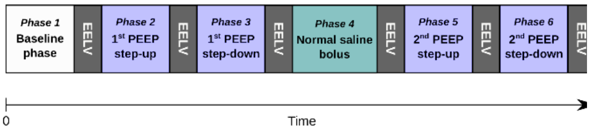

Fig. 1: Timeline of the study protocol. EELV – end-expiratory lung volume measurement.

Initial EELV measurement was conducted at the end of the baseline phase. Incremental PEEP step from 5 to 7 cmH_2O was performed and the second EELV measurement followed. PEEP was decreased back from 7 to 5 cmH_2O and EELV was measured again. Consequently, a bolus of 500 mL of normal saline was administered using a pressure infusion bag. The duration of the administration was 6 minutes on average. Three minutes after the end of the saline administration the EELV was measured, followed by the second incremental PEEP step from 5 to 7 cmH_2O. EELV was measured again, and PEEP was decreased back to the initial value. The last EELV measurement was done during the end phase when the PEEP was set back to 5 cmH_2O.

Data analysis and statistics

EIT data were pre-processed using EIT Data Analysis Tool (Dräger Medical, Lübeck, Germany). For each animal, a reference frame (also referred to as a baseline frame) was selected from the initial baseline phase of the experiment and was used for the reconstruction of EIT images and impedance waveforms. The data were exported to MATLAB (Mathworks Inc., Natick, MA, USA) where further processing was performed.

For each breath cycle, tidal variation (TV) image was calculated as a difference between the end-inspiratory and the previous end-expiratory EIT image [11].

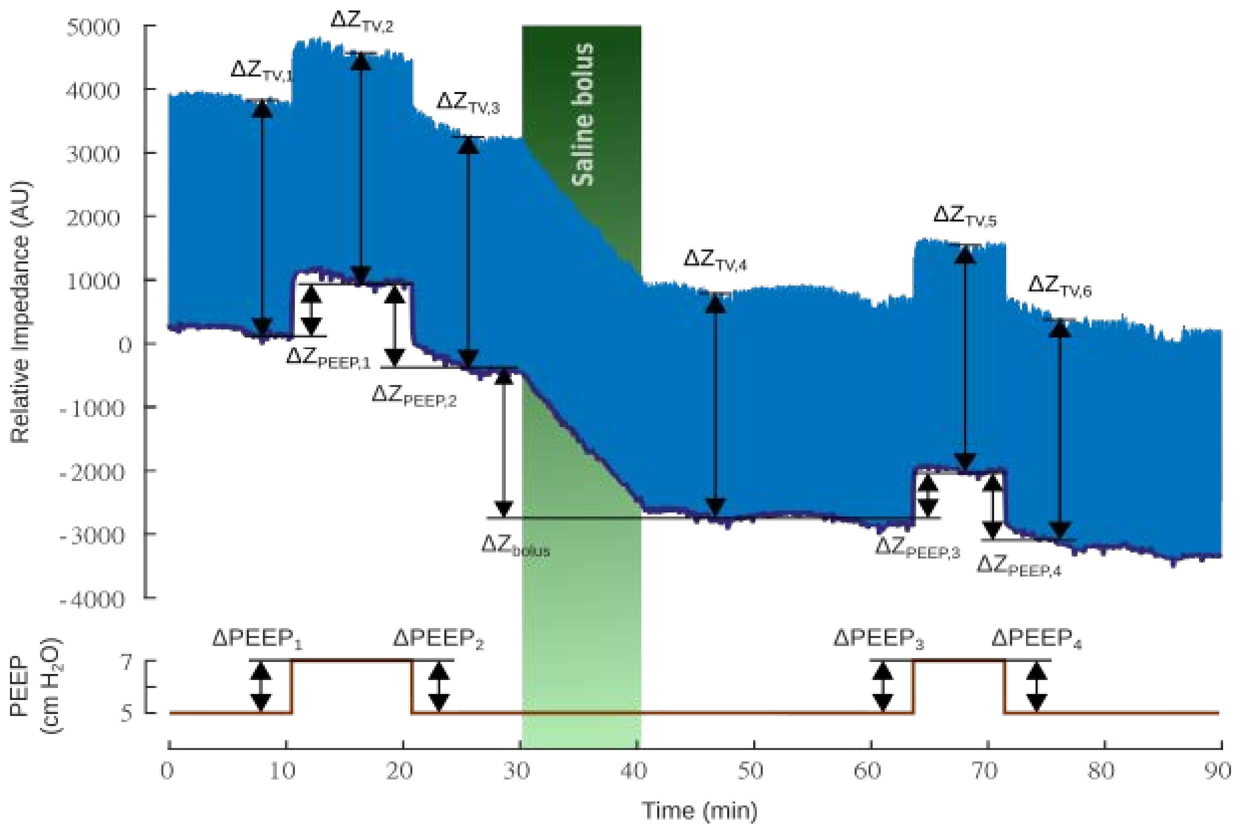

Fig. 2: Definition of variables for calculation of equivalent change in end-expiratory lung volume ($\Delta EELV_{equiv}$). Top graph: a representative relative impedance waveform with depicted end-expiratory lung impedance trend (dark blue). Bottom graph: a time course of positive end-expiratory pressure (PEEP).

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An equivalent end-expiratory volume change ($\Delta EELV_{equiv}$) was calculated from the end-expiratory lung impedance (EELI) changes caused by increase of PEEP, decrease of PEEP and the administration of 500 mL of normal saline.

The equivalent changes of end-expiratory lung volume caused by the administration of normal saline bolus were calculated as follows:

$$\Delta EELV_{equiv,bolus} = -\Delta Z_{bolus} \cdot \frac{1}{6}\sum_{j=1}^{6}\frac{V_{T,j}}{\Delta Z_{TV,j}}. \qquad (1)$$

The mean changes of end-expiratory lung impedance caused by the increase of PEEP and by the decrease of PEEP were calculated as follows:

$$\Delta Z_{PEEPup} = \frac{1}{2}(\Delta Z_{PEEP,1} + \Delta Z_{PEEP,3}), \qquad (2)$$

$$\Delta Z_{PEEPdown} = \frac{1}{2}(\Delta Z_{PEEP,2} + \Delta Z_{PEEP,4}). \qquad (3)$$

The equivalent changes of end-expiratory lung volume caused by the increase of PEEP and the decrease of PEEP were calculated as follows:

$$\Delta EELV_{equiv,PEEPup} = \Delta Z_{PEEPup} \cdot \frac{1}{6}\sum_{j=1}^{6}\frac{V_{T,j}}{\Delta Z_{TV,j}}, \qquad (4)$$

$$\Delta EELV_{equiv,PEEPdown} = \Delta Z_{PEEPdown} \cdot \frac{1}{6}\sum_{j=1}^{6}\frac{V_{T,j}}{\Delta Z_{TV,j}}. \qquad (5)$$

The definitions of the impedance changes $\Delta Z_{PEEP,1-4}$ and $\Delta Z_{TV,j}$ are depicted in the Fig. 2. $V_{T,j}$ is the tidal volume in the corresponding phase (see Fig. 1 for definitions of phases).

The values of $\Delta EELV_{equiv}$ were compared with reference EELV data measured using the FRC INview module of the ventilator ($\Delta EELV_{meas}$). Correlation between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ was calculated as Pearson's correlation coefficient.

ANOVA for repeated measures was used for the comparison of the differences between the measured and the estimated changes in EELV. A p-value < 0.05 was considered statistically significant. The values are presented as mean ± standard deviation unless stated otherwise.

Results

Nine animals completed the full study protocol, in one animal the 2nd PEEP maneuver was not carried out. Comparison of $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ in increase in PEEP, in decrease in PEEP and in administration of normal saline bolus is depicted in Fig. 3. Statistically significant difference between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ was observed only in administration of normal saline bolus. Weak correlation between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ was observed in the increase in PEEP, moderate correlation between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ was observed in the decrease in PEEP, as depicted in Fig. 4.

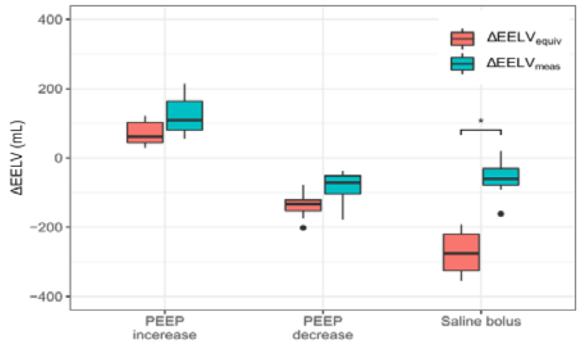

*Fig. 3: Comparison of $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ with PEEP increase, PEEP decrease and normal saline bolus. Statistically significant differences ($p < 0.05$) between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ are indicated by *.*

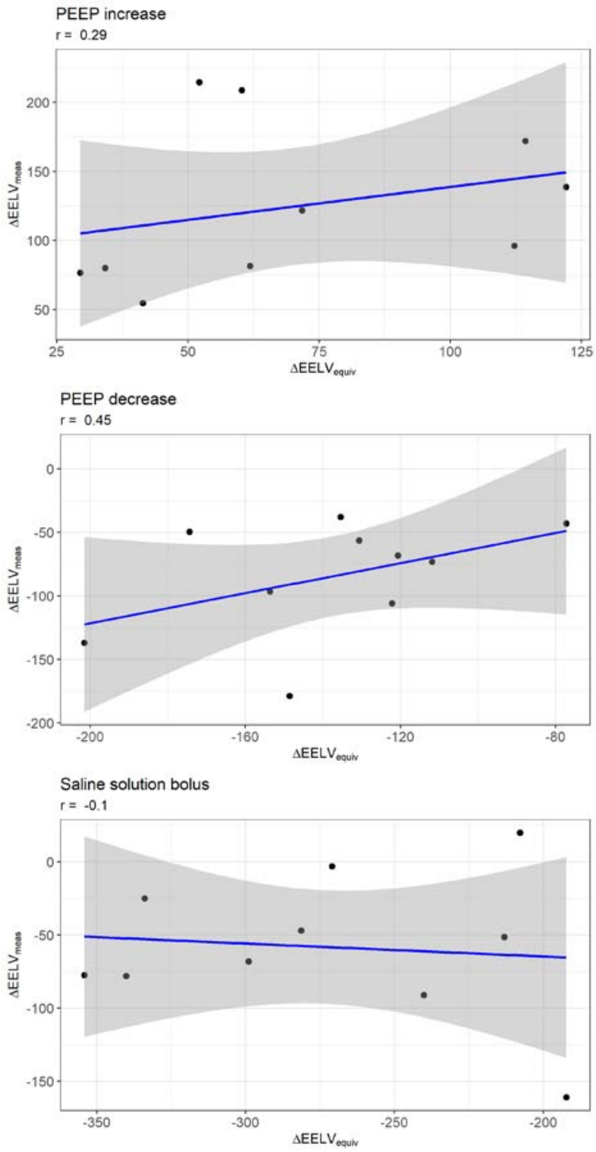

Fig. 4: Correlation between $\Delta EELVequiv$ a $\Delta EELVmeas$ in the increase in PEEP, in the decrease in PEEP and in the administration of normal saline bolus. „r“ is Pearson's correlation coefficient.

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Discussion

The main finding of the study is that changes in end-expiratory lung volume calculated from changes in end-expiratory lung impedance do not differ significantly from changes in EELV measured by nitrogen washout method when manipulating PEEP value. However, the correlation between the two methods was only moderate. In contrast, when the saline bolus was administered, the $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ values differed statistically significantly and no correlation was found between the two methods.

Several studies dealt with comparison of EELV calculated from values obtained by electrical impedance tomography with results obtained by a reference method of EELV measurement, e.g. by nitrogen washout method, but the results are contradictory. As noted above, Hinz *et al.* [6] found a very good correlation between the change in end-expiratory lung impedance and the change in end-expiratory lung volume measured by the multi-breath open-circuit nitrogen washout technique in ten patients on mechanical lung ventilation.

In contrast, Bikker *et al.* [7] demonstrated only a weak correlation between the change in end-expiratory impedance and the change in end-expiratory volume measured by nitrogen washout method in 30 patients on mechanical lung ventilation. Markhorst *et al.* [8] reported that no linear relationship was found between the change in end-expiratory impedance and EELV measured by the nitrogen washout method in an animal study in seven pigs. Grivans *et al.* [12] compared changes in end-expiratory lung volume, which was calculated based on spirometrically measured change in inspiratory and expiratory tidal volume, with changes in EELV calculated based on EELI changes, and found a very good correlation in both the lung model and patients on mechanical lung ventilation.

The results of our study are in agreement with the studies of Bikker *et al.* and Markhorst *et al.*, which did not show a linear relationship between EELV calculated from changes in EELI and EELV measured by the nitrogen washout method. Statistically insignificant differences between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ during PEEP maneuvers and at the same time low degree of correlation between these parameters may be due to inaccuracies in the measurement of EELV by the modified nitrogen washout. As can be seen from Figure 3, the variance of the $\Delta EELV_{meas}$ values is greater than the variance of the $\Delta EELV_{equiv}$ values. Although Olegard *et al.* [10] reports the error of repeated measurements at 2 PEEP levels of -22 mL with a 95% confidence interval [-38, 29 mL], the sensitivity of EELV measurements using a modified nitrogen washout method may be lower than changes in end-expiratory lung impedance measured by electrical impedance tomography. Another factor that may contribute to the low correlation between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ is the nonlinearity of the relationship between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$, which is also caused, among other reasons, by inhomogeneity of volume distribution in pulmonary recruitment. If the EIT is measured at only one chest level, it may not reflect changes in whole lung volume. This possible reason is also mentioned in work by Bikker *et al.*

Furthermore, the results obtained by analysis of the EIT data are affected by other factors, such as the choice of the baseline frame used for the EIT image reconstruction [13], presence of lung effusion [14], body and electrode belt position [15] and other factors.

When the saline bolus was administered, the size of $\Delta EELV_{meas}$ was minimal, while $\Delta EELV_{equiv}$ was significant. This is consistent with the assumption that EELI is affected not only by lung aeration but also by intravenous fluid administration. To verify this hypothesis was the main aim of a study by Sobota *et al.* [9], for which this study was conducted as a pilot to verify the relationship between EELV changes measured using a modified nitrogen washout technique and EELV changes calculated from EELI values.

The limitation of this study is the relatively small number of included experimental animals. Another limitation is the use of only one level of PEEP change and the relatively small step of PEEP change. Another limitation is that the study was conducted using laboratory animals and the findings may not be fully transferable to human patients.

Conclusion

The study showed that with changes in PEEP in the porcine model, there was no linear relationship between changes in end-expiratory lung volume measured by nitrogen washout method and calculated changes in end-expiratory lung volume based on changes in chest end-expiratory impedance measured by electrical impedance tomography. Although there was no linear relationship between $\Delta EELV_{equiv}$ and $\Delta EELV_{meas}$ with changes in PEEP, no statistically significant difference was demonstrated between the two methods, which justifies the use of $\Delta EELV_{equiv}$ as a parameter suitable for description and evaluation of electrical impedance tomography data.

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