COMPARISON OF METHODS TO QUANTIFY LUNG OVERDISTENSION AND TIDAL RECRUITMENT BASED ON EIT

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Abstract Protective ventilation strategies have been proposed to minimize the occurrence of lung overdistension (OD), as well as the presence of tidal recruitment (TR) of airways and alveolar units. In this context, Electrical Impedance Tomography (EIT) emerges as a noninvasive, radiation-free imaging technique, for bedside monitoring the regional distribution of ventilation in the lungs. Different EIT methods exist to quantify OD and TR: 1) PVShape quantifies the curvature of the pressure-volume curve during inspiration ($PVShape_{insp}$) and expiration ($PVShape_{exp}$); 2) the algorithm RACH is based on the estimation of the compliance changes in each element through the PEEP steps. Thus, the objective of this study is to compare these published algorithms to quantify changes in spatial distribution of OD and TR during mechanical ventilation. EIT was collected from 19 mechanically ventilated surgical patients during a decremental positive end-expiratory pressure (PEEP) titration maneuver. The proportion of TR and OD at each PEEP step was computed from EIT according with each algorithm. The spatial distribution of OD and TR was significantly affected by PEEP changes. Compared to the other methods, the estimates of TR were considerably higher with $PVShape_{insp}$ (more than 60% larger, $p<0.001$). While the higher significant proportion of OD was found in the $PVShape_{exp}$ (more than 6% larger, $p<0.001$). This study demonstrates a significant disagreement between TR and OD quantified by these three EIT-based methods. Despite the statistic difference between RACH and $PVShape_{exp}$, these methods present information that appears to be reasonably compatible.

Keywords: *Electric impedance tomography, Mechanical ventilation, Overdistension, Tidal recruitment.*

Introduction

Mechanical ventilation (MV, i.e. cyclic insufflation of the lungs) is routinely used in the clinic to maintain adequate levels of oxygen and carbon dioxide in the blood [1]. However, improper MV settings may lead to alveolar overdistension (OD) and tidal recruitment (TR), which increase the risk of ventilator-induced lung injury [1,2]. So called "protective" ventilation strategies have been proposed to minimize the occurrence of OD and TR [2,3]. However, emerging evidence is available that MV settings that appear protective from a "whole lung" perspective might result in regions of the lung submitted to injurious ventilation [4].

In this context, Electric Impedance Tomography (EIT) emerges as a non-invasive, radiation-free real-time imaging method for bedside estimation of regional lung mechanics [5]. Different EIT-based methods have been proposed to quantify OD and TR [6]. In order to investigate the agreement among these methods, in this study we compared two published algorithms to quantify how positive end-expiratory pressure (PEEP) affects the spatial distribution of OD and TR: 1) PVShape [5], which quantifies of how much local pressure-volume curves deviate from a linear relationship; 2) the recruitable alveolar collapse and hyperdistension (RACH) [7], which quantifies how much the local compliance decreases at each PEEP compared to its maximum value. The objective is to verify if both methods result in the same conclusions about PEEP-related changes in regional lung mechanics.

Methods

Experimental Protocol – EIT was acquired at the beginning of an elective abdominal surgery in 20 adult patients without any lung disease (one patient was removed from the analysis due to its EIT data poor quality), prior to the procedure, in Tredenlenburg position (supine, feet 30º higher than the head). The patients were under general anesthesia and controlled mechanical ventilation (mode: VCV, PEEP=4cmH_2O, respiratory rate=12cycles/min, FiO2=0.4, tidal volume6mL/kg BW, I:E=1:2). After a recruitment maneuver (10 cycles with PEEP=30cmH_2O, Peak pressure = 50 cmH_2O, respiratory rate 6 breaths/minute), a PEEP titration was performed starting at 20 cmH_2O and decreasing 2 cmH_2O each 2 minutes until 4 cmH_2O. Before each PEEP change, a slow inflation maneuver was performed using the ventilator built-in function (constant flow of 4 $L \cdot min^{-1}$ until reaching an inflation volume of 12 $mL \cdot kg^{-1}$ body weight), followed by a slow expiration maneuver with the same characteristics. During the procedure, EIT, airway pressure, respiratory volume and flow were collected at 50 Hz (Pulmovista 500, Draeger).

The study was approved by a local ethic committee (University of Leizig, Germany, No. 196-11-ff- 8042011), and patients signed an informed consent prior to the procedure.

EIT Processing – The EIT data was reconstructed using GREIT algorithm [8] with a human-shape tridimensional thorax finite-element mesh, resulting in 3402 elements whose impedance changes in time due to the ventilation dynamics. The region of interest (ROI) was identified at each PEEP level considering the variation of impedance between the beginning and the end of the slow inflation maneuver in each element. Then, if such change was more than 10% of the maximum change, the element was classified as a ventilated part of the lung and considered for analysis (for the RACH algorithm, a single ROI was established for all PEEPs, defined by the ROI of the highest PEEP).

PVShape - PVShape [5] characterizes the relation of the volume-independent and the volume-dependent terms of the elastance in each element "i"" of the ROI ($E_{1,i}$ and $E_{2,i}$, respectively), considering the following non-linear single-compartment model of the local impedance [9]

$$p(t) = E_{1,i} z_i(t) + E_{2,i}\, z(t)^2 + R_i \frac{\partial z_i(t)}{\partial t} + P_{0,i} \qquad (1)$$

where $z_i(t)$ is the impedance of the element, p(t) the airway pressure, R_i the resistance, and $P_{0,i}$ the end-expiratory pressure. For each PEEP, the coefficients of eq (1) are estimated using least squares considering two different epochs: beginning of the slow inflation maneuver (from start until reaching an inspired volume of 6 mL / kg PBW ,$PVShape_{insp}$) and end of the slow expiration maneuver (from a residual volume of 6 mL / kg PBW to the end of the expiration $PVShape_{exp}$).Then, for each epoch the PVShape was calculated as

$$PVShape_i = \frac{E_{2,i}.\max(z_i(t))}{|E_{2,i}|.\max(z_i(t))+E_{1,i}} 100\% \qquad (2)$$

Then, the percentage of lung undergoing TR and OD ($TR_{PVShape}$ and $OD_{PVShape}$), was estimated as the percentage of elements with PVShape<-10% and PVShape>20%, respectively. PVShape values in between are considered as linearly distended.

RACH. For the estimation of recruitable alveolar collapse and hyperdistension (RACH) [7], the first step is the quantification of the compliance C_i of each element "i" of the ROI at every PEEP step

$$C_i = \frac{\Delta z_i}{P_{plateau} - PEEP} \qquad (3)$$

where Δz_i is the local impedance variation and $P_{plateau}$ is the plateau pressure, both measured as median values of 26 tidal cycles. Then, for each element of the ROI, the highest compliance was identified ($C_{i,max}$) and the associated PEEP defined as the ideal PEEP for that element ($PEEP_{ideal}$). For PEEP>$PEEP_{ideal}$, the reduction in compliance was considered as due to OD, while for PEEP<$PEEP_{ideal}$ the reduction in compliance was assumed to be the effect of TR. Thus, for each PEEP step, the percentage of TR and OD of each element was calculated as

$$TR_{RACH,i} = \begin{cases} 0, if\ PEEP > PEEP_{ideal} \\ \frac{C_{i,\max} - C_i}{C_{i,\max}} \times 100, otherwise \end{cases};$$

$$OD_{RACH,i} = \begin{cases} 0, if\ PEEP < PEEP_{ideal} \\ \frac{C_{i,\max} - C_i}{C_{i,\max}} \times 100, otherwise \end{cases} \qquad (4)$$

and the cumulated percentage of TR and OD of all N elements in the ROI was computed as

$$TR_{RACH} = \frac{\sum_1^N (Tidal\ Recruitment_i * C_{i,\max})}{\sum_1^N C_{i,\max}} \times 100;$$
$$OD_{RACH} = \frac{\sum_1^N Overdistension_i * C_{i,\max})}{\sum_1^N C_{i,\max}} \times 100 \qquad (5)$$

Moreover, the respiratory system compliance (C_{RS}), for each subject, can be derived from the equation of motion as

$$p(t) = \frac{v(t)}{C_{RS}} + R_{RS} f(t) + P_0 \qquad (6)$$

where f(t) is the airflow and v(t) is the respiratory volume, R_{RS} is the respiratory system resistance and P_0 is the end-expiratory pressure.

Statistical Analysis - Results are shown as mean ± standard error. Both percentage of TR and OD were analyzed using a generalized linear mixed model (fixed effect: PEEP and method for estimation; random effect: subject). All the statistical analysis was performed using R considering a significance level of 0.05.

Results

Estimations of TR and OD – Figure 1 illustrates the comparison between the proportions of TR and OD estimated for each method as a function of the PEEP steps, also compared to the respiratory system compliance (Figure 1A).

It can be observed that, independently of the method considered, TR decreases with PEEP, while OD increases (and it is almost negligible for lower PEEP levels). The $PVShape_{insp}$ method (Figure 1C) detects a predominance of TR for all PEEP steps. For the other two methods ($PVShape_{exp}$ and RACH, Figure 1B and Figure 1D), the low PEEPs are associated with higher TR and lower OD, while the high PEEPs are associated with higher OD and lower TR, as expected.

Qualitative comparison of regional distribution of PVShape of and RACH – Figure 2 shows the maps of PVShape and RACH for a representative subject at different PEEPs. The maps obtained using $PVShape_{exp}$ and RACH are quite comparable, showing that for lower PEEPs there is a considerable presence of TR concentrated in the dorsal (dependent) region of the lung, which progressively reduces with increasing PEEP, with a parallel increase of OD in the ventral (nondependent) region of the lung.

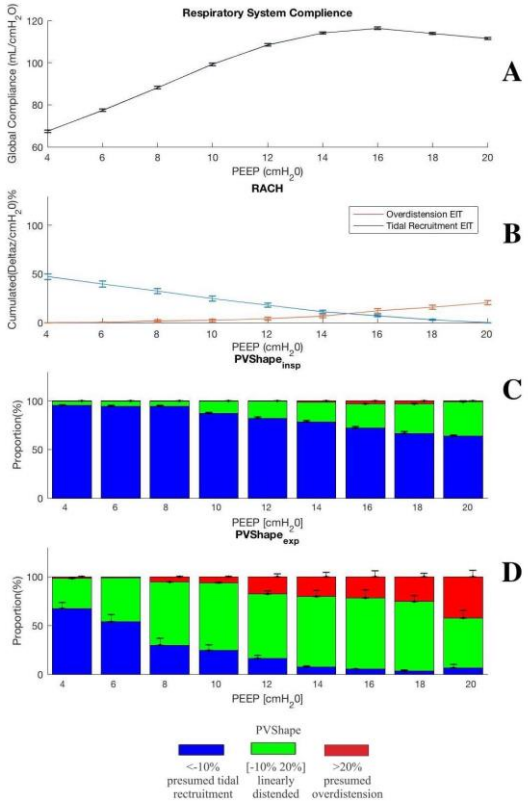

Figure 1: Effect of PEEP on lung mechanics (mean ± SE): A) respiratory system compliance; TR and OD estimated with B) RACH C) $PVShape_{insp}$ and D) $PVShape_{exp}$.

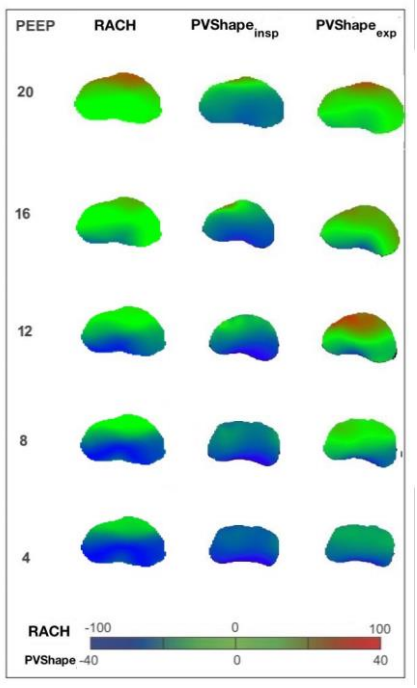

Figure 2: Representative example of EIT-derived maps of RACH (left), $PVShape_{insp}$ (center) and $PVShape_{exp}$ (right) at different PEEP levels.

Quantitative comparison between PVShape and RACH – Table 1 shows the results of the statistical analysis of the difference between the methods in the quantification of TR and OD. The comparison of TR and OD percentages obtained by each method demonstrates that PEEP-related changes significantly affected the lung airway regional distribution.

Moreover, as can be seen in Table 1, the comparison of the TR percentages indicates that, among the three methods, the one that estimated the higher percentage of TR was $PVShape_{insp}$. In contrast, the technique that estimated the lowest rates of TR was RACH.

Concerning the OD, it can be seen that the method that estimated the highest percentage was $PVShape_{exp}$; while, the $PVShape_{insp}$ evaluated the smallest proportions of OD.

Table 1: Statistical comparison of TR and OD estimated with different methods, using linear mixed model. The average effects are shown as (first method compared) – (second method compared). Values are shown as mean ± SE. ***P<0.001;

Parameter	Methods Compared	PEEP effect (mean±se)	Method effect (mean±se)
TR (%)	$PVShape_{insp}$ vs $PVShape_{exp}$	-3±0.2***	63.4±1.9***
	$PVShape_{exp}$ vs RACH	-3.6±0.2***	4.4±1.5***
	$PVShape_{insp}$ vs RACH	-3±0.2***	67.8±1.1***
OD (%)	$PVShape_{insp}$ vs $PVShape_{exp}$	1.3±0.2***	-15.6±1.6 ***
	$PVShape_{exp}$ vs RACH	1.9±0.1***	9.8±1.4***
	$PVShape_{insp}$ vs RACH	0.7±0.1***	-6.4±0.6***

Discussion

In the present study, we compared two approaches to quantify PEEP-related changes in spatial distribution of OD and TR: RACH and PVShape (the latter estimated both during inspiration and expiration). Our results suggest that: 1) at lower PEEPs, as expected, both algorithms detected higher TR and lower (or absent) OD [5,7,9]; 2) according to $PVShape_{insp}$, but not with the other methods, the estimated amounts of OD are practically zero even in higher PEEP values; 3) in agreement with Beda et al. [5] and Terragni et al. [9], in none of the PEEP steps, TR and OD were both simultaneously absent; 4) in general terms, the TR and OD estimations of different methods are not fully compatible.

In agreement with previous studies, for both methods higher PEEPs shifted the PVShape (inspiratory and expiratory) and RACH distributions toward increased OD and reduced TR [5,7,9]. At lower PEEPs, as expected [7,9], the TR proportions increased, while OD decreased (almost absent for the lower levels). In contrast to RACH and $PVShape_{exp}$, the $PVShape_{insp}$ detected a predominance of TR for all PEEP levels. Despite the differences, all methods considered indicate

that lung heterogeneity is present at all PEEP levels. This is particularly relevant because the lungs of the patients considered are healthy, and because it contradicts the conventional approach of seeking PEEP levels that result in an ideal homogenous scenario where TR and OD are simultaneously absent/negligible [9].

The RACH and the PVShape techniques are based on different approaches to quantify TR and OD. The RACH method requires a full PEEP titration maneuver to be quantified, because estimations of TR and OD are based on the comparison of compliance between PEEPs (i.e. they are relative to changes of TR and OD from an ideal condition). This implies that a wide range of PEEPs need to be tested in order to obtain a reliable estimation. In contrast, PVShape quantification is performed at each PEEP independently (i.e. absolute estimations of TR and OD). However, the method requires a slow inflation maneuver that only some mechanical ventilators can perform.

The comparison of RACH with $PVShape_{insp}$ and $PVShape_{exp}$ showed a significant quantitative disagreement between the proportions quantified as TR and OD. Especially with $PVShape_{insp}$, it can be noticed that PEEP-related changes are not reasonably compatible with RACH and $PVShape_{exp}$ findings.

The estimates of OD and TR with $PVShape_{exp}$ always moderately overestimate those of RACH, however the PEEP related changes are similar between the two methods (Figure 2). The differences can be related to the threshold used for $PVShape_{exp}$. Different threshold combinations might have resulted in higher similarity with RACH (i.e., increasing the threshold values decreases the number of pixels for TR and OD). Nevertheless, it seems that the two method are providing the same qualitative information about the effect of PEEP on local lung mechanics.

As for global respiratory mechanics, maximum compliance was reached on average at PEEP=14-16cmH_2O (Figure 2A), which suggests that the PEEP that optimizes global mechanics should be considerably high compared to conventional clinical practice in healthy patients with normal lungs. Possibly, this is a direct consequence of the Trendelenburg position, that results in increased gravitational effect of the abdominal content on the diaphragm [10].

Additionally, limitations in agreement between $PVShape_{insp}$ and $PVShape_{exp}$ are expected, since the inspiratory and expiratory pressure-volume curves are different due to lung hysteresis. Although differences in the estimated proportions of TR and OD were expected, the results show that the estimations of the different PVShape configurations are not physiologically comparable. This significant disagreement is again probably related to the body position. In the Trendelenburg position, the abdominal viscera push the diaphragm downward into the thoracic cavity [10]. This probably results in lower compliance at the beginning of inspiration, which it may lead to overestimation of TR as well as an underestimation of OD, compared to expiration.

Conclusion

This exploratory study suggests a significant disagreement between the TR and OD quantified by the RACH, $PVShape_{exp}$ and $PVShape_{insp}$ methods. Although estimations of RACH and $PVShape_{exp}$ were statistically different, these methods present information that appears to be reasonably compatible. Furthermore, in the Tredenlenburg position the EIT data from healthy subjects indicated lung heterogeneity.

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