

Transpulmonary pressures to predict the percentage of alveolar collapse and overdistension in acute respiratory distress syndrome

Clément Brault

Brault.clement@chu-amiens.fr

Amiens-Picardie University Hospital

Yoann Zerbib

Amiens-Picardie University Hospital

Romain Vallee

Amiens-Picardie University Hospital

Rosalie Schoux

Amiens-Picardie University Hospital

Alexis Lambour

Amiens-Picardie University Hospital

Benjamin Swinyard

Amiens-Picardie University Hospital

Valentin Dambrine

Amiens-Picardie University Hospital

Julien Demaier

Amiens-Picardie University Hospital

Loay Kontar

Amiens-Picardie University Hospital

Julien Maizel

Amiens-Picardie University Hospital

Michel Slama

Amiens-Picardie University Hospital

Research Article

Keywords: Acute respiratory distress syndrome, Positive end-expiratory pressure, Transpulmonary pressure, Electrical impedance tomography, Overdistension, Collapsus

Posted Date: July 3rd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10108489/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Critical Care on September 25th, 2026.
See the published version at <https://doi.org/10.1186/s13054-026-06356-4>.

Abstract

Background

Determining the optimal positive end-expiratory pressure (PEEP) to maximize alveolar recruitment while minimizing overdistension remains a clinical challenge. This study investigated the relationship between transpulmonary pressures and alveolar collapse/overdistension, as assessed by electrical impedance tomography (EIT), in patients with moderate-to-severe acute respiratory distress syndrome (ARDS).

Methods

We conducted a physiological study involving 38 mechanically ventilated ARDS patients. Each patient underwent a decremental PEEP trial (20 to 4 cmH₂O), with continuous EIT monitoring and esophageal pressure measurements to calculate end-expiratory ($P_{L,e}$) and end-inspiratory ($P_{L,i}$) transpulmonary pressures. Percentages of alveolar collapse and overdistension were derived from EIT data. The predictive value of $P_{L,e}$ and $P_{L,i}$ for critical alveolar collapse or overdistension (> 10%) was assessed. We also compared PEEP levels determined by EIT-guided (best compromise between overdistension and collapse) versus esophageal pressure-guided (lowest PEEP yielding a positive $P_{L,e}$) strategies.

Results

$P_{L,e}$ and $P_{L,i}$ strongly correlated with alveolar collapse ($r = -0.68$) and overdistension ($r = 0.60$), respectively (both $p < 0.001$). Receiver operating characteristic analysis showed good predictive performance of $P_{L,e}$ (AUC = 0.84) and $P_{L,i}$ (AUC = 0.80) for identifying critical collapse and overdistension. A $P_{L,e} < 2.0$ cmH₂O predicted collapse > 10%, while $P_{L,i} > 18.4$ cmH₂O predicted overdistension > 10%, both with $\geq 80\%$ specificity. PEEP levels determined using EIT were significantly higher than those based on esophageal pressure (12.0 [8.0–14.0] vs. 8.0 [4.8–11.3] cmH₂O; $p < 0.001$), resulting in reduced alveolar collapse, indicating more effective alveolar recruitment, and improved ventilation in dependent lung region. However, EIT-guided strategy also led to a slight increase in overdistension and reduced compliance in the non-dependent lung.

Conclusions

$P_{L,e}$ and $P_{L,i}$ accurately identified clinically relevant thresholds of collapse and overdistension, supporting their role as physiologic surrogates of regional lung stress in ARDS. However, EIT- and esophageal-guided strategies result in different PEEP settings, respiratory mechanics, and patterns of alveolar collapse and overdistension.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening condition characterized by diffuse alveolar damage, reduced lung compliance, and severe hypoxemia. Mechanical ventilation is an essential component of ARDS management, however, if not carefully optimized, it may exacerbate lung injury through ventilator-induced lung injury (VILI) [1]. The principal mechanisms underlying VILI include both alveolar collapse (atelectrauma) and overdistension (volutrauma and barotrauma), which frequently coexist within the heterogeneous lung parenchyma of patients with ARDS. Accurate identification and mitigation of these deleterious phenomena are fundamental to lung-protective ventilation strategies [1].

Positive end-expiratory pressure (PEEP) is applied to prevent alveolar collapse and maintain end-expiratory lung volume. Nonetheless, determining the optimal PEEP level in ARDS remains challenging and depends on individual's potential for lung recruitment. Excessive PEEP may cause alveolar overdistension, increasing lung stress and strain, whereas insufficient PEEP may fail to prevent cyclic alveolar collapse [2].

Electrical impedance tomography (EIT) is a non-invasive, bedside imaging technique that enables real-time assessment of regional ventilation distribution, providing estimates of alveolar collapse and overdistension during PEEP titration [3]. In contrast, esophageal pressure monitoring allows for the calculation of transpulmonary pressure, which is commonly used as a surrogate for the distending pressure applied to the lung parenchyma [4]. However, whether transpulmonary pressures reliably correlate with EIT-derived estimates of alveolar collapse and overdistension has not been definitively established.

The aim of this study was to investigate the relationship between transpulmonary pressures and the extent of alveolar collapse and overdistension assessed by EIT in patients with moderate-to-severe ARDS. We hypothesized that transpulmonary pressure measurements could serve as reliable predictors of alveolar status, thus helping clinicians in the individualized optimization of PEEP.

MATERIAL AND METHODS

Study population

We conducted a physiological study including all patients with moderate-to-severe ARDS, defined according to the Berlin criteria, who underwent a decremental PEEP trial with simultaneous recording of esophageal pressure and EIT between January 1, 2022, and October 31, 2025, in the intensive care unit (ICU) of Amiens University Hospital (Amiens, France). The study was approved by the local institutional review board (CPP Nord-Ouest II, Amiens, France; reference PI2025_843_0221).

Ventilator settings

A clinical protocol for management of ARDS patients was implemented in our ICU. Patients were ventilated in volume-control mode using V500/V600 (Dräger, Lübeck, Germany) ventilators. Sedation and analgesia were maintained by continuous intravenous infusion of midazolam or propofol. Neuromuscular blockade was achieved with continuous intravenous cisatracurium infusion. Tidal volume was set at 6 mL/kg predicted body weight, with plateau pressure (P_{plat}) maintained below 30 cmH₂O. The fraction of inspired oxygen (F_{iO_2}) level was adjusted to target a peripheral oxygen saturation (S_{pO_2}) between 88 and 92%.

Device installation

EIT was performed using the PulmoVista 500 system (Dräger, Lübeck, Germany) with a 16-electrode belt placed between the 4th and 5th intercostal spaces. The PEEP titration tool provided the relative percentages of lung collapse (decrease in local compliance with PEEP reduction) and overdistension (increase in local compliance with PEEP reduction) at each PEEP level during a decremental PEEP trial.

An esophageal balloon catheter (Nutrivent, Sidam, Modena, Italy) was positioned in the mid-esophagus (Supplementary Appendix 1) and connected to the PressurePod device (Dräger, Lübeck, Germany). Transpulmonary pressures and regional lung compliances were calculated as detailed in Supplementary Appendix 2 [4, 5]. Following the approach of Yoshida et al., the local transpulmonary pressure in the middle-to-dependent lung regions at the end of expiration ($P_{\text{L,e}}$) was derived from direct measurements of esophageal pressure, while the end-inspiratory transpulmonary pressure in the non-dependent region ($P_{\text{L,i}}$) was estimated using the elastance ratio method [6].

EIT and esophageal pressures were recorded synchronously at a sampling frequency of 50 Hz, and filtered using a low-pass filter with a cut-off frequency of 50 min⁻¹. Airway pressure, flow, and volume signals were collected via a dedicated cable connecting the V500/V600 ventilators to the PulmoVista 500 system. All data were extracted directly from the PulmoVista 500 system and analyzed offline using the EIT Data Analysis Tool (Dräger, Lübeck, Germany). Contraindications to study procedures, as specified by local protocol, are detailed in Supplementary Appendix 3.

Decremental PEEP trial

A decremental PEEP trial was performed in selected ARDS patients at the discretion of the attending physician, depending on operator expertise, and logistical constraints, including time of day and equipment availability. The trial was conducted in pressure-controlled ventilation with a fixed driving pressure of 15 cmH₂O. PEEP was initially set at 20 cmH₂O and subsequently reduced in 2 cmH₂O steps every 2 minutes to a minimum of 4 cmH₂O. In two patients, the trial started at PEEP 16 cmH₂O due to hemodynamic concerns from the clinical team. Passive ventilation was ensured by confirming the absence of spontaneous respiratory effort. The respiratory rate was transiently reduced to below 25

breaths/min to minimize dynamic hyperinflation. A single decremental PEEP trial was performed in each patient.

At each PEEP level, airway and esophageal pressures were recorded during end-expiratory and end-inspiratory occlusion maneuvers. In addition, regional ventilation distribution (i.e., proportion of tidal volume delivered to the dependent lung) and the extent of alveolar collapse and overdistension were assessed. The PEEP determined by the EIT-guided strategy ($PEEP_{EIT}$) was defined as the PEEP level achieving the best compromise between collapse and overdistension (i.e. the crossing point of the collapse and overdistension curves) [7]. The esophageal pressure-based optimal PEEP (P_{eso} -guided strategy) was defined as the lowest PEEP yielding a positive $P_{L,e}$.

Statistics

Normality of data distribution was assessed using the Shapiro–Wilk test. Continuous data were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range [IQR], as appropriate. Spearman's correlation coefficients were calculated to assess relationships between transpulmonary pressures and the extent of alveolar collapse and overdistension. Because each patient contributed repeated measurements across PEEP levels, within-subject relationships were further assessed using the repeated-measures correlation (rmcorr) and linear mixed-effects models with a random intercept for each patient, the latter estimating the change in collapse (or overdistension), in percentage points, per 1 cmH₂O change in the corresponding transpulmonary pressure. The robustness of these associations was tested in sensitivity analyses excluding the extreme PEEP measurements (PEEP 20 cmH₂O for the $P_{L,e}$ –collapse relationship and PEEP 4 cmH₂O for the $P_{L,i}$ –overdistension relationship). These extreme levels were excluded because of an inherent constraint of EIT-based analysis: collapse is computed relative to the highest PEEP level, which is therefore assigned a collapse value of 0% by definition, while overdistension is computed relative to the lowest PEEP level, which is likewise assigned an overdistension value of 0%. Finally, $P_{L,i}$ was additionally computed using the direct method ($P_{L,i} = P_{plat} - P_{eso}$).

Prespecified subgroup analyses were performed according to obesity (body mass index ≥ 30 kg/m²), respiratory system compliance (dichotomized at the median value of 35 cmH₂O/L), PaO₂/FiO₂ ratio (dichotomized at the median value of 153 mmHg), and the potential for lung recruitment assessed by the absolute reduction in collapse between PEEP 4 cmH₂O and PEEP 20 cmH₂O (dichotomized at the median value of 33%) [8]. Fisher's r-to-z transformation was used to compare correlation coefficients between subgroups.

Receiver operating characteristic (ROC) curves were generated to determine the performance of transpulmonary pressures in predicting critical alveolar collapse and overdistension, each defined as involving more than 10% of the lung. Areas under the ROC curve (AUC) with 95% confidence interval (CI) were calculated. Optimal cut-off values were identified using the Youden index. To avoid the dualism of a

single threshold, a gray-zone approach was applied to identify a range of transpulmonary pressures within which collapse and overdistension could not be reliably predicted.

Comparisons between optimal PEEP values derived from EIT-guided and P_{eso} -guided strategies were performed using the Wilcoxon signed-rank test. Statistical analyses were conducted using Prism (version 9.4.1, GraphPad Software, San Diego CA, USA) and R software version 4.0.5 (<http://www.R-project.org/>). A p-value < 0.05 was considered statistically significant.

RESULTS

Study population

Thirty-nine patients with moderate-to-severe ARDS were included. One patient was excluded due to technical issues during EIT and esophageal pressure recordings. All remaining patients (n = 38) successfully completed the decremental PEEP trial. Median age was 65 [53–71] years and body mass index were 28.2 [24.2–34.1] kg/m². Median P_aO_2/F_iO_2 ratio was 153 [119–179] mmHg and 6 (16%) patients had severe ARDS. Baseline demographic characteristics and respiratory mechanics are reported in Table 1.

Table 1
Characteristics of patients at time of study inclusion.

Parameters	All patients (n = 38)
Demographic data	
Age (years)	65 [53–71]
Male sex	30 (79)
BMI (Kg/m ²)	28.2 [24.2–34.1]
Obese	16 (42)
SAPS II (pts)	56 [43–64]
SOFA (pts)	8 [6–10]
Delay between intubation and inclusion (days)	1 [0–4]
Chronic pulmonary disease	11 (29)
Cause of ARDS	
Bacterial pneumonia	15 (39)
Influenza	4 (11)
COVID-19	4 (11)
Pneumonia without microbiological documentation	9 (24)
Extrapulmonary sepsis	2 (5)
Other	4 (11)
Ventilator settings	
V _T (mL)	410 [353–429]
V _T PBW (mL/kg)	6.0 [5.7–6.2]
RR (breaths/min)	28 [24–30]
Respiratory mechanics	
ΔP_{rs} : driving pressure of the respiratory system, AOP: airway opening pressure, BMI: body mass index, C_{rs} : respiratory system compliance, DP: driving pressure, F_iO_2 : fraction of inspiratory oxygen, P_aO_2 : partial arterial pressure of oxygen, P_aCO_2 : partial arterial pressure of carbon dioxide, P_{peak} : peak pressure, P_{plat} : plateau pressure, PBW: predicted body weight, PEEP: positive end-expiratory pressure, RR: respiratory rate, SAPS: simplified acute physiology score, V _T : tidal volume.	
Data are quoted as the median [interquartile range] or n (%).	

Parameters	All patients (n = 38)
Airway closure with AOP > 5 cmH ₂ O	11 (29)
P _{peak} (cmH ₂ O)	34.0 [30.3–37.0]
P _{plat} (cmH ₂ O)	22.0 [20.0–27.0]
PEEP (cmH ₂ O)	10.0 [9.0–11.0]
ΔP _{rs} (cmH ₂ O)	12.0 [10.0–16.0]
C _{rs} (mL/cmH ₂ O)	35 [24–42]
Mechanical power (J/min)	25.2 [19.8–28.2]
Gas exchange	
F _i O ₂ (%)	60 [53–90]
P _a O ₂ /F _i O ₂ (mmHg)	153 [119–179]
P _a CO ₂ (mmHg)	41.2 [35.5–48.6]
pH	7.30 [7.29–7.39]
Ventilatory ratio	1.80 [1.41–2.26]
ΔP_{rs}: driving pressure of the respiratory system, AOP: airway opening pressure, BMI: body mass index, C_{rs}: respiratory system compliance, DP: driving pressure, F_iO₂: fraction of inspiratory oxygen, P_aO₂: partial arterial pressure of oxygen, P_aCO₂: partial arterial pressure of carbon dioxide, P_{peak}: peak pressure, P_{plat}: plateau pressure, PBW: predicted body weight, PEEP: positive end-expiratory pressure, RR: respiratory rate, SAPS: simplified acute physiology score, V_T: tidal volume.	
Data are quoted as the median [interquartile range] or n (%).	

Correlation between transpulmonary pressures and alveolar collapse and overdistension.

During the decremental PEEP trial, the stepwise reduction in PEEP was associated with a progressive, linear decrease in P_{L,e}, from 8.3 ± 3.6 cmH₂O at PEEP 20 cmH₂O to – 1.8 ± 3.4 cmH₂O at PEEP 4 cmH₂O. In parallel, the percentage of alveolar collapse increased from 0 ± 0% to 31 ± 16% (Fig. 1A), and a negative correlation was observed between P_{L,e} and alveolar collapse (r = – 0.68 [95% CI: –0.74 to –0.62]; p < 0.001) (Fig. 1B, Supplementary Table E1).

Conversely, P_{L,i} decreased from 25.6 ± 4.8 cmH₂O at PEEP 20 cmH₂O to 10.0 ± 3.7 cmH₂O at PEEP 4 cmH₂O, while the percentage of alveolar overdistension decreased from 33 ± 11% to 0 ± 0% (Fig. 1C).

Accordingly, a positive correlation was observed between $P_{L,i}$ and alveolar overdistension ($r = 0.60$ [95% CI: 0.52 to 0.67]; $p < 0.001$) (Fig. 1D, Supplementary Table E1). Similar results were obtained when $P_{L,i}$ was calculated using the direct method (Supplementary Figure E1).

These relationships were confirmed by within-subject analyses. For alveolar collapse, the repeated-measures correlation with $P_{L,e}$ was strong ($rmcorr = -0.85$ [95% CI: -0.88 to -0.81]; $p < 0.001$), and in a linear mixed-effects model with a random intercept for each patient, each 1 cmH₂O decrease in $P_{L,e}$ was associated with a 3.0% increase in alveolar collapse ($p < 0.001$). Likewise, for overdistension, the repeated-measures correlation with $P_{L,i}$ was strong ($rmcorr = 0.89$ [95% CI: 0.86 to 0.91]; $p < 0.001$), and in the corresponding model, each 1 cmH₂O increase in $P_{L,i}$ was associated with a 1.9% increase in overdistension ($p < 0.001$). Both associations remained essentially unchanged in sensitivity analyses (Supplementary Table E1-E2 and Figure E2).

On subgroup analysis, the correlation between $P_{L,e}$ and alveolar collapse did not differ significantly across any subgroup. In contrast, the correlation between $P_{L,i}$ and overdistension was significantly higher in obese than in non-obese patients ($Z = 2.92$; $p = 0.004$), whereas no significant differences were observed across subgroups defined by respiratory system compliance, PaO₂/FiO₂ ratio, or lung recruitability (Supplementary Table E3, Figures E3–E4).

Predictive value of transpulmonary pressures for alveolar collapse and overdistension.

Receiver operating characteristic (ROC) analysis demonstrated that $P_{L,e}$ independently predicted alveolar collapse $> 10\%$, with an AUC of 0.84 [95% CI: 0.80 to 0.88] (Fig. 2A, Supplementary Table E4). A $P_{L,e} < 2.0$ cmH₂O predicted collapse $> 10\%$ with $\geq 80\%$ specificity, while a $P_{L,e} > 9.0$ cmH₂O predicted collapse $< 10\%$ with the same specificity (Fig. 2B).

$P_{L,i}$ also independently predicted overdistension $> 10\%$ with an AUC of 0.80 [95% CI: 0.75 to 0.84] (Fig. 2C, Supplementary Table E4). A $P_{L,i} > 18.4$ cmH₂O predicted overdistension $> 10\%$ with $\geq 80\%$ specificity, while a $P_{L,i} < 9.2$ cmH₂O predicted overdistension $< 10\%$ with the same specificity (Fig. 2D). Additional analyses of $P_{L,i}$ calculated using the direct method are provided in Supplementary Figure E1.

Comparison between PEEP strategies.

At the individual level, only three patients had identical PEEP values between the two strategies (Supplementary Figure E5). The EIT-guided strategy induced higher PEEP level compared to the P_{eso} -guided strategy (12.0 [8.0–14.0] vs. 8.0 [4.8–11.3] cmH₂O; $p < 0.001$), leading to higher $P_{L,e}$ and $P_{L,i}$ (3.4 [1.3–5.3] vs. 1.3 [0.9–1.6] cmH₂O; $p < 0.001$, and 15.9 [13.8–20.0] vs. 12.8 [8.9–17.3] cmH₂O; $p = 0.006$, respectively) (Table 2, Supplementary Figure E6).

Table 2
Comparison of respiratory mechanics, collapse and overdistension between PEEP strategies.

Parameters	PEEP _{EIT}	PEEP _{Peso}	p value
PEEP (cmH ₂ O)	12.0 [8.0–14.0]	8.0 [4.8–11.3]	< 0.001
Transpulmonary pressure			
P _{L,e} (cmH ₂ O)	3.4 [1.3–5.3]	1.3 [0.9–1.6]	< 0.001
P _{L,e} < 0 cmH ₂ O	4 (11)	0 (0)	0.115
P _{L,i} (cmH ₂ O)	15.9 [13.8–20.0]	12.8 [8.9–17.3]	0.006
P _{L,i} > 20 cmH ₂ O	9 (24)	6 (16)	0.387
Electrical tomography impedance			
Collapse (%)	6 [3–9]	16 [8–24]	< 0.001
Collapse > 10%	7 (18)	22 (58)	< 0.001
Overdistension (%)	10 [7–13]	4 [0–11]	0.012
Overdistension > 10%	15 (39)	10 (26)	0.222
Collapse + Overdistension (%)	17 [10–22]	22 [18–30]	< 0.001
Collapse + Overdistension > 20%	11 (29)	22 (58)	0.011
%V _{T,D} (%)	49 [42–58]	44 [38–52]	< 0.001
Compliance			
C _{rs} (mL/cmH ₂ O)	33 [25–47]	34 [25–52]	0.144
C _L (mL/cmH ₂ O)	40 [31–64]	43 [29–68]	0.102
C _{L,ND} (mL/cmH ₂ O)	19 [14–32]	24 [16–40]	0.014
C _{L,D} (mL/cmH ₂ O)	20 [17–27]	17 [13–32]	0.667
<i>C_L: lung compliance, C_{L,D}: dependent lung compliance, C_{L,ND}: non-dependent lung compliance, C_{rs}: respiratory system compliance, P_{eso}: esophageal pressure, P_{L,e}: end-expiratory transpulmonary pressure (direct method), P_{L,i}: end-inspiratory transpulmonary pressure (elastance-derived method), PEEP: positive end-expiratory transpulmonary pressure. PEEP_{EIT}: PEEP determined by the EIT-guided strategy, PEEP_{Peso}: PEEP determined by the esophageal pressure-guided strategy.</i>			
Data are quoted as the median [interquartile range] or n (%).			

Electrical impedance tomography revealed a significant reduction in collapse with the EIT-guided strategy (6 [3–9] vs. 16 [8–24] %; $p < 0.001$), suggesting greater alveolar recruitment. Ventilation was also more evenly distributed to the dependent lung region (49 [42–58] vs. 44 [38–52] %; $p < 0.001$), although this did not translate in a significant difference in compliance of the dependent lung (20 [17–27] vs. 17 [13–32] mL/cmH₂O; $p = 0.667$) (Table 2, Supplementary Figure E6).

Conversely, EIT-guided strategy led to an increase in overdistension (10 [7–13] vs. 4 [0–11] %; $p = 0.012$), associated with a lower compliance of the non-dependent lung (19 [14–32] vs. 24 [16–40] mL/cmH₂O; $p = 0.014$). However, global respiratory system and lung compliances remained similar between strategies (Table 2, Supplementary Figure E6).

DISCUSSION

In this physiological study, we investigated the relationship between transpulmonary pressures and alveolar status (specifically collapse and overdistension) as assessed by EIT, during a decremental PEEP trial in patients with moderate-to-severe ARDS. Our principal findings are as follows:

1. Both $P_{L,e}$ and $P_{L,i}$ were significantly associated with alveolar status and may serve as predictive markers of collapse and overdistension, respectively.
2. A $P_{L,e} < 2.0$ cmH₂O predicted collapse $> 10\%$, while a $P_{L,i} > 18.4$ cmH₂O predicted overdistension $> 10\%$, both with a specificity of at least 80%.
3. PEEP_{EIT} and PEEP_{PesO} guided strategies resulted in different PEEP level, transpulmonary pressures, and lung aeration.

Esophageal pressure monitoring provides a non-invasive estimate of pleural pressure, enabling calculation of transpulmonary pressures [4]. In both animal and human cadaver, Yoshida et al. demonstrated that direct measurement of transpulmonary pressure closely reflects the distending pressure in the dependent and middle lung regions [5]. A negative $P_{L,e}$ (resulting from low PEEP and/or elevated pleural pressure) is associated with alveolar de-recruitment and collapse in these areas, leading to hypoxemia, impaired compliance, and atelectrauma (i.e. the cyclic opening and closing of alveoli, a key mechanism of VILI) [9, 10]. Our results revealed a significant inverse correlation between $P_{L,e}$ and the extent of collapse: the lower the $P_{L,e}$, the higher the percentage of collapse. Specifically, a $P_{L,e} < 2.0$ cmH₂O – observed at a mean PEEP of 10.5 cmH₂O – was associated with a high likelihood of a critical amount of collapse ($> 10\%$), with a strong specificity.

These findings align with post hoc analyses from the EPVent-2 trial, where maintaining $P_{L,e}$ near 0 cmH₂O (± 2 cmH₂O) was associated with improved 60-day survival, while lower $P_{L,e}$ values correlated with increased mortality, presumably due to sustained collapse and its consequences [11]. As such, targeting a slightly positive $P_{L,e}$ (around 2 cmH₂O) may help prevent clinically significant collapse [12]. According to our results, targeting a $P_{L,e}$ at 2 cmH₂O might prevent critical collapse for most of patients.

However, to rule out collapse with high specificity, $P_{L,e}$ may need to exceed 9.0 cmH₂O, raising the potential for lung overdistension.

Esophageal pressure monitoring also enables estimation of $P_{L,i}$, a surrogate of lung stress during tidal insufflation. Excessive $P_{L,i}$ has been associated with increased risk of overdistension in non-dependent lung and the occurrence of barotrauma/volutrauma. Compared to direct measurement, the elastance-derived method more accurately reflects $P_{L,i}$ in non-dependent lung areas [5]. Our findings showed a positive correlation between the extent of overdistension and $P_{L,i}$, regardless of the calculation method used. Notably, a $P_{L,i} > 18.4$ cmH₂O – measured using the elastance-derived method and observed at a mean PEEP of 12.8 cmH₂O – reliably identified critical overdistension (> 10%). This threshold approximates pressures seen at total lung capacity in healthy individuals and may exceed safe limits in ARDS patient [11]. However, consensus on a definitive safety threshold for $P_{L,i}$ remains lacking [12].

Currently, no guidelines recommend setting PEEP level based on the minimization of lung collapse and/or overdistension. Nevertheless, meta-analyses suggest that optimizing PEEP using EIT may improve respiratory mechanics and clinical outcomes [13, 14]. These benefits may be partially related to the impact of PEEP on right ventricular afterload. By reducing both collapse and overdistension, PEEP_{EIT} brings lung volumes closer to functional residual capacity, thereby decreasing pulmonary vascular resistance and right ventricular afterload [15, 16]. In a recent study by Sousa et al using EIT in a porcine model of ARDS, PEEP was adjusted to achieve either minimal collapse (< 3%), minimal overdistension (< 3%), or an optimal balance [17]. After 12 hours, animals in the minimal overdistension group – for who higher levels of collapse were tolerated – demonstrated more frequent and higher dose epinephrine requirements, suggesting that excessive alveolar collapse impair cardiac function and potentially increase mortality. Thus, minimizing overdistension by tolerating a certain amount of alveolar collapse may have detrimental effects on lung and cardiac function in ARDS.

EIT may serve as a valuable tool in the management of ARDS, as it provides insights into the amount of collapse and overdistension at a given PEEP level. While EIT shows promising potential in the ICU, its current use remains largely restricted to research, partly due to high costs [18, 19]. Conversely, Pes monitoring is increasingly feasible, with integration into the modern ventilators enabling real-time pleural pressure measurement and automated calculation of both $P_{L,e}$ and $P_{L,i}$ [20]. Standardized procedures for catheter insertion and in vivo calibration have improved the reliability of measurements [21]. Additionally, the use of air-filled open catheters has been proposed as a cost-effective alternative [22]. Despite these advantages, PEEP_{Peso}-guided and PEEP_{EIT}-guided strategies are not interchangeable, as they are based on fundamentally different principles. EIT assesses regional ventilation within a transverse thoracic slice (approximately 5–10 cm), whereas esophageal pressure serves as a surrogate for pleural pressure in the periesophageal region. These methodological differences may partly explain why the two titration strategies selected different PEEP levels and resulted in distinct respiratory mechanics and transpulmonary pressures [23, 24]. The PEEP_{EIT}-guided strategy resulted in higher PEEP levels, which in turn increased both $P_{L,e}$ and $P_{L,i}$. The combined amount of collapse and overdistension was lower using

PEEP_{EIT}, primarily due to a significant reduction in alveolar collapse, indicating more effective alveolar recruitment and a more homogeneous ventilation pattern (i.e. a redistribution of tidal volume from non-dependent to dependent lung regions). However, PEEP_{EIT} also caused a slight increase in overdistension, contributing to reduced compliance in the non-dependent lung. Despite these differences, both respiratory system and lung compliances were similar between the two strategies.

Several limitations should be acknowledged. First, the 10% threshold used to define critical levels of collapse and overdistension was arbitrarily selected, and its prognostic validity has not been confirmed. Second, the absolute values of collapse and overdistension are influenced by the range of PEEP applied during the decremental trial [25]. The percentages might have differed if a broader PEEP range has been used (e.g. from PEEP 24 cmH₂O to PEEP 4 cmH₂O) [26, 27]. Third, esophageal pressure monitoring requires specialized training and time for calibration, which limits its routine clinical application [21]. A recent study shows that an end-expiratory positive-pressure occlusion test can falsely indicate esophageal balloon malposition when airway opening pressure (AOP) is higher than PEEP. In our cohort, however, only two patients had PEEP set below AOP during esophageal balloon calibration. Finally, because all measurements were performed in deeply sedated, paralyzed patients without spontaneous respiratory effort, our findings cannot be extrapolated to patients undergoing assisted ventilation.

CONCLUSION

Our findings support the physiological rationale that $P_{L,e}$ and $P_{L,i}$ are correlated with alveolar collapse and overdistension, respectively. These associations were consistent across the cohort, with particularly stronger correlation between $P_{L,i}$ and overdistension in obese patients. Transpulmonary pressures may serve as valuable tools for predicting alveolar status in patients with ARDS, when EIT is contraindicated (because of pacemaker, burns...) or unavailable. Nonetheless, the wide gray zones for both $P_{L,e}$ and $P_{L,i}$ highlight the inherent uncertainty in applying rigid thresholds in a heterogeneous ARDS population, and supports individualized approach for PEEP setting.

ABBREVIATIONS

AOP	Airway Opening Pressure
ARDS	Acute Respiratory Distress Syndrome
AUC	Area Under the Receiver Operating Characteristic Curve
CI	Confidence Interval
CPP	Comité de Protection des Personnes (French Institutional Review Board)
EIT	Electrical Impedance Tomography
FiO ₂	Fraction of Inspired Oxygen
ICU	Intensive Care Unit
IQR	Interquartile Range
PEEP	Positive End-Expiratory Pressure
PEEP _{EIT}	EIT-guided Positive End-Expiratory Pressure
PEEP _{Peso}	Esophageal pressure-guided Positive End-Expiratory Pressure
P _{L,e}	End-expiratory Transpulmonary Pressure
P _{L,i}	End-inspiratory Transpulmonary Pressure
P _{plat}	Plateau Pressure
P _{eso}	Esophageal Pressure
rmcorr	Repeated-measures Correlation
ROC	Receiver Operating Characteristic
SD	Standard Deviation
SpO ₂	Peripheral Oxygen Saturation
VILI	Ventilator-Induced Lung Injury

DECLARATIONS

Ethics approval and consent to participate

The study was approved by the local institutional review board (CPP Nord-Ouest II, Amiens, France; reference PI2025_843_0221). As the study reports data routinely acquired in usual care, signed informed consent was waived, according to local legislation.

Consent for publication

Not applicable.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Funding

This research did not receive any specific funding from agencies or organizations in the public, commercial, or not-for-profit sectors.

Author Contribution

CB, YZ, LK, JM and MS contributed to the conception and design of the study. CB, YZ, RV, RS, AL, BS, VD and JD were responsible for the recruitment and clinical care of the patients. CB, YZ, LK, JM and MS participated on the analysis and interpretation of the data. CB, YZ, and RV drafted the manuscript. All the authors reviewed and approved the final version of the manuscript.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med*. 2013;369:2126–36. <https://doi.org/10.1056/NEJMr1208707>.
2. Battaglini D, Roca O, Ferrer R. Positive end-expiratory pressure optimization in ARDS: physiological evidence, bedside methods and clinical applications. *Intensive Care Med*. 2024;50:762–5. <https://doi.org/10.1007/s00134-024-07397-5>.
3. Franchineau G, Jonkman AH, Piquilloud L, Yoshida T, Costa E, Rozé H, et al. Electrical Impedance Tomography to Monitor Hypoxemic Respiratory Failure. *Am J Respir Crit Care Med Am Thorac Soc - AJRCCM*. 2024;209:670–82. <https://doi.org/10.1164/rccm.202306-1118CI>.
4. Piquilloud L, Beitler JR, Beloncle FM. Monitoring esophageal pressure. *Intensive Care Med*. 2024;50:953–6. <https://doi.org/10.1007/s00134-024-07401-y>.
5. Yoshida T, Amato MBP, Grieco DL, Chen L, Lima CAS, Roldan R, et al. Esophageal Manometry and Regional Transpulmonary Pressure in Lung Injury. *Am J Respir Crit Care Med Am Thorac Soc - AJRCCM*. 2018;197:1018–26. <https://doi.org/10.1164/rccm.201709-1806OC>.

6. Yoshida T, Amato MBP, Grieco DL, Chen L, Lima CAS, Roldan R, et al. Esophageal Manometry and Regional Transpulmonary Pressure in Lung Injury. *Am J Respir Crit Care Med*. 2018;197:1018–26. <https://doi.org/10.1164/rccm.201709-1806OC>.
7. Francovich JE, Katira BH, Jonkman AH. Electrical impedance tomography to set positive end-expiratory pressure. *Curr Opin Crit Care*. 2025;31:319–27. <https://doi.org/10.1097/MCC.0000000000001255>.
8. Jonkman AH, Alcalá GC, Pavlovsky B, Roca O, Spadaro S, Scaramuzzo G et al. Lung Recruitment Assessed by Electrical Impedance Tomography (RECRUIT): A Multicenter Study of COVID-19 Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 208:25–38. <https://doi.org/10.1164/rccm.202212-2300OC>
9. Bikker I, Vd Berg B, Specht P, Bakker J, Gommers D. Transpulmonary pressure and ventilation distribution measured with EIT during a PEEP trial in porcine acute lung injury. *Crit Care*. 2010;14:P178. <https://doi.org/10.1186/cc8410>.
10. Rodriguez PO, Bonelli I, Setten M, Attie S, Madorno M, Maskin LP et al. Transpulmonary Pressure and Gas Exchange During Decremental PEEP Titration in Pulmonary ARDS Patients. *Respiratory Care*. Daedalus Enterprises for the American Association for Respiratory Therapy; 2013;58:754–63. <https://doi.org/10.4187/respcare.01977>
11. Sarge T, Baedorf-Kassis E, Banner-Goodspeed V, Novack V, Loring SH, Gong MN et al. Effect of Esophageal Pressure–guided Positive End-Expiratory Pressure on Survival from Acute Respiratory Distress Syndrome: A Risk-based and Mechanistic Reanalysis of the EPVent-2 Trial. *Am J Respir Crit Care Med* 204:1153–63. <https://doi.org/10.1164/rccm.202009-3539OC>
12. Ball L, Talmor D, Pelosi P. Transpulmonary pressure monitoring in critically ill patients: pros and cons. *Crit Care*. 2024;28:177. <https://doi.org/10.1186/s13054-024-04950-y>.
13. Gao Y, He H, Chi Y, Frerichs I, Long Y, Zhao Z. Electrical impedance tomography guided positive end-expiratory pressure titration in critically ill and surgical adult patients: a systematic review and meta-analysis. *BMC Pulm Med*. 2024;24:582. <https://doi.org/10.1186/s12890-024-03394-y>.
14. Songsangvorn N, Xu Y, Lu C, Rotstein O, Brochard L, Slutsky AS, et al. Electrical impedance tomography-guided positive end-expiratory pressure titration in ARDS: a systematic review and meta-analysis. *Intensive Care Med*. 2024;50:617–31. <https://doi.org/10.1007/s00134-024-07362-2>.
15. Sousa MLA, Menga LS, Schreiber A, Docci M, Vieira F, Katira BH, et al. Individualized PEEP can improve both pulmonary hemodynamics and lung function in acute lung injury. *Crit Care*. 2025;29:107. <https://doi.org/10.1186/s13054-025-05325-7>.
16. Jozwiak M, Teboul J-L. Heart–Lungs interactions: the basics and clinical implications. *Ann Intensive Care*. 2024;14:122. <https://doi.org/10.1186/s13613-024-01356-5>.
17. Sousa MLA, Katira BH, Bouch S, Hsing V, Engelberts D, Amato MBP, et al. Limiting Overdistention or Collapse When Mechanically Ventilating Injured Lungs: A Randomized Study in a Porcine Model. *Am J Respir Crit Care Med*. 2024;209:1441–52. <https://doi.org/10.1164/rccm.202310-1895OC>.

18. Aristovich K. Opinion: the Future of Electrical Impedance Tomography. *J Electr Bioimpedance*. 2022;13:1–3. <https://doi.org/10.2478/joeb-2022-0001>.
19. Wisse JJ, Scaramuzzo G, Pellegrini M, Heunks L, Piraino T, Somhorst P, et al. Clinical implementation of advanced respiratory monitoring with esophageal pressure and electrical impedance tomography: results from an international survey and focus group discussion. *ICMx*. 2024;12:93. <https://doi.org/10.1186/s40635-024-00686-9>.
20. Jonkman AH, Telias I, Spinelli E, Akoumianaki E, Piquilloud L. The oesophageal balloon for respiratory monitoring in ventilated patients: updated clinical review and practical aspects. *Eur Respir Rev Eur Respiratory Soc (ERS)*. 2023;32:220186. <https://doi.org/10.1183/16000617.0186-2022>.
21. Mojoli F, Torriglia F, Orlando A, Bianchi I, Arisi E, Pozzi M. Technical aspects of bedside respiratory monitoring of transpulmonary pressure. *Ann Transl Med*. 2018;6:377. <https://doi.org/10.21037/atm.2018.08.37>.
22. Massion PB, Berg J, Samalea Suarez N, Parzibut G, Lambermont B, Ledoux D, et al. Novel method of transpulmonary pressure measurement with an air-filled esophageal catheter. *Intensive Care Med Experimental*. 2021;9:47. <https://doi.org/10.1186/s40635-021-00411-w>.
23. Gibot S, Conrad M, Courte G, Cravoisy A. Positive End-Expiratory Pressure Setting in COVID-19-Related Acute Respiratory Distress Syndrome: Comparison Between Electrical Impedance Tomography, PEEP/FiO2 Tables, and Transpulmonary Pressure. *Front Med (Lausanne)*. 2021;8:720920. <https://doi.org/10.3389/fmed.2021.720920>.
24. Scaramuzzo G, Spadaro S, Dalla Corte F, Waldmann AD, Böhm SH, Ragazzi R, et al. Personalized Positive End-Expiratory Pressure in Acute Respiratory Distress Syndrome: Comparison Between Optimal Distribution of Regional Ventilation and Positive Transpulmonary Pressure. *Crit Care Med*. 2020;48:1148–56. <https://doi.org/10.1097/CCM.0000000000004439>.
25. Pavlovsky B, Desprez C, Richard J-C, Fage N, Lesimple A, Chean D, et al. Bedside personalized methods based on electrical impedance tomography or respiratory mechanics to set PEEP in ARDS and recruitment-to-inflation ratio: a physiologic study. *Ann Intensiv Care*. 2024;14:1. <https://doi.org/10.1186/s13613-023-01228-4>.
26. Scaramuzzo G, Pavlovsky B, Adler A, Baccinelli W, Bodor DL, Damiani LF, et al. Electrical impedance tomography monitoring in adult ICU patients: state-of-the-art, recommendations for standardized acquisition, processing, and clinical use, and future directions. *Crit Care*. 2024;28:377. <https://doi.org/10.1186/s13054-024-05173-x>.
27. Francovich JE, Katira BH, Jonkman AH. Electrical impedance tomography to set positive end-expiratory pressure. *Curr Opin Crit Care*. 2025;31:319. <https://doi.org/10.1097/MCC.0000000000001255>.

Figures

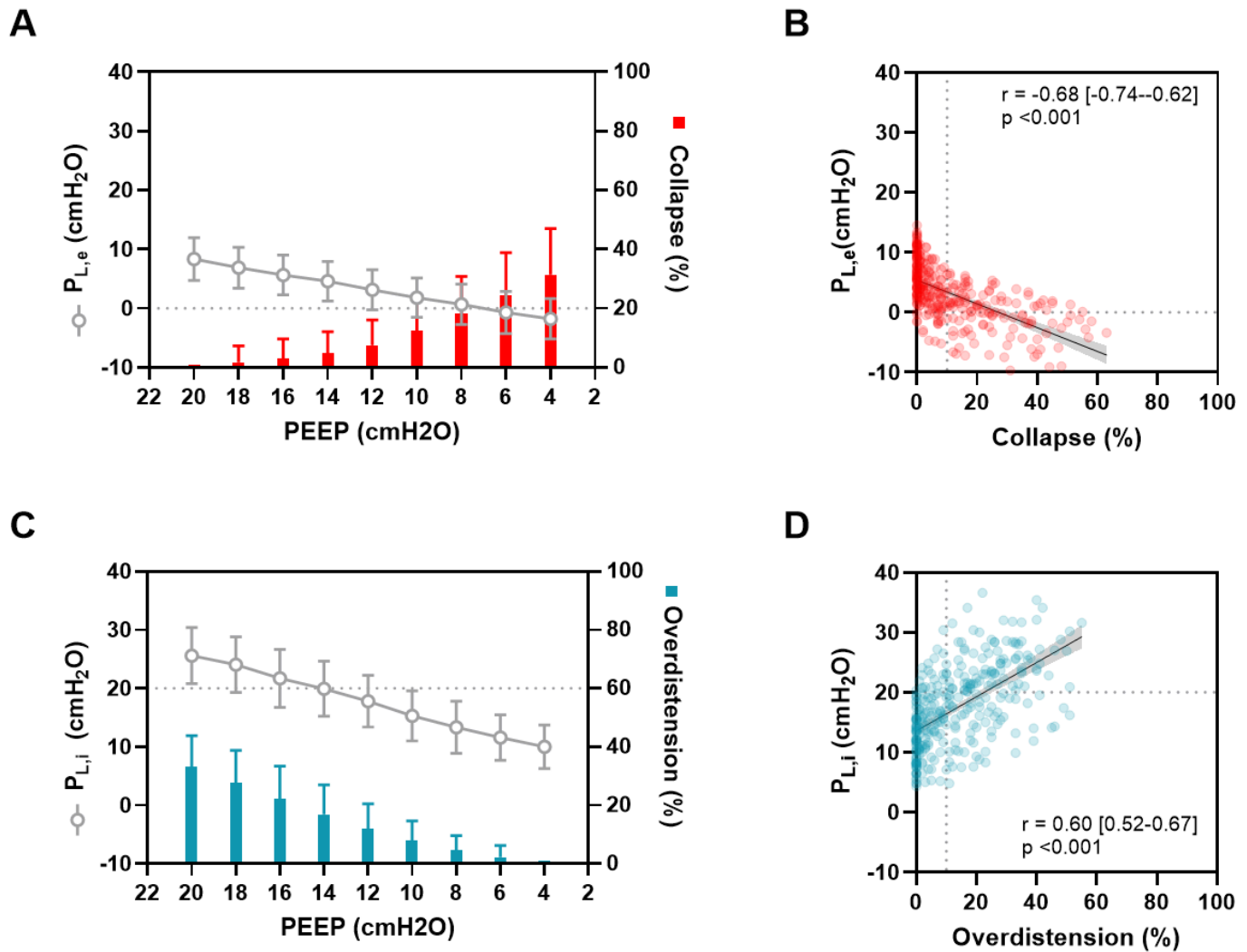


Figure 1

Relationship between transpulmonary pressures and the percentage of alveolar collapse and overdistension during the decremental positive end-expiratory pressure titration.

Panel A and C: evolution of transpulmonary pressures (grey circle) and alveolar collapse (red bar) or overdistension (blue bar) during the decremental PEEP titration. Data are expressed as mean $\pm$ SD. The horizontal dashed lines indicate $P_{L,e}$ of 0 cmH₂O and $P_{L,i}$ of 20 cmH₂O, respectively. Panel B: scatterplots depicting the correlation (and 95% confidence interval) between $P_{L,e}$ and the percentage of alveolar collapse. Solid line shows linear regression. Dashed vertical line shows 10% of collapsed lung units out of the total lung imaged by EIT. Dashed horizontal line shows $P_{L,e}$ at 0 cmH₂O – the theoretical threshold value beyond which the risk of alveolar collapse increase. Panel D: scatterplots depicting the correlation (and 95% confidence interval) between $P_{L,i}$ and the percentage of alveolar overdistension. Solid line shows linear regression. Dashed vertical line shows 10% of overdistended lung units out of the total lung imaged by EIT. Dashed horizontal line shows $P_{L,i}$ at 20 cmH₂O – the theoretical threshold value above which the risk of alveolar overdistension increase.

$P_{L,e}$: end-expiratory transpulmonary pressure (direct method), $P_{L,i}$: end-inspiratory transpulmonary pressure (elastance-derived method), PEEP: positive end-expiratory transpulmonary pressure.

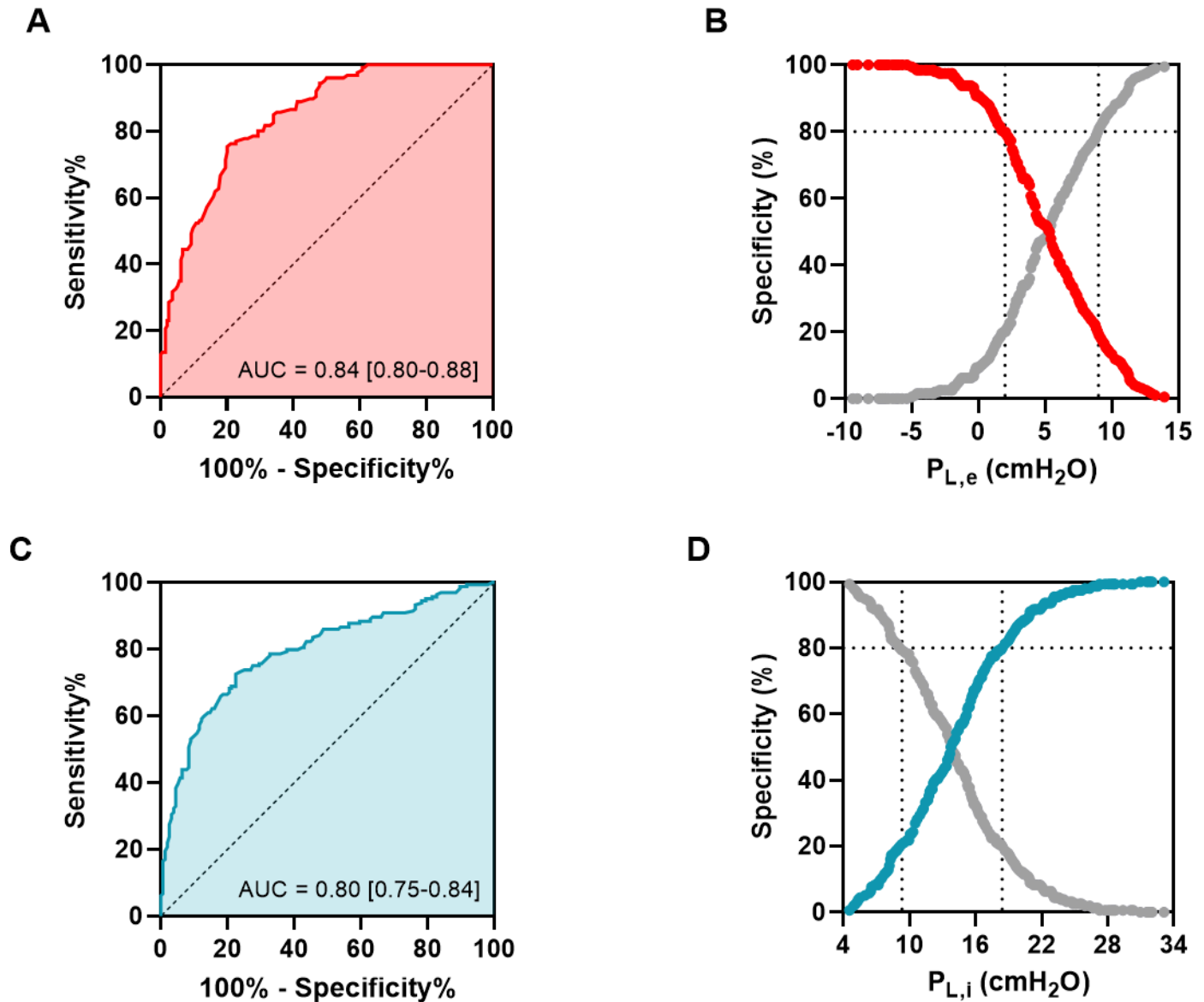


Figure 2

Ability of transpulmonary pressures to detect critical value (i.e. 10% out of the total lung imaged by electrical impedance tomography) of alveolar collapse and overdistension.

Panel A: receiver operating characteristic (ROC) curves for $P_{L,e}$ predicting alveolar collapse higher than 10%. Panel B: Specificity of $P_{L,e}$ to predict alveolar collapse lung units higher than 10% (red circles) or lower than 10% (grey circles) out of the total lung imaged by EIT. Pre-determined thresholds of interest (targeted specificity of 80% for both outcomes) are plotted. Panel C: receiver operating characteristic (ROC) curves for $P_{L,i}$ predicting alveolar overdistension higher than 10%. Panel D: Specificity of $P_{L,i}$ to predict alveolar overdistension lung units higher than 10% (blue circles) or lower than 10% (grey circles) out of the total lung imaged by EIT. Pre-determined thresholds of interest (targeted specificity of 80% for both outcomes) are plotted.

out of the total lung imaged by EIT. Pre-determined thresholds of interest (targeted specificity of 80% for both outcomes) are plotted.

AUC: area under the ROC curve, $P_{L,e}$: end-expiratory transpulmonary pressure (direct method), $P_{L,i}$: end-inspiratory transpulmonary pressure (elastance-derived method).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [TACOSSupplementaryMaterialv2.docx](#)