Critical Care

RESEARCH

Open Access

Optimum electrical impedance tomography-based PEEP and recruitment-to-inflation ratio in patients with severe ARDS on venovenous ECMO

Alexandre Coppens[1,2], Sarah Aissi James[2], Hadrien Roze[3,4], Charles Juvin[1,5], Benjamin Repusseau[4], Guillaume Lebreton[1,5], Charles-Edouard Luyt[1,2], Guillaume Hékimian[1,2], Juliette Chommeloux[1,2], Marc Pineton de Chambrun[1,2], Alain Combes[1,2], Guillaume Franchineau[6] and Matthieu Schmidt[1,2*]

Abstract

Rationale The significance of the Recruitment to Inflation (R/I) ratio in identifying PEEP recruiters in patients undergoing ultra-protective lung ventilation during venovenous ECMO is not well established.

Objectives To compare the concordance of the R/I ratio and Electrical Impedance Tomography (EIT) in determining optimum PEEP settings in severe ARDS patients on ECMO and ventilated with very low tidal volumes.

Methods Initially, a low-flow insufflation was performed to detect and measure the airway opening pressure (AOP). Subsequently, the R/I ratio was calculated from PEEP 15–5 cmH_2O, followed by a decremental PEEP trial (20–6 cmH_2O in 2 cmH_2O steps) monitored by EIT. The optimum EIT-based PEEP was defined as the intersection of the collapse and overdistension curves.

Main results Among 54 ECMO patients (tidal volume: 4.8 [3.0–6.0] mL/kg), 13 (24%) exhibited an airway opening pressure (AOP) of 11 (8–14) cmH_2O. The cohort's median R/I ratio was 0.43 (0.28–0.61). A tertile-based analysis of the R/I ratio (≤ 0.34; 0.34–0.54; > 0.54) revealed median optimum EIT-based PEEP of 8 [8–10], 10 [8–14], and 14 [12–16] cmH_2O, respectively. The R/I ratio demonstrated weak inverse correlations with lung overdistension ($R^2 = 0.19$) and positive correlations with lung collapse ($R^2 = 0.26$) measured by EIT ($p < 0.01$).

Conclusion The R/I ratio is feasible during ultra-protective ventilation and provides valuable indications for guiding PEEP titration. Specifically, an R/I ratio > 0.34 may help identify patients likely to benefit from further individualized PEEP optimization using EIT. In contrast, when the R/I ratio is ≤ 0.34, a moderate PEEP level (8–10 cmH_2O) may suffice.

Keywords Extracorporeal membrane oxygenation, Acute respiratory distress syndrome, Electrical impedance tomography, Recruitment-to-inflation ratio

*Correspondence:
Matthieu Schmidt
matthieu.schmidt@aphp.fr
Full list of author information is available at the end of the article

Introduction

Extracorporeal membrane oxygenation (ECMO is strongly recommended for patients with severe acute respiratory distress syndrome (ARDS) experiencing refractory hypoxemia or extremely high inspiratory airway pressures who cannot tolerate a volume- and pressure-limited ventilation strategy [1]. The key component of this therapy is the use of ultra-protective lung ventilation, designed to reduce the mechanical power applied to the lungs while allowing for lung healing [2–4]. This approach requires significantly reduced tidal volume, driving pressure, and plateau pressure. However, setting the appropriate positive end-expiratory pressure (PEEP) in these patients is particularly challenging. Insufficient PEEP can result in cyclic end-expiratory collapse and atelectrauma, while excessively high PEEP can cause overdistension, hyperinflation, barotrauma, and irreversible lung injury [5].

Electrical impedance tomography (EIT) offers individualized, non-invasive, real-time, bedside, radiation-free lung imaging with global and regional dynamic lung analyses [6, 7]. By evaluating the percentage of overdistension and lung collapse at different PEEP levels, EIT can help identify the optimum PEEP in patients with [5] and without ECMO [8]. However, this procedure is time-consuming and necessitates experienced physicians. Furthermore, despite its widespread availability, EIT is not yet present in all Intensive Care Units (ICUs).

The Recruitment-to-Inflation (R/I) ratio is another, simpler method that estimates the balance between recruited lung compliance and baseline compliance, reflecting the potential for alveolar recruitment with increasing PEEP [9]. To date, no studies have evaluated the R/I ratio in severe ARDS patients on ECMO, a scenario where tidal volume and minute ventilation are significantly reduced. Validating the concordance of this method with EIT could have immediate clinical applications for bedside physicians.

Our study aims to compare the concordance between EIT-determined optimum PEEP and R/I ratio to set PEEP in ECMO-supported severe ARDS patients receiving low tidal volume ventilation.

Material and method

Study design and ethical considerations

This bicentric prospective observational study was conducted from December 2021 to August 2023 in the 26-bed medical ICU of La Pitié Salpétrière Hospital, Paris, France, and the Surgical Thoracic ICU of the Pessac Hospital, France. This study was approved by an institutional review board (CPP 2022-A02589-34).

Patients

Intubated patients on VV ECMO were enrolled within the first week of ECMO. Inclusion criteria were 1) age > 18 years, 2) patients with severe ARDS on VV ECMO, and 3) controlled ventilation under continuous sedation with or without paralysis. Exclusion criteria were 1) contraindication for EIT (pacemaker, automatic implantable cardioverter defibrillator, thoracic or spinal cord trauma, recent thoracic surgery), 2) contraindications to high PEEP (undrained pneumothorax, bronchopleural fistula, 3) severe hemodynamic instability defined by systolic blood pressure (SBP) < 75 mmHg or mean arterial pressure (MAP) < 65 mmHg despite norepinephrine > 2 mg/h and/or heart rate < 50 beats/minute), 4) pregnancy or, 5) tidal volume < 2 mL/kg/ predicted body weight.

Data collection

At enrollment, demographics, clinical characteristics, and mechanical ventilation details were collected for all patients. ICU severity scores included simplified acute physiology score II (SAPS II) at ICU admission and sepsis organ failure assessment (SOFA) score on the day of enrollment. Follow-up data include ECMO and ICU length of stay, and mortality at days 30, 60, and 90.

Protocol

The patient was on passive pressure-controlled ventilation (PCV) with sedation using continuous infusion of propofol, sufentanil, and continuous neuromuscular blockades if necessary. Automated mattress movements, fluid boluses, and excessive diuresis were avoided to limit EIT signal interference. All patients were ventilated using a V500 or V800 ventilator (Drager, Lubeck, Germany). A silicone EIT belt, with 16 surface electrodes, was placed around the patient's thorax in one transversal plane corresponding to the fourth to fifth intercostal space then continuously connected to the EIT monitor (PulmoVista; Drager Medical GmbH) for bedside visualization. EIT data were generated by application of a small alternating electrical current (5 mA at 50 kHz). The data were digitally filtered using a low-pass filter with a cutoff frequency of 40/min to eliminate small impedance changes synchronous with the heart rate [5]. Synchronized recordings of EIT, airway pressure, and/or flow were continuously visualized on the Pulmovista screen and recorded in a single EIT patient file. The protocol was stopped if SaO_2 was < 85% or hemodynamic instability.

The research protocol is summarized in Fig. 1.

Step #1. The patients were ventilated following settings used in the ECMO arm of the EOLIA trial, using pressure-controlled ventilation with a constant driving

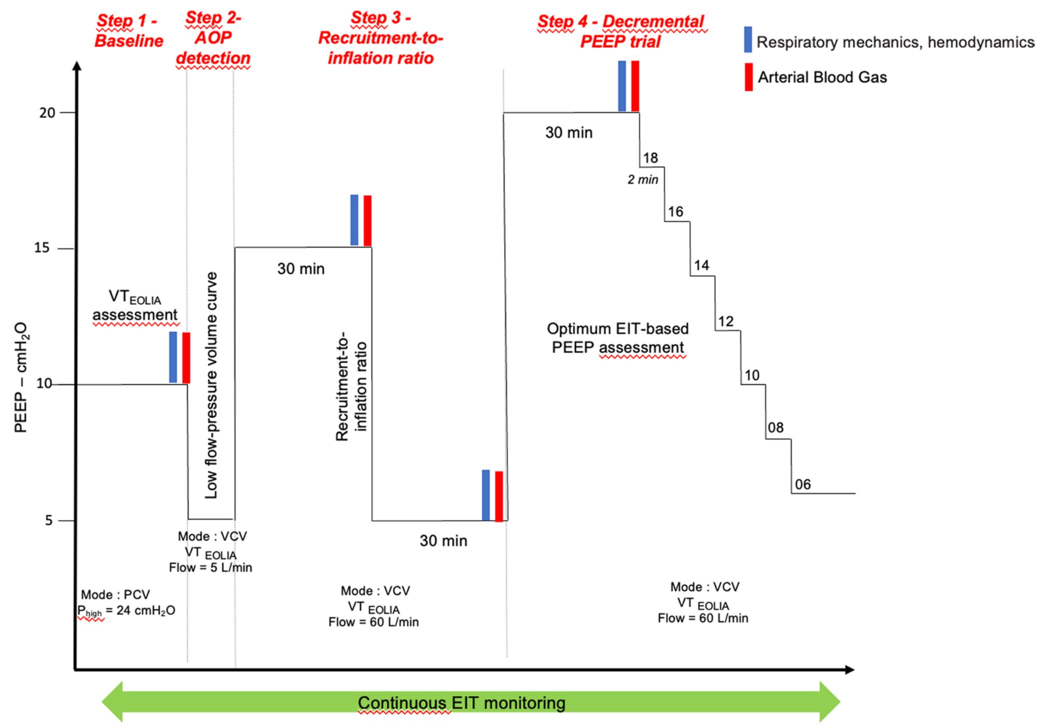

Fig. 1 Study protocol with applied positive end-expiratory pressure (PEEP) steps. For further details, see the METHODS section. AOP, airway occlusion pressure; PEEP, Positive End Expiratory Pressure; Pplat, plateau pressure; VTEOLIA, tidal volume obtained with a driving pressure set at 14 cmH_2O and a PEEP at 10 cmH_2O in pressure-controlled ventilation; PCV, Pressure controlled ventilation; VCV, volume-controlled ventilation; R/I ratio, recruitment to inflation ratio

pressure of 14 cmH_2O, a PEEP at 10 cmH_2O, and a respiratory rate set at 10 breaths/min to avoid auto-PEEP. The absence of auto-PEEP was assessed by real-time flow waveform monitoring and total PEEP measurements. To ensure that measured peak pressure accurately reflected plateau pressure, we verified that inspiratory flow was zero at the end of inspiration. The ECMO sweep gas flow was adjusted to maintain pH > 7.30 and $35 \leq PaCO_2 \leq 42$ mmHg. FiO_2 was minimized to maintain $PaO_2 > 80$ mmHg and $SaO_2 > 90\%$. The volume obtained with these settings, named VT_{EOLIA}, was recorded and used for all the following steps. Therefore, only the PEEP level and the flow will be modified during the following steps.

<u>*Step #2.*</u> A low-flow insufflation was performed to look for an airway opening pressure (AOP) [10]). Patients were ventilated in volume-controlled mode using the tidal volume determined in step #1 (i.e. VT_{EOLIA}). A PEEP of 5 cmH_2O was applied and flow was set at 5 L/min. If a significant alteration in compliance (close to that of the occluded ventilator circuit) at the beginning of the insufflation was detected on the pressure–volume curve (i.e., the initial linear portion of the pressure–volume curve), it reflected the presence of an expiratory airway collapse. AOP was measured as the airway pressure at which the volume delivered to the patient became 4 ml greater than the volume in the occluded circuit [10].

<u>*Step #3.*</u> For 30 min, the flow and the PEEP were set at 60 L/min, and 15 cmH_20 (i.e. $PEEP_{high}$), respectively. Respiratory mechanics (plateau pressure, total PEEP), hemodynamics (systolic and diastolic arterial pressure, and heart rate), and arterial blood gases were assessed after 30 min. A single breath maneuver during PEEP drops from 15 to 5 cmH_2O (i.e., $PEEP_{low}$) was performed and expired volume was measured (VT_{exp}). The recruited volume (ΔVT_{rec}) was calculated by subtracting the predicted volume in the absence of PEEP-induced recruitment and the VT_{EOLIA} from the $VT_{exp.}$ The ratio of the compliance of the recruited lung (Cr_{rec}) to the compliance of the baby lung with $PEEP_{low}$, called the R/I ratio was calculated [9]. The higher the R/I ratio, the greater the potential for lung recruitment.

In patients with complete airway closure and an AOP greater than $PEEP_{low}$, the same procedure was carried out using a $PEEP_{high}$ 10 cmH_2O above the AOP with a maximum PEEP of 20 cmH_2O. In this context, $PEEP_{low}$ was the level of AOP.

<u>*Step #4.*</u> A PEEP of 20cmH_2O, $VT_{EOLIA,}$ and a flow at 60 l/min were set for 30 min. Then, a decremental PEEP trial was performed from 20 to 6 cmH_2O

following successive 2-min steps of 2 cmH_2O. At each PEEP step, the percentage of overdistention and collapse was calculated with EIT as previously described [11]. The reported percentages of collapse or overdistention are derived from the calculus of relative changes in pixel compliance. For instance, the percentage of collapse refers to the percentage loss of pixel compliance over the range of applied PEEP from 20 to 6 cmH_2O. The minimal PEEP level (6 cmH_2O) was considered to have 0% overdistension. The percentages of overdistension at higher PEEP levels indicate the amount of overdistension that occurred compared to the low PEEP level. Optimum EIT-based PEEP was defined as the crossing point of the collapse and overdistension curves along the decremental PEEP trial [11]. If the crossing point was between two PEEP levels values were rounded up to the nearest integer. Similarly, in the case of similar results for two different PEEP levels, the one with the lowest percentage of collapse was selected as the optimum EIT-based PEEP. Noticeably, for patients with AOP, the decremental PEEP trial was conducted from 20 cmH_2O to the level of the AOP.

Endpoints and statistical analysis

The primary endpoint was the comparison of the means of the optimum EIT-based PEEP and the R/I ratio using a Student's t-test. Patients were stratified into tertiles of the R/I ratio (≤ 0.34, 0.34–0.54, and > 0.54) derived from our cohort. Secondarily, consistent with the original R/I ratio study [9], patients were categorized as high recruiters using the threshold of a R/I ratio > 0.50. We performed a ROC curve analysis to determine the optimal R/I ratio threshold for identifying patients with a high EIT-based PEEP (i.e., above the median PEEP of our cohort), applying Youden's Index.

The relationship between the R/I ratio and EIT-derived parameters such as total distension and collapse percentages was analyzed by linear regression. Similarly, the correlation between body mass index, number of days of mechanical ventilation before enrollment, number of ECMO days before enrollment, or tidal volume and optimum EIT-based PEEP, and the R/I ratio was evaluated by linear regression (Online Table 1).

Data were expressed as median (interquartile range) for continuous variables. Student's t-test or Mann–Whitney U test made comparisons between continuous variables as appropriate whereas categorical variables were

Table 1 Patient characteristics and outcomes according to recruitability estimated by the R/I ratio tertile

	All patients (n = 54)	Patients with R/I ratio ≤ 0.34 (n = 18)	Patients with R/I ratio 0.34–0.54 (n = 18)	Patients with R/I ratio > 0.54 (n = 18)	*P* value
Age, years	47 (39–58)	53 (41–59)	45 (37–58)	46 (37–59)	0.76
Male gender	34 (63%)	12 (67%)	10 (56%)	12 (67%)	0.73
BMI, kg/m^2	29.1 (24.6–35.7)	27.3 (23.4–36.0)	27.2 (24.7–31.1)	33.8 (26.1–36.2)	0.40
SAPS II	50 (41–69)	56.5 (41.5–76.8)	50 (40–57)	52.5 (33–70)	0.59
SOFA at enrolement	9 (8–12)	10.5 (7.8–12)	8 (4–10)	10.5 (8–13)	0.08
Risk factors of ARDS					
COVID-19	20 (37%)	7 (39%)	5 (28%)	8 (44%)	0.57
Bacterial pneumonia	19 (35%)	5 (28%)	6 (34%)	8 (44%)	0.57
Influenza	6 (11%)	2 (11%)	3 (17%)	1 (6%)	0.57
Other	9 (17%)	4 (22%)	4 (22%)	1 (6%)	0.30
ECMO parameters					
Femoro-jugular canulation	54 (100%)	18 (100%)	18 (100%)	18 (100%)	1.00
Flow, L/min	4.7 (4.2–5.1)	4.7 (4.2–5.0)	4.5 (4.3–5.3)	4.7 (4–5.2)	0.84
Sweep-Gas, L/min	4.0 (3.0–6.0)	4.0 (2.0–6.0)	5.0 (3.0–6.0)	4.0 (2.5–6.0)	0.61
Days on MV	7 (3–16)	8 (4–21)	4 (3–8)	8 (6–17)	0.12
Days on ECMO	2 (1–7)	5 (2–12)	1 (1–3)	4 (1–14)	0.06
Outcomes					
MV duration, days	40 (17–81)	43 (20–84)	21 (11–46)	55 (40–80)	0.06
ECMO duration, days	21 (7–49)	27 (16–58)	25 (8–42)	38 (14–61)	0.70
Mortality at day 30	10 (19%)	4 (22%)	3 (17%)	3 (17%)	0.88
Mortality at day 60	11 (20%)	4 (22%)	4 (22%)	3 (17%)	0.89
Mortality at day 90	13 (24%)	6 (33%)	4 (22%)	3 (17%)	0.49

BMI body mass index; *SAPS II* simplified acute physiology score II; *SOFA* sequential organ failure assessment; *ARDS* acute respiratory distress syndrome; *ECMO* extracorporeal membrane oxygenation; *PBW* predicted body weight; *MV* mechanical ventilation compared with $\chi 2$ test. A P value < 0.05 was considered statistically significant.

Statistical analyses were performed using JMP version 14.3 (SAS Institute, Cary, NC, USA) and Prism 8.3 software (GraphPad Software, San Diego, CA). The calculation of the AUC and Youden index was conducted using R version 4.4.2 with the pROC package.

Results

Study population

Out of 64 patients with severe ARDS on VV ECMO screened during the study period, 54 were included. Details on reasons for exclusion can be found in eFile 1. Their main characteristics are reported in Table 1. Briefly, the median age was 47 (39–58) years, 63% male, and SAPS II was 50 (41–69). The main etiology of ARDS was COVID-19-related pneumonia (n = 20) and bacterial pneumonia (n = 19). At enrollment, patients were on mechanical ventilation and ECMO for 7 (3–16) and 2 (1–7) days, respectively. Femoro jugular setting was used in all patients with an ECMO flow at 4.7 (4.2–5.1) L/min and a sweep gas flow set at 4.0 (3.0–6.0) L/min. ECMO duration was 26 (10–56) days with 31% of deaths within day-90.

Respiratory mechanics

With a driving pressure set at 14 cmH_2O and a PEEP at 10 cmH_2O in pressure-controlled ventilation mode in step #1 of our protocol, the resulting tidal volume (i.e., VT_{EOLIA}) was 4.8 (3.0–6.0) mL/kg predicted body weight. The compliance of the respiratory system was 21 (13–27) mL/cmH_2O.

Airway opening pressure

After a low-flow insufflation, 13 (24%) patients had an airway opening pressure (AOP) of 11 (8–14) cmH_2O while on VV ECMO. The AOP level did not significantly differ across R/I ratio tertiles (Table 2). Among these 13 patients, the optimum EIT-based PEEP was 14 (14–16) cmH_2O (eFile 2) vs 10 (8–12) cmH_2O in those without AOP ($p < 0.01$).

Recruitment to inflation ratio

In the whole cohort, the median R/I ratio was 0.43 (0.28–0.61). Respiratory mechanics stratified by R/I ratio tertiles (≤ 0.34, 0.34–0.54, > 0.54) are reported in Table 2. Compliance of the recruited lung differed significantly across tertiles (4 [1–8] mL/cmH_2O, 10 [6–14] mL/cmH_2O for 0.34–0.54, and 19 [12–28] mL/cmH_2O for R/I ratio ≤ 0.34, 0.34–0.54, or > 0.54 respectively; $p < 0.001$). The dichotomized analysis (R/I ratio ≤ 0.5 vs. > 0.5) is provided in the Supplementary Appendix (eFile 3 and 4), where patients with an R/I ratio > 0.5 had a significantly higher BMI (30.4 [24.2–34.8] vs. 28.5 [24.8–34.8] kg/m^2, $p = 0.05$).

Recruitment-to-inflation ratio and EIT-derived parameters

The R/I ratio exhibited a weak yet statistically significant negative correlation with lung overdistension ($R^2 = 0.19$; $p < 0.01$) and a positive correlation with lung collapse as assessed by EIT ($R^2 = 0.26$; $p < 0.01$) (Fig. 2). The BMI was positively correlated with optimum EIT-based PEEP ($R^2 = 0.14$, $p = 0.02$). Additionally, tidal volume showed an inverse correlation with the optimum EIT-based PEEP ($R^2 = 0.12$, $p = 0.03$). No significant correlation was identified between the number of days on mechanical ventilation or the number of days on ECMO before enrollment and the optimum EIT-based PEEP (eFile 5).

Optimum EIT-based PEEP and R/I ratio

Tertile-based analysis of the R/I ratio (≤ 0.34; 0.34–0.54; > 0.54) revealed median optimum EIT-based PEEP of 8 [8–10], 10 [8–14], and 14 [12–16] cmH_2O across the respective tertiles (Fig. 3). The optimum EIT-based PEEP was significantly lower in patients with an R/I ratio ≤ 0.5 [10 (8–14) cmH_2O, n = 32] compared to those with an R/I ratio > 0.5 [14 (12–16) cmH_2O, n = 22] ($p < 0.01$) (eFile 6). The ROC curve for the R/I ratio to classify patients into low or high PEEP groups based on EIT yielded an area under the curve (AUC) of 0.82 (eFile 7). The optimum R/I ratio threshold was 0.47, resulting in a sensitivity of 73.1% and a specificity of 85.7%.

Discussion

The main findings of this study can be summarized as follows: 1) In the cohort stratified by R/I ratio tertiles, optimal EIT-guided PEEP progressively increased from 8 [8–10] cmH_2O to 14 [12–16] cmH_2O when R/I ratio is ≤ 0.34 or > 0.54, respectively. 2) An R/I ratio ≤ 0.34 was consistently associated with lower optimum EIT-based PEEP, typically ranging from 8 to 10 cmH_2O. 3) The R/I ratio showed a weak inverse correlation with EIT-measured overdistension and a positive correlation with lung collapse. 4) Nearly 24% of patients exhibited an AOP.

Setting PEEP on VV ECMO remains a challenge for bedside clinicians. Franchineau et al. highlighted substantial variability in EIT-based optimum PEEP among 15 patients with severe ARDS, emphasizing the need for personalized ventilation strategies based on ARDS lesion distribution. EIT allows regional visualization of lung ventilation during VV ECMO [5]. Similarly, the RECRUIT trial in 108 COVID-19 ARDS patients demonstrated wide variability in recruitability, with non-recruiters showing no oxygenation improvement at any PEEP level [8]. While EIT provides critical physiological

Table 2 Response to positive end-expiratory pressure in patients on VV-ECMO according to the recruitability estimated by R/I ratio tertile

	All patients (n = 54)	Patients with R/I ratio ≤ 0.34 (n = 18)	Patients with R/I ratio 0.34–0.54 (n = 18)	Patients with R/I ratio > 0.54 (n = 18)	*P* value
Step #1					
VT_{EOLIA} ml	300 (190–380)	315 (243–360)	310 (188–365)	265 (150–420)	0.93
VT_{EOLIA}, ml/kg PBW	4.8 (3.0–6.0)	4.8 (4.0–5.4)	5.2 (2.9–6.0)	4.0 (2.9–6.0)	0.80
Crs, ml/cmH_2O	21 (13–27)	22.5 (17.3–25.7)	22.1 (13.4–26.1)	18.9 (10.7–30)	0.93
Step #2					
AOP level, cmH_2O	11 (8–14)	14 (13–14)	11 (8–13)	12 (10–14)	0.35
Presence of AOP	13 (24%)	2 (11%)	6 (33%)	5 (28%)	0.27
Step #3					
VTexp, mL	571 (381–846)	554 (346–770)	573 (385–778)	595 (329–867)	0.80
ΔVTrec, mL	90 (48–154)	42 (10–77)	84 (61–140)	174 (116–233)	< **0.001**
$PEEP_{low}$, cmH_2O	15	5 (5–5)	5 (5–10)	5 (5–10)	0.35
$PEEP_{high}$, cmH_2O	15 (15–16)	15 (15–15)	15 (15–20)	15 (15–20)	0.27
Compliance at low PEEP, mL/cmH_2O	24 (15–38)	26 (15–40)	22 (16–34)	24 (10–31)	0.76
Compliance of the recruited lung, mL/cmH_2O	10 (5–15)	4 (1–8)	10 (6–14)	19 (12–28)	< **0.001**
Recruitment to inflation ratio	0.43 (0.28–0.61)	0.20 (0.10–0.30)	0.44 (0.36–0.48)	0.68 (0.60–1.37)	< **0.001**
At the level of PEEPhigh					
pH	7.40 (7.35–7.44)	7.40 (7.33–7.45)	7.40 (7.38–7.45)	7.40 (7.34–7.44)	0.92
PO_2,mmHg	94 (75–117)	95 (75–113)	94 (70–114)	87 (73–129)	0.94
Systolic blood pressure, mmHg	116 (103–137)	115 (105–139)	112 (100–132)	121 (101–132)	0.90
Heart rate, mmHg	90 (75–104)	86 (68–104)	90 (76–105)	90 (76–105)	0.90
At the level of PEEPlow					
pH	7.40 (7.33–7.43)	7.40 (7.30–7.44)	7.42 (7.35–7.44)	7.37 (7.32–7.44)	0.75
PO_2, mmHg	85 (68–108)	93 (72–111)	88 (69–104)	73 (62–103)	0.16
Systolic blood pressure, mmHg	120 (109–135)	116 (107–131)	126 (109–144)	120 (110–132)	0.68
Heart rate, beats/min	86 (73–104)	85 (70–103)	86 (76–98)	90 (75–111)	0.83
Δ Systolic blood pressure between low and high PEEP, mmHg	0 (− 7 to 3)	1 (− 5 to 3)	− 1.5 (− 9 to 1)	0 (− 7 to 3)	0.36
ΔPO_2 between low and high PEEP, mmHg	0 (− 1–11)	0 (− 3 to 10)	1 (− 4 to 8)	0 (0 to 25)	0.67
Step #4					
Optimum EIT-based PEEP, cmH_2O	10 (8–14)	8 (8–10)	10 (8 to 14)	14 (12 – 16)	< **0.001**

Significant values are shown in bold

Crs compliance of the respiratory system; *PBW* predicted body weight; *VT* tidal volume; *AOP* airway occlusion pressure; *VTexp* expired volume measured during the recruitment-to-inflation ratio assessment; *ΔVrec* recruited volume calculated as the amount of upward shift in volume between two PEEP levels; *PEEP* positive end-expiratory pressure; *PEEPlow* lower positive end-expiratory pressure level used for recruitment-to-inflation ratio assessment, *PEEPhigh* higher positive end-expiratory pressure level used for recruitment-to-inflation ratio assessment; *EIT* electrical impedance tomography

insights, it requires specialized training, equipment, and time for bedside application [6].

The R/I ratio, derived from a single-breath maneuver, measures recruited volume over a PEEP range and identifies low versus high PEEP recruiters. This study reinforces the feasibility of using the R/I ratio in the context of ultra-protective ventilation, even with low tidal volumes. Its weak correlation with EIT-derived indices of overdistension and collapse is consistent with findings from Pavlosky et al. in 19 non-ECMO patients, supporting the notion that recruitability assessed by the R/I ratio does not directly reflect the balance between lung overdistension and collapse [12]. As the R/I ratio reflects global respiratory system compliance, it lacks the sensitivity to detect regional variations in lung mechanics and cannot reliably assess the risk of overdistension at the individual level, underscoring the complementary value of EIT in evaluating recruitment dynamics.

Although our results demonstrate a statistically significant relationship between the R/I ratio and EIT-derived optimum PEEP, the clinical utility is limited by the overlap in PEEP ranges observed when the R/I ratio

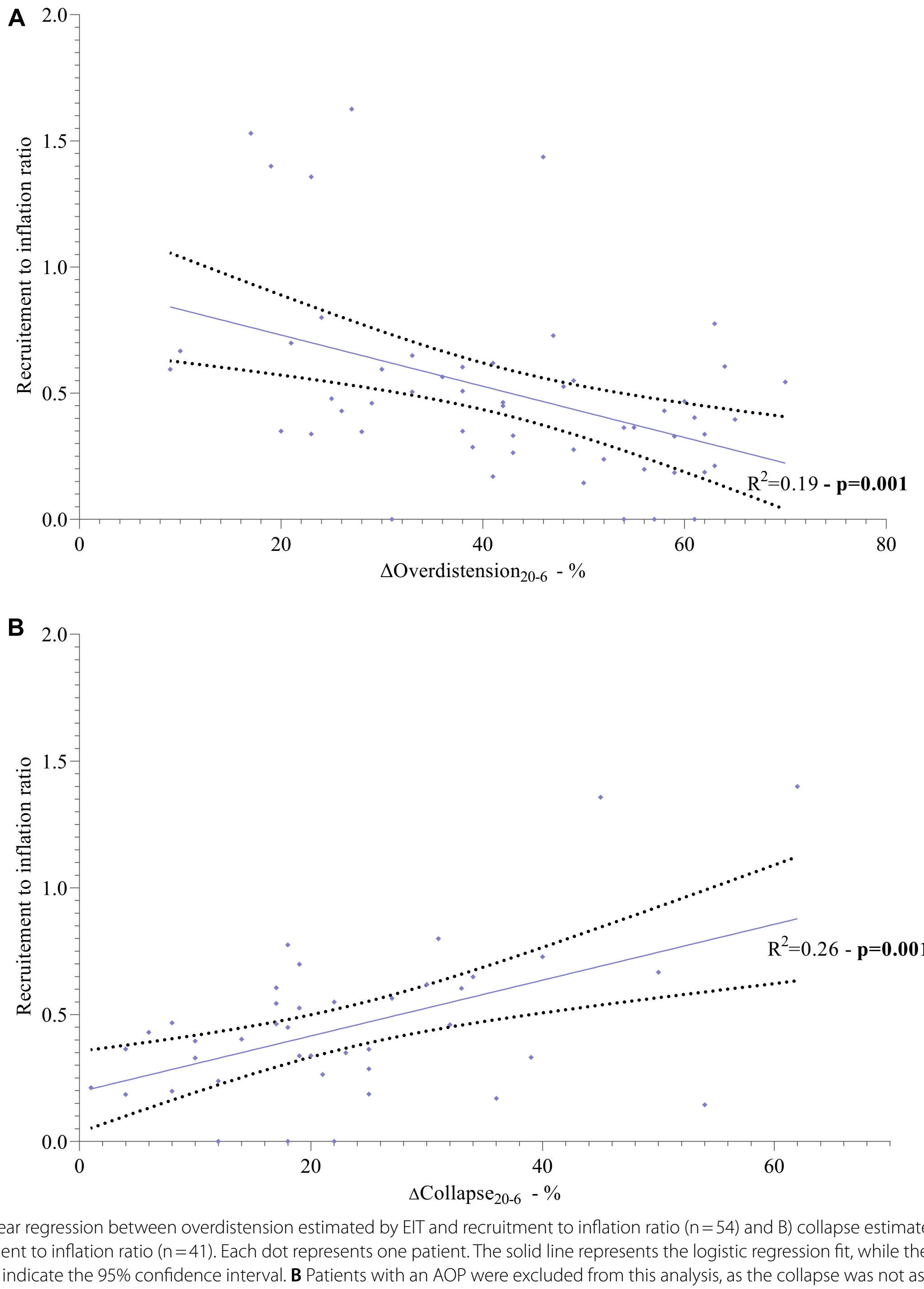

Fig. 2 **A** Linear regression between overdistension estimated by EIT and recruitment to inflation ratio (n = 54) and B) collapse estimated by EIT and recruitment to inflation ratio (n = 41). Each dot represents one patient. The solid line represents the logistic regression fit, while the curved dashed lines indicate the 95% confidence interval. **B** Patients with an AOP were excluded from this analysis, as the collapse was not assessed below the level of the AOP

exceeds 0.34 or even when divided according to the reference threshold of 0.5. Notably, a R/I ratio ≤ 0.34 was consistently associated with an EIT-derived PEEP of 8–10 cmH_2O—aligning with the lower PEEP levels recommended by the ELSO guidelines [13]. This finding suggests that, in patients with low R/I ratios, minimal PEEP settings may suffice, and further PEEP titration using EIT may offer limited added value. In contrast, when the R/I ratio exceeded 0.34, optimum EIT-derived PEEP values exhibited a broader distribution (e.g., 10

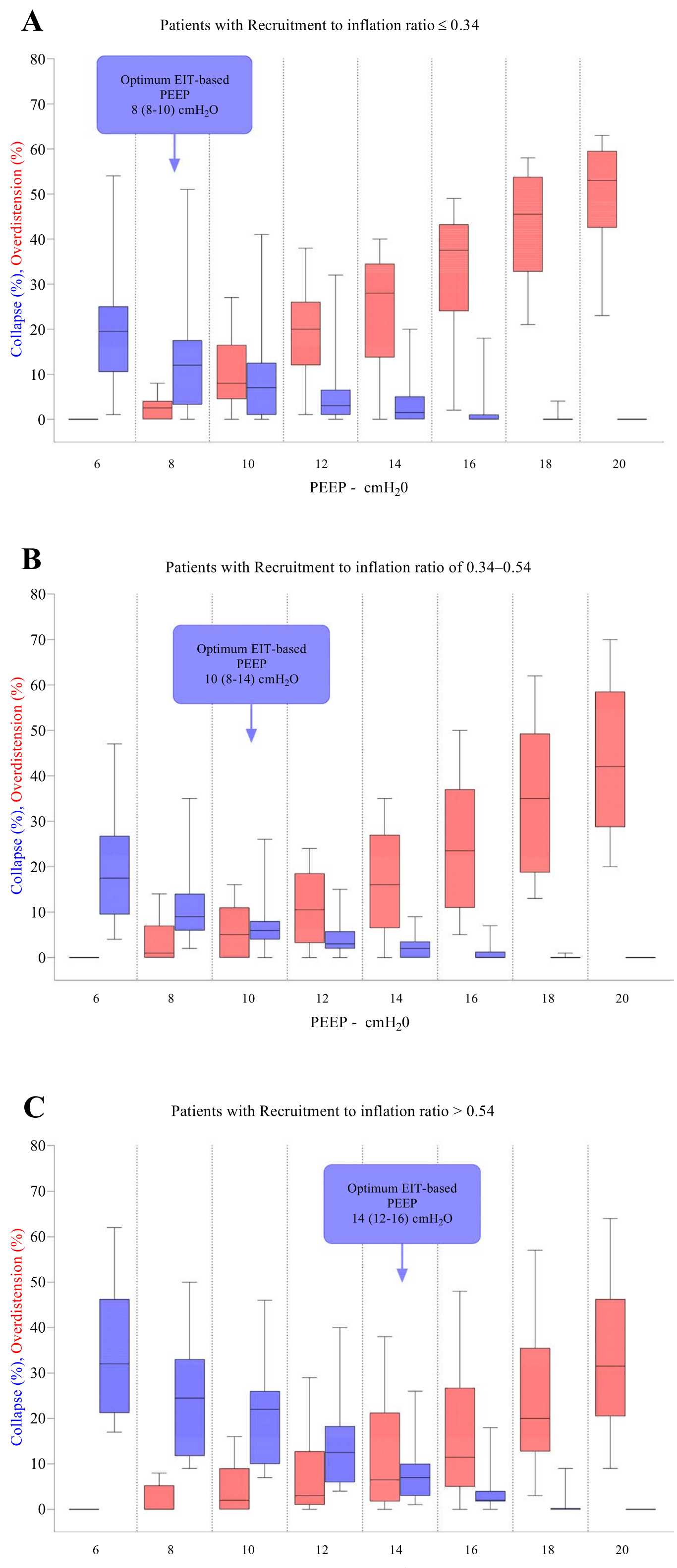

Fig. 3 Distribution of the percentage of lung collapse (blue) and overdistension (red) during the decremental positive end-expiratory pressure (PEEP) trial for **A** Patients with a R/I ratio ≤ 0.34 (n = 18), **B** Patients with R/I ratio between 0.34 and 0.54 (n = 18), and **C** Patients with R/I ratio > 0.54 (n = 18). The internal horizontal line of the box plot is the median whereas the lower and upper box limits represent quartile 1 and quartile 3, respectively. Bars represent maximum/minimum

[8–14] and 14 [12–16] cmH_2O for R/I ranges of 0.34–0.54 and > 0.54, respectively), providing less definitive guidance and highlighting the need for individualized assessment. In these cases, EIT-based titration may serve as a complementary tool to refine PEEP selection. Thus, the R/I ratio may be valuable as a preliminary screening method to stratify patients who could benefit from more detailed, EIT-guided PEEP optimization. Furthermore, given the dynamic nature of lung pathology during ECMO, regular reassessment of PEEP throughout the ECMO run is warranted.

The recently reported EITVent trial provides critical context for our findings [14]. While EIT-guided PEEP did not reduce mortality in the overall ARDS population, it significantly improved survival in the subgroup with higher lung recruitability (R/I ratio ≥ 0.5) [14]. This aligns with our observation that patients with an R/I ratio > 0.54, characterized by greater recruited lung compliance, received higher optimal PEEP and may represent a cohort where EIT adds clinical value. Conversely, low recruiters (R/I ratio ≤ 0.34) showed minimal recruitment potential, suggesting that standardized lower PEEP (8–10 cmH_2O) suffices for this subgroup. Collectively, these data underscore the R/I ratio's utility in identifying patients most likely to benefit from personalized PEEP strategies versus those where a simplified approach is adequate.

Although not the primary focus of our study, the 24% incidence of AOP identified in this VV ECMO cohort was lower than the 33–41% reported in non-ECMO ARDS populations [8, 9]. This discrepancy may be partially attributed to differences in BMI, as patients in our cohort had comparatively lower BMIs (30.5–33 kg/m^2). Furthermore, the use of ultra-low tidal volumes during VV ECMO could promote alveolar derecruitment and airway collapse, potentially affecting AOP prevalence. Additional research is needed to explore the effects of different tidal volume strategies and to assess AOP dynamics throughout ECMO support. Importantly, in patients with documented AOP, the R/I ratio was calculated using pressure measurements taken only above the AOP threshold. This approach may underestimate actual recruitability by omitting data from lower pressures where airway collapse may still be present. This methodological limitation could explain why AOP values did not significantly differ between R/I ratio subgroups (Table 2).

The strengths of our study include the broad inclusion of patients with varying respiratory system compliances and diverse ARDS etiologies. It represents the largest evaluation of AOP prevalence and R/I ratio assessment in a cohort of VV-ECMO patients undergoing ultra-protective lung ventilation. However, several limitations exist. First, a direct comparison of the R/I ratio and optimum EIT-based PEEP within the same interval was infeasible, as the R/I ratio is based on a 10 cmH_2O pressure drop. Second, a linear relationship between the R/I ratio and EIT-derived parameters was assumed, which is well established in COVID-19 ARDS [15] but less validated in other ARDS etiologies. Third, the threshold R/I ratio value distinguishing high and low PEEP recruiters remains debatable. Our threshold (0.47) differs from prior reports [9], reflecting variability influenced by ARDS etiology, timing of assessment, and disease severity. Moreover, the use of optimum EIT-based PEEP as the gold standard is contentious, as it assesses overdistension-collapsibility compromise rather than true recruitability. Notably, the PEEP limit of 20 cmH_2O in our protocol may have restricted the identification of patients who would benefit from higher pressures to achieve optimal alveolar recruitment. Finally, the median optimum EIT-based PEEP in our cohort (10 [8–14] cmH_2O) was lower than another VV-ECMO cohort's (14 [12–16] cmH_2O) [16], potentially due to our heterogeneous population, encompassing both COVID-19 and non-COVID-19 ARDS cases.

Conclusion

In this bicentric cohort study including 54 patients supported with VV-ECMO and ventilated with very low tidal volumes, the R/I ratio proved to be a useful indicator for guiding PEEP titration. Specifically, an R/I ratio > 0.34 may help identify patients likely to benefit from further individualized PEEP optimization using EIT. In contrast, when the R/I ratio is ≤ 0.34, a moderate PEEP level (8–10 cmH_2O) may suffice, making additional EIT-based assessment less critical. Prospective studies are warranted to confirm the clinical value of this stepwise approach combining R/I ratio screening and EIT-guided PEEP setting.

Abbreviations

ARDS	Acute respiratory distress syndrome
ECMO	Extracorporeal membrane oxygenation
EIT	Electrical impedance tomography
VV-ECMO	Venovenous-extracorporeal membrane oxygenation
ICU	Intensive care unit
SAPS	Simplified acute physiology score
SOFA	Sequential organ-failure assessment
PEEP	Positive end-expiratory pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05437-0.

Additional file1 (DOCX 545 KB)

Author contributions

A.C., S.A.J., H.R., G.F., and M.S. contributed to the conception of the study, data collection, data analysis, and interpretation, and drafted the manuscript. All authors contributed to data collection and interpretation and revised the manuscript critically for important intellectual content. All authors approved the final version of the manuscript.

Funding
None.

Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethics approval was obtained from the appropriate legal and ethical authorities (CPP 2022-A02589-34). According to local legislation, signed informed consent was waived as the study reports data routinely acquired in usual care.

Consent for publication
Not applicable.

Competing interests
Alain Combes reports grants from Getinge, and personal fees from Getinge, Baxter, and Xenios outside the submitted work. Matthieu Schmidt reports lecture fees from Getinge, Dräger, Baxter, and Fresenius Medical Care outside the submitted work. The other authors declare that they have no conflict of interest.

Author details
[1]UMRS_1166-ICAN, Service de Medecine Intensive Reanimation, iCAN, Institute of Cardiometabolism and Nutrition, INSERM, Hôpital de la Pitié–Salpêtrière, Sorbonne Universités, 47, Bd de L'Hôpital, 75651 Paris Cedex 13, France. [2]Medical Intensive Care Unit, Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Hospital, 75651 Paris Cedex 13, France. [3]Réanimation Polyvalente, Centre Hospitalier Côte Basque, Bayonne, France. [4]Department of Thoraco-Abdominal Anesthesiology and Intensive Care, Hopital Haut Leveque, Bordeaux University Hospital, University of Bordeaux, Bordeaux, France. [5]Cardiac Surgery Department, Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Hospital, 75651 Paris Cedex 13, France. [6]Intensive Care Unit, Centre Hospitalier Intercommunal de Poissy-Saint-Germain-en-Laye, 78300 Poissy, France.

Received: 16 February 2025 Accepted: 28 April 2025
Published online: 16 May 2025

References

1. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M, et al. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med. 2023;49:727–59.
2. Rudym D, Pham T, Rackley CR, Grasselli G, Anderson M, Baldwin MR, et al. Mortality in patients with obesity and acute respiratory distress syndrome receiving extracorporeal membrane oxygenation: the multicenter ECMObesity study. Am J Respir Crit Care Med. 2023;208:685–94.
3. Brodie D, Slutsky AS, Combes A. Extracorporeal life support for adults with respiratory failure and related indications: a review. JAMA. 2019;322:557.
4. Serpa Neto A, Schmidt M, Azevedo LCP, Bein T, Brochard L, et al. Associations between ventilator settings during extracorporeal membrane oxygenation for refractory hypoxemia and outcome in patients with acute respiratory distress syndrome: a pooled individual patient data analysis: mechanical ventilation during ECMO. Intensive Care Med. 2016;42:1672–84.
5. Franchineau G, Bréchot N, Lebreton G, Hekimian G, Nieszkowska A, Trouillet J-L, et al. Bedside contribution of electrical impedance tomography to setting positive end-expiratory pressure for extracorporeal membrane oxygenation–treated patients with severe acute respiratory distress syndrome. Am J Respir Crit Care Med. 2017;196:447–57.
6. 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. 2024;209:670–82.
7. Meier T, Luepschen H, Karsten J, Leibecke T, Großherr M, Gehring H, et al. Assessment of regional lung recruitment and derecruitment during a PEEP trial based on electrical impedance tomography. Intensive Care Med. 2008;34:543–50.
8. Jonkman AH, Alcala 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. 2023;208:25–38.
9. Chen Lu, Del Sorbo L, Grieco DL, Junhasavasdikul D, Rittayamai N, Soliman I, Sklar MC, Rauseo M, Ferguson ND, Fan E, Richard J-C, Brochard L. Potential for lung recruitment estimated by the recruitment-to-inflation ratio in acute respiratory distress syndrome. A clinical trial. Am J Respir Crit Care Med. 2020;201(2):178–87. https://doi.org/10.1164/rccm.201902-0334OC.
10. Chen L, Del Sorbo L, Grieco DL, Shklar O, Junhasavasdikul D, Telias I, et al. Airway closure in acute respiratory distress syndrome: an underestimated and misinterpreted phenomenon. Am J Respir Crit Care Med. 2018;197:132–6.
11. Costa ELV, Borges JB, Melo A, Suarez-Sipmann F, Toufen C, Bohm SH, et al. Bedside estimation of recruitable alveolar collapse and hyperdistension by electrical impedance tomography. Intensive Care Med. 2009;35:1132–7.
12. 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 Intensive Care. 2024;14:1.
13. Tonna JE, Abrams D, Brodie D, Greenwood JC, Mateo-Sidron JAR, Usman A, et al. Management of adult patients supported with venovenous extracorporeal membrane oxygenation (VV ECMO): guideline from the extracorporeal life support organization (ELSO). ASAIO J. 2021;67:601–10.
14. Yuan X, Zhong M, Li Z, Sang L, Huang X, Zhang R, et al. Electrical impedance tomography-guided PEEP and mortality of patients with the acute respiratory distress syndrome. Pre-print, The Lancet.
15. Pettenuzzo T, Sella N, Lorenzoni G, Calore A, Zarantonello F, Andreatta G, De Cassai A, Gregori D, Boscolo A, Navalesi P. The recruitment-to-inflation ratio is correlated with EIT-derived collapse and overdistention in COVID-19 ARDS. Am J Respir Crit Care Med. 2022;206(10):1284–6. https://doi.org/10.1164/rccm.202203-0555LE.
16. Franchineau G, Bréchot N, Hekimian G, Lebreton G, Bourcier S, Demondion P, et al. Prone positioning monitored by electrical impedance tomography in patients with severe acute respiratory distress syndrome on veno-venous ECMO. Ann Intensive Care. 2020;10:12.

Publisher's Note