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SYSTEMATIC REVIEW

Electrical impedance tomography-guided positive end-expiratory pressure titration in ARDS: a systematic review and meta-analysis

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Abstract

Purpose: Assessing efficacy of electrical impedance tomography (EIT) in optimizing positive end-expiratory pressure (PEEP) for acute respiratory distress syndrome (ARDS) patients to enhance respiratory system mechanics and prevent ventilator-induced lung injury (VILI), compared to traditional methods.

Methods: We carried out a systematic review and meta-analysis, spanning literature from January 2012 to May 2023, sourced from Scopus, PubMed, MEDLINE (Ovid), Cochrane, and LILACS, evaluated EIT-guided PEEP strategies in ARDS versus conventional methods. Thirteen studies (3 randomized, 10 non-randomized) involving 623 ARDS patients were analyzed using random-effects models for primary outcomes (respiratory mechanics and mechanical power) and secondary outcomes (PaO_2/FiO_2 ratio, mortality, stays in intensive care unit (ICU), ventilator-free days).

Results: EIT-guided PEEP significantly improved lung compliance ($n=941$ cases, mean difference (MD) = 4.33, 95% confidence interval (CI) [2.94, 5.71]), reduced mechanical power ($n=148$, MD = − 1.99, 95% CI [− 3.51, − 0.47]), and lowered driving pressure ($n=903$, MD = − 1.20, 95% CI [− 2.33, − 0.07]) compared to traditional methods. Sensitivity analysis showed consistent positive effect of EIT-guided PEEP on lung compliance in randomized clinical trials vs. non-randomized studies pooled (MD) = 2.43 (95% CI − 0.39 to 5.26), indicating a trend towards improvement. A reduction in mortality rate (259 patients, relative risk (RR) = 0.64, 95% CI [0.45, 0.91]) was associated with modest improvements in compliance and driving pressure in three studies.

Conclusions: EIT facilitates real-time, individualized PEEP adjustments, improving respiratory system mechanics. Integration of EIT as a guiding tool in mechanical ventilation holds potential benefits in preventing ventilator-induced lung injury. Larger-scale studies are essential to validate and optimize EIT's clinical utility in ARDS management.

Keywords: Mechanical ventilation, Ventilator-induced lung injury, ARDSNet

Introduction

Acute respiratory distress syndrome (ARDS) is a severe pulmonary condition characterized by respiratory failure and a significant mortality rate of 35–45% [1]. Mechanical ventilation is a critical intervention for ARDS patients; however, it may potentially exacerbate lung injury, giving rise to ventilator-induced lung injury (VILI) [2]. This underscores the need for personalized mechanical ventilation strategies to optimize patient outcomes

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[3]. A key strategy in supporting critically ill patients with ARDS is the application of positive end-expiratory pressure (PEEP), which helps to maintain alveolar recruitment [4–6] and improve oxygenation [7]. Nevertheless, the optimal level of PEEP remains the subject of ongoing debate and research [8, 9].

Traditionally, PEEP levels have been selected using conventional strategies, such as the ARDSNet PEEP/FiO_2 table, which has become the standard approach for ARDS management [10]. Although various methods have been explored to personalize PEEP, including lung compliance, trans-pulmonary pressure, and inflection points on pressure–volume curves, these approaches do not fully account for the heterogeneous nature of lung disease in ARDS patients and consequently, may not be optimal for all ARDS patients [11]. Recently, electrical impedance tomography (EIT), a non-invasive imaging technique providing real-time regional lung information, has emerged as a promising tool to guide PEEP settings [12] for individualize intervention, potentially leading to improved respiratory mechanics, a crucial determinant of VILI, in patients with ARDS.

Despite the potential benefits of EIT-guided PEEP, its effectiveness compared to conventional methods of PEEP titration remains unclear [11]. To provide a more comprehensive understanding of these approaches and guide clinicians in delivering the best possible care for ARDS patients, we conducted a meta-analysis of randomized trials and observational studies comparing EIT-guided PEEP titration to conventional methods to guide PEEP titration aiming to enable improving respiratory system mechanics and thus the risk of VILI.

Take-home message

This meta-analysis highlights the electrical impedance tomography (EIT)'s potential in optimizing personalized positive end-expiratory pressure settings for patients with acute respiratory distress syndrome (ARDS), advancing pulmonary function and respiratory system mechanics. The study underscores the need for further integration of EIT into clinical practice to minimize ventilator-induced lung injury, bridging the gap between scientific understanding and practical application in ARDS care

Materials and methods

Data sources

We conducted through searches of multiple databases (Scopus, PubMed, MEDLINE through Ovid, Cochrane Central Register of Controlled Trials, and LILACS) spanning from January 2012 to May 1, 2023. Our literature search combined terms (EIT OR "electrical impedance tomography") AND (ARDS OR "acute respiratory distress syndrome" OR "acute respiratory failure" OR "acute lung injury") AND ("mechanical ventilat*" OR peep OR "positive end-expiratory pressure" OR recruitment OR "tidal volume") in titles, abstracts, and keywords. The focus was on human studies from 2012 onwards, with no language restrictions. Additionally, we scrutinized the reference lists of eligible studies to uncover potentially relevant ones.

Study selection

We included randomized controlled trials (RCTs) and non-randomized studies (NRS) involving adult ARDS patients on invasive mechanical ventilation, defined by the Berlin definition [13]. These studies compared EIT-guided PEEP selection with conventional PEEP titration methods and reported at least one primary or secondary outcome of interest. Conventional methods encompassed ARDSNet FiO_2/PEEP table [13, 14], pressure–volume (PV) curve analysis, transpulmonary pressure adjustments, or other techniques. Exclusions comprised case reports, case series, conference abstracts, and review articles. Additionally, studies lacking control groups, those not specifically evaluating the impact of EIT-guided PEEP, or employed EIT solely for monitoring purposes were excluded.

Primary outcomes assessed respiratory system mechanics, including lung compliance, driving pressure (DP), plateau pressure, PEEP level, and mechanical power (MP). Secondary outcomes included PaO_2/FiO_2 ratio, 28-day all-cause mortality, in-hospital mortality, intensive care unit (ICU) lengths of stay, ventilator-free days, and EIT-based lung mechanics as reported by study authors. These EIT metrics included % of Silent Spaces, quantifying hypoventilated lung units, and %COV (coefficient of ventilation), indicating ventilation distribution along a gravitational axis [15–17].

Data abstraction and quality assessment

Two review authors (NS, CL) independently screened all titles and abstracts for eligibility. Subsequently, the full texts of the identified studies meeting initial screening criteria were assessed. The same two authors then independently determined eligibility for inclusion in the meta-analysis, with disagreements resolved through discussion or consultation with field experts (LB and HZ).

Data were extracted from included studies using a standardized form, with one author (NS) performing extraction and another author (CL) cross-checking the data. Information included patient characteristics (demographic and clinical), study population, intervention and control PEEP titration strategies, and outcomes (respiratory system mechanics measurements, PaO_2/FiO_2 ratio, mortality, lengths of stay, and ventilator-free days). We did not seek supplementary data beyond what was publicly available in the published articles.

Two authors (NS, CL) independently assessed the risk of bias (ROB) for each study. The Cochrane ROB-2 tool was used to for RCTs [18], while the Risk Of Bias In Non-randomized Studies-of Interventions (ROBINS-I) tool was applied to NRS [19]. ROB was categorized as low, of some concern, or high, with disagreements resolved through consensus.

Data synthesis

Random-effects models were employed to pool data in Review Manager Web [20]. We chose this model to account for potential variability across studies. This includes differences in study designs, patient populations, and interventions. Risk ratio (RR) for dichotomous outcomes and mean difference (MD) for continuous outcomes were reported, with 95% confidence intervals (CIs). Median and interquartile range data were converted to estimated mean and standard deviation where necessary [21]. A two-sided p value ≤ 0.05 indicated statistical significance.

Statistical heterogeneity was assessed using the Chi-square test (p value ≤ 0.1 considered significant) and I^2 statistic (0–40% not important, 30–60% moderate heterogeneity, 50–90% substantial heterogeneity, 75–100% considerable heterogeneity) [22]. Potential publication bias was evaluated using Egger's test and funnel plots in Stata when ≥ 10 studies were identified [23].

Sensitivity and subgroup analyses

Sensitivity analyses gauged the impact of RCT quality, high ROB, use of recruitment maneuvers before PEEP titration, studies with significant positive treatment effect, obese versus non-obese patients, ODCL method versus conventional method, EIT-guided PEEP versus ARDSNet PEEP/FiO_2 table, and ODCL method versus ARDSNet PEEP/FiO_2 table. Subgroup analyses were performed to investigate the sources of heterogeneity in the outcomes. These analyses were restricted to outcomes that were reported in a substantial number of studies, specifically those with a minimum of 10 studies contributing data. Aligning with our criteria of heterogeneity, we directed our subgroup analyses toward instances characterized by 'substantial heterogeneity' (I^2 values ranging from 50 to 90%) and 'considerable heterogeneity' (I^2 values between 75% and 100%). Subgroup analyses were conducted based on participant characteristics (age, body mass index, cause of ARDS, coronavirus disease 2019 (COVID-19), ARDS severity, duration of mechanical ventilation before data collection, duration of mechanical ventilation before inclusion) and interventions across studies (tidal volume, recruitment maneuver, incremental/decremental PEEP, conventional intervention, EIT intervention). Subgroup effects were assessed using the Chi-square test of heterogeneity (p value ≤ 0.1 indicating significance). Considerations included the number of trials and participants per subgroup, interaction plausibility, interaction importance, and potential confounding, guiding the decision to present or omit the subgroup analyses [22].

Results

Study identification

The search identified 421 records with 243 unique citations after removing duplicates. Of these, we excluded 218 records that did not meet eligibility criteria. We retrieved 25 full-text articles for closer review and excluded 12 studies that evaluated EIT monitoring [15, 24–27], included non-ARDS patients [28–30], had no control group [31, 32], or were letters with insufficient data [33, 34]. Consequently, we included 13 studies ($n = 623$ patients) in the analysis [35–47] (Fig. 1).

Characteristics of the included studies

Of the 13 included studies, 3 were RCTs, and 10 were non-randomized studies. Four studies specifically included patients with COVID-19-related ARDS. The average age of participants in the included studies ranged from 41 to 70 years. The average baseline PaO_2/FiO_2 ratio in 12 studies [35–44, 46, 47] was within the moderate ARDS range with only one study [45] reporting an average baseline PaO_2/FiO_2 ratio of 70 mmHg. One study [39] included patients on extracorporeal membrane oxygenation (ECMO). Although 2 studies reported average body mass index (BMI) within the normal range, 6 studies reported BMI within the overweight range and 5 studies within the obesity range. All participants in the included studies received sedation and neuromuscular blocking agents. Tidal volume administration varied across the studies. Ten studies [36–38, 41–47] utilized tidal volumes ranging from 6 to 8 ml/kg predicted body weight (PBW), while 2 studies [35, 40] used tidal volumes of 4–6 ml/kg PBW. Additionally, 1 study [39] utilized tidal volumes of 3–4 ml/kg PBW (Table 1).

In the control groups of the included trials, PEEP was titrated using PEEP/FiO_2 tables in 7 studies [36–38, 41–43, 47], PV curves in 2 studies [40, 45], end-expiratory transpulmonary sliding table in 2 studies [42, 44], and physician-set PEEP or clinical PEEP in 3 studies [35, 39, 46].

In the intervention group, PEEP titration was guided by EIT. Eight studies [35–37, 39–41, 45, 46] used the intercept point of cumulated collapse and overdistension percentages curves by Costa et al. to guide PEEP titration [12], while the remaining 5 studies utilized

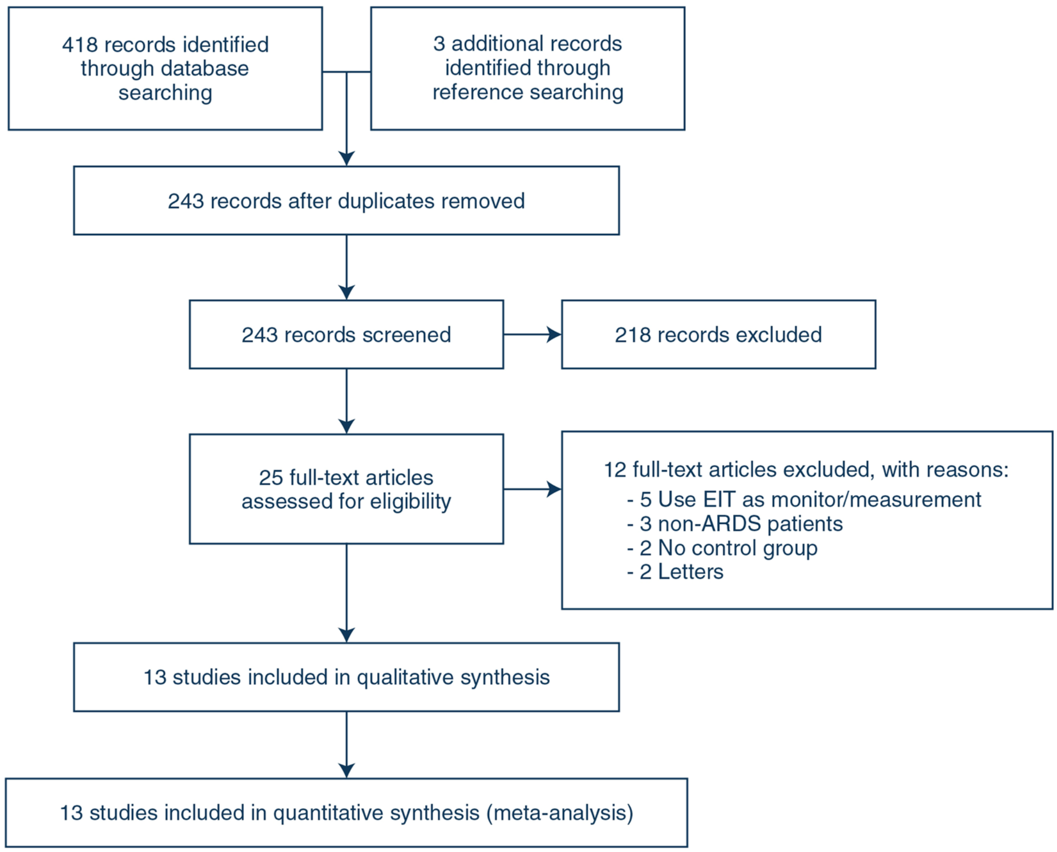


Fig. 1 Study selection process diagram: Initially, 421 records were identified, which were then deduplicated to yield 243 unique citations. Subsequently, 218 records were excluded based on eligibility criteria. Following a comprehensive review of 25 full-text articles, an additional 12 studies were excluded based on specific criteria. This resulted in 13 studies that met the inclusion criteria and were included in the analysis

various techniques including total percentage of collapse and distension [42, 44], global inhomogeneity (GI) index [38], regional compliance [43], and end-expiratory lung impedance (EELI) techniques [47]. Seven studies [35–37, 39, 43, 46, 47] performed a recruitment maneuver before PEEP titration, while the remaining six studies [38, 40–42, 44, 45] did not. The EIT belt was placed in the 4–5th intercostal space in 9 studies [35–37, 39–41, 44–46], in the 5–6th intercostal space in 1 study [47], and was not reported in 3 studies [38, 42, 43]. The position of the patient was reported in 9 studies [35–42, 44], with all patients in the supine position.

Risk of bias in included studies

The overall risk of bias was (supplemental Figures E1 and E2) judge to some concern. Notably, the main concern revolves around the potential bias due to confounding factors.

Primary outcomes

The pooled results of 12 studies indicated that compared to conventional methods, EIT-guided PEEP significantly increased lung compliance ($n=941$ analyzed cases, MD = 4.33, 95% CI [2.94, 5.71], $P<0.00001$, and $I^2=0\%$) (Fig. 2). EIT-guided (vs. conventional) PEEP titration significantly decreased mechanical power ($n=148$ analyzed cases, MD = − 1.99, 95% CI [− 3.51, − 0.47], $P=0.01$, and $I^2=0\%$) and DP ($n=903$ analyzed cases, MD = − 1.20, 95% CI [− 2.33, − 0.07], $P=0.04$, and $I^2=89\%$) (Figs. 3 and 4). However, there were no statistically significant differences between PEEP titration techniques regarding plateau pressure and PEEP level amidst significant heterogeneity (supplemental Figure E3 and E4).

Secondary outcomes

Three studies [40, 41, 45] ($n=259$ patients) provided mortality data. The meta-analysis of all-cause hospital mortality, based on two studies ($n=142$) with 62

Table 1 The main characteristics of the studies included in the meta-analysis

References	Design	Age (EIT guided vs. control, years)	Gender (male ratio)	Population	Baseline PaO_2/FiO_2 ratio	PEEP trial		Analyzed population	Outcomes
						EIT guided	Control		
Jonkman [35]	NRS	61 [51, 68]	65/108	*N* = 108 COVID-19 with moderate to severe ARDS	114 [92, 140]	ODCL	Physician-set PEEP	108 (108 vs 108)	The effects of PEEP on recruitability, respiratory mechanics and gas exchange, results of methods for EIT-based PEEP selection
Jimenez [36]	RCT	62 [50, 72] vs 59.5 [46, 67]	5/6 vs 4/6	*N* = 16 ARDS $PaO_2/FiO_2 < 150$ and PEEP > 8 cm/H_2O	130 [112–140]	ODCL	High-PEEP/FiO_2 tables	12 (6 vs 6)	Change in MP, 4ΔP + RR index, elastic–static, elastic–dynamic, and resistive powers, ΔP, Pplat, PaO_2/FiO_2ratio, and Crs
Somhorst [37]	NRS	64 [54–71]	59/75	*N* = 75 COVID-19 with moderate to severe ARDS	162 [110–201]	ODCL	High-PEEP/ FiO_2 tables	75 (75 vs 75)	Compare $PEEP_{base}$ with $PEEP_{set}$, respiratory mechanics (ΔP, Pplat, and Crs) and oxygenation (PaO_2/ FiO_2, PaO_2)
Liu [38]	NRS	70 ± 8	13/14	*N* = 14 ARDS with COPD	195.7 ± 47	GI index	Low- PEEP/ FiO_2 tables	14 (14 vs 14)	Respiratory mechanics, Gas exchange, Ventilation distribution
Di Pierro [39]	NRS	C-ARDS: 55 [43.5–60], NC-ARDS 41 [31–59]	14/24	*N* = 24 C-ARDS and NC-ARDS undergoing V-V ECMO	NR (reported as PaO_2: C-ARDS 86[72–96], NC-ARDS 76 [66–79])	ODCL	Physician-set PEEP	31 EIT evaluations (13 vs 13 C-ARDS, 18 vs 18 NC-ARDS)	Clinical features before and after to set PEEP in both patients with C-ARDS and NC-ARDS
Hsu [40]	RCT	55.7 ± 16.6 vs 62.2 ± 15.3	28/42 vs 36/45	*N* = 93 Moderate to severe ARDS PaO_2/FiO_2 ratio < 200	129.5 ± 39.4 vs 119.4 ± 38.9	ODCL	Point of maximal hysteresis in PV loop	87 (42 vs 45)	Respiratory system compliance, oxygenation, all-cause hospital mortality, weaning success rate, ICU length of stay, length of mechanical ventilation, presence of barotrauma

Table 1 (continued)

References	Design	Age (EIT guided vs. control, years)	Gender (male ratio)	Population	Baseline PaO_2/FiO_2 ratio	PEEP trial		Analyzed population	Outcomes
						EIT guided	Control		
He [41]	RCT	61 [44, 68] vs 66.5 [50, 73]	42/61 vs 35/56	*N* = 126 ARDS $PaO_2/FiO_2 < 300$	165 [106, 213] vs 176 [139, 222]	ODCL	Low $PEEP/FiO_2$ tables	117 (61 vs 56)	All-cause mortality 28 days after randomization, ventilator-free days at day 28, ICU length of stay, new onset barotrauma, oxygenation and respiratory mechanics, ΔD1-SOFA, ΔD2-SOFA
Gibot [42]	NRS	65 [62–71]	15/17	*N* = 17 COVID-19 related moderate to severe ARDS	136 [103–155]	Lowest total percentage collapsed + distended	Low/high PEEP/FiO_2, PL/FiO_2 tables	17 (17 vs 17)	Compared PEEP settings based on $PEEP/FiO_2$ tables, P_L/FiO_2 table, and EIT, MP, Δ*P*, Pplat, and Crs, %silent spaces
Becher [43]	NRS	65 ± 15	11/20	*N* = 20 ARDS	151 ± 5	Regional Crs	Low $PEEP/FiO_2$ tables	20 (20 vs 20)	Number of patients with stress below 27 mbar and release-derived strain below 2 after 4 h of ventilation, changes in SD_{RVD}, Crs, ΔP, PaO_2/FiO_2
Scaramuzzo [44]	NRS	63 [53–72]	13/20	*N* = 20 ARDS	149 [96–211]	SStot	P_L/FiO_2 tables	20 (20 vs 20)	ΔP, ΔP_L, MP, %silent spaces, regional compliance, COV, PaO_2/FiO_2
Zhao [45]	NRS	50.5 ± 13.3 vs 61.5 ± 19.2	15/24 vs 22/31	*N* = 55 ARDS $PaO_2/FiO_2 < 100$	70.85 ± 18.44	ODCL	2 cmH_2O above LIP on PV curve	55 (24 vs 31)	Respiratory mechanics and oxygenation, all-cause hospital mortality, barotrauma, weaning success rate, respiratory strategies (nitric oxide, ECMO, NMBA) after initial PEEP titration

Table 1 (continued)

References	Design	Age (EIT guided vs. control, years)	Gender (male ratio)	Population	Baseline PaO_2/ FiO_2 ratio	PEEP trial		Analyzed population	Outcomes
						EIT guided	Control		
Heines [46]	NRS	65 ± 15	25/39	*N* = 39 ARDS	147 ± 61	ODCL	Physician-set PEEP	39 (39 vs 39)	Oxygenation, PaO_2/ FiO_2 ratio and Crs before and after EIT analysis
Eronia [47]	NRS	66 ± 11	14/16	*N* = 16 AHRF PaO_2/ FiO_2 < 300 of non-cardiogenic origin, PEEP ≥ 5 cmH_2O (ARDS = 12)	160 ± 60	EELI	PEEP/FiO_2 table	14 (14 vs 14); (ARDS 11)	Compared the effects of selected PEEP on gas exchange, respiratory mechanics, hemodynamics and tidal recruitment/de-recruitment and overdistension

Mean ± standard deviation, median [interquartile range]

RCT randomized controlled trials, *NRS* non-randomized studies, *ARDS* acute respiratory distress syndrome, *C-ARDS* COVID-19-related acute respiratory distress syndrome, *NC-ARDS* ARDS from other etiologies, *V-V ECMO* veno venous extracorporeal membrane oxygenation, *COPD* chronic obstructive pulmonary disease, *ODCL* intercept point of cumulated collapse and overdistension percentages curves, *GI index* global inhomogeneity index, *SStot* total silent spaces (collapse + overdistension) using lowest PEEP level associated with a total percentage of SStot less than or equal to 15%, *EELI* end-expiratory lung impedance, *PEEP* positive end-expiratory pressure, *PEEP/*FiO_2 *tables* ARDS Network PEEP–fraction of inspired oxygen table, P_L/FiO_2 *tables* positive end-expiratory transpulmonary–fraction of inspired oxygen table, *MP* mechanical power, *ΔP* driving pressure, *RR* respiratory rate, *Pplat* plateau pressure, *Crs* lung compliance, PaO_2/FiO_2 arterial partial pressure of oxygen to fraction of inspired oxygen ratio, ΔD1-SOFA and ΔD2-SOFA difference in Sequential Organ Failure Assessment score at day 1 and day 2 compared with baseline, SD_{RVD} standard deviation of regional ventilation delay, ΔP_L transpulmonary driving pressure, *COV* center of ventilation, *NMBA* neuromuscular blocking agent, *PV* pressure–volume, *AHRF* acute hypoxemic respiratory failure

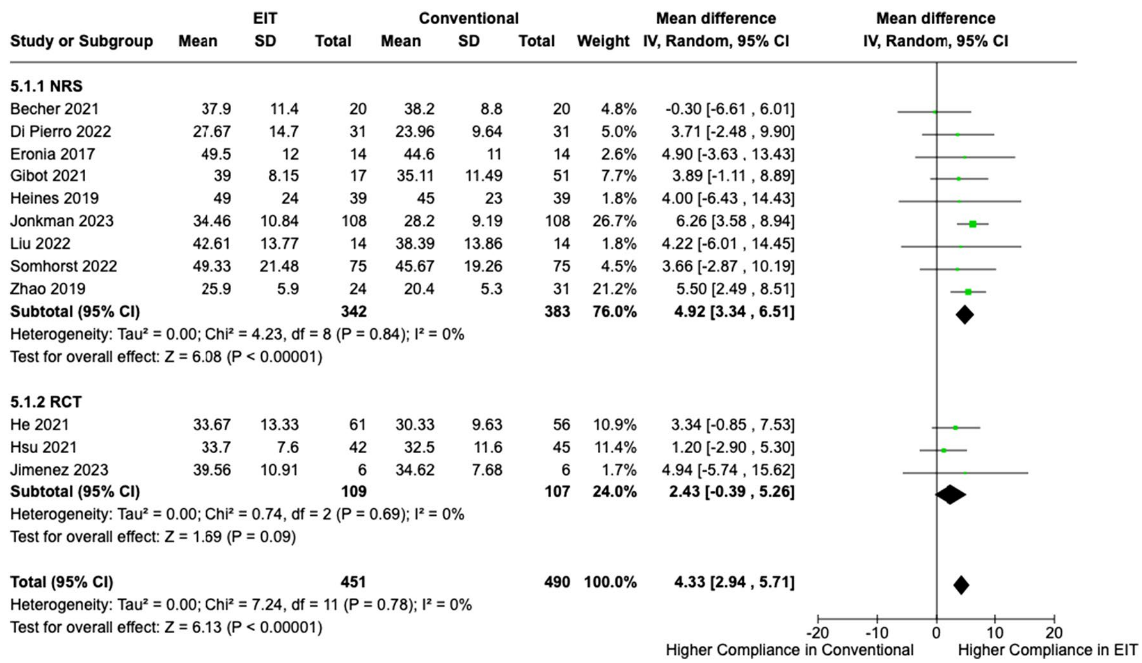


Fig. 2 Comparison of lung compliance between EIT-guided and conventional PEEP titration. *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

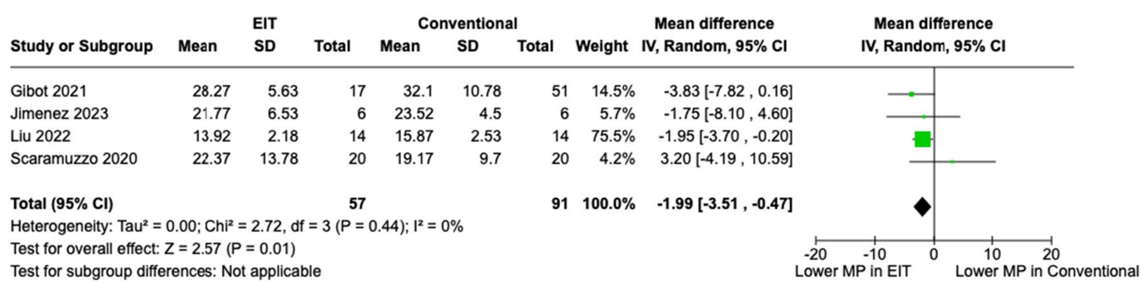


Fig. 3 Comparison of mechanical power between EIT-guided and conventional PEEP titration. *MP* mechanical power, *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

deaths, revealed a pooled relative risk (RR) of 0.59 (95% CI [0.39, 0.89], $P=0.01$, and $I^2=0\%$). Only 1 study [41] ($n=117$) with 28 deaths reported all-cause mortality within 28 days, yielded a RR of 0.80 (95% CI [0.42, 1.52], $P=0.49$). Post-hoc, pooling of the most protracted mortality (the combined overall effect estimates of both outcomes) including 259 patients and 90 deaths revealed a RR of 0.64, 95% CI [0.45, 0.91], $P=0.01$, and $I^2=0\%$ (supplemental Figure E5). Within these three studies, a trend towards higher lung compliance was noted, with one study demonstrating a significant improvement [45]. Concerning DP, two studies indicated a significant reduction [40, 45], while one study found no difference.

EIT-guided (vs. conventional) PEEP titration significantly reduced the % of silent spaces. (MD = − 5.23, 95% CI [− 8.72, − 1.74], $P=0.003$, and $I^2=5\%$) (supplemental Figure E6). However, the effect of EIT-guided PEEP on PaO_2/FiO_2 ratio, lengths of ICU stay, and % COV was not significantly different from conventional methods, and heterogeneity was observed in the forest plot (supplemental Figures E7–E9). One study each reported ventilator-free days at day 28 [41] and duration of ventilation [40] with nonsignificant between group differences.

Sensitivity and subgroup analyses

Sensitivity analysis of RCTs (vs NRS) consistently demonstrated a positive effect of EIT-guided PEEP on lung

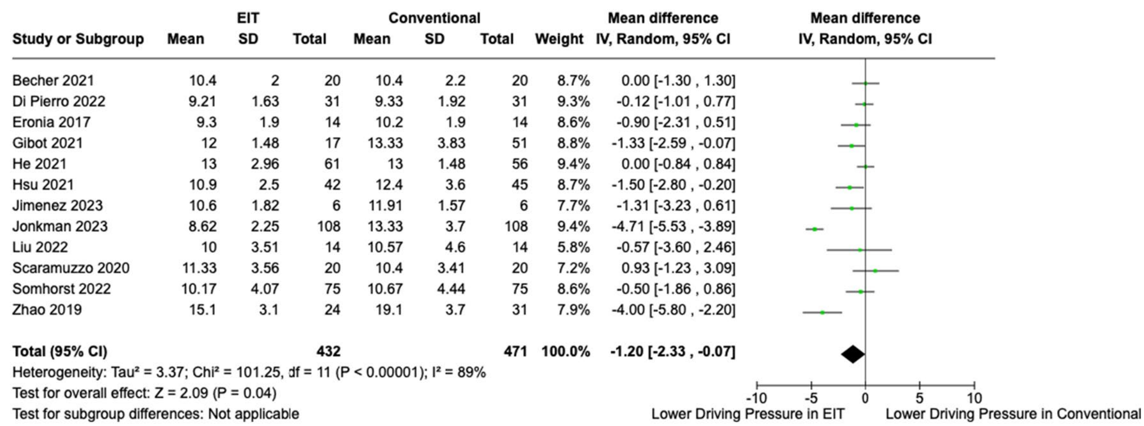


Fig. 4 Comparison of driving pressure between EIT-guided and conventional PEEP titration. *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

compliance, with the pooled (MD) of 2.43 (95% CI − 0.39 to 5.26), indicating a trend towards improvement, but with some uncertainty in the estimate (Fig. 2). To further assess the robustness of these findings, additional analyses were conducted: excluding studies with high risk of bias affirmed the consistency of the treatment effect (MD = 4.01, 95% CI [2.45, 5.57], $P < 0.00001$, and $I^2 = 0\%$), enhancing confidence in the results (Fig. 5a); isolating the impact of EIT-guided PEEP from potential confounders by excluding studies with recruitment maneuver before PEEP trials still showed a positive trend (MD = 3.85, 95% CI [1.95, 5.75], $P < 0.0001$, and $I^2 = 0\%$), thereby reinforcing the direct impact of EIT-guided PEEP on lung compliance (Fig. 5b); and removing studies with significant positive treatment effects revealed that the overall positive trend was not driven solely by a few outlier studies, as the impact on lung compliance remained consistently positive and statistically significant (MD = 2.86, 95% CI [0.95, 4.78], $P = 0.003$, and $I^2 = 0\%$) (Fig. 5c). We performed a sensitivity analysis for obese patient subgroup to test the hypothesis that EIT-guided PEEP might be particularly advantageous for this specific subgroup due to their distinct respiratory challenges, such as lung atelectasis, nonhomogeneous ventilation, and an increased risk of VILI. However, our results demonstrated that EIT-guided PEEP improves respiratory system compliance in both obese (MD = 5.27, 95% CI [3.22, 7.33], $P < 0.00001$, and $I^2 = 0\%$) and non-obese patients (MD = 3.54, 95% CI [1.66, 5.41], $P = 0.0002$, and $I^2 = 0\%$), compare with conventional PEEP methods (Fig. 5d). We conducted a thorough examination comparing different PEEP titration strategies: ODCL method versus conventional method, EIT-guided PEEP versus ARDSNet PEEP/FiO_2 table, and ODCL method versus ARDSNet PEEP/FiO_2 table. In comparing ODCL method to conventional method, we observed MD in lung compliance of 4.62 (95% CI [3.10, 6.14], $P < 0.00001$, and $I^2 = 0\%$) (Fig. 5e). Similarly, when comparing EIT-guided PEEP to the ARDSNet PEEP/FiO_2 table, MD was 3.17 (95% CI [0.76, 5.58], $P = 0.01$, and $I^2 = 0\%$) (Fig. 5f). Finally, the comparison between ODCL method and ARDSNet PEEP/FiO_2 table resulted in MD of 3.58 (95% CI [0.23, 6.93], $P = 0.04$, and $I^2 = 0\%$) (Fig. 5g). These analyses, with their respective statistical metrics, highlighted consistent trends in lung compliance outcomes across different methods, demonstrating the robustness and consistency of our findings. Furthermore, we did sensitivity analysis for DP by excluding studies with high risk of bias and those using tidal volume less than 6. Excluding the high risk of bias study altered the MD to − 0.96 (95% CI [− 2.12, 0.19], $P = 0.10$, $I^2 = 89\%$) (supplemental Figure E10), and after removing studies using tidal volumes less than 6 changed the statistics to MD − 0.82 (95% CI [− 1.63, − 0.02], $P = 0.04$, $I^2 = 61\%$) (supplemental Figure E11).

For DP, there was a statistically significant subgroup effect observed in the severity of ARDS, incremental/decremental PEEP, and conventional intervention (supplemental Table E1). Regarding PEEP, there was a statistically significant subgroup effect observed in cause of ARDS, the severity of ARDS, recruitment maneuver before PEEP trial, and conventional and EIT interventions. For PaO_2/FiO_2 ratio, there was a statistically significant subgroup effect observed in recruitment maneuver before PEEP trial and EIT intervention. Notwithstanding, covariates were unevenly distributed across subgroups, indicating that the subgroup analysis might not produce valid results. However, the covariate distribution was not concerning for the comparison of EIT (vs. conventional)-guided PEEP in PaO_2/FiO_2 ratio classified in the presence and absence of a recruitment maneuver. Although

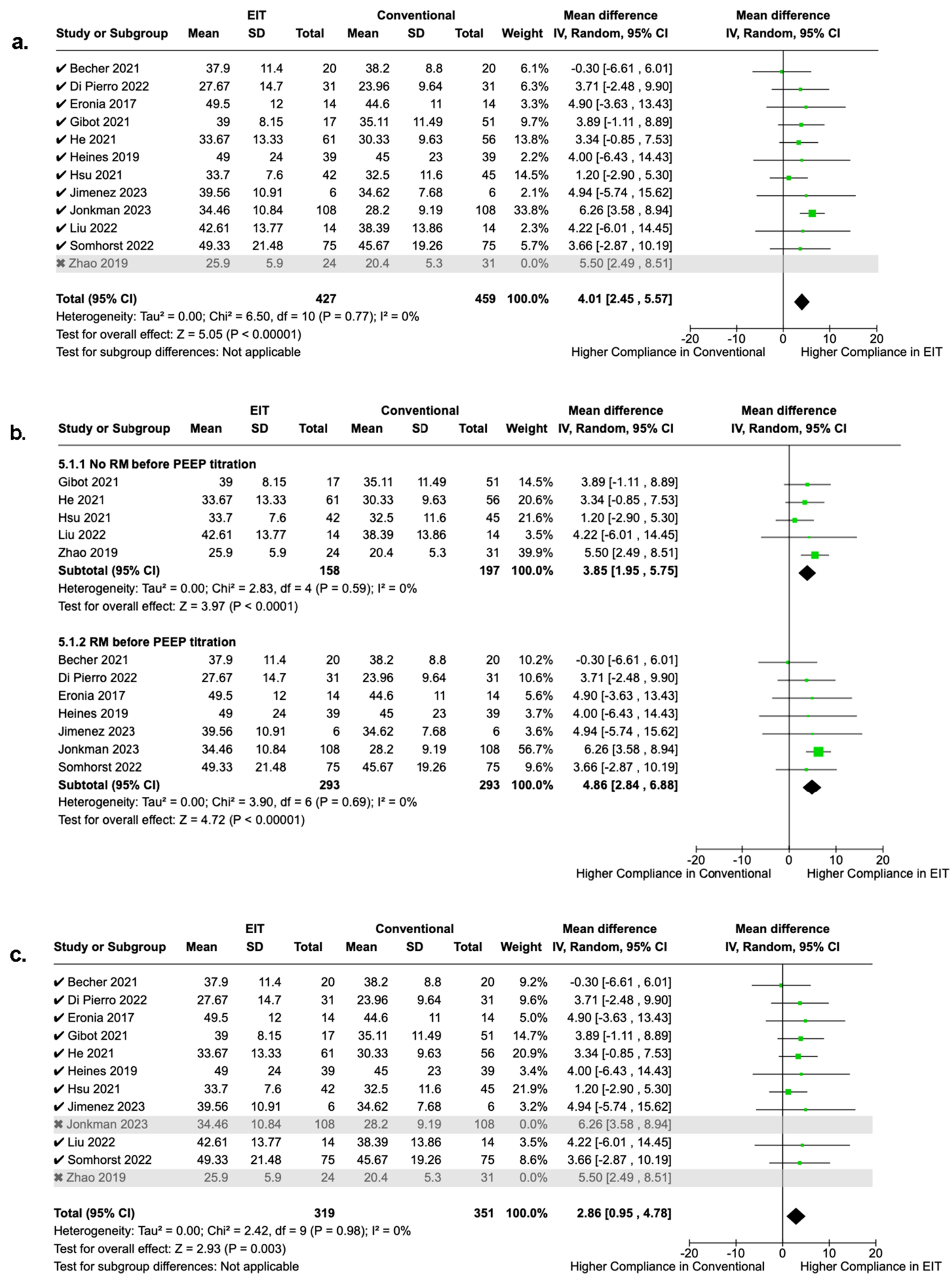
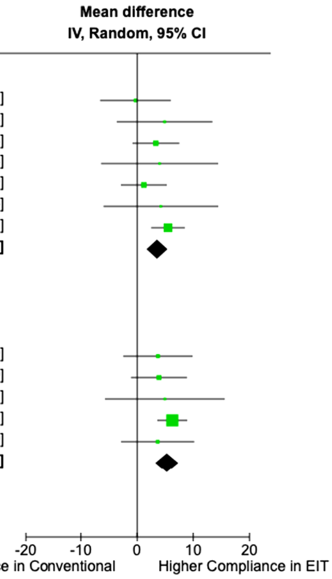


Fig. 5 Forest plots of sensitivity analysis for lung compliance: **a** Excluding studies with high risk of bias, **b** excluding studies with recruitment maneuver before PEEP, **c** excluding studies with significant positive treatment effect, **d** obese and non-obese patients, e ODCL method versus conventional method, **f** EIT-guided PEEP versus ARDSNet PEEP/FiO2 table, **g** ODCL method versus ARDSNet PEEP/FiO_2 table. *RM* recruitment maneuver, *BMI* body mass index, *ODCL* intercept point of cumulated collapse and overdistension percentages curves, *CI* confidence interval, *df* degrees of freedom, I^2 heterogeneity statistic, *IV* inverse variance method

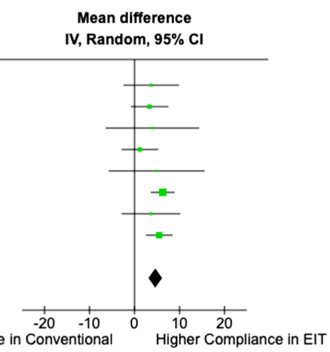
d.

Study or Subgroup	EIT Mean	EIT SD	EIT Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean difference IV, Random, 95% CI
5.1.1 BMI less than 30								
Becher 2021	37.9	11.4	20	38.2	8.8	20	8.8%	-0.30 [-6.61 , 6.01]
Eronia 2017	49.5	12	14	44.6	11	14	4.8%	4.90 [-3.63 , 13.43]
He 2021	33.67	13.33	61	30.33	9.63	56	20.0%	3.34 [-0.85 , 7.53]
Heines 2019	49	24	39	45	23	39	3.2%	4.00 [-6.43 , 14.43]
Hsu 2021	33.7	7.6	42	32.5	11.6	45	20.9%	1.20 [-2.90 , 5.30]
Liu 2022	42.61	13.77	14	38.39	13.86	14	3.4%	4.22 [-6.01 , 14.45]
Zhao 2019	25.9	5.9	24	20.4	5.3	31	38.8%	5.50 [2.49 , 8.51]
Subtotal (95% CI)			**214**			**219**	**100.0%**	**3.54 [1.66 , 5.41]**
Heterogeneity: Tau² = 0.00; Chi² = 4.44, df = 6 (P = 0.62); I² = 0%								
Test for overall effect: Z = 3.70 (P = 0.0002)								
5.1.2 BMI more than 30								
Di Pierro 2022	27.67	14.7	31	23.96	9.64	31	11.0%	3.71 [-2.48 , 9.90]
Gibot 2021	39	8.15	17	35.11	11.49	51	16.9%	3.89 [-1.11 , 8.89]
Jimenez 2023	39.56	10.91	6	34.62	7.68	6	3.7%	4.94 [-5.74 , 15.62]
Jonkman 2023	34.46	10.84	108	28.2	9.19	108	58.6%	6.26 [3.58 , 8.94]
Somhorst 2022	49.33	21.48	75	45.67	19.26	75	9.9%	3.66 [-2.87 , 10.19]
Subtotal (95% CI)			**237**			**271**	**100.0%**	**5.27 [3.22 , 7.33]**
Heterogeneity: Tau² = 0.00; Chi² = 1.30, df = 4 (P = 0.86); I² = 0%								
Test for overall effect: Z = 5.04 (P < 0.00001)								



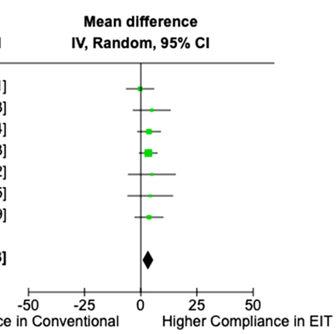
e.

Study or Subgroup	ODCL Mean	ODCL SD	ODCL Total	Conventional Mean	Conventional SD	Conventional Total	Weight	Mean difference IV, Random, 95% CI
Di Pierro 2022	27.67	14.7	31	23.96	9.64	31	6.0%	3.71 [-2.48 , 9.90]
He 2021	33.67	13.33	61	30.33	9.63	56	13.1%	3.34 [-0.85 , 7.53]
Heines 2019	49	24	39	45	23	39	2.1%	4.00 [-6.43 , 14.43]
Hsu 2021	33.7	7.6	42	32.5	11.6	45	13.7%	1.20 [-2.90 , 5.30]
Jimenez 2023	39.56	10.91	6	34.62	7.68	6	2.0%	4.94 [-5.74 , 15.62]
Jonkman 2023	34.46	10.84	108	28.2	9.19	108	32.1%	6.26 [3.58 , 8.94]
Somhorst 2022	49.33	21.48	75	45.67	19.26	75	5.4%	3.66 [-2.87 , 10.19]
Zhao 2019	25.9	5.9	24	20.4	5.3	31	25.5%	5.50 [2.49 , 8.51]
Total (95% CI)			**386**			**391**	**100.0%**	**4.62 [3.10 , 6.14]**
Heterogeneity: Tau² = 0.00; Chi² = 4.99, df = 7 (P = 0.66); I² = 0%								
Test for overall effect: Z = 5.96 (P < 0.00001)								
Test for subgroup differences: Not applicable								



f.

Study or Subgroup	EIT Mean	EIT SD	EIT Total	PEEP/FiO2 table Mean	PEEP/FiO2 table SD	PEEP/FiO2 table Total	Weight	Mean difference IV, Random, 95% CI
Becher 2021	37.9	11.4	20	38.2	8.8	20	14.6%	-0.30 [-6.61 , 6.01]
Eronia 2017	49.5	12	14	44.6	11	14	8.0%	4.90 [-3.63 , 13.43]
Gibot 2021	39	8.15	17	35.33	11.08	34	20.1%	3.67 [-1.70 , 9.04]
He 2021	33.67	13.33	61	30.33	9.63	56	33.1%	3.34 [-0.85 , 7.53]
Jimenez 2023	39.56	10.91	6	34.62	7.68	6	5.1%	4.94 [-5.74 , 15.62]
Liu 2022	42.61	13.77	14	38.39	13.86	14	5.5%	4.22 [-6.01 , 14.45]
Somhorst 2022	49.33	21.48	75	45.67	19.26	75	13.6%	3.66 [-2.87 , 10.19]
Total (95% CI)			**207**			**219**	**100.0%**	**3.17 [0.76 , 5.58]**
Heterogeneity: Tau² = 0.00; Chi² = 1.53, df = 6 (P = 0.96); I² = 0%								
Test for overall effect: Z = 2.58 (P = 0.010)								
Test for subgroup differences: Not applicable								



g.

Study or Subgroup	ODCL Mean	ODCL SD	ODCL Total	PEEP/FiO2 table Mean	PEEP/FiO2 table SD	PEEP/FiO2 table Total	Weight	Mean difference IV, Random, 95% CI
He 2021	33.67	13.33	61	30.33	9.63	56	63.9%	3.34 [-0.85 , 7.53]
Jimenez 2023	39.56	10.91	6	34.62	7.68	6	9.8%	4.94 [-5.74 , 15.62]
Somhorst 2022	49.33	21.48	75	45.67	19.26	75	26.3%	3.66 [-2.87 , 10.19]
Total (95% CI)			**142**			**137**	**100.0%**	**3.58 [0.23 , 6.93]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 2 (P = 0.96); I² = 0%								
Test for overall effect: Z = 2.10 (P = 0.04)								
Test for subgroup differences: Not applicable								

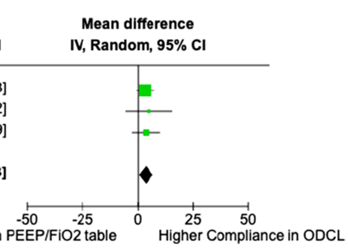


Fig. 5 continued

EIT (vs conventional) PEEP titration had a significantly higher PaO_2/FiO_2 ratio, there was moderate between trial heterogeneity within the recruitment maneuver subgroup, resulting in uncertainty regarding the validity of the treatment effect estimate.

Publication bias

The Egger's test yielded a non-significant *p* value of 0.26, suggesting the absence of publication bias. Inspection of the contour-enhanced funnel plot analysis, our findings suggest a mixed pattern of study results with regard to lung compliance. Some studies demonstrated significant positive treatment effects with higher compliance, while others showed non-significant effects with potentially varied compliance levels. The absence of significant publication bias, as indicated by the Egger's regression test, lends support to the validity of our results (Supplemental Figure E12).

Discussion

In this meta-analysis, we noted a significant enhancement in lung compliance and a reduction in mechanical power when employing EIT-guided PEEP titration compared to conventional methods. These effects were observed in the absence of heterogeneity. Additionally, a noteworthy reduction in DP was identified, despite the presence of substantial heterogeneity.

In the pooled analysis, patients afflicted with ARDS, who received optimized PEEP adjustments guided by EIT, exhibited elevated lung compliance compared to those whose PEEP was titrated using conventional methods. This augmentation in compliance is noteworthy, as it signifies an enhanced recruitment of lung tissue and the potential mitigation of lung overdistension. This finding aligns with the underlying physiological rationale of real-time monitoring of EIT which enables personalized adjustments of PEEP based on the localized distribution of lung ventilation [48–50]. As such, the capacity of EIT to visualize ventilation distribution within distinct lung regions facilitates data-driven insights into PEEP titration and ventilator management. Specifically, EIT enables quantification of lung inhomogeneity, analysis of regional and global ventilation patterns, and identification of potentially recruitable lung areas [31, 51, 52].

Recent investigations have demonstrated the feasibility of employing EIT-guided PEEP titration in ARDS patients [25, 53]. To this end, Franchineau et al. have shown the feasibility and additional support provided by EIT-driven PEEP titration, even in severe ARDS patients undergoing ECMO. The strategies for EIT-guided PEEP titration involved various approaches, including the assessment of overdistension and collapse through regional compliance analysis, the trend of EELI identifying the point of significant EELI reduction as an indicator of lung volume loss, the determination of minimum GI index quantifying homogeneity of ventilation distribution across the lung, and regional compliance assessment. The main goal of utilizing these diverse approaches is to strike a harmonious balance between lung recruitment and the prevention of overdistension. According to a recent study by Jonkman et al. [35], EIT demonstrates notable advantages in guiding PEEP selection for ARDS patients. It furnishes essential information beyond the scope of targeting the highest compliance during PEEP trials. Therefore, EIT-guided PEEP may present greater precision and safety compared to the approach of optimizing for the best compliance.

Although there was a lack of difference in the level PEEP obtained with the EIT and conventional approaches observed in the inhomogeneous population, it is worth note that EIT-derived PEEP strategies have reduced MP [36] and DP [40], with lowered PEEP levels compared to conventional PEEP methods in the RCTs. The potential clinical significance of EIT-derived PEEP strategies, particularly in specific subgroups underlines the importance of considering not only the overall population but also subgroup analyses to elucidate the impact of EIT-derived strategies on PEEP and its implications for VILI-related variables. Our findings related to reduced MP, and to a lesser extent DP, provide support for the assertion that EIT-guided PEEP optimization holds promise for advancing lung-protective ventilation strategies. It is postulated that curtailing MP and DP might confer potential survival advantages in individuals grappling with ARDS [54–59].

Several additional findings from our study warrant commentary. First, the attenuation in the percentage of silent spaces favoring EIT-guided PEEP titration harmonizes with the overarching concept of curtailing lung collapse and areas prone to overdistension. This dynamic contributes to an ameliorated gas exchange capacity and a mitigated risk for VILI. However, it is noteworthy to acknowledge that our conclusions regarding silent spaces stem from a limited number of studies with a relatively small sample size, which inherently imposes constraints on the robustness of this finding. Second, we did not find effects between PEEP titration strategies on secondary endpoints, including PaO_2/FiO_2 ratio, ICU stay, and %COV. These findings suggest that while the optimization of PEEP guided by EIT may exert an effect on respiratory system mechanic parameters, its ramifications on other clinical indicators may be limited and were variably reported. Nevertheless, we did note a reduction in all-cause mortality rate may coincide with improvements in compliance and DP driving across three studies. Due to the limited sample size, limited inferences can be made regarding the impact of the alternative PEEP titration strategies on mortality. It is worth noting that recent studies suggest that lowering DP might provide patients potential survival benefits [1, 54, 59, 60].

Our meta-analysis distinguishes itself from the study conducted by Yu M et al. [61], through several key differences. Specifically, we opted to exclude four studies that were encompassed in the prior meta-analysis for specific reasons: (1) Weber [30]—this study was omitted because it concentrated on patients undergoing general anesthesia for otorhinolaryngeal surgery. This deviation from our study criteria, which focuses on adult ARDS patients on invasive mechanical ventilation as defined by the Berlin definition, led to its exclusion. (2) Karsten [29]—exclusion of this study was warranted as it involved patients with mild-to-moderate impairment of oxygenation. This variance in patient characteristics did not align with our targeted population of adult ARDS patients. (3) Jacopo Fumagalli [26]—we chose to exclude this study since it utilized EIT to assess the effects of PEEP titration strategies, rather than focusing on PEEP titration per our analysis criteria. (4) Becher [62]—given that this was a meeting abstract with insufficient data for inclusion in our paper, we opted not to incorporate it into our meta-analysis. These exclusions were made to ensure the alignment of our study criteria with the specific parameters outlined in the Berlin definition for adult ARDS patients on invasive mechanical ventilation.

Our study exhibits notable strengths. The inclusion of ARDS patients with diverse demographics and etiologies enhances the generalizability of our findings to heterogeneous patient cohorts. The sensitivity analysis reinforces the positive impact of EIT-guided PEEP titration on respiratory system mechanics, thereby emphasizing its potential as a promising area for future investigation. The absence of significant bias and publication bias further underscores the reliability and trustworthiness of our conclusions.

Our study is not without limitations. First, beyond the analyses related to lung compliance and mechanical power, heterogeneity persisted due to variations in participant characteristics (such as age, BMI, etiology of ARDS, baseline PaO_2/FiO_2 ratio, and duration of mechanical ventilation before inclusion) and interventions (including intervention methods, tidal volume, recruitment maneuver before PEEP trial, and incremental/decremental PEEP) among the included studies. This diversity restricts the extent of inferences that can be drawn from the collective results. The differences in conventional methods within the control group and the varied EIT-guided PEEP titration techniques employed in the intervention group contribute to this inter-study variation.

Second, our findings regarding the impact of EIT-guided PEEP on mechanical power are constrained by the small sample size. Third, variability in reporting outcomes limited our ability to pool data effectively. Lastly, we acknowledge that we did not assess the certainty of our findings through the grading of recommendations, assessment, development, and evaluations.

In conclusion, our systematic review and meta-analysis provide evidence endorsing the effectiveness of EIT-guided mechanical ventilation in ARDS. The real-time lung function assessment facilitated by EIT allows for personalized PEEP settings, resulting in enhanced lung compliance while concurrently reducing MP and DP. For future research, large-scale RCTs are warranted to validate these findings, with a particular focus on clinical outcomes such as mortality rate, the duration of mechanical ventilation, and overall ICU stay. Moreover, a critical need exists for standardizing EIT methodology for PEEP titration to ensure consistency in application and interpretation across studies.

Supplementary Information

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Author contributions

NS and HZ contributed to the conception or design of the work; NS and CL: acquisition, analysis, or interpretation of data for the work; NS, YX, CL, OR, LB, AS, KB, and HZ: drafting the work or reviewing it critically for important intellectual content. All authors have final approval of the version to be published and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Availability of data and materials

Availability of data and materials does not apply.

Declarations

Conflicts of interest

All authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Ethics approval and consent to participate does not apply.

Consent for publication
Consent for publication does not apply.

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