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Optimal positive end-expiratory pressure titration of intraoperative mechanical ventilation in different operative positions of female patients under general anesthesia

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ABSTRACT

Objective: This study aimed to compare the effectiveness and safety of different titrated methods used to determine individual positive end-expiratory pressure (PEEP) for intraoperative mechanical ventilation in female patients undergoing general anesthesia in different operative positions, and provide reference ranges of optimal PEEP values based on the titration.

Methods: A total of 123 female patients who underwent elective open abdominal surgery under general anesthesia were included in this study. After endotracheal intubation, patients' body position was adjusted to the supine position, Trendelenburg positions at 10° and 20° respectively. PEEP was titrated from 20 cmH_2O to 4 cmH_2O, decreasing by 2 cmH_2O every 1 min. Electrical impedance tomography (EIT), hemodynamic and respiratory mechanics parameters were continuously monitored and recorded. Optimal PEEP values and reference ranges were respectively calculated based on optimal EIT parameters, mean arterial pressure (MAP), and lung dynamic compliance (Cdyn).

Results: EIT-guided optimal PEEP was found to have higher values than those of the MAP-guided and Cdyn-guided methods for all three body positions ($P < 0.001$), and it was observed to more significantly inhibit hemodynamics ($P < 0.05$). The variable coefficients of EIT-guided optimal PEEP values were smaller than those of the other two methods, and this technique could provide better ventilation uniformity for dorsal/ventral lung fields and better balance for pulmonary atelectasis/collapse. The 95% reference ranges of EIT-guided optimal PEEP values were 4.6–13.8 cmH_2O, 7.0–15.0 cmH_2O and 8.6–17.0 cmH_2O for the supine position, Trendelenburg 10°, and Trendelenburg 20° positions, respectively.

Conclusion: EIT-guided optimal PEEP titration was found to be a superior method for lung protective ventilation in different operative positions under general anesthesia. The calculated reference ranges of PEEP values based on the EIT-guided method can be used as a reference for intraoperative mechanical ventilation.

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1. Introduction

Pulmonary atelectasis is a common occurrence during the perioperative period, affecting approximately 90% of patients receiving general anesthesia [1]. In fact, even before any surgical operation has taken place, 15–20% of the base of the lung typically collapsed following anesthesia induction. Atelectasis that develops during anesthesia persists into the postoperative period [2], contributing to perioperative lung dysfunction and potential injury, which may increase the morbidity of postoperative pulmonary complications (PPCs) and mortality rates of surgical patients. In addition, this results in longer hospital stays and higher costs [3,4]. With more than 320 million people undergoing surgery globally every year [5], the potential for PPCs is significant.

The Trendelenburg position is widely used in various surgical procedures [6], particularly in gynecological surgery, due to its ability to tilt the intra-abdominal bowel away from the surgical area [7]. However, this position may cause uplift of the diaphragm, decreased respiratory compliance, and a reduction in functional residual capacity, all of which can aggravate atelectasis, ventilation/perfusion mismatch, and PPCs [8,9]. Compared to conventional positive end-expiratory pressure (PEEP), higher PEEP may improve the fraction of regional ventilation in the most dorsal region during the Trendelenburg position [10].

The use of lung protective ventilation strategy (LPVS) intraoperatively is unanimously recommended by experts, and a consensus was reached among them on the use of low tidal ventilation, alveolar recruitment maneuvers (RM), and individualized PEEP [11]. Individualized PEEP is important to prevent alveolar collapse, as RM reverses alveolar collapse but has limited effect without adequate PEEP [12]. Although specific methods of using small tidal volumes and RM have been defined, the setting of an appropriate PEEP remains a controversial issue. No consensus has been reached on the optimal strategy for personalizing PEEP in protective mechanical ventilation.

Several methods of personalizing PEEP have been tested in clinical practice and preclinical studies, including pulse oximetry (SpO_2) [13], transpulmonary pressure [14], pulmonary compliance [15], dead-space fraction [16], inflection points on the pressure/volume curve (P/V) [17], and the slope of the expiratory flow curve using airway pressure release ventilation (APRV) [18], each with its own advantages and disadvantages. Although computed tomography (CT) scans are considered the gold standard for assessing the effect of a PEEP trial on lung aeration, their use is not feasible in the operating room [19].

Electrical impedance tomography (EIT) is a functional imaging tool that can continuously quantify ventilation homogeneity and lung volume changes at the bedside [20]. EIT images are highly consistent with CT Scan [21,22] and are regional, real-time, non-invasive, and radiation-free [23], making EIT is reliable method for setting PEEP in general anesthesia [24–26]. Recent studies have emphasized the benefits of using EIT for PEEP titration to identify the optimal PEEP setting that achieves maximized alveolar recruitment while minimizing overdistention [27,28]. However, to our knowledge, published studies have only discussed the feasibility, advantages, and disadvantages of PEEP titration based on EIT, and have not provided specific references for clinical practice for hospitals lacking EIT equipment.

Therefore, this study aimed to use EIT to titrate the optimal PEEP for different positions during surgery (primarily gynecological surgery) in female patients, set the medical reference value range of PEEP, and compare this method with other PEEP titration methods to provide a theoretical reference for subsequent clinical applications.

2. Materials and methods

2.1. Subjects and study design

This single-center, prospective, open-label clinical study was conducted at the Second Affiliated Hospital of Chongqing Medical University in the Republic of China. The study aimed to compare the effectiveness and safety of different titration methods to determine individual PEEP effectiveness for intraoperative mechanical ventilation in various surgical positions under general anesthesia, and provide reference ranges of optimal PEEP values based on the titration. This study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Chongqing Medical University (Approval Document No. 2020-98). The trial was registered before patient enrolment in the China Clinical Trial Center (Registration No. ChiCTR2000040460). The study personnel evaluated the eligibility of patients and individually approached them to obtain written informed consent prior to surgery.

From December 2020 to March 2021, a total of 127 female patients who underwent elective surgery at the Second Affiliated Hospital of Chongqing Medical University were recruited. The inclusion criteria were as follows: female patients who underwent elective surgery under general anesthesia, American Society of Anesthesiologists physical status (ASA-PS) I–II, between 20 and 60 years of age, able to understand and sign the informed consent, and able to cooperate with the experiment. The exclusion criteria were: undergoing emergency surgery, history of severe restrictive lung disease or severe chronic obstructive pulmonary disease (GOLD grade III or IV) requiring oxygen inhalation, severe or uncontrolled bronchial asthma, pulmonary infection within one month before surgery, bronchiectasis, lung metastases, preoperative use of positive pressure ventilation, thoracic deformities and intrathoracic disease, oxygen saturation $\leq$95% without oxygen inhalation, severe neuromuscular disease, New York Heart Association (NYHA) grade III or IV severe cardiac disease or acute coronary syndrome, sustained ventricular tachyarrhythmia, liver cirrhosis (Child B or C), glaucoma, chronic renal failure requiring dialysis, hemoglobin less than 10 g/dl, pacemaker or other source surgical implants, and patients who could not provide informed consent. The exit criteria were: serious adverse events, patient or family requesting to withdraw from the study, systolic blood pressure (SBP) less than 80 mmHg, or inability to tolerate peak inspiratory pressure (PIP) $\geq$40 cmH_2O during PEEP titration.

2.2. Anesthesia

The participants underwent a 12-h fasting period and an 8-h restriction from drinking any liquids before the operation. Upon entering the operating room, two groups of peripheral venous channels were established, and normal saline was infused at a rate of 10 mL/kg/h. After local anesthesia was administered, the left radial artery was cannulated, and the invasive arterial blood pressure was monitored. The 16-electrode strip of EIT was wrapped around the 4th and 5th rib thorax, ensuring a good fit between the electrodes and the skin. Electrodes 8 and 9 were positioned near the spine, while electrodes 15 and 16 were placed near the sternum.

All patients underwent routine general anesthesia induction according to the protocol, which included intravenous midazolam (0.05 mg/kg), sufentanil (0.2 μg/kg), and propofol (1–2 mg/kg). The patient was intubated after administering rocuronium (0.6 mg/kg), and additional rocuronium (0.15 mg/kg) was given every 60 min for further muscle relaxation, but it was discontinued at least 1 h before the end of the surgical suture. An intraoperative continuous infusion of propofol (4–12 mg/kg/h), remifentanil (0.05–0.3 μg/kg/min) and sevoflurane inhalation (concentration between 1% and 3%) was maintained under anesthesia to keep the patient's Patient Status Index between 25 and 50. Continuous monitoring of vitals was performed using dedicated monitors that included invasive blood pressure, invasive cardiac output, SpO_2, heart rate (HR), end-tidal carbon dioxide fraction and electrocardiogram. The ventilator was set to volume-controlled ventilation mode, the tidal volume (TV) was set to 6 mL/kg, fractional inspired oxygen tension (FiO_2) was equal to 0.5, and the inspiratory-to-breath ratio was set at 1:2. The respiratory rate (RR) was adjusted (starting at 12 breaths/min) to maintain normal blood carbonic acid levels and end-tidal carbon dioxide between 35 and 45 mmHg.

2.3. PEEP titration

After induction of anesthesia and endotracheal intubation, an EIT belt was placed and the EIT monitoring (Pulmo Vista 500, Drager, Lubeck, Germany) was started with continuous recording. The patient was then placed in the supine, Trendelenburg 10°, Trendelenburg 20° positions, and the optimal PEEP value for each position was titrated. A decremental PEEP titration following Sergio et al. 's study was then performed [29]. Before each titration, a lung recruitment maneuver was performed following 10–15 min of baseline ventilation. This involved switching the end-expiratory pressure to 0 and increasing FiO_2 to 100% for 3–5 min, followed by increasing PEEP to 15 cmH_2O for 2 min, and further increasing it to 20 cmH_2O for an additional 2 min if plateau airway pressure (Pplat) < 40 cmH_2O. The titration procedure started with a PEEP value of 20 cmH_2O and decreased by 2 cmH_2O every 1 min, and was titrated down to 4 cmH_2O to complete the data collection (Fig. 1B). EIT calibration was performed right after intubation for each patient. After storage as an EIT file, PEEP titration analysis was conducted using PulmoVista 500 Software 1.20 (Drager, Lubeck, Germany).

2.4. Primary outcome

The primary outcome of this study was the optimal PEEP value.

2.5. Secondary outcomes

The secondary outcomes of this study were SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, systemic vascular resistance (SVR), stroke volume (SV), cardiac cycle efficiency (CCE), stroke volume variation (SVV), the derivative of pressure over time (dp/dt), SpO_2, PIP, Pplat, mean inspiratory pressure (Pmean), pulmonary dynamic compliance (Cdyn), RR、VT, minute ventilation (MV), inspiratory time (Ti), driving pressure (DP), tidal volume region of interest 1 (TV ROI1), TV ROI2, TV ROI3, and TV ROI4.

2.6. Statistical analysis

All normally distributed continuous data were presented as the mean (standard deviation) and non-normally distributed continuous data were presented as median (25th–75th percentile). Qualitative data were summarized as the number of subjects. Comparative analysis was performed using SPSS software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY). Paired samples *t*-test was used to compare groups of normally distributed data, while Wilcoxon rank sum test was used for non-normally distributed data. The Chi-square test was used for comparison between groups, and Fisher's exact probability method was used when the theoretical frequency was less than five. Repeated measures ANOVA or Friedman's test were used to compare changes with more than two levels. Bonferroni correction was used to adjust the *P* values for multiple comparisons. A *P* value smaller than 0.05 was considered statistically significant.

3. Results

3.1. Study population

A total of 127 female patients were included in this study. Three patients with SBP $<$80 mmHg and one patient with PIP$>$40 cmH_2O during PEEP titration were excluded, resulting in 123 eligible patients for statistical analysis (Fig. 1A). The demographic and baseline data of all subjects are shown in Table 1.

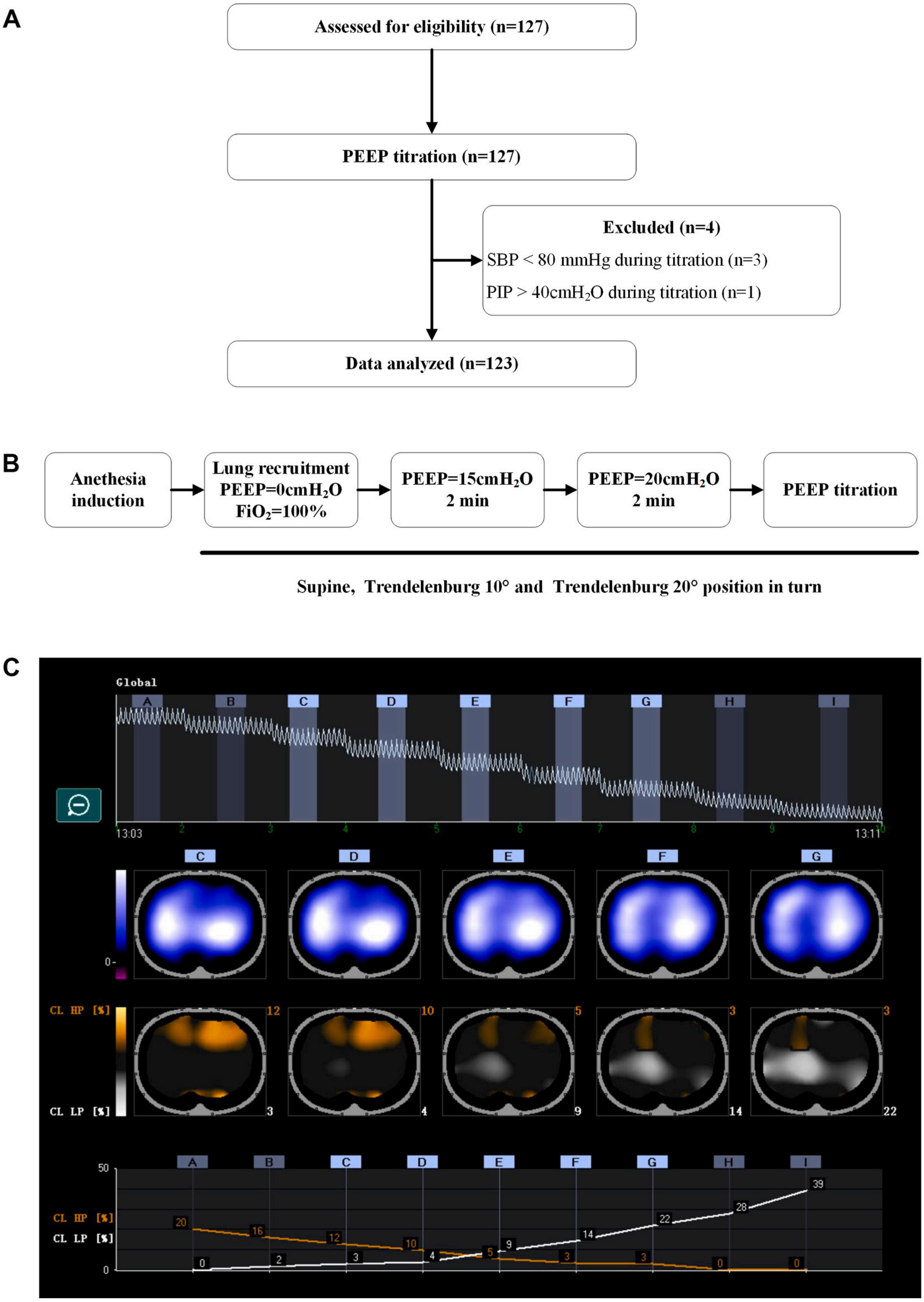

Fig. 1. Flow diagram representing patient enrollment (A), study protocol (B) and criteria for titrating positive end-expiratory pressure (PEEP) with electrical impedance tomography (C).

Table 1
Participants' characteristics.

Characteristics		n = 123
Age	Year, mean (SD)	37.6 (9)
Sex	Male, n (%)	0 (0)
	Female, n (%)	123 (100)
Height	cm, mean (SD)	158.8 (5.02)
Weight	kg, mean (SD)	57.1 (6.90)
BMI	kg/m^2, mean (SD)	22.7 (2.51)
ASA	I, n (%)	45 (36)
	II, n (%)	78 (64)
Type of surgery	Gynecological n (%)	101 (81)
	Thyroid n (%)	3 (2)
	Hepatobiliary n (%)	14 (11)
	Urology n (%)	5 (4)
Medical history	Hypertension n (%)	3 (2.4)
	Diabetes n (%)	4 (3.2)
Smoking	Never n (%)	123 (100)
	Occasionally n (%)	0 (0)
	Often n (%)	0 (0)

3.2. Optimal PEEP titrated by EIT, MAP, and Cdyn in different body positions

The 95% reference range of the optimal PEEP titrated by EIT was found to be 8.0–15.4 cmH_2O with a coefficient of variation of 16.15% in the supine position, 10.3–17.5 cmH_2O with a coefficient of variation of 13.09% in the Trendelenburg position at 10°, and 12.5–19.3 cmH_2O with a coefficient of variation of 11.07% in the Trendelenburg position at 20°. The 95% reference range of the optimal PEEP titrated by MAP was found to be 0.2–12.2 cmH_2O with a coefficient of variation of 49.35% in the supine position, 0.7–13.1 cmH_2O with a coefficient of variation of 46.09% in the Trendelenburg position at 10°, and 2.8–18.8 cmH_2O with a coefficient of variation of 37.74% in the Trendelenburg position at 20°. The 95% reference range of the optimal PEEP titrated by Cdyn was found to be 4.6–13.8 cmH_2O with a coefficient of variation of 25.76% in the supine position, 7.0–15.0 cmH_2O with a coefficient of variation of 18.64% in the Trendelenburg position at 10°, and (8.6–17.0) cmH_2O with a coefficient of variation of 16.72% in the Trendelenburg position at 20°. The optimal PEEP titrated by EIT was highest, followed by Cdyn and MAP, in each of the three positions ($P < 0.001$) (Table 2).

3.3. Comparison of hemodynamics mechanics between PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn in different positions

The hemodynamics mechanics of PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn were compared in the supine position, Trendelenburg 10°, and Trendelenburg 20° respectively (Table 3).

The MAP, SBP, DBP, CO, SV, and Dp/dt in the PEEP-EIT group were significantly lower ($P < 0.001$), while HR was significantly higher ($P < 0.001$) than those in the PEEP = 4 cmH_2O group. There was no significant difference in SVR ($P = 0.264$, 0.6, and 0.052, respectively) between these two groups in all three positions. CCE was significantly lower in the supine ($P < 0.001$) and Trendelenburg 10° ($P < 0.01$) positions, but not in the Trendelenburg 10° ($P = 0.703$). SVV was significantly higher in supine ($P < 0.001$), but not Trendelenburg 10° ($P = 0.108$) and Trendelenburg 20° ($P = 0.248$) position.

The MAP, SBP, DBP, CO, SV, and Dp/dt in the PEEP-EIT group were significantly lower ($P < 0.01$ or $P < 0.001$), while HR was significantly higher ($P < 0.001$) than those in the PEEP-MAP group. There was no significant difference in SVR ($P = 0.104$, 0.216, and 0.056, respectively) and SVV ($P = 0.291$, 0.756, and 0.526 respectively) between these two groups in all three positions. CCE was significantly lower in the supine and Trendelenburg 10° ($P < 0.01$) positions, but not Trendelenburg 20° ($P = 0.554$) position.

The MAP, SBP, DBP, CO, SV, and Dp/dt in the PEEP-EIT group were significantly lower ($P < 0.05$, $P < 0.01$, or $P < 0.001$), while HR was again significantly higher ($P < 0.05$ or $P < 0.001$) than those in the PEEP-Cdyn group. There was no significant difference in SVR

Table 2
Optimal PEEP titrated by EIT, MAP and Cdyn and 95% reference range for each position.

	PEEP-EIT			PEEP-MAP			PEEP-Cdyn		
	Optimal PEEP mean (SD)	95% reference range	Variation (%)	Optimal PEEP mean (SD)	95% reference range	Variation (%)	Optimal PEEP mean (SD)	95% reference range	Variation (%)
Supine	11.7 (1.89)	[8.0, 15.4]	16.15	6.2 (3.06) *	[0.2, 12.2]	49.35	9.2 (2.37) *#	[4.6, 13.8]	25.76
Trendelenburg 10°	13.9 (1.82)	[10.3, 17.5]	13.09	6.9 (3.18) *	[0.7, 13.1]	46.09	11.0 (2.05) *#	[7.0, 15.0]	18.64
Trendelenburg 20°	15.9 (1.76)	[12.5, 19.3]	11.07	10.6 (4.00) *	[2.8, 18.8]	37.74	12.8 (2.14) *#	[8.6, 17.0]	16.72

*$P < 0.05$ versus PEEP-EIT, #$P < 0.05$ versus PEEP-MAP.

Table 3

Comparison of hemodynamics mechanics between PEEP-EIT, PEEP = 4 cmH$_2$O, PEEP-MAP, and PEEP-Cdyn in different positions.

	Supine				Trendelenburg 10°				Trendelenburg 20°			
	PEEP-EIT Mean (SD) Median [IQR]	PEEP = 4 cmH$_2$O Mean (SD) Median [IQR]	PEEP-MAP Mean (SD) Median [IQR]	PEEP-Cdyn Mean (SD) Median [IQR]	PEEP-EIT Mean (SD) Median [IQR]	PEEP = 4 cmH$_2$O Mean (SD) Median [IQR]	PEEP-MAP Mean (SD) Median [IQR]	PEEP-Cdyn Mean (SD) Median [IQR]	PEEP-EIT Mean (SD) Median [IQR]	PEEP = 4 cmH$_2$O Mean (SD) Median [IQR]	PEEP-MAP Mean (SD) Median [IQR]	PEEP-Cdyn Mean (SD) Median [IQR]
MAP (mmHg)	70.3 (7.52)	77.7 (7.41) ***	76.2 (7.12) ***	73.0 (7.93) ***	76.3 (8.67)	83.2 (9.10) ***	82.4 (9.09) ***	78.3 (8.85) ***	83.0 (9.20)	88.1 (8.41) ***	86.3 (8.49) ***	84.5 (8.52) ***
SBP (mmHg)	98.7 (11.11)	107.3 (9.1) ***	105.3 (10.24) ***	102.0 (10.89) ***	105.7 (10.45)	113.5 (10.85) ***	112.7 (10.76) ***	108.5 (10.81) ***	113.1 (11.27)	118.7 (10.89) ***	116.7 (10.55) ***	115.4 (10.91) ***
DBP (mmHg)	56.1 (6.86)	60.9 (6.52) ***	60.1 (6.62) ***	58.1 (6.94) ***	61.4 (6.69)	65.6 (7.16) ***	64.9 (6.94) ***	63.1 (7.22) ***	66.6 (7.27)	69.8 (7.15) ***	68.0 (7.00) ***	67.3 (7.03) ***
HR (times/min)	69.6 (10.63)	64.6 (8.64) ***	66.3 (9.87) ***	68.1 (9.87) ***	65.8 (8.47)	63.4 (9.02) ***	63.1 (8.57) ***	64.8 (8.49) ***	63.9 (9.95)	62.2 (9.28) ***	62.0 (9.26) **	62.4 (9.46) *
CO (L/min)	3.94 (0.61)	4.36 (0.62) ***	4.23 (0.68) ***	4.15 (0.65) **	4.13 (0.58)	4.53 (0.72) ***	4.49 (0.73) ***	4.30 (0.61) ***	4.28 (0.71)	4.69 (0.94) ***	4.6 (0.8) **	4.50 (0.79) *
SVR (dyn*s/cm^2)	1314.4 (221.58)	1369.5 (205.76)	1377.9 (241.07)	1331.84 (219.98)	1339.3 (250.13)	1386.9 (225.30)	1395.2 (233.13)	1376.8 (235.80)	1396.9 (271.25)	1476.2 (212.60)	1427.9 (233.4)	1405.4 (235.07)
SV (mL)	57.7 (12.40)	65.5 (9.97) ***	62.2 (12.47) ***	61.1 (12.54) ***	62.3 (9.41)	70.0 (13.01) ***	69.3 (12.88) ***	65.7 (11.14) ***	64.8 (10.77)	70.5 (12.16) ***	69.8 (11.1) **	68.5 (10.24) **
CCE	0.30 [0.14–0.41]	0.35 [0.22–0.48] ***	0.34 [0.17–0.45] **	0.31 [0.21–0.42] *	0.32 [0.14–0.41]	0.36 [0.17–0.50] **	0.36 [0.14–0.48] **	0.33 [0.14–0.47]	0.31 [0.09–0.42]	0.30 [0.07–0.44]	0.3 [0.1–0.4]	0.34 [0.10–0.43] *
SVV (%)	9.09 [5.90–9.09]	8.54 [5.45–10.90] ***	5.93 [9.05–12.80]	9.34 [6.80–12.80]	10.70 [7.26–12.50]	8.81 [5.57–11.53]	9.64 [6.61–12.70]	9.68 [6.50–12.70]	9.60 [5.86–13.65]	7.62 [5.08–12.05]	8.8 [4.9–12.5]	8.82 [5.43–12.68]
Dp/dt	0.65 (0.18)	0.74 (0.19) ***	0.71 (0.20) ***	0.69 (0.20) ***	0.69 (0.16)	0.76 (0.17) ***	0.75 (0.17) ***	0.72 (0.17) ***	0.70 (0.17)	0.73 (0.18) ***	0.73 (0.17) ***	0.72 (0.16) *

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ *versus* PEEP-EIT.

($P = 0.350$, 0.440, and 0.524, respectively) and SVV ($P = 0.593$, 0.860, and 0.372 respectively) between these two groups in all three positions. CCE was significantly lower in the supine and Trendelenburg 20° ($P < 0.05$) positions, but not in the Trendelenburg 10° ($P = 0.080$) position.

3.4. Trends in hemodynamics during PEEP titration in different positions

Hemodynamics parameters during PEEP titration were compared in different positions. MAP, SV and SVR increased gradually, while SVV decreased gradually as PEEP levels decreased during the titration process in different positions. MAP was highest in the Trendelenburg 20° position, second highest in the Trendelenburg 10° position, and lowest in the supine position during 20 to 4 cmH_2O PEEP titration ($P < 0.001$). The difference in MAP was always statistically significant when compared to the MAP of the PEEP = 4 cmH_2O group when the PEEP decreased from 20 cmH_2O to 6 cmH_2O in the supine and Trendelenburg 10° positions. In the Trendelenburg 20° position, the difference between the corresponding MAP and that of the PEEP = 4 cmH_2O group was statistically significant until PEEP dropped from 20 to 8 cmH_2O ($P > 0.05$, Fig. 2A). SV gradually increased as the PEEP level decreased during the titration. SV was consistently higher in the Trendelenburg 20° and Trendelenburg 10° positions than in the supine position at the same PEEP level ($P < 0.05$). Compared to that of PEEP = 4 cmH_2O, SV was continuously lower from 20 to 8 cmH_2O PEEP titration than in the supine position, from 20 to 10 cmH_2O in the Trendelenburg 10° position and from 20 to 14 cmH_2O in the Trendelenburg 20° position (Fig. 2B). SVR was consistently higher in the Trendelenburg 20° position than in the supine position. On the other hand, in the Trendelenburg 10° position, only PEEP at 20 and 18 cmH_2O was higher than that of the supine position. SVR was continuously lower from 20 to 14 cmH_2O PEEP titration compared to that of PEEP = 4 cmH_2O in the supine position, and to that of 20 to 16 cmH_2O PEEP titration in the Trendelenburg 10° and Trendelenburg 20° positions (Fig. 2C). SVV was lower from 20 to 16 cmH_2O PEEP titration in the Trendelenburg 20° position than that of the supine position, and higher at PEEP = 6 cmH_2O in the Trendelenburg 10° than that of the supine position. SVV was continuously lower from 20 to 12 cmH_2O PEEP titration compared to that of PEEP = 4 cmH_2O in the supine position, and from 20 to 14 cmH_2O in the Trendelenburg 10° position (Fig. 2D).

3.5. Comparison of respiratory mechanics between PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn in different positions

The respiratory mechanics between PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn were compared in the supine, Trendelenburg 10°, and Trendelenburg 20° positions. In all three positions, PIP, Pplat, and Cdyn in the PEEP-EIT were significantly higher ($P < 0.05$ or $P < 0.001$) than those in the PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn groups. DP was lower in the PEEP-EIT group ($P < 0.001$) than that in the PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn groups in the supine and Trendelenburg 10° positions. In the Trendelenburg 20° position, DP in the PEEP-EIT group was lower than that in the PEEP = 4 cmH_2O ($P < 0.001$) and PEEP-MAP ($P < 0.01$) groups, but not the PEEP-Cdyn group ($P = 0.220$) (Table 4).

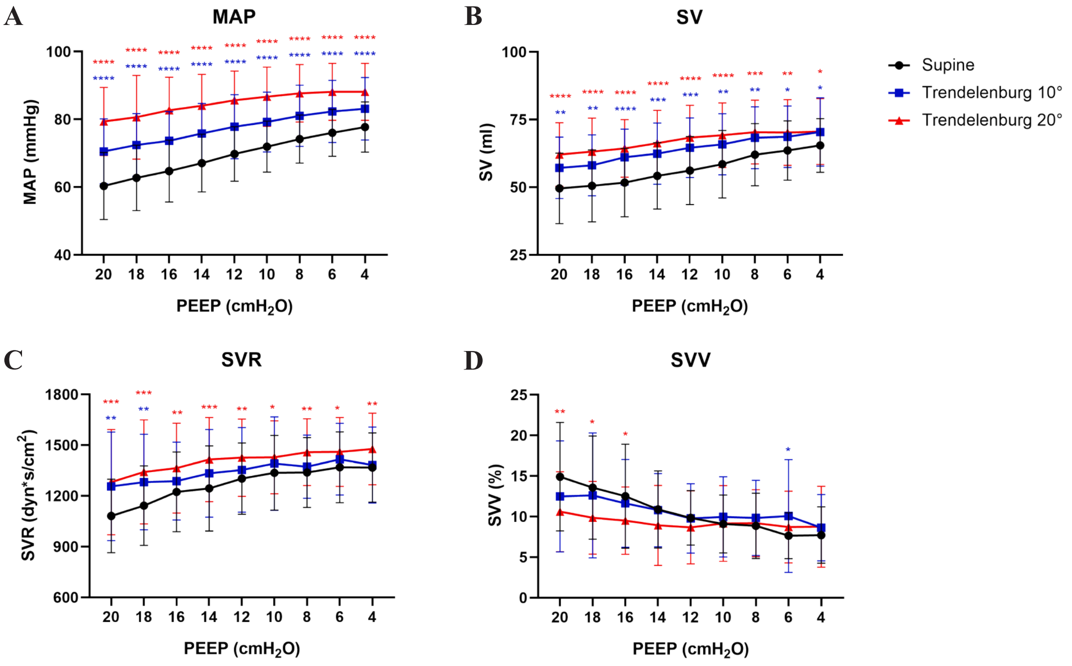

Fig. 2. Hemodynamics parameters during positive end-expiratory pressure (PEEP) titration in different positions. Mean arterial pressure (MAP) (A), stroke volume (SV) (B), systemic vascular resistance (SVR) (C), and stroke volume variation (SVV) (D) during the 20 to 4 cmH_2O PEEP titration process in different positions. Error bars represent the standard deviation. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ vs supine.

Table 4

Comparison of respiratory mechanics between PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP, and PEEP-Cdyn in different positions.

	Supine				Trendelenburg 10°				Trendelenburg 20°			
	PEEP-EIT Mean (SD)	PEEP = 4 cmH_2O Mean (SD)	PEEP-MAP Mean (SD)	PEEP-Cdyn Mean (SD)	PEEP-EIT Mean (SD)	PEEP = 4 cmH_2O Mean (SD)	PEEP-MAP Mean (SD)	PEEP-Cdyn Mean (SD)	PEEP-EIT Mean (SD)	PEEP = 4 cmH_2O Mean (SD)	PEEP-MAP Mean (SD)	PEEP-Cdyn Mean (SD)
PIP (cmH_2O)	19.3 (2.69)	12.9 (1.54) ***	14.7 (3.01) ***	17.0 (2.86) ***	21.9 (2.80)	13.9 (1.98) ***	15.9 (3.08) ***	19.2 (2.65) ***	24.3 (2.79)	15.2 (2.47) ***	20.4 (3.97) ***	21.3 (2.89) ***
Pplat (cmH_2O)	19.0 (2.74)	12.6 (1.56) ***	14.5 (3.05) ***	16.7 (2.92) ***	21.5 (2.67)	13.5 (1.90) ***	15.7 (3.01) ***	18.8 (2.56) ***	23.8 (3.40)	14.9 (2.46) ***	20.1 (3.92) ***	21.0 (2.88) ***
Cdyn (mL/ cmH_2O)	69.8 (11.03)	63.3 (10.28) ***	66.4 (11.36) ***	74.0 (11.29) ***	66.7 (10.40)	55.8 (9.21) ***	61.8 (11.35) ***	70.7 (10.46) ***	61.8 (11.03)	48.2 (9.18) ***	59.9 (11.97) *	66.3 (10.66) ***
DP (cmH_2O)	7.5 (1.23)	8.6 (1.56) ***	8.2 (1.72) ***	7.5 (1.24) ***	7.9 (1.23)	9.6 (1.88) ***	8.6 (1.79) ***	7.7 (1.17) ***	8.3 (1.38)	10.9 (2.46) ***	8.8 (2.08) **	8.1 (1.48)

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ *versus* PEEP-EIT.

3.6. *Trends in respiratory mechanics during PEEP titration in different positions*

The respiratory mechanics parameters during PEEP titration were compared in different positions. Cdyn increased and then decreased, DP decreased and then increased, while dp/dt increased slowly during PEEP titration as PEEP decreased. In the supine position, Cdyn increased from 49.55 to 71.57 mL/cmH_2O at PEEP = 8 cmH_2O and then decreased to 63.34 mL/cmH_2O at PEEP = 4cmH_2O. In the Trendelenburg 10° position, Cdyn increased from 52.12 to 68.88 mL/cmH_2O at PEEP = 12 cmH_2O and then decreased to 55.78 mL/cmH_2O at PEEP = 4 cmH_2O. In the Trendelenburg 20° position, Cdyn increased from 53.43 to 63.98 mL/cmH_2O at PEEP = 14 cmH_2O and then decreased to 48.17 mL/cmH_2O at PEEP = 4 cmH_2O (Fig. 3A). Moreover, dp/dt increased slowly during PEEP titration, and dp/dt was higher in the Trendelenburg 10° position than in the supine position at PEEP = 20 to 14 cmH_2O, and higher in the Trendelenburg 20° position than in the supine position at PEEP = 20 to 10 cmH_2O (Fig. 3B). DP decreased from 9.30 to 7.47 cmH_2O at PEEP = 10 cmH_2O and then increased to 8.63 cmH_2O at PEEP = 4 cmH_2O in the supine position. In the Trendelenburg 10° position, DP decreased from 9.13 to 7.78 mL/cmH_2O at PEEP = 12 cmH_2O and then increased to 9.51 cmH_2O at PEEP = 4 cmH_2O. In the Trendelenburg 20° position, DP decreased from 9.16 to 8.16 cmH_2O at PEEP = 14 cmH_2O and then increased to 10.91 mL/cmH_2O at PEEP = 4 cmH_2O (Fig. 3C).

4. Discussion

In the present study, the 95% reference range for optimal PEEP titrated by EIT was found to be 8.0–15.4 cmH_2O with a coefficient of variation of 16.15% in the supine position, 10.3–17.5 cmH_2O with a coefficient of variation of 13.09% in the Trendelenburg position at 10°, and 12.5–19.3 cmH_2O with a coefficient of variation of 11.07% in the Trendelenburg position at 20°.

Previous studies have employed several approaches for PEEP titration by EIT [30–32]. The reference used in this study is based on the "Costa algorithm" published in 2009, which measures regional lung compliance during PEEP titration to identify the loss of compliance that accompanies a decrease or increase in PEEP [21]. By identifying regional alveolar collapse and hyperinflation, the optimal PEEP is the one closest to the point where the alveolar hyperinflation and collapse curves cross above the PEEP, corresponding to the lowest lung atrophy and hyperinflation [33] (Fig. 1C).

The MAP, SBP, DBP, CO, SV and dp/dt were significantly lower, and the HR was significantly higher in the best PEEP group compared to those of PEEP = 4 cmH_2O group as determined by EIT titration in the supine, Trendelenburg at 10° and Trendelenburg at 20° positions. There was no statistically significant difference in SVR between the two groups. Previous studies have also confirmed significant alterations in hemodynamics during PEEP titration and pulmonary resuscitation maneuvers using EIT, which can be restored to baseline levels through aggressive rehydration and the use of vasoactive drugs [29]. According to the Frank-Starling mechanism, diastolic ventricular filling, elongation of the myocardial segments, and an increase in the initial length of the myocardium increase the overlapping portion of thick and thin myofilaments and the number of myosin and actin crosslinks, resulting in increased myocardial contractility [34]. In contrast, when PEEP-EIT was used in our study, it caused an increase in intrathoracic pressure and pulmonary circulatory resistance, which led to a decrease in return blood volume and a limitation of left ventricular diastole, resulting in to a decrease in SV, cardiac contractility, CO, and blood pressure. Therefore, preoperative rehydration should be ensured before using PEEP-EIT to maintain an adequate effective circulating blood volume. Moreover, PEEP-EIT is not recommended for elderly people who are hemodynamically unstable, have poor vascular elasticity, or have a history of heart disease.

In the supine, Trendelenburg 10°, and Trendelenburg 20° positions, PIP, Pplat and Cdyn were significantly higher in the PEEP-EIT group than in the PEEP = 4 cmH_2O group. In addition, the PEEP-EIT group had a lower DP, which has been associated with the lowest risk of PPCs [35]. These findings indicate that optimal PEEP determined by EIT titration not only provides positive effect on intraoperative lung protection, but also helps in preventing PPCs.

Furthermore, this study investigated the use of MAP to titrate optimal PEEP. Anesthesiologists should consider the hemodynamic impact of its use in clinical practice, and determine how to set it in hemodynamically unstable patients who require PEEP. We explored the maximum PEEP achievable while maintaining the MAP at the same level as PEEP = 0 cmH_2O. With the assumption that hemodynamics were not affected, we investigated whether the respiratory mechanics parameters corresponding to this PEEP (PEEP-MAP)

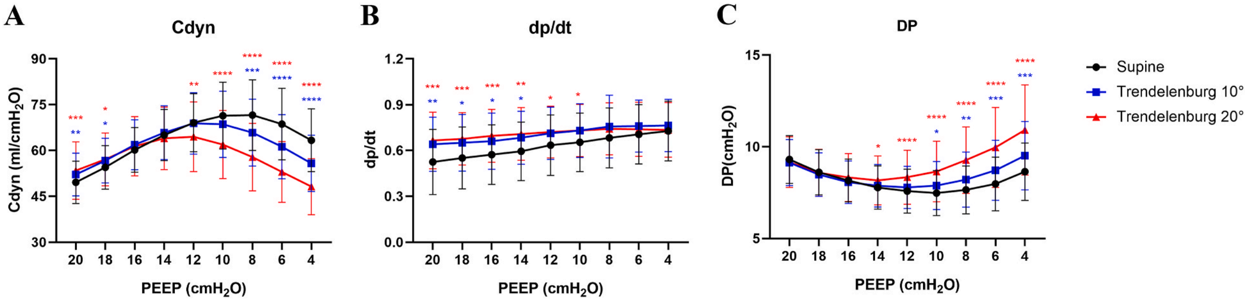

Fig. 3. Respiratory mechanics parameters during positive end-expiratory pressure (PEEP) titration in different positions. Pulmonary dynamic compliance (Cdyn) (A), the derivative of pressure over time (dp/dt) (B), and driving pressure (DP) (C) during the 20 to 4 cmH_2O PEEP titration process in different positions. Error bars represent the standard deviation. $^*P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ vs supine.

could be significantly improved compared to those of PEEP = 4 cmH_2O. The results showed significant variations in PEEP-MAP among individuals. We also compared the respiratory mechanics of PEEP-MAP with those of the PEEP = 4 cmH_2O group and found that PIP, Pplat, and Cdyn were significantly higher in the PEEP-MAP group. Additionally, the PEEP-MAP group had a significantly lower DP than that of the PEEP = 4 cmH_2O group in the supine, Trendelenburg 10°, and Trendelenburg 20° positions. These findings suggest that optimal PEEP titrated according to the MAP can improve respiratory mechanics parameters to some extent and positively impact lung protection. In conclusion, using maximal PEEP in hemodynamically unstable patients is positive when ensuring hemodynamic stability to the greatest extent possible.

The Cdyn at each PEEP level was recorded, and the PEEP of maximum Cdyn was selected as the optimal PEEP by Cdyn (PEEP-Cdyn). Hemodynamics and respiratory mechanics parameters were compared among the PEEP-EIT, PEEP = 4 cmH_2O, PEEP-MAP and PEEP Cdyn groups in different positions. The PEEP-EIT group had a slightly lower Cdyn than that of the PEEP-Cdyn group but higher than those of the PEEP = 4 cmH_2O and PEEP-MAP groups, and a DP comparable to that of the PEEP-Cdyn group but lower than those of the PEEP = 4 cmH_2O and PEEP-MAP groups. Concurrently, PEEP-EIT had the most pronounced hemodynamic inhibition (lowest MAP, SBP, DBP, CO, SV and dp/dt, and the highest HR).

The changes in hemodynamics and respiratory mechanics during PEEP titration also varied depending on the position. As the PEEP level gradually decreased, hemodynamic parameters such as MAP, SV, SVR, and dp/dt were improved gradually; however, the hemodynamic effects were greater in the supine and Trendelenburg 10° positions, and a smaller PEEP was required to restore the baseline. Furthermore, as the PEEP level decreased during titration, Cdyn initially increased and then gradually decreased, suggesting that alveolar hyperinflation occurs and lung compliance decreases when PEEP is too high. The minimum required PEEP level for maximum pulmonary compliance and minimum DP was found in the supine position, while it was the maximum in the Trendelenburg 20° position. This is, probably because the diaphragm shifts upward in the head-down position, causing a decrease in respiratory compliance, and functional residual air volume and requiring greater PEEP to reopen collapsed alveoli.

This study has strengths and limitations. Some of the strengths include its prospective own control-based design, relatively large sample size, strict inclusion and exclusion criteria, and use of high-quality data. However, there are several limitations that need to be addressed. First, this study only included female patients undergoing surgery at one university-affiliated hospital, and thus the generalizability of the findings to male patients and other hospitals is uncertain. Second, all participants were Chinese, so the reference value range may not be applicable to other races. Third, as none of the subjects smoked, the data may not apply to smokers. Fourth, the age range of the participants was 20–60 years old, and age-stratified analysis could not be performed with the present sample size. Fifth, the BMI range was limited to 17.5 to 28, so the results may not be applicable to obese patients. Sixth, as PEEP decreased by 2 cmH_2O every 1 min, the hemodynamic data were in the process of dynamic change and were not yet stable when recorded. Lastly, no postoperative and post-discharge data was collected to assess the long-term impact of PEEP-EIT.

Overall, our study highlights that titrating optimal PEEP using EIT significantly improves lung compliance and decreases DP in patients, but with a greater impact on hemodynamics. Therefore, preoperative rehydration is recommended to ensure adequate effective circulating blood volume before using this method to titrate PEEP. Optimal PEEP titrated by EIT is not recommended for older adults who are hemodynamically unstable or have poor vascular elasticity or a history of heart disease. For such patients, the optimal PEEP titrated according to MAP can be used while ensuring hemodynamic stability, as this approach results in a significant improvement in respiratory mechanics parameters.

5. Conclusion

1. Optimal PEEP titrated by EIT significantly increased pulmonary compliance and decreased DP in patients.
2. The 95% reference range of the optimal PEEP titrated by EIT was found to be 8.0–15.4 cmH_2O with a coefficient of variation of 16.15% in the supine position, 10.3–17.5 cmH_2O with a coefficient of variation of 13.09% in the Trendelenburg position at 10°, and 12.5–19.3 cmH_2O with a coefficient of variation of 11.07% in the Trendelenburg position at 20°.
3. The optimal PEEP titrated by EIT has a greater hemodynamic impact, mainly due to a decrease in SV and dp/dt caused by a reduction in effective circulating blood volume, suggesting that aggressive rehydration is preferable to correct the circulatory depression caused by PEEP.

Ethics statement

This study involving human participants was reviewed and approved by the Medical Ethics Committee of The Second Affiliated Hospital of Chongqing Medical University. The patients/participants provided their written informed consent to participate in this study.

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CRediT authorship contribution statement

Bin Shu: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Yang Zhang:** Conceptualization, Investigation. **Qian Ren:** Investigation. **Xuemei Zheng:** Data curation, Resources. **Yamei Zhang:**

Data curation, Resources. **Qi Liu:** Data curation, Resources. **Shiqi Li:** Data curation, Resources. **Jie Chen:** Resources. **Yuanjing Chen:** Resources. **Guangyou Duan:** Conceptualization, Data curation, Formal analysis, Methodology, Writing – review & editing. **He Huang:** Conceptualization, Formal analysis, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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