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SYSTEMATIC REVIEW

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Impact of a positive end-expiratory pressure on oxygenation, respiratory compliance, and hemodynamics in obese patients undergoing laparoscopic surgery in reverse Trendelenburg position: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background High and individual positive end-expiratory pressure (PEEP) during laparoscopic surgery may improve oxygenation and respiratory mechanics.

Methods We searched RCTs in PubMed, Cochrane Library, Web of Science, and Google Scholar from from from January 2000 to December 2023 comparing the different intraoperative PEEP (low PEEP (LPEEP): 0–5 mbar; moderate PEEP (MPEEP): 6–9 mbar; high PEEP (HPEEP): >=10 mbar; individualized PEEP (iPEEP): PEEP set by special physiological technique) on arterial oxygenation, respiratory compliance (Cdyn) or driving pressure, mean arterial pressure (MAP), and heart rate (HR) in patients during laparoscopic surgery in reverse Trendelenburg position. We calculated mean differences (MD) with 95% confidence intervals (CI), and predictive intervals (PI) using random-effects models. The Cochrane Bias Risk Assessment Tool was applied.

Results 8 RCTs ($n = 425$) met the inclusion criteria. HPEEP vs. LPEEP increased PaO_2/FiO_2 (+ 129.93 [+ 75.20; +184.65] mmHg, $p < 0.0001$) with high variation of true effect (Chi^2 34.92, $p < 0.0001$; I^2 89%). iPEEP vs. LPEEP also increased PaO_2/FiO_2 + 130.23 [+ 57.18; +203.27] mmHg, $p = 0.0005$) with high variation of true effect (Chi^2 26.95, $p < 0.0001$; I^2 93%). HPEEP vs. LPEEP increased Cdyn (+ 15.06 [5.47; +24.65] ml/mbar, $p = 0.002$) with high variation of true effect (Chi^2 93.16, $p < 0.0001$; I^2 96%). iPEEP vs. LPEEP increased Cdyn (+ 22.46 [+ 8.56; +36.35] ml/mbar, $p = 0.002$) with high

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variability of the true effect (Chi^2 53.92, $p<0.0001$; I^2 96%). HPEEP group had higher MAP as compared to LPEEP) + 4.36 [+0.36;+8.36], $p=0.03$), variability of the true effect was nonsignificant. HR did nit differ between all comparisons.

Conclusion In patients with obesity undergoing surgery in the reverse Trendelenburg position HPEEP and iPEEP may improve oxygenation, decrease driving pressure, and increase dynamic compliance compared to LPEEP with high variation of true effect without relevant hemodynamic compromise. Data with MPEEP comparisons are inconclusive.

PROSPERO Registration CRD42023488971; registered December 14, 2023.

Keywords Positive end-expiratory pressure, PEEP, Laparoscopic surgery, Lung protective ventilation, Compliance, Oxygenation, Obese, Obesity, Pneumoperitoneum, Meta-analysis

Introduction

Every year around 230 million patients worldwide undergo surgery under general anesthesia with mechanical ventilation [1]. Since their introduction in the late 1980s, laparoscopic procedures have gained widespread acceptance in surgery due to their numerous advantages over traditional open surgeries, including reduced postoperative pain, shorter hospital stays, and faster recovery times [2]. However, despite these benefits, laparoscopic surgeries present unique challenges, particularly in obese patients.

During laparoscopic surgery, carbon dioxide insufflation is commonly used to create a working space within the abdominal cavity. However, this insufflation displaces the diaphragm upward, leading to decreased functional residual capacity (FRC), compliance, and worsening ventilation-perfusion (V/Q) ratio. This can ultimately result in atelectasis, where portions of the lung collapse due to inadequate ventilation [3]. Moreover, the positioning of patients on the operating table, such as the Trendelenburg position commonly used during laparoscopic procedures, can further exacerbate pulmonary complications [4]. Studies have shown that the Trendelenburg position contributes to the development of atelectasis, worsened oxygenation, and reduced respiratory compliance, particularly in non-obese patients [5].

Obesity adds another layer of complexity to these challenges. Obese patients are more prone to postoperative pulmonary complications (PPCs) due to their significantly reduced FRC [6]. As body mass index (BMI) increases, FRC decreases exponentially, resulting in V/Q mismatch, intrapulmonary shunting, and arterial hypoxemia. During general anesthesia, these respiratory changes are further accentuated, with obese patients experiencing a notable decrease in FRC by approximately 50%, compared to 20% in non-obese patients [7]. The patient's respiratory mechanics phenotype could further influence V/Q mismatch [8]. One of the factors that causes V/Q mismatch is the airway closure leading to expiratory flow limitation (EFL) which was found in about 38% of patients who underwent laparoscopic gynecological surgery in the Trendelenburg position [9].

Mechanical ventilation, while essential during surgery, poses inherent risks to lung tissue and respiratory muscles. Prolonged mechanical ventilation can lead to ventilator-associated lung injury, including barotrauma, volutrauma, and atelectotrauma, as well as stress injuries caused by repeated alveolar collapse and reopening. To mitigate these risks, clinicians employ protective ventilation strategies, including the use of PEEP in conjunction with low tidal volume ventilation. PEEP helps to recruit and maintain alveoli open, improving oxygenation, and increasing FRC and lung compliance [10–12]. Multiple strategies can be employed for the titration of PEEP, such as electric impedance tomography or lung ultrasonography, to attain elevated dynamic compliance, enhanced oxygenation index, and minimized driving pressure [6, 10, 13]. Dynamic compliance may serve as an indirect indicator of the quantity of ventilated alveoli. Yueyi and colleagues conducted a meta-analysis comparing various PEEP levels, reporting that individualized PEEP, determined through titration and imaging techniques, conferred advantages to patients undergoing thoracic surgeries. However, determining the optimal level of PEEP for obese patients during laparoscopic surgery remains a subject of debate [10–12].

Recent studies have suggested that individualized PEEP strategies, tailored to the patient's specific physiological needs, may offer benefits in terms of improved oxygenation, and reduced postoperative pulmonary complications [14–16]. However, the efficacy and safety of these approaches require further investigation.

Given the complexities and uncertainties, the aim of this systematic review and meta-analysis is to comprehensively evaluate the effects of fixed and individualized PEEP strategies on respiratory mechanics, oxygenation, and hemodynamics in obese patients undergoing laparoscopic surgery. Through careful analysis of randomized controlled trials (RCTs), we aim to provide valuable insights that can inform clinical practice and improve patient outcomes in this high-risk group.

Methods

We conducted a systematic review and meta-analysis following the guidelines outlined in Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). The protocol for this meta-analysis was previously registered in the International Prospective Register of Systematic Reviews database (CRD42023488971; registered December 14, 2023).

Search strategy

We conducted a search for English-language randomized controlled trials (RCTs) that investigated the impact of varying PEEP levels on blood oxygenation, respiratory compliance, and hemodynamics in obese patients undergoing laparoscopic surgery. Studies were identified through electronic searches of PubMed, Google Scholar, Cochrane Library, and Embase databases from the 2000s to December 2023. Two researchers independently conducted the search without delving into the study details. All articles identified on this platform were initially assessed for relevance based on their titles and abstracts. Full-text articles were obtained and analyzed for potentially relevant studies. Additionally, related reviews and meta-analyses were examined, and all relevant titles and links were manually reviewed.

The following search terms or combinations of search terms were used:

Keywords: ((((((((((((“Tidal Volume“[Mesh]) OR Tidal Volumes) OR Volume, Tidal) OR Volumes, Tidal))) OR ((((((((((((((((“Positive-Pressure Respiration“[Mesh]) OR Positive-Pressure Respiration) OR Positive-Pressure Respirations) OR Respiration, Positive Pressure) OR Respirations, Positive-Pressure) OR Positive Pressure Ventilation) OR Positive-Pressure Ventilation) OR Positive-Pressure Ventilations) OR Ventilation, Positive Pressure) OR Ventilations, Positive-Pressure) OR Positive End-Expiratory Pressure) OR End-Expiratory Pressure, Positive) OR End-Expiratory Pressures, Positive) OR Positive End-Expiratory Pressure) OR Positive End-Expiratory Pressures) OR Pressure, Positive End-Expiratory) OR Pressures, Positive End-Expiratory))))) AND Randomized Controlled Trial[Publication Type]) NOT (((animals [Mesh] not (humans [Mesh] and animals [Mesh])))))))) AND laparoscopic AND (obese AND obesity). This study adheres to the PRISMA 2020 statement (see Supplement 2).

Selection process

Two independent authors conducted a literature search, selecting and excluding irrelevant articles. Titles and abstracts were independently screened to identify potentially relevant studies evaluating the effects of PEEP levels on the respiratory system and hemodynamics in obese patients undergoing laparoscopic surgery. Reviewers subsequently compared their initial selections; any disagreements were resolved through consensus among reviewers during discussions. Finally, potentially relevant randomized controlled trials (RCTs) published in full text in English were evaluated against the final inclusion criteria. We included only studies that reported on various parameters including PEEP, arterial partial pressure of oxygen (PaO_2) or the PaO2 to inspiratory oxygen fraction ratio (PaO_2/FiO_2), dynamic respiratory compliance (Cdyn), static respiratory compliance (Cstat), plateau pressure (Pplat), peak inspiratory pressure (PIP), driving pressure (DP), mean arterial pressure (MAP), and heart rate (HR) in obese adults undergoing laparoscopic surgery. This encompassed studies with a defined subgroup focusing on laparoscopic colorectal resection within mixed surgical procedures, as well as studies categorizing patient groups as ‘colorectal’ despite only abdominal incisions being performed, excluding perineal incisions.

Inclusion/exclusion criteria

We included studies with the following PICOS criteria:

1. Population: obese adult patients who underwent general anesthesia with mechanical ventilation with tidal volumes ≤ 8 ml/kg during laparoscopic surgery in reverse Trendelenburg position (published from January 2000 to December 2023).
2. Intervention: PEEP level during mechanical ventilation.
3. Comparison: the lung ventilation strategies were divided by PEEP levels according to the most common stratification in the included studies: (low PEEP (LPEEP): 0–5 mbar; moderate PEEP (MPEEP): 6–9 mbar; high PEEP (HPEEP): >=10 mbar; individualized PEEP (iPEEP): PEEP set by special physiological technique– best compliance, electrical impedance tomography or ultrasound guided).
4. Outcomes: SpO_2 or PaO_2/FiO_2, Cdyn, Cstat, Pplat, PIP, DP, MAP, HR.
5. Study design: randomized controlled trial.

We excluded studies that were not in English, not available as full text, or involved the use of a laryngeal mask for mechanical ventilation during general anesthesia.

Data collection

The primary objective of the study was to compare the effects of different PEEP strategies on oxygenation and respiratory mechanics in obese adult patients undergoing laparoscopic surgery under general anesthesia with mechanical ventilation in the reverse Trendelenburg position. The secondary objective was to evaluate the effect of PEEP on hemodynamics.

Oxygenation was evaluated through intraoperative measurements of PaO2 or PaO2/FiO2 during pneumoperitoneum. Respiratory compliance was assessed using static compliance (Cstat, measured via Pplat), dynamic compliance (Cdyn, measured via PIP), or driving pressure (DP). Hemodynamics were evaluated through non-invasive measurements of mean arterial pressure (MAP) and heart rate (HR).

When data were missing, studies were excluded from the meta-analysis. Studies that lacked standard deviations (SD) and where it was impossible to extract them were excluded from the meta-analysis, as they could significantly impact the overall results. For studies with different units of oxygenation measurement, the data were converted to a common unit (mmHg). We used GetData Graph Digitizer 2.25 (http://getdata-graph-digitizer.com/) to quantify the data presented only in graphical form.

Statistical analysis

Data were analyzed using Review Manager (RevMan, version 5.4) and Stata 17.0 (StataCorp, College Station, TX, USA). Pooled continuous data were presented as mean differences (MD) with 95% confidence intervals (CI) and standardized mean differences (SMD). 95% predictive intervals (PI) were used to describe the true significance of the effect within studies. A random-effects model was assumed due to the expected heterogeneity between studies. Heterogeneity was assessed using the Chi-squared test (χ^2), the variance of the true effect size (T^2), and the ratio of excess variance to total variance (I^2). We considered that the true effect varies if the p-value for the Chi-squared test was < 0.10. We conducted Egger's test to statistically evaluate the presence of publication bias by examining the asymmetry of the funnel plot. Funnel plots were drawn to explore publication bias, and forest plots were used to visualize the effect sizes and confidence intervals of individual studies, as well as the overall effect estimate in the meta-analysis. Sensitivity analysis was performed by excluding one study at a time to assess the robustness of the results.

Quality assessment

We used the Cochrane Risk of Bias Assessment Tool (RevMan, version 5.4) to assess the quality of the included studies in seven domains: random sequence generation [D1], allocation concealment [D2], performance bias [D3], detection bias [D4], incomplete outcome data [D5], selective reporting [D6] and other bias [D7] [17]. Also, we rated each domain as high risk, low risk, or some concern using the Risk of Bias Assessment Tool [17]. We performed a P-curve analysis, and False Discovery Rate (FDR) adjustments to assess the likelihood of publication bias and the potential impact of multiple comparisons by the online software using R code (https://www.p-curve.com/app4/ and https://tools.carbocation.com/FDR, respectively).

Results

Studies characteristics

Overall 38 RCTs were identified, that were published from January 2000 until December 2023, from which only 8 studies met inclusion criteria, and were analyzed for this meta-analysis (Fig. 1). These studies included 425 obese patients during laparoscopic surgery in the reverse Trendelenburg position under general anesthesia and volume-controlled mechanical ventilation with different PEEP levels, three of them used recruitment maneuvers. Four studies used individualized PEEP settings according to Cdyn. These studies aimed to assess the effect of different PEEP strategies on oxygenation (PaO_2/FiO_2 all, except Stankiewicz-Rudnicki - they used SpO_2) [6], static respiratory compliance (Cstat and/or DP) or dynamic compliance, hemodynamics (HR and MAP), and postoperative pulmonary complications. The types of procedures included laparoscopic bariatric surgery (gastric bypass or sleeve) in most patients. Table 1 demonstrates the baseline parameters of these studies [6, 13–16, 18–21]. The study made by Elokda SA and Farag HM [11] was excluded from the meta-analysis due to the lack of statistically relevant data.

Evidence quality and the risk of bias

Six of the included studies had a low risk [13, 14, 16, 18, 20, 21], and two studies had some concerns [6, 19] regarding random sequence generation (Fig. 2). Due to the complete outcome data, the risk of attrition bias was assessed as low. Three studies did not provide information on allocation concealment [16, 19, 20]. Five trials lacked details on the blinding of participants and personnel [6, 16, 18, 19, 21], and one trial exhibited a high risk of performance bias [13]. Two studies did not report the blinding of outcome assessment [19, 21], and one study showed a high risk of detection bias [6]. Due to the nearly complete outcome data, the risk of attrition bias was assessed as low. One study demonstrated an increased risk of selective bias [20], and three trials had some concerns [6, 18, 21]. For more information see Supplement 3.

Oxygenation

All studies used PaO_2/FiO_2 as a method for oxygenation evaluation, except the study by Stankiewicz-Rudnicki et al. (the authors used SpO_2 measurements only).

Meta-analysis of 5 studies comparing the influence of LPEEP vs. HPEEP ($n = 200$) on PaO_2/FiO_2 showed an increase in PaO_2/FiO_2 in every particular study in the HPEEP group and overall increase in effect was (+ 129.93 (+ 75.20; +184.65) mmHg, $p < 0.0001$), but variability of true effect was also evident (Chi^2 34.92, $p < 0.0001$). The

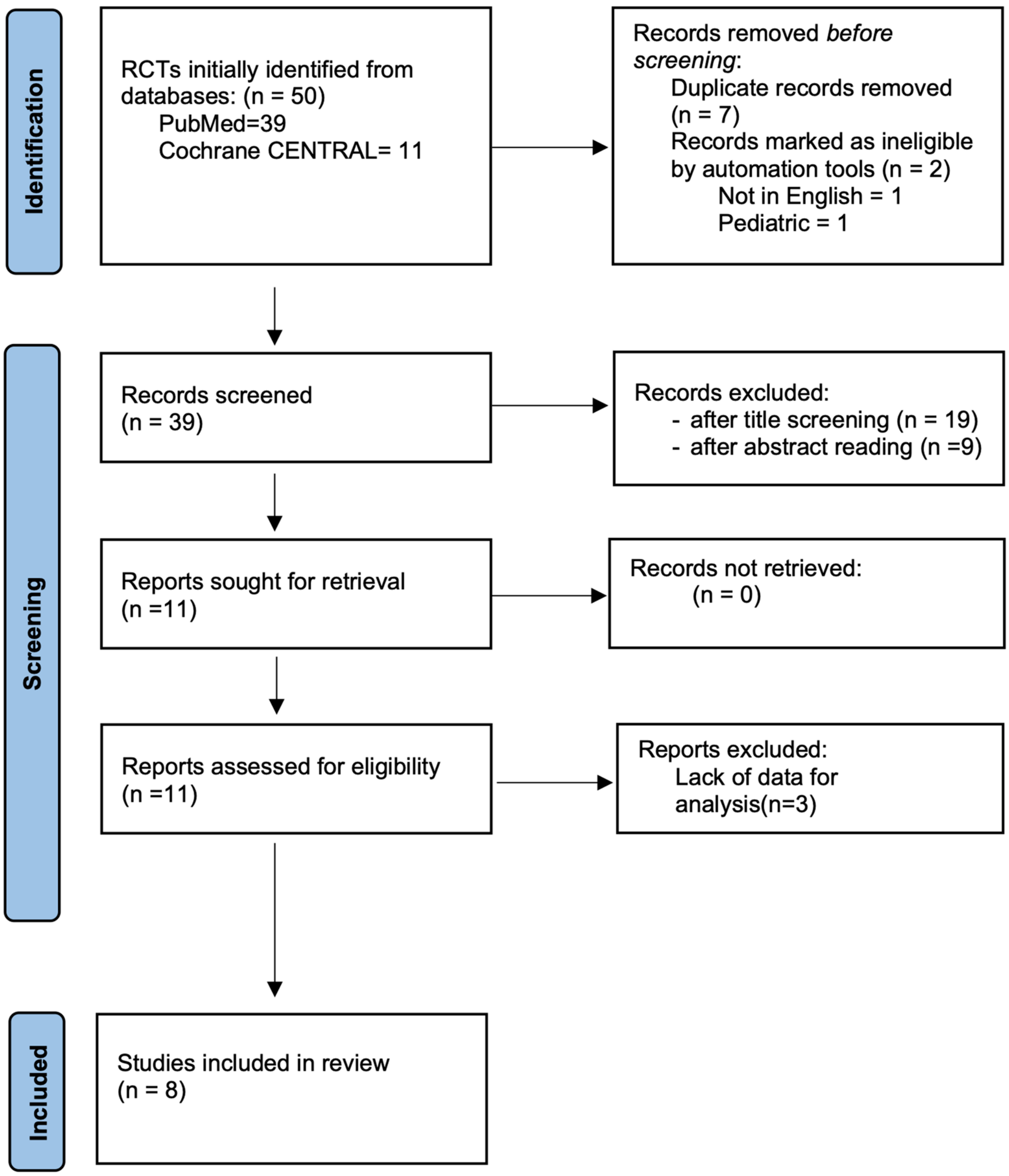

Fig. 1 PRISMA flow chart of the included studies

distribution of true effect size was wide ($T^2 = 3334.08$ and I^2 89%), which reveals a high real variation of the true effect of PaO_2/FiO_2 increase in the HPEEP group (Fig. 3a). Estimation of the prediction interval of true effect showed a broad distribution of predicted effect (Fig. S1). The precision was low, and the risk of publication bias was high (Fig. S2). A similar picture was seen in 3 studies comparing iPEEP versus LPEEP ($n = 159$), as iPEEP studies in fact used HPEEP. In the iPEEP group, PaO_2/FiO_2 was higher than in LPEEP (+ 130.23 (+ 57.18; +203.27) mmHg, $p = 0.0005$), also PaO_2/FiO_2 was higher in every single study with high variation of the true effect (Chi^2 26.95, $p < 0.0001$), wide distribution of true effect size ($T^2 = 3828.72$ and I^2 93%) (Fig. 3b), and wide predictive interval of the effect (Fig. S3). The precision was low, and the risk of publication bias was high (Fig. S4). In two studies a comparison between HPEEP and iPEEP did not find a difference in PaO_2/FiO_2 (+ 21.99 (-105.69; +149.67) mmHg, $p = 0.74$), but meta-analysis revealed variation of the true effect size (Chi^2 11.97, $p = 0.0005$) with very high heterogeneity of the true effect ($T^2 = 7779.79$, I^2 92%) (Fig. 3c), and wide predictive interval (Fig. S5). The precision and the risk of publication bias are presented in Fig. S6. Only one study [21] that included 36 patients in two arms, comparing LPEEP (zero PEEP) (alone or with the recruitment maneuvers) and moderate PEEP, did not

Table 1 Study characteristics

Study	Study design	Surgery	Position	*N* total	TV (ml/kg)	PEEP (cmH2O)	RM	Mean age (years)	BMI (kg/m2)	*n*	ASA	Strategy classification	HD complications	RM	PPC events (include hypoxemia SpO2 < 90%)
Whalen FX et al. (2006)	single centre	laparoscopic bariatric Roux-en-Y surgeries	RT	20	8	4	no	38 ± 11	53 ± 11	10	II-III	LPEEP	NA	After PNP, PEEP increased in a stepwise fashion for 2 min— to 10 cm H2O(3 breaths), to 15 cm H2O(3 breaths), to 20 cm H2O(10 breaths) until PIP reached 50 cm H2O. RM were repeated if Pao2 showed an increasing trend after the 1st RM, a series of up to 4 sequential RM was performed	2(1 - respiratory failure, 1 - atelectasis requiring bronchoscopy)
					8	12	yes	44 ± 9	48 ± 6	10		HPEEP			3 (1- pulmonary embolism, 2 - respiratory failure)
Stankiewicz-Rudnicki M et al.(2016)	single centre	laparoscopic gastric banding	RT	49	8	0	no	38 (32,5–43,5)	42.8 (40.8–46.9)	24		LPEEP	NA	Before mechanical ventilation was started a RM was performed (2 sustained inflations for 10 s, each with PIP of 40 cm H2O)	
					8	10	yes	40 (31–47)	41.7 (38.8–46.8)	25		HPEEP			
Nestler C et al. (2017)	single centre	laparoscopic surgery	RT	50	8	5	no	46.2 (19–63)	53.8 (8.2)	25	I-III	MPEEP	42% had BP complications, 20% had bradycardia	PIP 50 cm H2O, PEEP 30 cm H2O, respiratory rate 6 bpm, for 10 cycles	0
					8	EIT	yes	44.9 (23–62)	48.3 (7.1)	25		IPEEP	40% had BP complications, 28% had bradycardia		2 (8%) - pneumonia or the need for invasive or non-invasive ventilation for acute respiratory failure

Table 1 (continued)

Study	Study design	Surgery	Position	*N* total	TV (ml/kg)	PEEP (cmH2O)	RM	Mean age (years)	BMI (kg/m2)	*n*	ASA	Strategy classification	HD complications	RM	PPC events (include hypoxemia SpO2 < 90%)
Wei K et al. (2018)	single centre	laparoscopic sleeve gastrectomy	RT	34	8	0	no	37 (19–57)	45 ± 6	12	II-III	LPEEP	1 patient was excluded for persistent hypotension	After PNP and repeated every 30 min: increasing PEEP in a stepwise fashion- to 5 cmH2O, to 10 cmH2O, and then to 15 cmH2O with 3 breaths on each point. If PIP > 40cmH2O, the next level of PEEP was halted. If MAP decreased by > 25% of baseline value, the RM was stopped	1 (8%) – 1patient with postop resp failure requiring oxygen therapy
					8	0	yes	35 (18–46)	48 ± 8	11		LPEEP			0
					8	8	yes	39 (21–50)	43 ± 6	11		HPEEP			0
Van Hecke D et al. (2019)	single centre	laparoscopic bariatric surgery	RT	100	8	10	yes	40 (27–47)	42 (39–45)	50	II-III	HPEEP	NA	RM were applied whenever the SpO2 < 95%, using to the protocol described by Whalen et al.(2006)	1.3% -hypoxemia time
					8	Cdyn guided	no	42 (31–48)	42 (40–45)	50		IPEEP			2.1%
Elshazly M et al. (2020)	single centre	laparoscopic bariatric surgery	RT	40	6	4	no	35.6 (7.80)	43.85 (3.76)	20	II	LPEEP	1 patient from control group developed hypotension		5 (25%) - hypoxia
					6	US-guided	no	37.00 (4.71)	43 (2.83)	20		IPEEP			0

Table 1 (continued)

Study	Study design	Surgery	Position	*N* total	TV (ml/kg)	PEEP (cmH2O)	RM	Mean age (years)	BMI (kg/m2)	*n*	ASA	Strategy classification	HD complications	RM	PPC events (include hypoxemia SpO2 < 90%)
Simon P et al.(2021)	single centre	73 - gastric bypass, 16 - sleeve gastrec-tomy, 1- rectal cancer surgery	RT	90	7–8	EIT	yes	44.9 ± 10.3	48.2 ± 7.0	25		IPEEP	hypotension in 10 patients (40%), bradicardia 7 (28%)	I: E, 1:1;, 50 cm H2O; PEEP, 30 cm H2O; RR, 6 bpm	2 (8%)
						12	yes	43.6 ± 11.3	51.4 ± 13.4	21		HPEEP	hypotension in 7 patients (33%), bradicardia – 10(48%)	I: E, 1:1;PEEP, 12 cm H2O; RR, 6 bpm; increasing VT in steps of 4 ml/kg of predicted body weight until Pplateau reaches 40 cm H2O followed by 3 breaths while maintain-ing Pplateau of 40–50 cmH2O	1 (5%)
						4–5	no	46.5 ± 14.1	51.0 ± 9.5	44		LPEEP	hypotension in 22 patients (50%), bradicardia 11(25%)		2 (5%)
Li Xiang et al. (2023)	single centre	laparoscopic bariatric surgery	RT	40	8	8	yes	27 ± 7	40.1 ± 3.5	20	II-III	MPEEP	8 (40%) hypoten-sion during RM	PC ventilation mode, with a stepwise increase PEEP from 10 to 25 by 5 cm H2O every 30 s and a driving pres-sure of 15 cm H2O	20%
					8	Cdyn guided	yes	28 ± 7	41.9 ± 5.6	20		IPEEP	6 (30)		20%

Abbreviations: ASA: American Society of Anaesthesiologists physical status; BMI: body mass index; HD: hemodynamics; PC: pressure controlled ventilation; Cdyn: dynamic compliance; BP: blood pressure; MAP: mean arterial pressure; PIP: peak inspiratory pressure; EIT: electrical impedance tomography; iPEEP: individualized positive end-expiratory pressure group; LPEEP: low positive end-expiratory pressure group; MPEEP: moderate positive end-expiratory pressure group; HPEEP: high positive end-expiratory pressure group; PEEP: positive end-expiratory pressure; NA: not applicable; Pes: esophageal pressure; TV: tidal volume; RT: reverse Trendelenburg; PNP: carboxyperitoneum

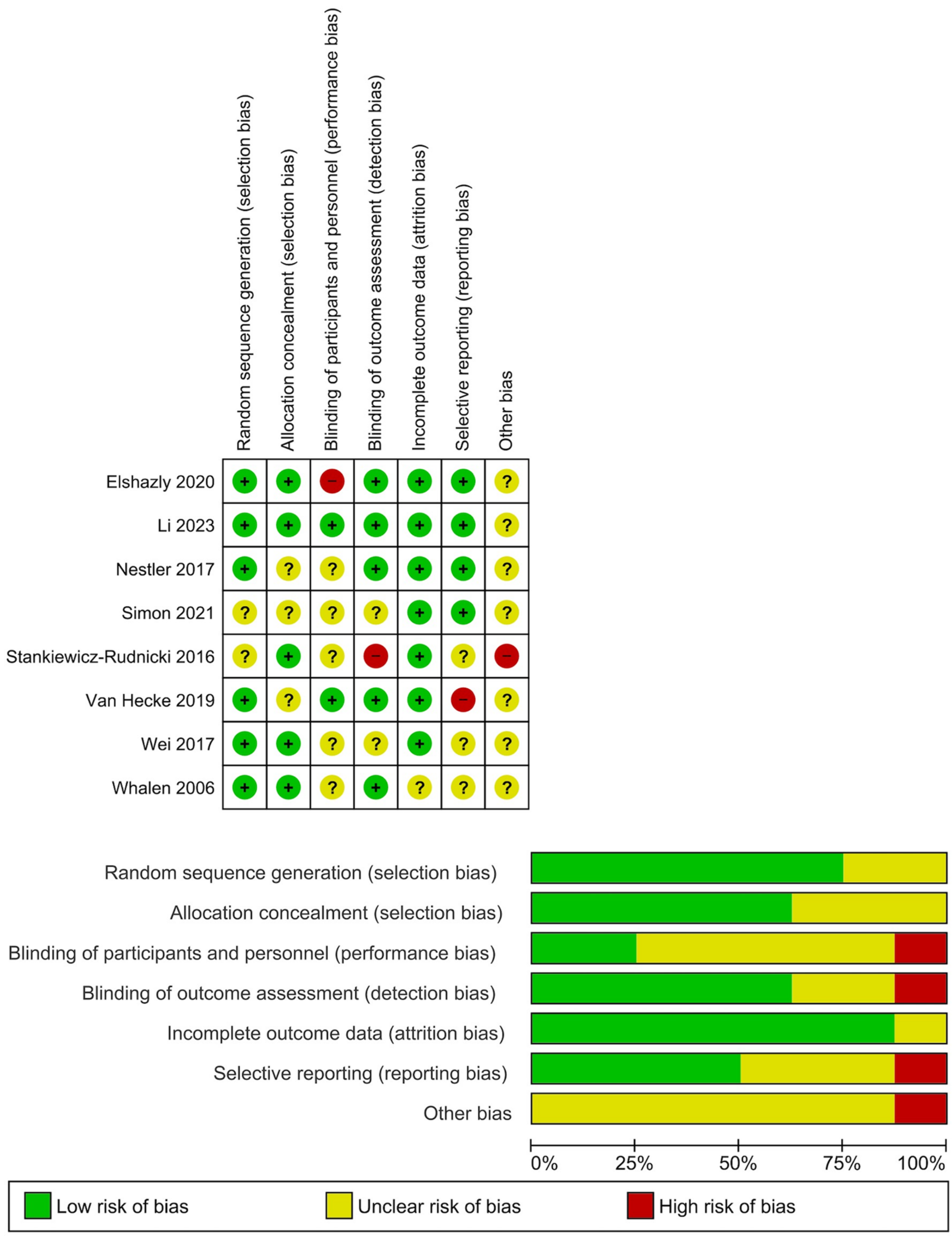

Fig. 2 Cochrane risk of bias assessment tool

show the difference in PaO_2/FiO_2 ($p = 0.13$), variation of the true effect was not significant (Chi^2 2.01, $p = 0.16$) (Fig. 3d). We did not draw any conclusion by the predictive interval and funnel plot because only two studies were included Fig S7-8.

Dynamic respiratory compliance

Meta-analysis of 5 studies comparing the influence of LPEEP vs. HPEEP ($n = 90$) on Cdyn has shown a significant increase in Cdyn in the HPEEP group (+ 15.06 (5.47; +24.65) ml/mbar, $p = 0.002$) but high variability of the true effect (Chi^2 93.16, $p < 0.0001$). The distribution of true effect size was wide ($T^2 = 113.75$), and I^2 96%, which can correspond to a high real proportion of true effect

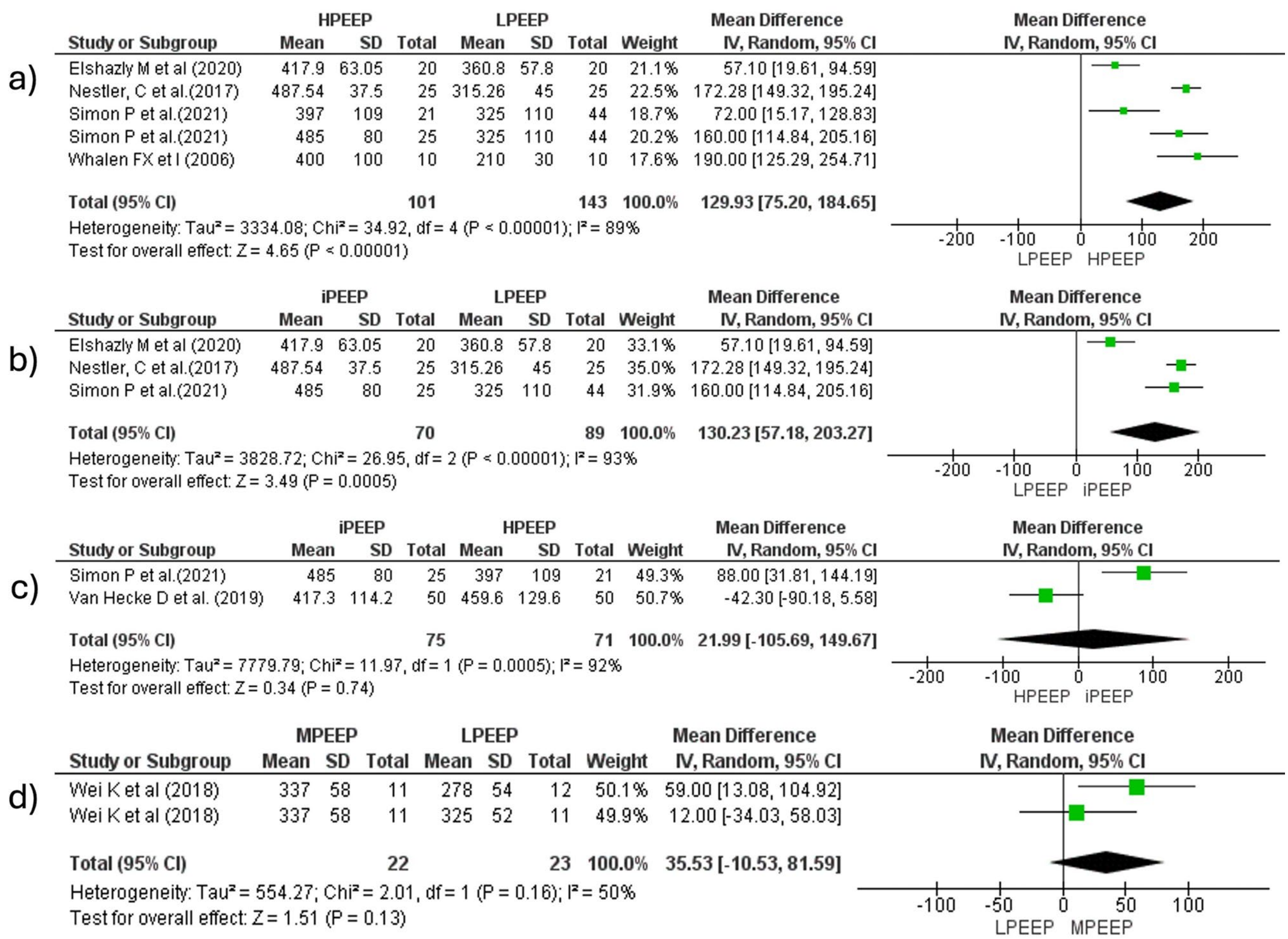

Fig. 3 Forest plot for PaO_2/FiO_2 comparing different PEEP strategy groups: (**a**) LPEEP vs. HPEEP; (**b**) LPEEP vs. iPEEP; (**c**) HPEEP vs. iPEEP; (**d**) LPEEP vs. MPEEP. Data are presented as mean differences and 95% confidence intervals. The vertical line represents no effect with the value of 0. The diamond represents the pooled mean effect estimate with 95% CI. It provides an overall measure of the difference in PaO_2/FiO_2 values between different PEEP strategy groups. *Abbreviations*: CI: confidence interval; SD: standard deviation; I^2: the ratio of excess dispersion to total dispersion; Tau^2: the variance of the true effect sizes; Chi^2: observed weighted sum of squares; df: degrees of freedom; PaO_2/FiO_2: arterial oxygen partial pressure to fractional inspired oxygen ratio; LPEEP: low positive end-expiratory pressure group; MPEEP: moderate positive end-expiratory pressure group; HPEEP: high positive end-expiratory pressure group; iPEEP: individualized positive end-expiratory pressure group

variation (Fig. 4a). The prediction interval of true effect was wide (Fig. S9), and a high risk of publication bias (Fig. S10). Comparison of LPEEP and iPEEP in three studies ($n = 159$) showed similar results Fig. 4b): increase in Cdyn in iPEEP group (+ 22.46 (+ 8.56; +36.35) ml/mbar, $p = 0.002$) with high variability of the true effect (Chi^2 53.92, $p < 0.0001$) and wide distribution of true effect ($T^2 = 144.52$) and high proportion of true effect variation (I^2 96%), wide predictive interval (Fig. S11), and high risk of publication bias (Fig. S12). Meta-analysis of another two studies comparing HPEEP and iPEEP ($n = 146$) revealed no difference in Cdyn (+ 12.92 (-5.01; +30.85) ml/mbar, $p = 0.16$)(Fig. 4c), with high variability of the true effect (Chi^2 24.56, $p < 0.0001$), wide distribution of true effect ($T^2 = 160.63$) with high proportion of real true effect variation (I^2 96%), also wide predictive interval (Fig. S13) and high risk of publication bias (Fig. S14).

Driving pressure

Meta-analysis of three studies ($n = 190$) revealed significant decrease in driving pressure in HPEEP group as compared with LPEEP (-10.12(-13.17;-7.06), $p < 0{,}0001$) with high variability of the true effect (Chi^2 23.53, $p < 0.0001$), but relatively narrow distribution of true effect ($T^2 = 6.52$), high real proportion of the true effect variation ($I^2 = 92\%$)(Fig. 5a), but predictive interval was wide (Fig. S15). The funnel plot of LPEEP vs. HPEEP studies reveals high publication bias (Fig. S16). LPEEP vs. iPEEP meta-analysis ($n = 119$) found a decrease in driving pressure in the iPEEP group (-8.26 (-9.63;-6.89), $p < 0{,}0001$) but low variability and narrow distribution of the true effect (Chi^2 2.42, $T^2 = 0.58$, $p = 0.12$), high real proportion of true effect variation ($I^2 = 59\%$) (Fig. 5b). LPEEP vs. iPEEP studies in DP had a narrow predictive interval for the true effect (Fig. S17), and low risk

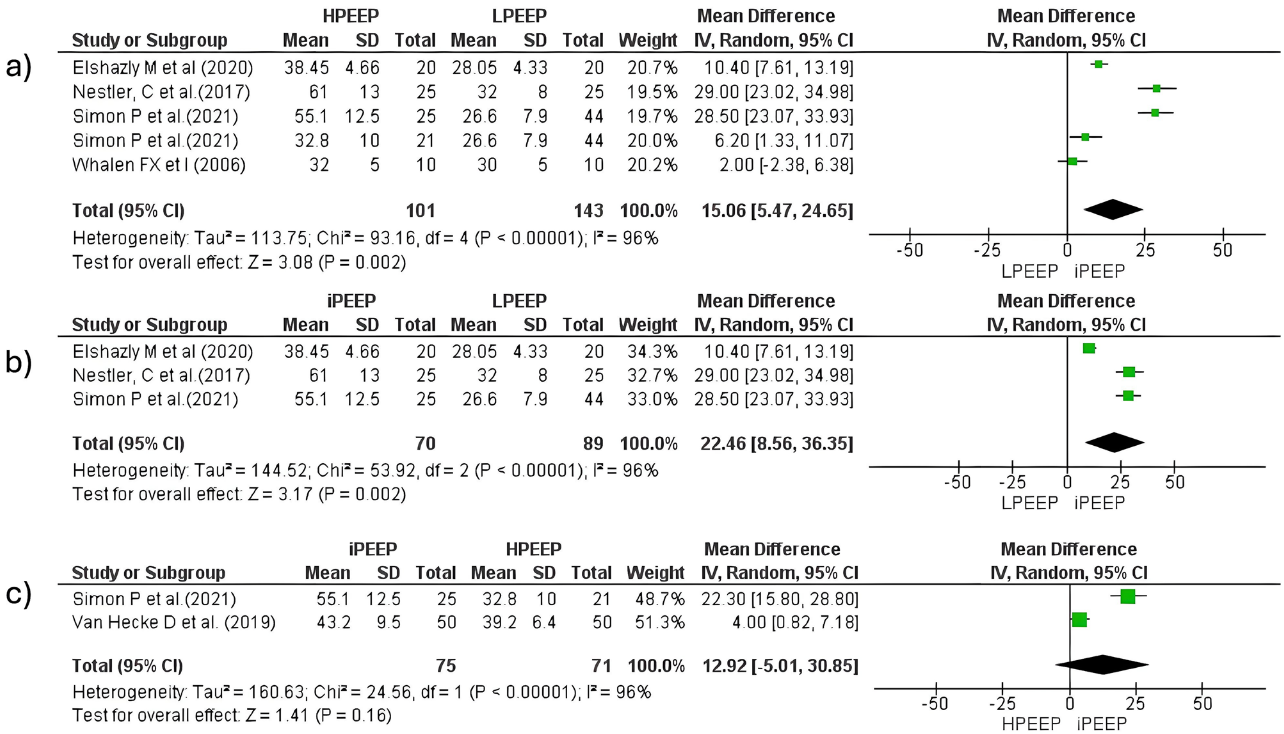

Fig. 4 Forest plot for Cdyn comparing different PEEP strategy groups: (**a**) LPEEP vs. HPEEP; (**b**) LPEEP vs. iPEEP; (**c**) HPEEP vs. iPEEP. Data are presented as mean differences and 95% confidence intervals. The vertical line represents no effect with the value of 0. The diamond represents the pooled mean effect estimate with 95% CI. It provides an overall measure of the difference in Cdyn values between different PEEP strategy groups. *Abbreviations*: CI: confidence interval; SD: standard deviation; I^2: the ratio of excess dispersion to total dispersion; Tau^2: the variance of the true effect sizes; Chi^2: observed weighted sum of squares; df: degrees of freedom; Cdyn: dynamic compliance; LPEEP: low positive end-expiratory pressure group; MPEEP– moderate positive end-expiratory pressure group; HPEEP: high positive end-expiratory pressure group

of publication bias (Fig. S18). Meta-analysis of one RCT with three arms did not found significant decrease in driving pressure in MPEEP group as compared with LPEEP (-3.12(-9.48; 3.25), p = 0,34) with high variability of the true effect (Chi^2 13.31, $p = 0.0003$), but relatively narrow distribution of true effect ($T^2 = 19.54$), high real proportion of the true effect variation ($I^2 = 92\%$)(Fig. 5c). Data on the predictive interval and funnel plot are inconclusive (Fig. S19-S20).

Plateau pressure

Meta-analysis of five studies ($n = 229$) comparing differences in plateau pressure between LPEEP and HPEEP studies found small but significant increase in plateau pressure (Pplat) in HPEEP group (+3.10(+0.37;+5.82), $p = 0.03$) with high variability of the true effect (Chi^2 23.47, $p < 0.0001$), relatively narrow distribution of true effect ($T^2 = 7.80$), and high real proportion of the true effect variation ($I^2 = 83\%$)(Fig. S21), but predictive interval was wide (Fig. S22). The funnel plot of LPEEP vs. HPEEP studies concerning Pplat reveals high publication bias (Fig. S23). LPEEP vs. iPEEP meta-analysis ($n = 159$) did not find significant changes in plateau pressure in the iPEEP group (+3.12 (-1.23;+7.48), $p = 0.16$) with high variability and high distribution of the true effect (Chi^2 23.30, $T^2 = 13.54$, $p < 0.0001$), high real proportion of true effect variation ($I^2 = 91\%$)(Fig. S24).The predictive interval for the true effect of LPEEP vs. iPEEP comparison in Pplat was wide (Fig. S25), and included studies had a high risk of publication bias (Fig. S26). LPEEP vs. MPEEP meta-analysis ($n = 45$) did not find significant changes in plateau pressure ($p = 0.05$) and significant variation of true effect (Chi^2 2.47, $T^2 = 4.77$, $p = 0.12$)(Fig. S27). The predictive interval for the true effect of LPEEP vs. MPEEP comparison in Pplat is presented in Fig. S28. Data on the risk of publication bias is inconclusive (Fig. S29).

Peak inspiratory pressure

Meta-analysis of five studies ($n = 199$) comparing differences in peak inspiratory pressure (PIP) between LPEEP and HPEEP studies found small increase in PIP pressure in HPEEP group (+3.92(+1.95;+5.89), $p < 0.0001$) with high variability of the true effect (Chi^2 11.76, $p = 0.02$), narrow distribution of true effect ($T^2 = 3.27$), moderate real proportion of the true effect variation ($I^2 = 66\%$)(Fig. S30), and wide predictive interval for the true effect (Fig. S31). The risk of publication bias for LPEEP vs. HPEEP studies concerning PIP was high (Fig. S32). Meta-analysis ($n = 159$) found a significant PIP increase in the iPEEP group as compared with LPEEP (+4.51 (+2.35;+6.68),

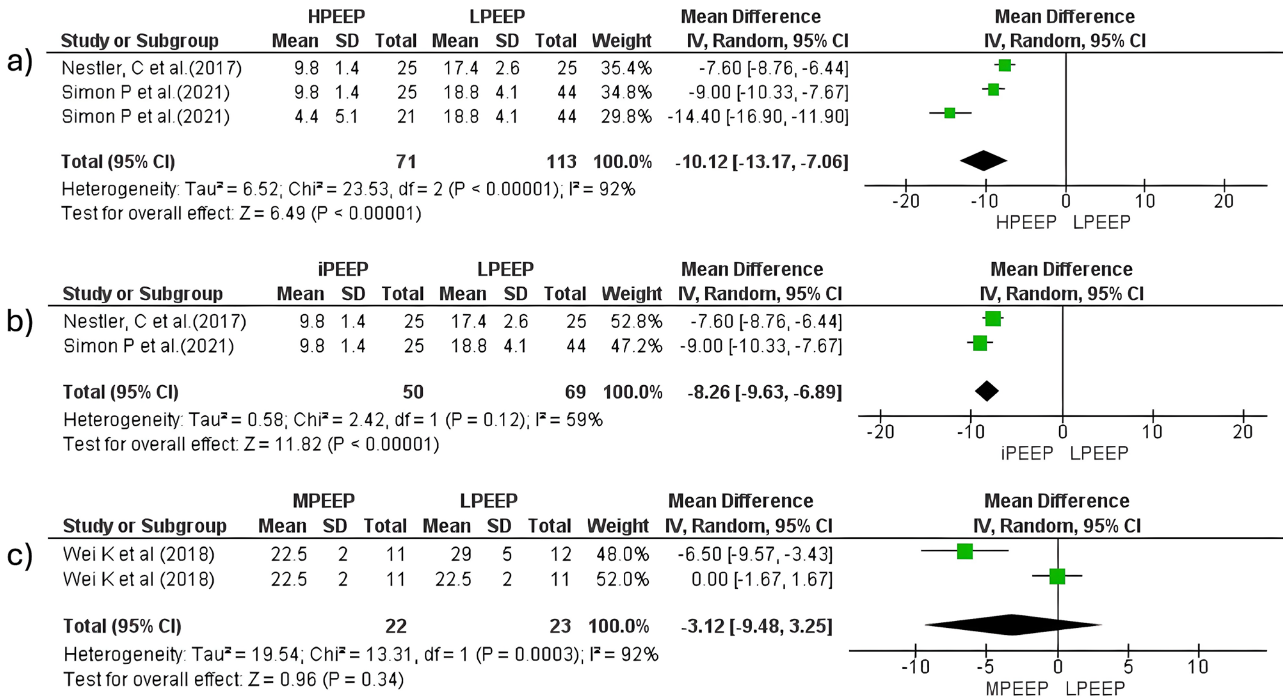

Fig. 5 Forest plot for DP comparing different PEEP strategy groups: (**a**) LPEEP vs. HPEEP; (**b**) LPEEP vs. iPEEP; (**c**) LPEEP vs. MPEEP. Data are presented as mean differences and 95% confidence intervals. The vertical line represents no effect with the value of 0. The diamond represents the pooled mean effect estimate with 95% CI. It provides an overall measure of the difference in DP values between different PEEP strategy groups. *Abbreviations*: CI: confidence interval; SD: standard deviation; I^2: the ratio of excess dispersion to total dispersion; Tau^2: the variance of the true effect sizes; Chi^2: observed weighted sum of squares; df: degrees of freedom; DP: driving pressure; Cdyn: dynamic compliance; MPEEP: moderate positive end-expiratory pressure; iPEEP: individualized positive end-expiratory pressure group

$p<0.0001$) with insignificant variability of the true effect (Chi^2 5.01, $T^2=2.20$, $p=0.08$, $I^2=60\%$) (Fig. S33). The predictive interval for the true effect of LPEEP vs. iPEEP comparison in PIP was wide (Fig. S34), but included studies had a low risk of publication bias (Fig. S35). PIP was low in LPEEP vs. MPEEP meta-analysis ($n=34$)($p=0.02$), but variation of true effect was insignificant (Chi^2 0.06, $T^2=0.00$, $p=0.80$)(Fig. S36). The predictive interval for the true effect of LPEEP vs. MPEEP comparison in PIP is presented in Fig. S37. Data on the risk of publication bias is inconclusive (Fig. S38).

Mean arterial pressure and heart rate

Meta-analysis of five studies ($n=249$) showed significant increase in MAP in HPEEP groups as compared to LPEEP groups (+4.36 (+0.36;+8.36), $p=0.03$), variability of the true effect was nonsignificant (Chi^2 9.26, $T^2=10.59$, $p=0.10$) (Fig. 6a), but predictive interval for the true effect showed wider range crossing zero line (Fig. S39). The risk of publication bias for LPEEP vs. HPEEP studies in MAP comparison was low (Fig. S40). Comparison of MAP in LPEEP vs. iPEEP meta-analysis ($n=159$) found nonsignificant differences (+1.58 (-1.95;+5.11), $p=0.38$) with nonsignificant heterogeneity of the true effect (Chi^2 2.43, $T^2=1.80$, $p=0.30$) (Fig. 6b), the predictive interval for true effect was wide, crossing zero line (Fig. S41), and the publication bias was low (Fig. S42). MAP in LPEEP vs. MPEEP meta-analysis ($n=34$) did not differ (+1.29 (-4.12;+6.70), $p=0.64$) and heterogeneity of the true effect was nonsignificant (Chi^2 0.02, $T^2=0.00$, $p=0.89$) (Fig. 6c), the predictive interval for true effect was wide, crossing zero line (Fig. S43), and the data on publication bias was inconclusive (Fig. S44).

Three meta-analyses comparing the heart rate in LPEEP vs. HPEEP, LPEEP vs. iPEEP, and LPEEP vs. MPEEP did not find significant differences between groups (Fig. 7a and c, respectively), all predictive intervals for the true effect showed a wider range crossing zero line (Figs. S45, S47, S49, respectively), and the rest of publication bias for all comparisons was low (Figs. S46, S48, S50, respectively).

Postoperative pulmonary complications

Methods for PPC detection were heterogeneous between studies, thus we did not perform a meta-analysis. Overall, all studies except Li et al. [14] and Elshazly et al. [13] have not found any differences in PPCs. These abovementioned studies have found a decrease in postoperative atelectasis and early postoperative hypoxemia.

P-curve analysis, and FDR analysis to assess the likelihood of publication bias and the potential impact of multiple comparisons are presented in the Supplement

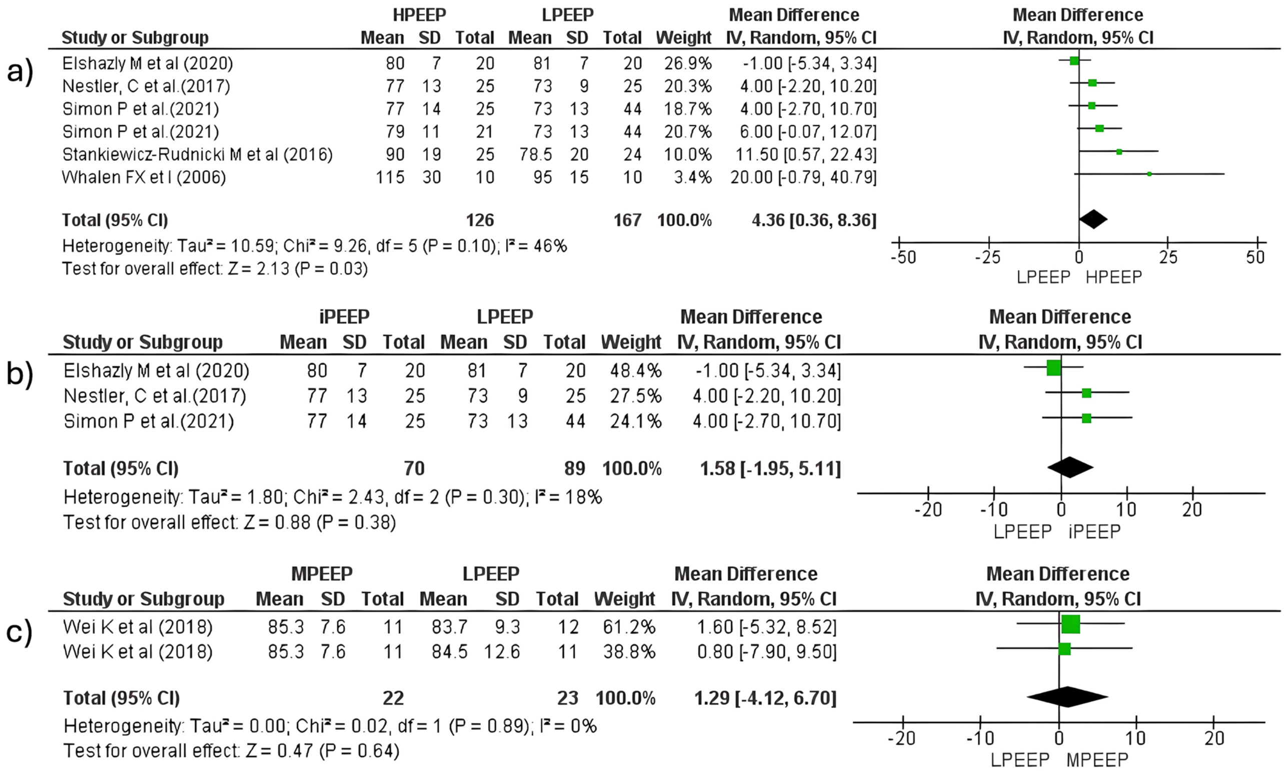

Fig. 6 Forest plot for MAP comparing different PEEP strategy groups: (**a**) LPEEP vs. HPEEP; (**b**) LPEEP vs. iPEEP; (**c**) LPEEP vs. MPEEP. Data are presented as mean differences and 95% confidence intervals. The vertical line represents no effect with the value of 0. The diamond represents the pooled mean effect estimate with 95% CI. It provides an overall measure of the difference in MAP values between different PEEP strategy groups. *Abbreviations*: CI: confidence interval; SD: standard deviation; I^2: the ratio of excess dispersion to total dispersion; Tau^2: the variance of the true effect sizes; Chi^2: observed weighted sum of squares; df: degrees of freedom; MAP: mean arterial pressure; LPEEP: low positive end-expiratory pressure; MPEEP: moderate positive end-expiratory pressure; HPEEP: high positive end-expiratory pressure group; iPEEP: individualized positive end-expiratory pressure group

4. These analyses found that the effects observed in the studies measuring plateau pressure are likely genuine, with minimal publication bias and no major issues with false positives. However, missing studies (like those with unreported p-values) might slightly affect the overall effect size. Sensitivity analysis are presented in the Supplement 5. For the meta-analyses with less than five studies we additionally used fixed-effects model. For studies with high risk of biases which concerned blinding of participants and personnel (performance bias) and blinding for the outcome (detection bias) we performed additional metaanalyses after removing these studies. After changing the statistical model for the meta-analyses and removing studies with high risk of bias overall estimates remained robust.

Discussion

Mechanical ventilation during anesthesia can lead to several side effects, including airway closure and atelectasis in dependent regions, which may result in hypoxemia and pneumonia [22]. These conditions are among the main postoperative pulmonary complications (PPCs) [23]. In obese patients, mechanical ventilation during anesthesia often results in increased pleural pressure and decreased respiratory compliance, as demonstrated in physiological studies [24]. The pneumoperitoneum associated with laparoscopic surgery can further decrease respiratory compliance and increase pleural pressure due to elevated intra-abdominal pressure [25]. Therefore, the careful selection of PEEP levels during anesthesia is crucial for this patient population, as it can enhance respiratory compliance and reduce the risk of PPCs [26–28].

An intraoperative increase in venous admixture due to decreased respiratory compliance, atelectasis, or airway closure can be managed by increasing the inspiratory oxygen fraction. However, a reduction in respiratory compliance (or an increase in its inverse for constant tidal volume, known as driving pressure) can lead to lung overdistension (also known as strain) during mechanical ventilation [29]. This overdistension can be mitigated by selecting an appropriate PEEP level during pneumoperitoneum (PNP). Conversely, excessive PEEP levels may exacerbate lung overdistension and reduce blood flow in alveolar vessels [30]. A large analysis of several RCTs in ARDS patients found that higher driving pressure was associated with increased mortality [31]. Similarly, in

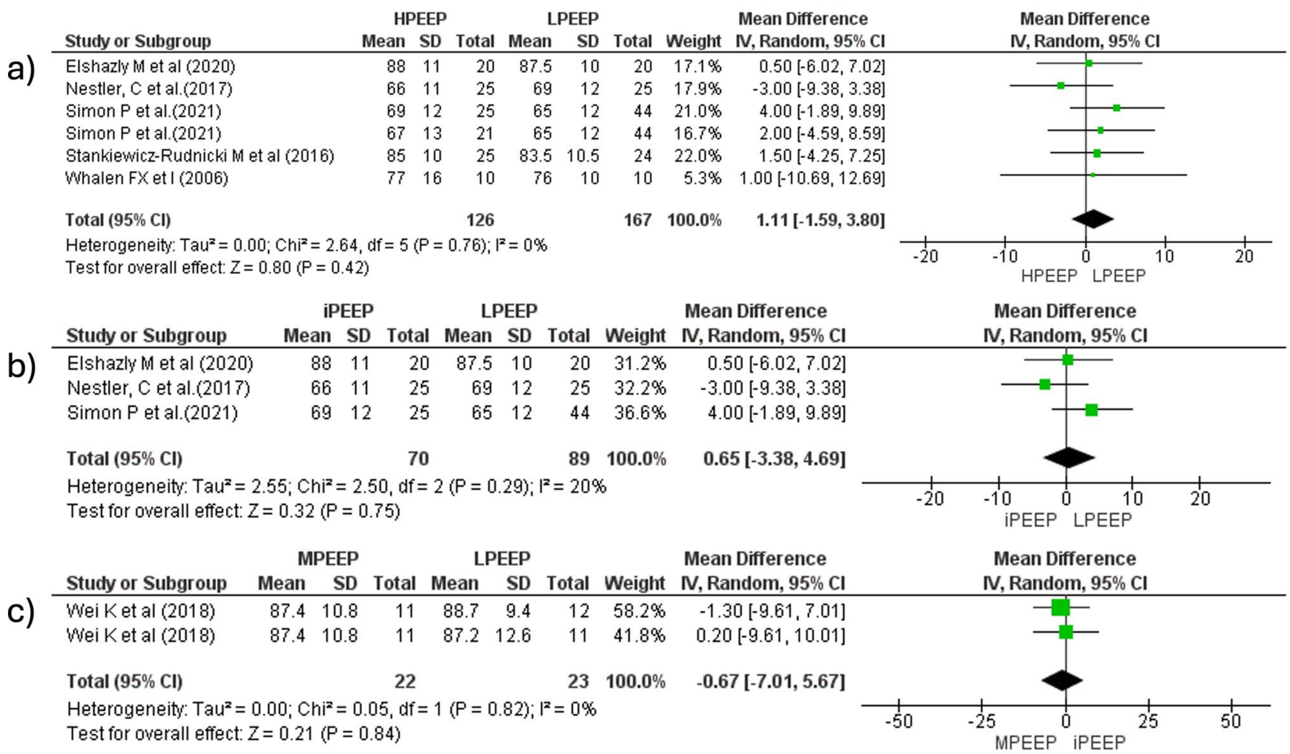

Fig. 7 Forest plot for HR comparing different PEEP strategy groups: (**a**) LPEEP vs. HPEEP; (**b**) LPEEP vs. iPEEP; (**c**) LPEEP vs. MPEEP. Data are presented as mean differences and 95% confidence intervals. The vertical line represents no effect with the value of 0. The diamond represents the pooled mean effect estimate with 95% CI. It provides an overall measure of the difference in HR values between different PEEP strategy groups. *Abbreviations* CI: confidence interval; SD: standard deviation; I^2: the ratio of excess dispersion to total dispersion; Tau^2: the variance of the true effect sizes; Chi^2: observed weighted sum of squares; df: degreeы of freedom; HR: heart rate; LPEEP: low positive end-expiratory pressure group; MPEEP: moderate positive end-expiratory pressure group; HPEEP: high positive end-expiratory pressure group; iPEEP: individualized positive end-expiratory pressure group

elective surgical patients undergoing general anesthesia, higher driving pressure was linked to a greater risk of postoperative respiratory failure [32].

PEEP could help counterbalance not only the increased pleural and abdominal pressure but also the expiratory flow limitation caused by airway closure. EFL can be detected, and airway opening pressure (AOP) can be measured through a simple analysis of the pressure curve during intraoperative ventilation with a constant flow if «conductive pressure» exceeds resistive pressure [33]. The prevalence of the AOP in obese patients during PNP was 22–38% [9, 34]. In these patients, lung inflation begins if the airway pressure exceeds AOP. PEEP level that could reverse EFL and decrease shunt reached 8–15 cmH2O during PNP and Trendelenburg position [9]. Intraoperative atelectasis formation is linearly related to body mass index within a range from 18 to 30 kg/m^2 at zero PEEP [35]. Both PNP and obesity reduce transpulmonary pressure, leading to conditions that favor lung collapse (36–37). In obese patients during PNP and Trendelenburg position, end-expiratory transpulmonary pressure close to zero or above zero was achieved at the mean PEEP 9.1 cm H2O for BMI 25 to 29.9, PEEP 11.2 cm H2O for BMI 30 to 34.9, PEEP 12.8 cm H2O for BMI 35 to 39.9, and PEEP 16.8 cm H2O for BMI 40 or above [38]. Postoperative atelectasis in patients with morbid obesity was observed after 24 h from the operation with PNP and reverse Trendelenburg position with the tidal volume of 10 ml/kg and PEEP 6 cm H2O. Still, this was not the case for non-obese patients [37]. Spadaro S. et al. found a significant shunt reduction during laparoscopic surgery in a flat position was observed at PEEP 10 cmH2O compared to PEEP 5 cmH2O, or zero PEEP [39]. The authors also showed that PEEP 5 cmH2O was sufficient to decrease the shunt during laparotomy, and a further increase in PEEP had no positive effect on the shunt.

The position of the patient during PNP also affects lung volumes. The supine position was associated with a marked decrease in FRC as compared to the sitting position [40], and it could be more pronounced in the Trendelenburg position [41] with the formation of zones of no ventilation in dorsal parts of the lungs [42]. Shono A. et al. found with the EIT that these zones during PNP and the Trendelenburg position were partially reversed by PEEP about 15 cmH_2O in a study by [43]. On the contrary, another EIT study showed that reverse Trendelenburg position could improve lung ventilation in obese patients with PNP [6]. PEEP 10 cm H_2O was insufficient to improve respiratory mechanics compared with PEEP 5 cmH_2O during gynecological robotic surgery with deep Trendelenburg position and PNP [44].

«Traditional» tidal volume (VT) (10–15 ml/kg of predicted body weight (PBW)) has been widely used intraoperatively to prevent atelectasis formation as it was demonstrated almost 50 years ago as compared to low tidal volume [45]. It has been shown in 2000 that traditional VT increased mortality in ARDS patients [46] due to lung overdistension (volutrauma) as an important cause of ventilator-associated lung injury [47]. In the experimental study, the volutrauma (or strain) was more pronounced during zero PEEP as compared to PEEP 10 cm H2O with the same VT used [48]. The use of low VT with PEEP 6–8 cmH2O as compared to 10 ml/kg PBW and zero PEEP in intermediate-risk and high-risk patients undergoing major abdominal surgery was associated with a reduction of postoperative pulmonary complications in a large RCT [49]. Secondary analysis of RCT in laparoscopic abdominal surgery demonstrated a lower rate of PPCs with VT 6 ml/kg PBW and PEEP 5 cm H2O vs. 10 ml/kg PBW and PEEP 5 cm H2O [50]. These findings may be associated with lower driving pressure but not lower VT per se, as was demonstrated in a large registry study [51]. Driving pressure is a reverse measure for respiratory compliance during ventilation with the stable tidal volume, and it is particularly associated with lung strain [36].

A transient increase in airway pressure or volume (recruitment maneuvers) aimed to increase transpulmonary pressures to open (recruit) poorly or non-ventilated lung regions. Besides this aim, the types and methodology of RM are heterogeneous, and the PEEP level after RM differs significantly (6, 16, 18, 20–21). Futier E et al. has shown that using RM combined with a PEEP of 10 cm H_2O, compared to PEEP of 10 cm H_2O alone, increased end-expiratory lung volume in patients undergoing laparoscopic surgery in the Trendelenburg position, regardless of whether they are obese or non-obese [52]. Additionally, RM with PEEP in patients during PND and Trendelenburg position decreased elastance of the lung and chest wall, improving oxygenation without causing clinically significant hemodynamic compromise [53]. Differences in the methodology of RMs combined with the different PEEP strategies make the results of meta-analyses inconclusive.

In our meta-analysis, we focused on a highly specific cohort: obese patients undergoing pneumoperitoneum (PNP) in the reverse Trendelenburg position. Our findings indicate that both high PEEP (HPEEP) and individualized PEEP (iPEEP) strategies improved oxygenation, reduced driving pressure, and increased dynamic compliance during carboxyperitoneum compared to low PEEP (LPEEP). Despite these improvements, there was considerable variability in the true effects, and no significant differences were found between HPEEP and iPEEP. Additionally, neither HPEEP nor iPEEP adversely affected mean arterial pressure (MAP) or heart rate (HR) relative to LPEEP. However, the predictive intervals for the true effects on oxygenation, respiratory compliance, and MAP in comparisons of HPEEP and iPEEP versus LPEEP showed a broad range, suggesting that these strategies might pose a risk of harm to some patients. Postoperative pulmonary complications were comparable across all PEEP groups, and the data comparing low PEEP (LPEEP) and moderate PEEP (MPEEP) were inconclusive.

Most studies and meta-analyses exploring PEEP levels in abdominal surgery focused on hypoxemia, hypotension, and postoperative pulmonary complications. First of all, the meta-analysis in non-cardiac surgery found that intraoperative ventilation with low tidal volume and PEEP was associated with the reduction in PPCs, but higher levels of PEEP as compared to lower PEEP had no additional positive effect [54]. Another meta-analysis for the influence of intraoperative PEEP in non-cardiothoracic and non-neurological surgery that included the biggest multicenter randomized controlled trials up-to-date (PROVHILO, iPROVE, and PROBESE) demonstrated that patients in the higher PEEP group had less frequent decrease in oxygen saturation but higher risk of intraoperative hypotension without influence on postoperative pulmonary complications [55]. These meta-analyses are not applicable to the population of patients selected for our meta-analysis. To begin with, it used heterogeneous populations of patients concerning type of surgery, body position, and body weight. Of note, in the latter meta-analysis in a subgroup of laparoscopic surgery postoperative pulmonary complications were significantly lower. Furthermore, large RCTs focusing on PEEP levels intraoperatively did not provide relevant data concerning obese patients and PNPs. For example, patients with obesity and PNP were excluded from the PROVHILO study [56]. Moreover, the PROBESE trial included a mixed population of obese surgical patients (BMI > 40 kg/m^2), including not only PNP but also open abdominal and non-abdominal surgery [57]. Two other recent meta-analyses found better oxygenation, higher respiratory compliance, fewer postoperative pulmonary complications, and a decrease in markers of inflammation (such as IL-6) in the individualized PEEP groups in non-selected patients who underwent abdominal surgery (58–59). Our recent meta-analysis of PEEP selection during PNP in non-obese patients found that HPEEP and iPEEP (that was higher than HPEEP) improved oxygenation, and reduced driving pressure as compared to LPEEP, but did not lead to overdistension or affect hemodynamics (MAP or HR) in all studies without significant variability of true effect [5]. However, further investigation using meta-regression found that not HPEEP per se, but the combination of HPEEP with higher tidal volume (above 8 mL/kg) may cause overdistension and decrease MAP. Meta-analysis of trials in non-obese patients undergoing surgery with PNP showed improvement in oxygenation and respiratory compliance with HPEEP with low heterogeneity of true effect variation. On the opposite, this meta-analysis in obese patients undergoing surgery with PNP and reverse Trendelenburg position also showed improvement in oxygenation and respiratory mechanics generally, but the true effect variation was high. We may assume that «high» PEEP levels in non-obese patients may be sufficient to maintain oxygenation and respiratory mechanics, but in obese patients, these values may be lower than needed. Also, we have to keep in mind that this meta-analysis included only patients with the reverse Trendelenburg position which had a smaller negative impact on respiratory mechanics than the Trendelenburg position.

Before RCTs, some observational studies had shown promising results using HPEEP or iPEEP in patients with obesity and pneumoperitoneum. For instance, an EIT study found that the optimal PEEP level for these patients was approximately 15 cm H_2O after intra-abdominal gas inflation and before surgery [60]. This PEEP level was effective in maintaining normal functional residual capacity, minimizing shunt, and keeping the PaO_2/FiO_2 ratio stable before and after surgery. Additionally, a cross-over study by Boeing C et al. found that in super-obese patients undergoing laparoscopic bariatric surgery, individualized PEEP based on the best compliance method improved respiratory mechanics, lung volumes, and oxygenation without causing hemodynamic compromise, compared to a fixed PEEP level of 8 cm H_2O [61]. In this study, the iPEEP level in the reverse Trendelenburg position was also around 15 cm H_2O (15.8 ± 2.5), consistent with the previously mentioned EIT study.

A recent study compared iPEEP using electrical impedance tomography alone ($PEEP_{EIT}$) with $PEEP_{EIT}$ combined with recruitment maneuvers during bariatric laparoscopic surgery. This study found a slight increase in oxygenation with no significant differences in the EIT data; however, it also observed an increase in vasopressor use in the $PEEP_{EIT}$ combined with recruitment maneuvers group [62].

In a sub-study of the PROBESE RCT, PEEP set at 12 cm H_2O reduced driving pressure, intra-tidal recruitment, elastance, and mechanical power compared to PEEP set at 4 cm H_2O in obese patients undergoing abdominal surgery [63].

One recent meta-analysis of obese patients undergoing bariatric surgery appears comparable to ours [64]. However, in that meta-analysis, the authors compared PEEP with and without recruitment maneuvers. The PEEP levels, tidal volumes, and methods of recruitment maneuvers varied widely among studies, leading to inconsistent interpretations.

Another meta-analysis focused on PEEP levels in obesity [65]. However, the authors of this meta-analysis did not focus on the type of surgery (open or laparoscopic) or region of excision and excluded many relevant studies that were included in our meta-analysis due to «wrong intervention», «wrong patient population», and «wrong study design».

More comprehensive results on the impact of ventilation strategies on lung function in obese patients were presented by Wang J et al. [66]. They examined a diverse group of surgical patients, including those undergoing open abdominal, laparoscopic, cardiothoracic, and peripheral surgeries. The study not only compared different PEEP strategies but also assessed the effects of ventilation modes and recruitment maneuvers. The authors concluded that volume-controlled ventilation combined with individualized PEEP and recruitment maneuvers was the optimal strategy for improving oxygenation and respiratory compliance in obese patients. However, only the combination of volume-controlled ventilation, high PEEP, and recruitment maneuvers effectively reduced postoperative atelectasis caused by inflammation.

Our study has several limitations. First, the included studies exhibited high heterogeneity regarding PEEP levels and recruitment maneuvers, and were small. Second, there was variability in the measures of respiratory compliance used (e.g., Cdyn, DP, Cstat), along with methodological issues such as estimating plateau pressure without measuring driving pressure or assessing peak inspiratory pressure without calculating dynamic compliance. Third, different methodologies for recruitment maneuvers were employed across studies. Fourth, all studies were heterogeneous concerning FiO_2, including fixed FiO_2 (50% [18, 20] and 80% [21]), or FiO_2 not less than 40% to obtain $SpO_2 > 90–92\%$ [16, 19]; one study did not report FiO_2 values [13]. This heterogeneity could impact PaO_2/FiO_2 because of the dependency of PaO_2/FiO_2 on FiO_2 [67]. Additionally, postoperative pulmonary complications (PPCs) were not included in our meta-analysis. Finally, some meta-analyses may be underpowered and have a high risk of publication bias, although P-curve and FDR analyses did not reveal these concerns. Generalizability of our findings may be limited due to the small sample sizes of the included istudies.

Our study has several strengths. We conducted our meta-analysis focusing on a highly specific group: obese patients undergoing laparoscopic surgery in the reverse Trendelenburg position. This approach minimized potential heterogeneity related to the Trendelenburg position or variations in body weight. We demonstrated that both HPEEP and iPEEP strategies improved oxygenation and respiratory compliance during surgery compared to LPEEP with the high heterogeneity in the true effects observed. Importantly, these strategies did not result in hemodynamic compromise. Additionally, we utilized predictive intervals to provide a more accurate representation of the true effects.

Conclusions

In patients with obesity undergoing surgery in the reverse Trendelenburg position, HPEEP and iPEEP strategies, when compared to the LPEEP strategy, may improve oxygenation, decrease driving pressure, and increase dynamic compliance. These improvements occur with a high variation of true effect, without causing relevant hemodynamic compromise. Data comparing MPEEP are inconclusive.

Abbreviations

ARDS	Acute respiratory distress syndrome
BMI	Body mass index
Cdyn	Dynamic compliance
Cstat	Static respiratory compliance
CI	Confidence intervals
DP	Driving pressure
EELV	End–expiratory volume lung volume
EIT	Electrical impedance tomography
FiO_2	Fraction of inspired oxygen
FRC	functional residual capacity
HPEEP	High positive end–expiratory pressure
HR	Heart rate
IAP	Intra–abdominal pressure
iPEEP	Individualised positive end–expiratory pressure
ICU	Intensive care unit
LPEEP	Low positive end–expiratory pressure
LPV	Lung protective ventilation
MAP	Mean arterial pressure
MD	Mean difference
MPEEP	Moderate positive end–expiratory pressure
SMD	Standardized mean difference
PaO_2	Arterial partial pressure of oxygen
PBW	Predicted body weight
PEEP	Positive end–expiratory pressure
$PEEP_{EIT}$	Positive end–expiratory pressure selected by EIT
Pes	Esophageal pressure
PIP	Peak inspiratory pressure
PNP	Pneumoperitoneum (carboxyperitoneum)
PPC	Postoperative pulmonary complication
Pplat	Plateau pressure
PRISMA	Preferred Reporting Items for Systematic Review and Meta–analysis
RCT	Randomized controlled study
RM	Recruitment maneuver
RR	Risk ratio
SpO_2	Peripheral oxygen saturation
TV	Tidal volume
V/Q	Ventilation–perfusion
ZEEP	Zero end–expiratory pressure

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

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Author contributions
GAY: study design, data collection, analysis, manuscript writing, and revision; AMM: data analysis and interpretation; SIK: data collection; MBZ: data collection; GSB: data collection; SBS: data analysis and interpretation; DSZ: data analysis and interpretation; IYM: manuscript revision; YAY: data analysis and interpretation; DAK: data collection; AIY: study design, data analysis and interpretation, manuscript writing and revision. All authors revised the drafted manuscript, and all read and approved its final version.

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Declarations

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Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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