Individualized positive end-expiratory pressure reduces driving pressure in obese patients during laparoscopic surgery under pneumoperitoneum: a randomized clinical trial

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Introduction: During pneumoperitoneum (PNP), airway driving pressure (ΔP_{RS}) increases due to the stiffness of the chest wall and cephalic shift of the diaphragm, which favors atelectasis. In addition, depending on the mechanical power (MP) formulas, they may lead to different interpretations.

Methods: Patients >18 years of age with body mass index >35 kg/m^2 were included in a single-center randomized controlled trial during their admission for bariatric surgery by abdominal laparoscopy. Intra-abdominal pressure was set at 15 mmHg at the pneumoperitoneum time point (PNP). After the recruitment maneuver, the lowest respiratory system elastance (E_{RS}) was detected during the positive end-expiratory pressure (PEEP) step-wise decrement. Patients were randomized to the 1) CTRL group: ventilated with PEEP of 5 cmH$_2$O and 2) PEEP$_{IND}$ group: ventilated with PEEP value associated with E_{RS} that is 5% higher than its lowest level. Respiratory system mechanics and mean arterial pressure (MAP) were assessed at the PNP, 5 min after randomization (T1), and at the end of the ventilation protocol (T2); arterial blood gas was assessed at PNP and T2. ΔP_{RS} was the primary outcome. Three MP formulas were used: MP$_A$, which computes static PEEP × volume, elastic, and resistive components; MP$_B$, which computes only the elastic component; and MP$_C$, which computes static PEEP × volume, elastic, and resistive components without inspiratory holds.

Results: Twenty-eight patients were assessed for eligibility: eight were not included and 20 patients were randomized and allocated to CTRL and PEEP$_{IND}$ groups (*n* = 10/group). The PEEP$_{IND}$ ventilator strategy reduced ΔP_{RS} when compared with the CTRL group (PEEP$_{IND}$, 13 ± 2 cmH$_2$O; CTRL, 22 ± 4 cmH$_2$O; *p* < 0.001). Oxygenation improved in the PEEP$_{IND}$ group when

compared with the CTRL group ($p = 0.029$), whereas MAP was comparable between the $PEEP_{IND}$ and CTRL groups. At the end of surgery, MP_A and MP_B were correlated in both the CTRL (rho = 0.71, $p = 0.019$) and $PEEP_{IND}$ (rho = 0.84, $p = 0.020$) groups but showed different bias (CTRL, −1.9 J/min; $PEEP_{IND}$, +10.0 J/min). At the end of the surgery, MP_A and MP_C were correlated in both the CTRL (rho = 0.71, $p = 0.019$) and $PEEP_{IND}$ (rho = 0.84, $p = 0.020$) groups but showed different bias (CTRL, −1.9 J/min; $PEEP_{IND}$, +10.0 J/min).

Conclusion: Individualized PEEP was associated with a reduction in ΔP_{RS} and an improvement in oxygenation with comparable MAP. The MP, which solely computes the elastic component, better reflected the improvement in ΔP_{RS} observed in the individualized PEEP group.

Clinical Trial Registration: The protocol was registered at the Brazilian Registry of Clinical Trials (U1111-1220-7296).

Introduction

Millions of laparoscopic procedures are performed globally every year (Boberg et al., 2022), which involve the insufflation of carbon dioxide into the peritoneal cavity to produce a pneumoperitoneum (PNP). PNP can cause dramatic changes in respiratory mechanics due to the stiffness of the chest wall and cephalic shift of the diaphragm, which favors atelectasis (Andersson et al., 2005; Cinnella et al., 2013). Furthermore, the combination of laparoscopic surgery, PNP, and obesity may further increase the negative consequences for the respiratory system (Regli et al., 2019), as observed by an increase in airway driving pressure (ΔP_{RS}). In addition, the cardiac output may decrease with a subsequent decrease in the mean arterial pressure (MAP) after an increase in intra-abdominal pressure (IAP) during the PNP procedure (Regli et al., 2019). Different ventilatory strategies have been adopted during the intraoperative period. The recruitment maneuver (RM) followed by the fixed positive end-expiratory pressure (PEEP) level has been associated with an improvement in intraoperative oxygenation in morbidly obese patients and also with hemodynamic instability (Whalen et al., 2006) or functional improvement occurred only after repetitive RM followed by fixed PEEP level titration (Almarakbi et al., 2009; Talab et al., 2009; Edmark et al., 2016). Individualization of the PEEP level after the application of RM has also been done in laparoscopic surgeries in obese patients using pulse oximetry (Ferrando et al., 2018), electrical impedance tomography (EIT) (Nestler et al., 2017), best respiratory system compliance (D Antini et al., 2018; Boesing et al., 2023), or by transpulmonary pressure (Eichler et al., 2018; Mazzinari et al., 2020). However, the use of these variables requires equipment that is not widely available in operating rooms or the introduction of an esophageal balloon, which is not feasible during bariatric surgery under PNP. In addition, the PEEP level has been individualized in laparoscopic surgery in obese patients using several techniques but with minimal changes in real-life ventilator settings in the perioperative period in obese patients. For instance, during the secondary analysis of the international multicenter LAS VEGAS study (Ball et al., 2018), 2,012 obese patients were ventilated with PEEP of $4\,cmH_2O$. Recently, RM followed by PEEP titration according to the lowest respiratory system elastance (E_{RS}) reduced

ΔP_{RS} and cardiovascular performance of the right ventricle in an experimental obesity model and in obese patients (Magder et al., 2021). Nevertheless, the PEEP value associated with minimal E_{RS} may not be feasible during laparoscopic surgery due to hemodynamic instability. Whether ventilating at the PEEP level that corresponds to a 5% increase in E_{RS} according to its minimal value obtained during PEEP titration can maintain the beneficial effects on respiratory system mechanics throughout the surgery without causing hemodynamic instability is not known. Therefore, we hypothesized that a ventilatory strategy based on individualized PEEP ($PEEP_{IND}$; that is, the PEEP level associated with E_{RS} that is 5% higher than the minimal E_{RS}) can reduce airway driving pressure compared with PEEP of $5\,cmH_2O$ and would be hemodynamically feasible.

Material and methods

Study design

This is a single-center, randomized controlled trial that evaluated obese patients admitted for bariatric surgery by abdominal laparoscopy at the Hospital Federal dos Servidores do Estado do Rio de Janeiro between September 2018 and December 2019. This study was approved by the Co-substantiated Ethics and Research Committee of the Hospital Federal dos Servidores do Estado do Rio de Janeiro on 14 December 2015 (CAAE: 51623015.9.0000.5252), and written informed consent was obtained from all subjects participating in the trial. The trial was registered prior to patient enrollment at the Brazilian Registry of Clinical Trials (number U1111-1220-7296; http://www.ensaiosclinicos.gov.br/rg/RBR-68y7cz/; principal investigator: Tiago Batista Xavier; date of registration: 28 September 2018). This report follows the CONSORT 2010 Statement: updated guidelines for reporting parallel group randomized trials (Schulz et al., 2010).

Patient eligibility

The inclusion criteria were patients >18 years of age, with body mass index >35 kg/m², and signed consent provided. The exclusion

FIGURE 1
Timeline of the experimental procedures. ABG, arterial blood gases; CTRL, control group ventilated with PEEP of 5 cmH$_2$O; E$_{RS}$, respiratory system elastance; MV, mechanical ventilation; PEEP, positive end-expiratory pressure; PEEP$_{IND}$, PEEP adjusted at E$_{RS}$ that is 5% higher than the PEEPminE$_{RS}$; PNP, pneumoperitoneum; RM, recruitment maneuver; T1, at the beginning of surgery; T2, at the end of surgery.

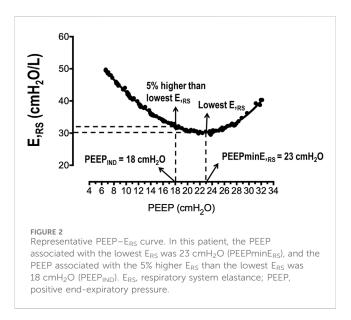criteria were chronic obstructive pulmonary disease with forced expiratory volume at first second (FEV$_1$) <80% or FEV$_1$ divided by forced vital capacity 70% lower after a bronchodilator challenge; heart disease with an ejection fraction <65%; structural chest wall alterations due to obesity such as kyphosis, scoliosis, or hyperlordosis; the absence of consent; and pregnancy.

Experimental protocol

On the day of surgery, the procedure for anesthesia and pre-surgery care, such as fasting period, was followed according to the hospital protocols (Figure 1). Briefly, patients were intubated by endo-tracheal intubation (inner diameter, 7.0 mm), according to a rapid sequence intubation protocol with intravenous administration of fentanyl 1–2 µg/kg, lidocaine 1 mg/kg, propofol 1–2 mg/kg, and succinylcholine 1 mg/kg. General anesthesia was maintained with inhaled sevoflurane in expired concentrations ≥1.4% and intravenous fentanyl 1–2 µg/kg, according to the adequacy of the depth of anesthesia. Neuromuscular blockade after tracheal intubation was maintained with intravenous administration of rocuronium 0.1–0.3 mg/kg or cisatracurium 0.02–0.05 mg/kg every 20–30 min during PNP inflation. The lungs were mechanically ventilated (Aisys, Datex-Ohmeda, Madison, WI, United States) in the 35° dorsal recumbent position using the following parameters at baseline: volume-controlled ventilation (VCV), tidal volume (V$_T$) = 8 mL/kg of the predicted body weight (PBW), the respiratory rate (RR) adjusted to between 10 and 20 bpm to achieve end-tidal carbon dioxide (P$_{ET}$CO$_2$) of 35–45 mmHg, the inspiratory/expiratory (I:E) ratio of 1:2, PEEP 5 cmH$_2$O, and FiO$_2$ 0.5–0.6. The heart rate (HR), P$_{ET}$CO$_2$, MAP, and peripheral oxygen saturation (SpO$_2$) were monitored using a multiparameter monitor (S/5; Datex-Ohmeda). After baseline, abdomen insufflation was done using a clinical CO$_2$ insufflator (Baxter), which maintained the IAP at 15 mmHg (~20 cmH$_2$O) during the surgery. After clinical stabilization, the arterial blood was sampled (1 mL) at the PNP time point, and all patients underwent the initial RM, as is described later. After the initial RM, an additional RM was followed by PEEP titration to detect the PEEP level associated with the lowest E$_{RS}$ (so-called

FIGURE 2
Representative PEEP−E$_{RS}$ curve. In this patient, the PEEP associated with the lowest E$_{RS}$ was 23 cmH$_2$O (PEEPminE$_{RS}$), and the PEEP associated with the 5% higher E$_{RS}$ than the lowest E$_{RS}$ was 18 cmH$_2$O (PEEP$_{IND}$). E$_{RS}$, respiratory system elastance; PEEP, positive end-expiratory pressure.

PEEPminE$_{RS}$). At this point, randomization and open allocation into the CTRL and PEEP$_{IND}$ groups were performed according to a computer-generated random number list: 1) the CTRL group was ventilated with the baseline ventilator parameters; 2) the PEEP$_{IND}$ group was ventilated with the same baseline ventilator parameters and the PEEP value associated with E$_{RS}$ that is 5% higher than its lowest level (Figure 2). The surgery was started after both PEEP adjustments were made. No further changes to the ventilation settings were made during the surgery. At the end of surgery, the arterial blood was sampled (1 mL) again, which was still under PNP pressure (15 mmHg).

Initial recruitment maneuver

For the initial RM, pressure-controlled ventilation was adjusted according to the following parameters: delta inspiratory pressure, 15 cmH$_2$O; RR, 10 bpm; I:E ratio, 1:1; PEEP, 5 cmH$_2$O; and FiO$_2$, 1. PEEP was increased to 10 cmH$_2$O for 10 s, followed by an increase to 20 cm H$_2$O for 10 s and to 30 cmH$_2$O for 30 s. After the initial maneuver, the ventilator parameters were adjusted according to the baseline condition.

PEEP titration maneuver

After a similar initial RM, the ventilation mode was rapidly adjusted to VCV under a square flow curve, V_T of 8 mL/kg of PBW, RR of 20 bpm, I:E ratio of 1:1, and FiO_2 = 1 and PEEP was reduced in steps of 2 cmH_2O every 30 s, when feasible according to the MAP safe levels (>65 mmHg), starting at PEEP of 26 cmH_2O down to PEEP of 6 cmH_2O and ending at PEEP of 5 cmH_2O.

$PEEP_{IND}$

The parameter chosen to individualize PEEP was E_{RS}. The E_{RS} at different PEEP levels during the PEEP titration maneuver was estimated in real time by the Bdalog software written in LabVIEW version 8.2 (National Instruments, Austin, TX, United States) using the least square fitting method according to the homogeneous one-compartmental linear model as follows:

$$Paw = Raw \times flow + E_{RS} \times volume + P0,$$

where Paw is the airway pressure, Raw is the airway resistance, E_{RS} is respiratory system elastance, and P0 is the airway pressure when the flow and volume are equal to zero. A PEEP–E_{RS} curve was obtained for all patients. The $PEEPminE_{RS}$ was recognized as the PEEP level associated with the lowest E_{RS}. $PEEP_{IND}$ represented the lowest PEEP level associated with E_{RS} that is 5% higher than the minimum E_{RS} (Figure 2).

Data acquisition

Airflow, Paw, HR, $P_{ET}CO_2$, MAP, and SpO_2 data were collected using a multiparameter monitor. Airflow and Paw were also recorded using the serial port of the mechanical ventilator and the Bdalog software. Airflow and CO_2 sensors were calibrated by the anesthesiologists. The time points were baseline, PNP, T1, and T2. Baseline and PNP were the time points after endotracheal intubation and during PNP, respectively. T1 and T2 were the time points at the beginning and end of surgery, respectively.

Mechanical power (MP, J/min) was calculated using the following formulas:

$$MP_A = 0.098 \times RR \times V_T \times (Ppeak,_{RS} - 0.5\Delta P,_{RS}).$$
$$MP_B = 0.098 \times RR \times V_T \times \Delta P,_{RS}.$$
$$MP_C = 0.098 \times V_T \times RR \times (Ppeak,_{RS} + PEEP + F/6)/20.$$

The formulas were obtained from previous clinical studies (Gattinoni et al., 2016; Guerin et al., 2016; Giosa et al., 2019). MP_A computes the static PEEP $\times$ volume, elastic, and resistive components (Gattinoni et al., 2016), whereas MP_B computes only the elastic component (Guerin et al., 2016). MP_C computes the static PEEP $\times$ volume, elastic, and resistive components with the additional benefit that inspiratory holds are not necessary (Giosa et al., 2019).

Statistical analysis

According to previous pilot data from the respiratory physiology laboratory at the Institute of Biophysics Carlos Chagas, a sample of 10 patients per arm would provide the information (1 − β = 0.9) to identify significant (α = 0.05) differences in ΔP_{RS} as the primary outcome between CTRL and $PEEP_{IND}$ (pilot data: CTRL, 12.0 ±

4.2 cmH_2O vs. $PEEP_{IND}$, 20.3 ± 4.5 cmH_2O), taking into account an effect size d = 1.84, a two-sided test, and a sample size ratio of 1 (G*Power 3.1.9.2; University of Düsseldorf, Germany).
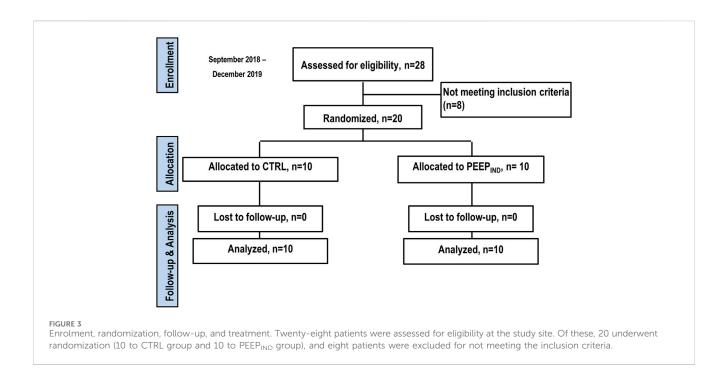
The primary outcome was airway driving pressure, while secondary outcomes were arterial blood gas and hemodynamic. The normality of the data was tested using the Shapiro–Wilk test. The number and relative frequency were compared by Fisher's exact test ($p < 0.05$). The Student's t-test and Mann–Whitney rank-sum test were used to compare parametric and non-parametric data, respectively. The mechanical data obtained at baseline and PNP time points were compared by paired Student's t-test. Arterial blood gases, respiratory variables, and MAP obtained from the CTRL and $PEEP_{IND}$ groups at PNP and subsequent time points were compared by two-way ANOVA followed by the Holm–Sidak multiple comparisons test ($p < 0.05$).

Pearson correlation and Bland–Altman analyses were done between the MP_A and MP_B formulas and between the MP_A and MP_C formulas to determine the levels of agreement and bias obtained. The data are expressed as means and standard deviation (SD), medians and interquartile range (IQR), or number and relative frequency (%), as appropriate. The SPSS 25 (SPSS, IBM Inc., Armonk, NY, United States) and GraphPad Prism 9.0 for MacIOS (GraphPad Software, La Jolla, CA, United States) were used. A $p < 0.05$ was considered significant.

Results

From September 2018 to December 2019, 28 patients were assessed for eligibility at the study site. Eight patients did not meet the inclusion criteria due to chronic obstructive pulmonary disease ($n = 4$), heart disease with an ejection fraction <65% ($n = 3$), and pregnancy ($n = 1$); 20 patients underwent randomization (Figure 3). Overall, 90% of the patients were females, and the median age was 45 years (IQR, 45–52 years), the mean body mass index was 47.6 kg/m^2 (SD, ±7.2 kg/m^2), and most patients were American Society of Anesthesiologists physical status classification level III. Few patients were diagnosed with restrictive lung disease (15%), with 65% and 55% of them having arterial hypertension and diabetes mellitus, respectively. The surgery time was 71.5 min (IQR, 55.5–77.0 min) (Supplementary Table S1).

ΔP_{RS}, MP_A, and MP_B increased after the PNP procedure when compared with the baseline ($p < 0.001$, $p = 0.004$, and $p < 0.001$, respectively) (Supplementary Figure S1). Supplementary Figure S2 depicts the PEEP–E_{RS} curve for all the patients. The primary outcome ΔP_{RS} was lower in the $PEEP_{IND}$ group at T1 and T2 than in the CTRL group ($p < 0.001$) (Table 1). PaO_2/FiO_2 was higher in the $PEEP_{IND}$ group than in the CTRL group at T2 ($p = 0.029$). pHa had decreased in both groups over time ($p = 0.002$ for both). HCO_3^- was lower in the $PEEP_{IND}$ group than in the CTRL group at T2 ($p = 0.016$). No differences were observed in $PaCO_2$ and lactate levels (Table 1). MAP decreased in the CTRL group at T1 and T2 in relation to the respective PNP time points ($p = 0.011$ and $p = 0.002$, respectively). In addition, MAP decreased in the $PEEP_{IND}$ group at T2 in relation to the respective PNP time point ($p = 0.032$). No difference was observed between the $PEEP_{IND}$ and CTRL groups at T2 ($p = 0.445$) (Table 1).

FIGURE 3
Enrolment, randomization, follow-up, and treatment. Twenty-eight patients were assessed for eligibility at the study site. Of these, 20 underwent randomization (10 to CTRL group and 10 to PEEP$_{IND}$ group), and eight patients were excluded for not meeting the inclusion criteria.

No difference was observed in V_T among the groups and over time (Table 1). RR increased in the PEEP$_{IND}$ group at T2 in relation to the PNP time point ($p = 0.019$). PEEP was higher in the PEEP$_{IND}$ group at T1 and T2 than in the CTRL group ($p < 0.001$ for both). Ppeak$_{RS}$ was higher in the PEEP$_{IND}$ group at T1 than in the CTRL group ($p = 0.048$). E$_{RS}$ was lower in the PEEP$_{IND}$ group at T1 and T2 than in the CTRL group ($p < 0.001$). Raw decreased in the PEEP$_{IND}$ group at T1 and T2 in relation to the respective PNP time points ($p < 0.001$ for both). MP$_A$ and MP$_C$ were higher, whereas MP$_B$ was lower in the PEEP$_{IND}$ group than in CTRL groups at T1 and T2 (Table 1).

In the CTRL group at T2, MP$_A$ and MP$_B$ showed a positive correlation (rho = 0.71, $p = 0.019$), whereas the Bland–Altman plot showed a bias of -1.9 J/min between both the formulas for mechanical power (Figures 4A and B). In the PEEP$_{IND}$ group at T2, MP$_A$ and MP$_B$ showed a positive correlation (rho = 0.84, $p = 0.020$), while the Bland–Altman plot showed a bias of $+10.0$ J/min between both the formulas for MP (Figures 4C and D).

In the CTRL group at T2, MP$_A$ and MP$_C$ showed a positive correlation (rho = 0.98, $p < 0.001$), whereas the Bland–Altman plot showed a bias of $+1.18$ J/min between both formulas for MP (Figures 5A and B). In the PEEP$_{IND}$ group at T2, MP$_A$ and MP$_C$ showed a positive correlation (rho = 0.98, $p < 0.001$), whereas the Bland–Altman plot showed a bias of $+1.41$ J/min between both the formulas for MP (Figures 5C and D). Figure 6 shows a summary of the respiratory variables in the PEEP$_{IND}$ group in relation to the CTRL group at T2 in percentage. The increase in MP$_A$ ($+50\%$) was highly influenced by the increase in PEEP ($+346\%$) and did not follow the decrease in ΔP_{RS} and E$_{RS}$ (-41% and -42%, respectively). The decrease in MP$_B$ (-31%) followed the decrease in ΔP_{RS} and E$_{RS}$. MP$_A$ and MP$_C$ showed comparative increments.

Discussion

This single-center, randomized clinical trial on obese patients under PNP for bariatric surgery by abdominal laparoscopy showed that 1) a ventilatory strategy based on the PEEP level associated with E$_{RS}$ that is 5% higher than the lowest E$_{RS}$ was feasible and reduced ΔP_{RS} when compared with a CTRL group ventilated at PEEP of 5 cmH$_2$O; 2) oxygenation improved in the PEEP$_{IND}$ group compared with the CTRL group, with similar MAP; 3) the MP$_A$ and MP$_C$ formulas used to compute the static PEEP $\times$ volume, elastic, and resistive components did not follow the improvement observed in ΔP_{RS}, whereas the MP$_B$ formula, which computes only the elastic component, did.

Laparoscopic surgery involves CO_2 insufflation into the peritoneal cavity, producing a PNP. IAP of 15 mmHg during PNP increased ΔP_{RS}, likely due to the cranial shift of the diaphragm, reduction of the lung tissue could sustain the strain, and formation of atelectasis (D Antini et al., 2018). After an increase in IAP, the cardiac output may decrease with a subsequent fall in MAP (Regli et al., 2019). Although the PEEP$_{IND}$ group showed increased levels of PEEP compared with the CTRL group, with the MAP being comparable in the two groups. Thus, we can infer that IAP was the main factor responsible for the reduction in MAP, likely due to the compression of the inferior vena cava.

RM followed by a fixed PEEP level of 12 cmH$_2$O has been associated with improved oxygenation in morbidly obese patients, but it is associated with hemodynamic instability (Whalen et al., 2006). In a study on obese patients undergoing laparoscopic gastric banding (Almarakbi et al., 2009), the respiratory mechanics and oxygenation benefits were only achieved by repetitive RM followed by 10 cmH$_2$O PEEP (Talab et al., 2009; Edmark et al., 2016). Nestler et al. (2017) showed that RM followed by individualized PEEP using EIT restored end-expiratory lung volume (EELV), regional ventilation distribution, and oxygenation during anesthesia. Hemodynamic instability was reported during surgery. It

TABLE 1 Primary and secondary outcomes during PNP, T1, and T2.

	CTRL or PEEP$_{IND}$	PNP	T1	T2	p-value: time effect	p-value: group effect	p-value: time × group effect
Primary outcome							
ΔP$_{RS}$ (cmH$_2$O)	CTRL	21 ± 3	21 ± 4	22 ± 4	<0.001	0.001	<0.001
	PEEP$_{IND}$	20 ± 3	13 ± 1[a,b]	13 ± 2[a,b]			
Secondary outcomes							
PaO$_2$/FiO$_2$ (mmHg)	CTRL	236 ± 51	—	266 ± 70	<0.001	0.156	—
	PEEP$_{IND}$	243 ± 87	—	359 ± 104*#			
pHa	CTRL	7.37 ± 0.04	—	7.32 ± 0.04	<0.001	0.736	—
	PEEP$_{IND}$	7.37 ± 0.04	—	7.31 ± 0.04			
PaCO$_2$ (mmHg)	CTRL	41 ± 4	—	41 ± 6	0.017	0.974	—
	PEEP$_{IND}$	44 ± 4	—	44 ± 6			—
HCO$_3^-$ (mEq/L)	CTRL	24 ± 2	—	23 ± 1	<0.001	0.035	—
	PEEP$_{IND}$	23 ± 1	—	21 ± 1*#			
Lactate (mmol/L)	CTRL	1.0 ± 0.3	—	1.2 ± 0.5	0.266	0.086	—
	PEEP$_{IND}$	1.6 ± 0.9	—	1.6 ± 0.7			
MAP (mmHg)	CTRL	106 ± 21	91 ± 15[b]	88 ± 11[b]	<0.001	0.088	
	PEEP$_{IND}$	92 ± 19	85 ± 7	79 ± 14[b]			
V$_t$ (mL/kg PBW)	CTRL	7.8 ± 0.4	7.8 ± 0.4	7.9 ± 0.3	0.635	0.841	—
	PEEP$_{IND}$	8.0 ± 0.7	7.8 ± 0.4	7.9 ± 0.4			
RR (bpm)	CTRL	15 ± 2	16 ± 2	17 ± 2	0.010	0.170	—
	PEEP$_{IND}$	16 ± 2	17 ± 3	18 ± 3[b]			
Ppeak$_{RS}$ (cmH$_2$O)	CTRL	32 ± 4	31 ± 5	33 ± 4	0.004	0.183	<0.001
	PEEP$_{IND}$	31 ± 5	36 ± 3[a,b]	36 ± 4[b]			
PEEP (cmH$_2$O)	CTRL	4.7 ± 1.8	4.8 ± 1.2	4.7 ± 1.3	<0.001	<0.001	<0.001
	PEEP$_{IND}$	4.3 ± 0.9	16.3 ± 2.5[a,b]	16.3 ± 2.5[a,b]			
E$_{RS}$ (cmH$_2$O/L)	CTRL	52 ± 10	51 ± 10	55 ± 10	<0.001	<0.001	<0.001
	PEEP$_{IND}$	47 ± 9	31 ± 7[a,b]	32 ± 8[a,b]			
Raw (cmH$_2$O/L/s)	CTRL	18 ± 6	18 ± 5	18 ± 5	0.002	0.244	0.004
	PEEP$_{IND}$	18 ± 6	14 ± 3[b]	15 ± 4[b]			
MP$_A$ (J/min)	CTRL	13 ± 3	13 ± 2	14 ± 2	<0.001	0.002	<0.001
	PEEP$_{IND}$	14 ± 4	20 ± 5[a,b]	21 ± 5[a,b]			
MP$_B$ (J/min)	CTRL	14 ± 3	14 ± 3	16 ± 3	<0.001	0.047	<0.001
	PEEP$_{IND}$	15 ± 5	10 ± 3[a,b]	11 ± 3[a,b]			
MP$_C$ (J/min)	CTRL	12 ± 2	12 ± 2	13 ± 2	<0.001	0.001	<0.001
	PEEP$_{IND}$	12 ± 3	18 ± 4[a,b]	19 ± 4[a,b]			

Data are means ± standard deviation of 10 individuals per group. Comparisons were done by two-way ANOVA followed by Holm–Sidak multiple comparisons test ($p < 0.05$). CTRL, control group ventilated with PEEP of 5 cmH$_2$O; PEEP, positive end-expiratory pressure; PEEP$_{IND}$, PEEP adjusted at E$_{RS}$ that is 5% higher than the PEEPminE$_{RS}$; PNP, pneumoperitoneum; T1, at the beginning of surgery; T2, at the end of surgery; ΔP$_{RS}$, driving pressure; PaO$_2$/FiO$_2$, ratio of arterial oxygen partial pressure to fractional inspired oxygen; pHa, arterial pH; PaCO$_2$, carbon dioxide partial pressure; HCO$_3^-$, bicarbonate levels; MAP, mean arterial pressure; V$_T$, tidal volume; PBW, predicted body weight; RR, respiratory rate; Ppeak$_{RS}$, peak airway pressure; E$_{RS}$, respiratory system elastance; Raw, airway resistance; MP$_A$, mechanical power formula: 0.098 × RR × V$_T$ × (Ppeak$_{RS}$ − 0.5 ΔP$_{RS}$); MP$_B$, mechanical power formula: 0.098 × RR × V$_T$ × ΔP$_{RS}$); MP$_C$, mechanical power formula: 0.098 × V$_T$ × RR × (Ppeak$_{RS}$ + PEEP + F/6)/20.

[a]Versus CTRL.

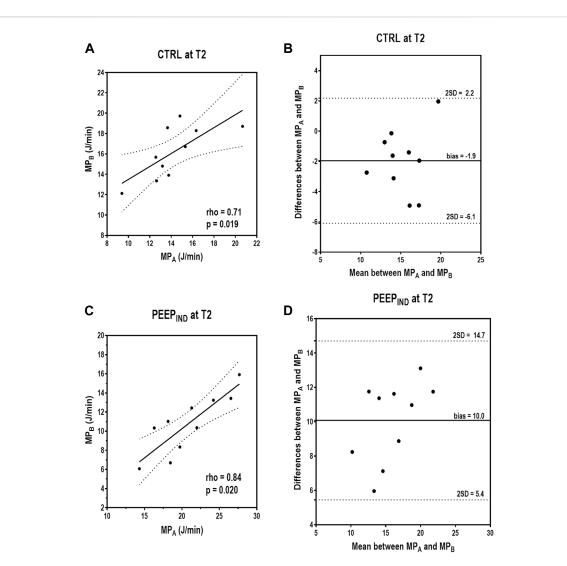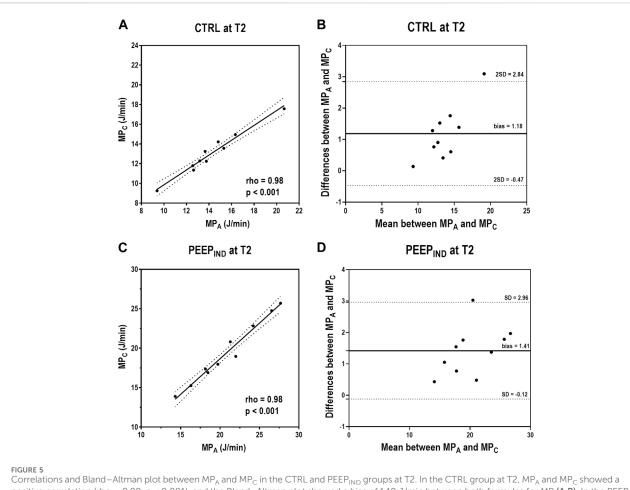[b]Versus the respective PNP time point.

FIGURE 4
Correlations and Bland−Altman plot between MP_A and MP_B in CTRL and $PEEP_{IND}$ groups at T2. In the CTRL group at T2, MP_A and MP_B showed a positive correlation (rho = 0.71, p = 0.019), and the Bland−Altman plot showed a bias of −1.9 J/min between both formulas for mechanical power **(A,B)**. In the $PEEP_{IND}$ group at T2, MP_A and MP_B showed a positive correlation (rho = 0.84, p = 0.020), and the Bland−Altman plot showed a bias of +10.0 J/min between both formulas for mechanical power **(C,D)**. CTRL, control group ventilated with PEEP of 5 cmH_2O; MP_A, mechanical power formula: $0.098 \times RR \times V_T \times (Ppeak_{RS} − 0.5 \Delta P_{RS})$; MP_B, mechanical power formula: $0.098 \times RR \times V_T \times \Delta P_{RS})$; PEEP, positive end-expiratory pressure; $PEEP_{IND}$, PEEP adjusted at E_{RS} that is 5% higher than the $PEEPminE_{RS}$; RR, respiratory rate; T2, at the end of surgery; V_T, tidal volume.

has been shown that PEEP levels up to 10 cmH_2O (7.3 mmHg) cannot prevent a decline in functional residual capacity caused by grade I intra-abdominal hypertension (12–15 mmHg); they are associated with reduced oxygen delivery as a consequence of reduced cardiac output (Regli et al., 2019). To maintain EELV according to EIT or to keep E_{RS} stable, as observed in our study, PEEP levels were adjusted to 18.5 cmH_2O and 16.3 cmH_2O, respectively. It has been shown that targeted PEEP levels of 10, 14, and 17 cmH_2O at IAP of 8, 12, and 15 mmHg, respectively, resulted in lower transpulmonary driving pressure (Mazzinari et al., 2020). However, PEEP was not titrated and, thus, not individualized. PEEP can counteract the negative effects of intra-abdominal hypertension on lung volume, and the present study favors setting PEEP to allow E_{RS} that is 5% higher than the minimal E_{RS}.

The intraoperative ΔP_{RS}, the ratio of V_T to respiratory system compliance, reflects the strain applied on lung tissue available for ventilation during general anesthesia (Silva and Rocco, 2018). After

RM and $PEEP_{IND}$, ΔP_{RS} decreased, likely due to an increase in lung tissue availability to accommodate V_T. Because V_T did not change, we may infer that overall respiratory system compliance improved. There are currently no data from large trials regarding safe ΔP_{RS} levels for obese patients undergoing mechanical ventilation. Nevertheless, ΔP_{RS} should ideally be limited to a maximum value of 15 cmH_2O in non-acute respiratory distress syndrome (ARDS) obese patients (Ball and Pelosi, 2019). The ΔP_{RS} observed in our $PEEP_{IND}$ group was 13 cmH_2O, which is within the protective range, while ΔP_{RS} was. In addition, hemodynamic instability is more frequent than respiratory impairment in obese patients without ARDS (Cinnella et al., 2013). In swine with obesity, the RM followed by PEEP titration according to the lowest E_{RS} reduced the inspiratory load on the right ventricle. A similar behavior was observed in obese patients under protective ventilation (Magder et al., 2021), and likely the protection may not only be restricted to the lungs but may also protect the heart.
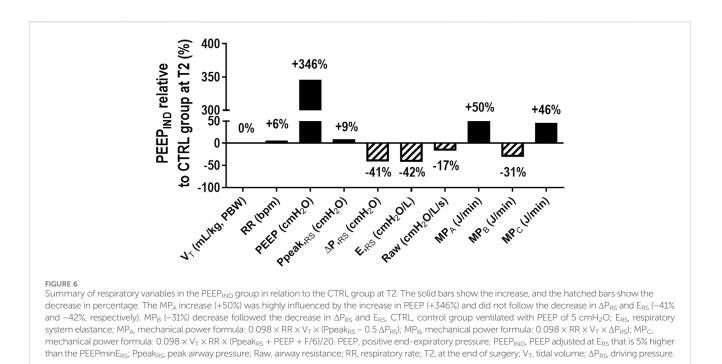
FIGURE 5
Correlations and Bland–Altman plot between MP_A and MP_C in the CTRL and $PEEP_{IND}$ groups at T2. In the CTRL group at T2, MP_A and MP_C showed a positive correlation (rho = 0.98, $p < 0.001$), and the Bland–Altman plot showed a bias of 1.19 J/min between both formulas for MP **(A,B)**. In the $PEEP_{IND}$ group at T2, MP_A and MP_C showed a positive correlation (rho = 0.98, $p < 0.001$), and the Bland–Altman plot showed a bias of 1.41 J/min between both formulas for MP **(C,D)**. CTRL, control group ventilated with PEEP of 5 cmH$_2$O; MP_A, mechanical power formula: $0.098 \times RR \times V_T \times (Ppeak_{RS} - 0.5 \Delta P_{RS})$; MP_C, mechanical power formula: $0.098 \times V_T \times RR \times (Ppeak_{RS} + PEEP + F/6)/20$; PEEP, positive end-expiratory pressure; $PEEP_{IND}$, PEEP adjusted at E_{RS} that is 5% higher than the $PEEPminE_{RS}$; RR, respiratory rate; T2, at the end of surgery; V_T, tidal volume.

MP refers to the energy transferred to the respiratory system and, similarly, to ΔP_{RS}, but there are no data regarding safe MP levels for obese patients. The suggested overall protective threshold is 17–20 J/min. ΔP_{RS} and MP are dependent on chest wall elastance, which is increased in obese patients, especially during PNP (Loring et al., 2014; Ball et al., 2018). There are different formulas for MP (Gattinoni et al., 2016; Guerin et al., 2016; Giosa et al., 2019). The fundamental role of calculating MP is to inform lung protection and likely follow the behavior of key variables, such as ΔP_{RS}. Here, $PEEP_{IND}$ led to not only a reduction in ΔP_{RS} toward the protective range but also an increase in MP (>20 J/min) when the MP_A and MP_C formulas were used. The explanation relies on the contribution of the MP formula components during $PEEP_{IND}$ ventilation. $PEEP_{IND}$ led to a reduction in ΔP_{RS} (elastic component) by 41% when compared with the CTRL. However, to achieve that reduction, PEEP (static PEEP × volume) had to increase by 346% when compared with the CTRL and bypass the improvement observed in the elastic component (Figure 6). No major changes were observed in Raw (resistive component). On applying the MP_B formula, agreement with the behavior of ΔP_{RS} was observed. Thus, the choice of the MP formula may have an impact on interpreting the results, as noted by the bias in the $PEEP_{IND}$ (+10.0 J/min) group. The MP_C formula has the additional

benefit that inspiratory holds are not necessary, which may facilitate the inclusion of an algorithm in mechanical ventilators (Giosa et al., 2019). Because MP_C also computes the PEEP × volume and resistive components, it showed a similar behavior to the MP_A formula and did not follow the improvement observed in ΔP_{RS}. The rationale for using only the dynamic elastic component or including static elastic and resistive components has been debated extensively (Huhle et al., 2018; Vasques et al., 2018). In addition, a study of 4,549 patients with ARDS showed the concept of using $4 \times \Delta P_{RS} + 1 \times RR$ (4DPRR) to quantify the impact of changes in the ventilatory strategy on ventilator-induced lung injury (Costa et al., 2021). The 4DPRR formula only computes the dynamic elastic component, similar to the MP_B used here. Thus, we believe that our data may provide additional discussion about ventilator settings in obese patients under laparoscopy.

Limitations

We did not compute the postoperative complications, which are highly prevalent in obese patients after laparoscopic surgeries under mechanical ventilation (Bluth et al., 2019). EIT measurements were not

FIGURE 6
Summary of respiratory variables in the PEEP$_{IND}$ group in relation to the CTRL group at T2. The solid bars show the increase, and the hatched bars show the decrease in percentage. The MP$_A$ increase (+50%) was highly influenced by the increase in PEEP (+346%) and did not follow the decrease in ΔP_{RS} and E$_{RS}$ (−41% and −42%, respectively). MP$_B$ (−31%) decrease followed the decrease in ΔP_{RS} and E$_{RS}$. CTRL, control group ventilated with PEEP of 5 cmH$_2$O; E$_{RS}$, respiratory system elastance; MP$_A$, mechanical power formula: 0.098 × RR × V$_T$ × (Ppeak$_{RS}$ − 0.5 ΔP_{RS}); MP$_B$, mechanical power formula: 0.098 × RR × V$_T$ × ΔP_{RS}); MP$_C$, mechanical power formula: 0.098 × V$_T$ × RR × (Ppeak$_{RS}$ + PEEP + F/6)/20. PEEP, positive end-expiratory pressure; PEEP$_{IND}$, PEEP adjusted at E$_{RS}$ that is 5% higher than the PEEPmin$_{RS}$; Ppeak$_{RS}$, peak airway pressure; Raw, airway resistance; RR, respiratory rate; T2, at the end of surgery; V$_T$, tidal volume; ΔP_{RS}, driving pressure.

done and could add important information about the distribution of V$_T$ and EELV in obese patients. However, we conducted the PEEP titration according to the PEEP–E$_{RS}$ curve. We did not measure the transpulmonary pressure because there was no wide-caliber probe to keep the pylorus open, and thus, we could not pass the esophageal balloon. In addition, we did not measure invasive cardiac output and the related variables due to the absence of hemodynamic devices in the operating room.

Conclusion

The present single-center, randomized clinical trial on obese patients under abdominal laparoscopy showed that individualized PEEP was associated with a reduction in ΔP_{RS} and improvement in oxygenation with comparable MAP. The MP, which solely computes the elastic component, better reflected the improvement in ΔP_{RS} observed in individualized PEEP group.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Co-substantiated Ethics and Research Committee of the Hospital Federal dos Servidores do Estado do Rio de Janeiro, on 14 December 2015 (CAAE: 51623015.9.0000.5252), and written informed consent was obtained from all subjects participating in the trial. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

TX: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, software, supervision, validation, manuscript writing—original draft, review, and editing. LeC: Data curation, formal analysis, investigation, methodology, manuscript writing—original draft, review, and editing. DF: Data curation, formal analysis, investigation, methodology, manuscript writing—original draft, review, and editing. JC: Data curation, formal analysis, investigation, methodology, manuscript writing—original draft, review, and editing. MD: Conceptualization, data curation, formal analysis, investigation, methodology, manuscript writing—original draft, review, and editing. LS: Formal analysis, methodology, validation, visualization, manuscript writing—original draft, review, and editing. GM-R: Data curation, formal analysis, methodology, software, validation, manuscript writing—original draft, review, and editing. LuC: Conceptualization, data curation, formal analysis, investigation, methodology, manuscript writing—original draft, review, and editing. AC: Conceptualization, data curation, formal analysis, investigation, software, validation, visualization, manuscript writing—original draft, review, and editing. PS: Data curation, formal analysis, funding acquisition, resources, supervision, validation, visualization, manuscript writing—original draft, review, and editing.

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Conflict of interest

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Supplementary material

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Glossary

ARDS	acute respiratory distress syndrome
ASA	American Society of Anesthesiologists
E_{RS}	respiratory system elastance
EELV	end-expiratory lung volume
EIT	electrical impedance tomography
FEV_1	forced expiratory volume at the first second
HR	heart rate
IAP	intra-abdominal pressure
I:E	inspiratory/expiratory
IQR	interquartile range
MAP	mean arterial pressure
MP	mechanical power
MP_A	MP that includes the static PEEP × volume, elastic, and resistive components
MP_B	MP considering only the elastic component
MP_C	MP that includes the static PEEP × volume, elastic, and resistive components without inspiratory holds
$PaCO_2$	carbon dioxide arterial pressure
PaO_2/FiO_2	oxygenation index
Paw	airway pressure
PBW	predicted body weight
PEEP	positive end-expiratory pressure
$PEEP_{IND}$	individualized PEEP
$PEEPminE_{RS}$	PEEP level associated with the lowest E_{RS}
$P_{ET}CO_2$	end-tidal carbon dioxide
pHa	arterial pH
PNP	pneumoperitoneum
$Ppeak_{RS}$	airway peak pressure
Raw	airway resistance
REBEC	Brazilian Registry of Clinical Trials
RM	recruitment maneuver
RR	respiratory rate
SD	standard deviation
SpO_2	peripheral oxygen saturation
T1	time point at the beginning of surgery
T2	time point at the end of surgery
VCV	volume-controlled ventilation
V_T	tidal volume
P_{RS}	airway driving pressure