

## Research Article

# Improved oxygenation and lung compliance with recruitment maneuvers in robotic prostate surgery: A randomized trial

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## Summary

**Background:** This randomized controlled trial investigated the effects of recruitment maneuvers on arterial oxygenation and lung compliance in patients undergoing robotic-assisted prostatectomy in the steep Trendelenburg position. Hemodynamic parameters were also monitored, with no significant differences observed among groups.

**Methods:** Sixty patients were randomly assigned to three groups (n = 20 each).

- Group 1 received 0 cm H<sub>2</sub>O positive end-expiratory pressure (PEEP),
- Group 2 received 5 cm H<sub>2</sub>O PEEP,
- Group 3 received 5 cm H<sub>2</sub>O PEEP combined with two recruitment maneuvers, applied 5 minutes after CO<sub>2</sub> insufflation and 5 minutes after desufflation.

Pneumoperitoneum was maintained at 12 mmHg. Anesthesia was maintained with sevoflurane and remifentanyl infusion (FI<sub>O</sub><sub>2</sub> 50%), titrated to maintain end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>) between 30–36 mmHg. Balanced crystalloid solutions were administered at 4–6 mL/kg/h, adjusted according to hemodynamic parameters. Hemodynamic variables, arterial blood gases, and respiratory mechanics were recorded at predefined intraoperative and postoperative time points.

**Results:** Group 3 demonstrated significantly higher PaO<sub>2</sub> and improved static and dynamic lung compliance compared to Group 1 (PaO<sub>2</sub> at T3: 155.0 ± 51.3 mmHg vs. 121.2 ± 25.2 mmHg; p = 0.014). EtCO<sub>2</sub> and peak heart rate (PHR) were significantly lower in Group 3 than in Group 1 (p = 0.018 and p = 0.007, respectively), though these findings were interpreted cautiously given potential vagal stimulation. Groups 2 and 3 both showed significantly better compliance and oxygenation than Group 1 (p < 0.001 and p = 0.006, respectively). No significant hemodynamic instability was observed.

**Conclusion:** Recruitment maneuvers, when combined with moderate PEEP, may enhance intraoperative oxygenation and lung compliance during robotic prostatectomy without inducing significant hemodynamic compromise; however, the clinical relevance of these physiological improvements warrants further investigation in larger-scale studies.

**Key words:** Lung, oxygenation, PEEP, recruitment maneuver, robotic-assisted laparoscopic radical prostatectomy, steep Trendelenburg position



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## Introduction

Robotic-assisted laparoscopic radical prostatectomy (RALRP) is a widely utilized minimally invasive technique for the surgical management of localized prostate cancer. It offers several perioperative advantages, including reduced blood loss, lower complication rates, and favorable functional outcomes, such as preservation of urinary continence and erectile function (Türkoğlu et al. 2012).

To optimize surgical exposure during RALRP, carbon dioxide (CO<sub>2</sub>) is insufflated into the peritoneal cavity to create pneumoperitoneum, and patients are placed in a steep Trendelenburg position. While these maneuvers facilitate access to the pelvic cavity, they are associated with significant physiological alterations. The combined effects of pneumoperitoneum and steep Trendelenburg positioning can impair respiratory mechanics by reducing functional residual capacity (FRC), promoting atelectasis, increasing airway resistance, and decreasing pulmonary compliance. These changes may lead to a ventilation-perfusion mismatch and compromised gas exchange, posing challenges for intraoperative respiratory management (Awad et al. 2009; Gainsburg et al. 2012).

Alveolar recruitment maneuvers (RMs) have been proposed to counteract atelectasis and improve oxygenation by transiently increasing airway pressure to reopen collapsed alveoli. Various techniques, including positive end-expiratory pressure (PEEP), continuous positive airway pressure (CPAP), and pressure-controlled ventilation, have been used to perform RMs (Talab et al. 2009). However, the efficacy and safety of RMs during RALRP, particularly in steep Trendelenburg positioning, remain under investigation.

This randomized controlled trial aimed to evaluate the effects of recruitment maneuvers on arterial oxygenation and lung compliance in patients undergoing RALRP. We hypothesized that adding RMs to standard PEEP would improve intraoperative respiratory parameters without inducing significant hemodynamic instability.

## Materials and methods

This randomized controlled trial was conducted at Ankara Atatürk Training and Research Hospital between 2019 and 2020, following approval from the University of Yıldırım Beyazıt Ethics Committee (Approval No: 26379996-246). Written informed consent was obtained from all participants.

### Study population and design

Sixty adult patients (ASA physical status I–II) scheduled for elective robotic-assisted laparoscopic radical prostatectomy in the steep Trendelenburg position were enrolled and randomized into three groups (n = 20 per group):

- Group 1: 0 cm H<sub>2</sub>O PEEP
- Group 2: 5 cm H<sub>2</sub>O PEEP
- Group 3: 5 cm H<sub>2</sub>O PEEP with recruitment maneuvers (RMs) applied twice: 5 minutes after CO<sub>2</sub> insufflation and 5 minutes after desufflation. Demographic characteristics and comorbidities were recorded preoperatively.

## Anesthesia and monitoring

Standard monitoring included ECG, non-invasive blood pressure, SpO<sub>2</sub>, EtCO<sub>2</sub>, and invasive arterial pressure via right radial artery cannulation. Baseline values were recorded before induction (T<sub>0</sub>).

Anesthesia was induced with lidocaine (1–1.5 mg/kg IV), propofol (2 mg/kg IV), remifentanyl (1 µg/kg IV), and rocuronium (0.6–1.2 mg/kg IV). After 3 minutes of preoxygenation with 100% O<sub>2</sub>, endotracheal intubation was performed. Anesthesia was maintained with sevoflurane in 50% FiO<sub>2</sub> and remifentanyl infusion, titrated to maintain EtCO<sub>2</sub> between 30–36 mmHg. An adequate depth of anesthesia was maintained throughout the procedure, targeting a Bispectral Index (BIS) range of 40–60.

## Ventilation and recruitment maneuvers

All patients were ventilated with a tidal volume of 6–8 mL/kg, a respiratory rate of 12 breaths/min, and FiO<sub>2</sub> 50%. Pneumoperitoneum was established with CO<sub>2</sub> at 12 mmHg. Ventilator settings were adjusted to maintain EtCO<sub>2</sub> within the target range and Ppeak <38 cmH<sub>2</sub>O.

In Group 3, recruitment maneuvers were performed twice: 5 minutes after insufflation and 5 minutes after desufflation. During RMs, PEEP was increased stepwise to 10, 15, and 20 cm H<sub>2</sub>O while maintaining VT at 6–8 mL/kg and respiratory rate at 12/min. At each PEEP level, 10 breaths were delivered, ensuring plateau and peak pressures remained below 30 cmH<sub>2</sub>O and 50 cm H<sub>2</sub>O, respectively.

## Data collection

Arterial blood gas samples were collected at the following time points:

- T<sub>0</sub>: Pre-induction
- T<sub>1</sub>: 5 minutes post-intubation
- T<sub>2</sub>: 5 minutes post-insufflation
- T<sub>3</sub>: 15 minutes post-insufflation
- T<sub>4</sub>: 5 minutes post-desufflation
- T<sub>5</sub>: 15 minutes post-desufflation
- T<sub>6</sub>: Postoperative 1<sup>st</sup> hour

Hemodynamic (SAP, DAP, MAP, HR) and respiratory (SpO<sub>2</sub>, FiO<sub>2</sub>, EtCO<sub>2</sub>, P<sub>peak</sub>, P<sub>plato</sub>) parameters were recorded every 5 minutes intraoperatively. Static (C<sub>S</sub>) and dynamic (C<sub>D</sub>) lung compliance were calculated at T<sub>1</sub>–T<sub>5</sub> using the following formulas:

- $C_S = VT / (P_{plato} - PEEP)$
- $C_D = VT / (P_{peak} - PEEP)$

## Intraoperative management

Fluid therapy consisted of balanced crystalloid solutions at 4–6 mL/kg/h, adjusted according to hemodynamic status. Hemodynamic stability was maintained within ±30% of baseline MAP and HR. Bradycardia (HR <50 bpm)

was treated with 0.5 mg IV atropine. Hypotension (MAP decrease >25% from baseline) was managed with a fluid bolus and 5–10 mg IV ephedrine. Hypertension was treated with 100–200 µg IV nitroglycerin boluses as needed. Mean surgical duration per group was recorded and expressed as mean ± standard deviation.

### Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean ± standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables.

The normality of the data distribution was assessed using both visual methods (histograms and probability plots) and analytical tests (the Kolmogorov–Smirnov test). For variables not normally distributed:

- The Wilcoxon Signed-Rank Test was used to compare two related groups.
- Kruskal-Wallis Test was applied for comparisons among three independent groups.
- When the Kruskal-Wallis Test indicated statistical significance, Bonferroni correction was applied for post-hoc pairwise comparisons, and adjusted p-values were reported accordingly.

For normally distributed variables:

- Paired Samples t-test was used to compare two related groups.
- One-Way Analysis of Variance (ANOVA) was employed for comparisons among three independent groups.
- In the presence of significant ANOVA results, Tukey's Honestly Significant Difference (HSD).

Test was used for post-hoc analysis.

To evaluate changes over time and between groups, a Two-Way Repeated Measures ANOVA was conducted. Results from repeated measures ANOVA are presented with F-values, degrees of freedom, and exact p-values. A p-value of less than 0.05 was considered statistically significant.

## Results

A total of 60 patients were included in the study. The mean age was  $61.10 \pm 7.98$  years (range: 39–76), and the mean body mass index (BMI) was  $27.36 \pm 3.99$  kg/m<sup>2</sup> (range: 19.57–38.06). All patients were classified as ASA physical status II. The study groups were comparable in terms of age, height, and BMI ( $p > 0.05$ ). No statistically significant differences were observed among the groups regarding the presence of comorbidities such as hypertension (HT), coronary artery disease (CAD), diabetes mellitus (DM), or the presence of multiple comorbid conditions ( $p > 0.05$ ) (Table 1).

There were no significant differences among the groups regarding mean arterial pressure (MAP) changes ( $p = 0.078$ ), peripheral oxygen saturation

**Table 1.** Distribution of some descriptive and clinical characteristics by study groups.

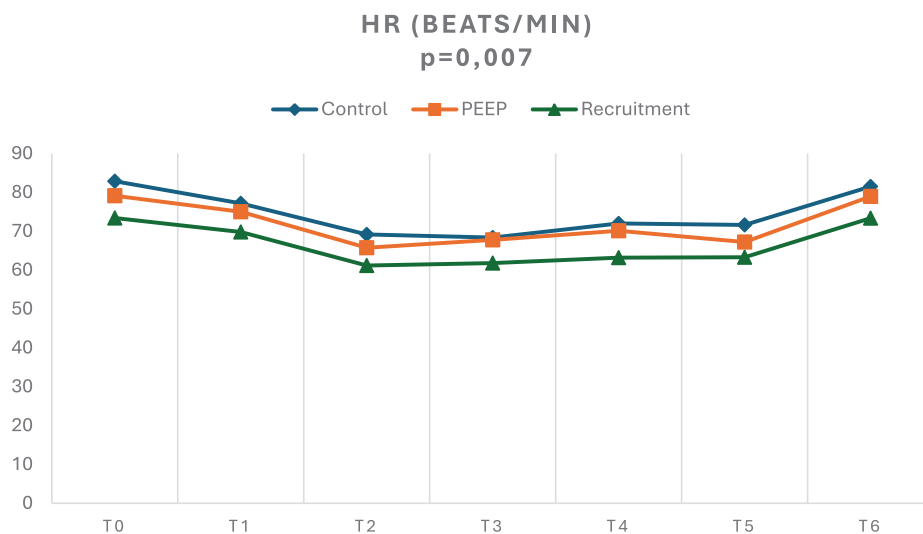
	C (n = 20)	PEEP (n = 20)	R (n = 20)	p
Age (years)	60.60 ± 8.73	60.00 ± 9.11	62.70 ± 5.85	0.539
Height (cm)	171.45 ± 6.36	173.45 ± 5.99	172.45 ± 6.12	0.593
Body weight (kg)	81.00 ± 11.63	82.10 ± 13.31	81.20 ± 13.78	0.960
BMI (kg/m <sup>2</sup> )	27.55 ± 3.55	27.27 ± 4.27	27.28 ± 4.31	0.971
Presence of comorbid disease				0.619
Absent	7 (35.0)	10 (50.0)	8 (40.0)	
Present	13 (65.0)	10 (50.0)	12 (60.0)	
Comorbid diseases (n = 35)				
Hypertension (HT)	9 (69.2)	6 (60.0)	7 (58.3)	0.833
Coronary artery disease (CAD)	3 (23.1)	2 (20.0)	2 (16.7)	0.923
Diabetes mellitus (DM)	0	2 (20.0)	1 (8.3)	0.236
COPD / Asthma	1 (7.7)	0	0	–
Other	0	0	2 (16.7)	–
Presence of second comorbid disease (n = 35)				0.152
Absent	9 (69.2)	10 (100)	10 (83.3)	
Present	4 (30.8)	0	2 (16.7)	
Second comorbid diseases (n = 6)				
Diabetes mellitus	2 (50.0)	0	1 (50.0)	–
Coronary artery disease	1 (25.0)	0	1 (50.0)	–
Other	1 (25.0)	0	0	–

Footnotes: Continuous variables are presented as mean ± standard deviation, and categorical variables as number (column percentage). One-Way Analysis of Variance (ANOVA). C: Control group; R: Alveolar recruitment group.

(SpO<sub>2</sub>) measured by pulse oximetry (p = 0.890), peak airway pressure (Ppeak) (p = 0.582), plateau pressure (Pplato) (p = 0.763), or arterial pH (p = 0.878).

We found a statistically significant difference in peak heart rate (PHR) among the groups (p = 0.007), with Group 3 showing significantly lower PHR than Group 1 (Fig. 1). End-tidal carbon dioxide (EtCO) values were also significantly lower in Group 3.

Tidal volume values at time points T2 and T3 differed significantly among the groups (p < 0.05), while values at T1, T4, and T5 were similar (p > 0.05). Post-hoc pairwise comparisons revealed significant differences at T2 and T3

**Figure 1.** Distribution of heart rate over time among the study groups.

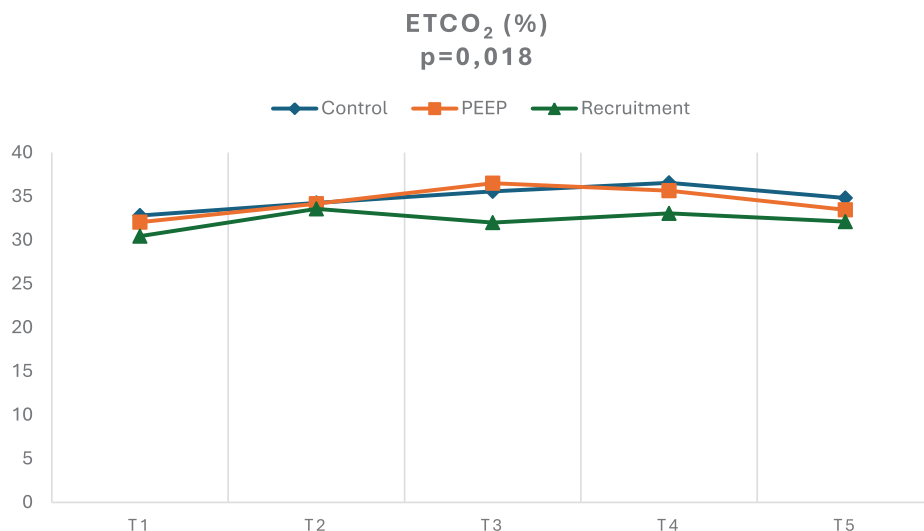


Figure 2. Distribution of end-tidal carbon dioxide over time among study groups.

between Group 1 and Group 2, with Group 1 exhibiting higher tidal volumes at these time points (Table 2).

Compliance values decreased at T2 in all groups but increased at T4 and T5, with more pronounced improvements observed in Groups 2 and 3. Static compliance (Cstat and dynamic compliance (Cdyn) were significantly higher in Groups 2 and 3 compared to Group 1 ( $p < 0.001$  for both) (Fig. 3).

Table 2. Distribution of tidal volume over time between study groups and within each group.

Tidal Volume	Control (n = 20) Mean ± SD	PEEP (n = 20) Mean ± SD	Recruitment (n = 20) Mean ± SD	p
T1	501.25 ± 17.15	500.0 ± 14.04	497.50 ± 13.81	0.913
T2	#457.50 ± 14.28*y	#445.0 ± 15.38*	#446.25 ± 16.77*	0.029
T3	457.50 ± 14.28*y	445.0 ± 15.38*	446.25 ± 16.77*	0.029
T4	#501.25 ± 17.15	#500.0 ± 14.04	#497.50 ± 13.81	0.913
T5	501.25 ± 17.15	500.0 ± 14.04	497.50 ± 13.81	0.913

T1: 5 minutes after intubation; T2: 5 minutes after insufflation; T3: 15 minutes after insufflation; T4: 5 minutes after deflation; T5: 15 minutes after deflation; X̄: Mean; SD: Standard deviation; K: Control; R: Alveolar recruitment; y: Statistically significant difference compared with the PEEP group in post-hoc pairwise comparison; \*:  $p < 0.05$  compared with T0; #:  $p < 0.05$  compared with the previous value.

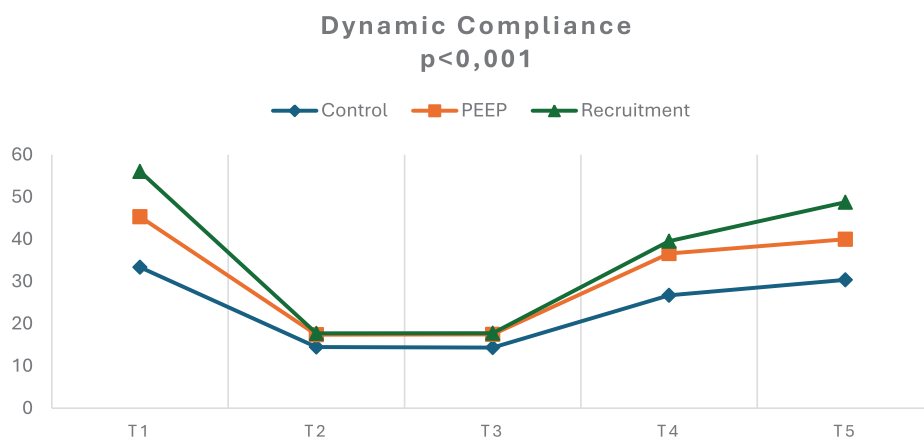


Figure 3. Distribution of dynamic compliance over time among study groups.

**Table 3.** Distribution of partial oxygen pressure ( $pO_2$ ) values over time between study groups and within each group.

$pO_2$	Control (n = 20) Mean $\pm$ SD	PEEP (n = 20) Mean $\pm$ SD	Recruitment (n = 20) Mean $\pm$ SD	p
T0	75.64 $\pm$ 6.30	75.53 $\pm$ 9.91	77.99 $\pm$ 10.10	0.619
T1	#167.31 $\pm$ 45.84* <sup>z</sup>	#203.21 $\pm$ 53.35*	#207.85 $\pm$ 47.42*	0.022
T2	#126.27 $\pm$ 28.98*	#157.90 $\pm$ 53.99*	#159.47 $\pm$ 55.02*	0.053
T3	121.20 $\pm$ 25.24* <sup>y</sup>	162.31 $\pm$ 55.14*	155.00 $\pm$ 51.32*	0.014
T4	#138.91 $\pm$ 35.27* <sup>yz</sup>	#186.77 $\pm$ 49.71*	#179.59 $\pm$ 51.50*	0.003
T5	#153.89 $\pm$ 32.31* <sup>z</sup>	#197.86 $\pm$ 47.27*	187.46 $\pm$ 58.44*	0.013
T6	#101.80 $\pm$ 22.22*	#110.67 $\pm$ 20.57*	#106.44 $\pm$ 26.89*	0.491

T0: Before operation; T1: 5 minutes after intubation; T2: 5 minutes after insufflation; T3: 15 minutes after insufflation; T4: 5 minutes after deflation; T5: 15 minutes after deflation; T6: 1 hour after operation;  $\bar{X}$ : Mean; SD: Standard deviation; K: Control; R: Alveolar recruitment;  $pO_2$ : Partial oxygen pressure; y: Statistically significant difference compared with the PEEP group in post-hoc pairwise comparison; z: Statistically significant difference compared with the Recruitment group in post-hoc pairwise comparison; \*:  $p < 0.05$  compared with T0; #:  $p < 0.05$  compared with the previous value;  $\gamma$ : Source of difference is the Control group.

Arterial partial pressure of oxygen ( $PaO_2$ ) was significantly higher in Groups 2 and 3 compared to Group 1 ( $p = 0.006$ ), with the most notable improvement observed in Group 3 at T3 (121.2  $\pm$  25.2 mmHg vs. 155.0  $\pm$  51.3 mmHg;  $p = 0.014$ ) (Table 3).

## Discussion

This randomized controlled trial demonstrated that ventilation with recruitment maneuvers (RMs) applied in conjunction with a controlled increase in positive end-expiratory pressure (PEEP) after  $CO_2$  insufflation and desufflation significantly improved intraoperative oxygenation and lung compliance in patients undergoing robot-assisted radical prostatectomy (RARP) in the steep Trendelenburg position, without inducing significant hemodynamic instability.

In our study, peak heart rate (PHR) was significantly lower in the RM group (Group 3) compared to Group 1 during the maneuver, likely due to vagal stimulation. While Whalen et al. reported no significant difference in PHR, they observed that the RM group required higher vasopressor doses, possibly due to reduced preload (Whalen et al. 2006). Suh et al. reported that end-tidal  $CO_2$  ( $EtCO_2$ ) levels increased following insufflation and remained elevated during the Trendelenburg position (Suh et al. 2010), consistent with findings by Uğur et al. (2006). In line with previous studies, tidal volume adjustments were made to maintain  $EtCO_2$  within target ranges (Haris et al. 1996). In our study,  $EtCO_2$  values were significantly lower in Group 3 than in Group 1, suggesting that RMs contributed to more effective ventilation. Notably, this occurred without significant differences in mean arterial pressure, supporting the safety of the intervention.

Functional residual capacity (FRC) is known to decrease by approximately 20% in the supine position, with an additional 10% reduction following anesthesia induction (Imberger et al. 2010). Pneumoperitoneum further exacerbates this decline. Mäkinen and Yli-Hankala (1998) reported a 30% reduction in respiratory compliance with 12 mmHg  $CO_2$  pneumoperitoneum, while Luis et al. observed a 40% reduction (Luis et al. 1992). Çakmakkaya et al. demonstrated that respiratory mechanics did not return to baseline after desufflation in laparoscopic nephrectomy. However, normal compliance values were restored

following a 40 cm H<sub>2</sub>O RM applied for 10 seconds (Çakmakkaya et al. 2009). Similarly, Whalen et al. found that RMs followed by 12 cm H<sub>2</sub>O PEEP improved intraoperative oxygenation and dynamic compliance in morbidly obese patients undergoing laparoscopic surgery (Whalen et al. 2006).

Regarding PaCO<sub>2</sub> dynamics, Hirvonen et al. (1995) and Pelosi et al. (1996) observed increases beginning at the 5<sup>th</sup> minute of pneumoperitoneum, while Joris et al. (1991) reported changes starting from the 15<sup>th</sup> minute. Monk et al. (1993) maintained constant EtCO<sub>2</sub> but still observed elevated PaCO<sub>2</sub> in patients placed in the Trendelenburg position. Özdemir et al. (2013) reported significant increases in PaCO<sub>2</sub> and the development of acidosis during RARP. In our study, although no significant intergroup differences in PaCO<sub>2</sub> were found, intragroup analysis revealed significant increases at T2–T4 and decreases at T5–T6, likely reflecting the effects of CO<sub>2</sub> insufflation and subsequent washout.

The steep Trendelenburg position and pneumoperitoneum cause cephalad displacement of the diaphragm and thoracic compression. Additionally, chest bandaging to prevent patient slippage further reduces FRC, thoracic compliance, and diffusion capacity. These anatomical and mechanical changes increase dead space ventilation, contributing to a decrease in arterial oxygen tension (PaO<sub>2</sub>).

In all groups, PaO<sub>2</sub> decreased after CO<sub>2</sub> insufflation and increased after desufflation. However, the application of PEEP and RMs in Groups 2 and 3 mitigated these decreases, resulting in significantly higher PaO<sub>2</sub> values compared to Group 1. These findings are consistent with previous reports indicating that CO<sub>2</sub> insufflation reduces lung volumes and compliance due to diaphragmatic elevation, increased airway resistance, and ventilation-perfusion mismatch, ultimately impairing oxygenation (Wittgen et al. 1991). Moreover, anesthetic-induced apnea may further exacerbate oxygen desaturation. Şahingöz (2011) reported a significant increase in oxygen saturation following desufflation.

In our study, static (Cstat) and dynamic compliance (Cdyn) were significantly lower in Group 1 compared to Groups 2 and 3. These results suggest that the adverse effects of general anesthesia, Trendelenburg positioning, and pneumoperitoneum on lung mechanics can be attenuated by PEEP and RMs. Similar findings were reported in a study, in which 15 cm H<sub>2</sub>O PEEP improved intraoperative ventilation homogeneity and physiological parameters during RARP, although it did not enhance postoperative lung function (Shono et al. 2020).

Choi et al. demonstrated that adding RMs to PEEP significantly reduced perioperative pulmonary complications in elderly patients undergoing RARP (Choi et al. 2017). Cinnella et al. emphasized the importance of individualizing PEEP settings based on body mass index (BMI) and surgical context (Choi et al. 2017). Other studies have shown that RMs improve lung compliance during the transition from the horizontal lithotomy to the steep Trendelenburg position (Kudoh et al. 2020), and Jung et al. (2021) confirmed that RMs enhance compliance at the end of laparoscopic procedures. The lower PHR in Group 3 may reflect vagal stimulation and should not be overinterpreted as a beneficial effect. Although statistically significant improvements in oxygenation and compliance were observed, the clinical relevance of these findings requires further investigation in larger trials. Our discussion also considered the findings of Whalen et al. (2006), highlighting differences in patient populations and RM protocols. The lower PHR observed in Group 3 may reflect vagal stimulation and should not be misinterpreted as a beneficial effect. Although statistically significant improvements in

oxygenation and compliance were demonstrated, the clinical relevance of these findings remains uncertain and requires confirmation in larger trials. A previous study by Whalen et al. (2006) showed that recruitment maneuvers improved oxygenation and respiratory mechanics during general anesthesia, but the effects were transient and of limited clinical significance. In contrast, Shono et al. (2020) reported significant intraoperative improvements in arterial oxygenation in patients with healthy lungs, confirming the safety of recruitment maneuvers in this setting. However, the impact on postoperative outcomes was not established.

Normal breathing ratio (I: E): In healthy spontaneous breathing, inspiration is shorter than expiration (about 1:2). IRV principle: In IRV, the inspiratory phase is prolonged (e.g., 2:1, 3:1, or higher), meaning the lungs stay inflated longer.

This increases mean airway pressure, helps keep alveoli open (“recruitment”), and improves oxygenation in patients with poor lung compliance or severe respiratory failure. Often applied in critical care or during surgeries (like laparoscopic procedures in obese patients) to enhance gas exchange (Jinghua et al. 2024). While IRV can improve oxygenation, it requires careful monitoring because prolonged inspiration may reduce venous return and affect hemodynamics. Inverse ratio ventilation (IRV) improves oxygenation and lung compliance in obese patients undergoing laparoscopic surgery, thereby reducing peak airway pressures without compromising hemodynamic stability (Jinghua et al. 2024). Overall, IRV appears to be a safe and effective ventilation strategy for this high-risk population. In our study, we used a gentler recruitment maneuver that did not impair venous return.

These differences highlight variability in patient populations and RM protocols, underscoring the need for cautious interpretation. A key limitation of our study is the absence of imaging modalities to directly assess alveolar recruitment, which may be considered a limitation. Nevertheless, physiological parameters such as  $C_{dyn}$  and  $C_{stat}$  were used as surrogate endpoints. Although the optimal role and effectiveness of PEEP and RMs remain subjects of ongoing debate, our findings support their physiological benefits during intraoperative use. Further large-scale, prospective studies are needed to validate these results and assess their impact on postoperative outcomes.

## **Additional information**

### **Conflict of interest**

The authors have declared that no competing interests exist.

### **Ethical statements**

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors’ representatives: Sağlık Bilimleri University of Ankara Bilkent City Hospital.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

## Use of AI

No use of AI was reported.

## Funding

No funding was reported.

## Author contributions

Halil Islamoglu: Conceptualization, methodology, research, writing – original draft, review and editing. Bilge Aslan: Conceptualization, research, writing – original draft, review and editing. Ayça Dumanlı Özcan: Methodology, research, writing – review and editing. Abdülkadir But: Research, writing – reviewing and editing.

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## Data availability

All of the data that support the findings of this study are available in the main text.

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