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CLINICAL TRIAL REPORT

Impact of Individualized Positive End-Expiratory Pressure Guided by Driving Pressure on Postoperative Atelectasis Assessed by Lung Ultrasound in Laparoscopic Surgery Patients: A Randomized Controlled Trial

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Purpose: Pulmonary atelectasis frequently develops during laparoscopic procedures under general anesthesia, often leading to postoperative pulmonary complications (PPCs). Given the connection between high driving pressure and these complications, this study employed ultrasonography to assess whether individualized positive end-expiratory pressure (PEEP) titration by minimum driving pressure reduces postoperative atelectasis.

Patients and Methods: Adult patients with medium-to-high-risk PPCs who were scheduled for laparoscopic procedures were allocated to receive either a fixed PEEP of 5 cmH_2O (Group C) or minimum driving pressure-guided individualized PEEP (Group D). The primary outcome was the lung ultrasound score (LUS) on postoperative day 1, and LUSs at other postoperative time points were also recorded. The secondary outcomes were occurrence of atelectasis evaluated by ultrasonography and occurrence of PPCs within 7 days postoperatively.

Results: A total of 106 participants were assigned randomly, with 102 included in the final analysis. Individualized PEEP resulted in better intraoperative respiratory mechanics. Compared with Group C, Group D demonstrated a more substantial decrease in the LUS on postoperative day 1 (4[3–6] vs 6[5–8], $P < 0.001$), and this benefit persisted until postoperative day 3. Moreover, the occurrence of atelectasis evaluated by ultrasonography in Group D was considerably lower than that in Group C at 15 min after extubation (58.8% vs 80.4%, $P = 0.018$), and this advantage persisted until postoperative day 2. Compared with Group C, Group D experienced fewer PPCs within 7 days after surgery (13.7% vs 31.4%, $P = 0.033$), whereas other postoperative recovery indicators were not significantly different.

Conclusion: In adult patients undergoing laparoscopic surgery, compared with a fixed PEEP of 5 cmH_2O, the driving pressure-guided individualized PEEP strategy improved postoperative LUSs and reduced incidences of early postoperative atelectasis assessed by ultrasound. Furthermore, it was associated with fewer PPCs and lower rates of atelectasis in the first 7 postoperative days.

Keywords: laparoscopy, postoperative complications, pulmonary atelectasis, positive-pressure respiration, driving pressure, ultrasonography

Introduction

Atelectasis is a common complication following general anesthesia. The combination of peumoperitoneum and Trendelenburg position significantly affects respiratory mechanics, which can increase the occurrence and aggravate the degree of atelectasis in laparoscopic procedures.[1,2] Atelectasis may lead to hypoxemia and often continues in

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postanaesthetic care unit (PACU) or even longer after procedure. The occurrence of atelectasis in the PACU after laparoscopic gynecological surgery is as high as 40–50%.[3] Postoperative persistent and severe atelectasis is closely related to postoperative pulmonary complications (PPCs). Therefore, the early identification and prevention of postoperative atelectasis are crucial.

Lung-protective ventilation strategies (LPVSs) mitigate postoperative atelectasis and PPCs in patients under general anesthesia, benefiting both injured and healthy lungs.[4] According to the 2019 international expert panel-based consensus,[5] individualized PEEP is the most recommended LPVS, but there is no consensus on the method to guide the optimal PEEP. A meta-analysis revealed that higher driving pressure independently contributes to the risk of PPCs.[6] Moreover, previous randomized controlled trials indicate that minimum driving pressure-guided individualized PEEP can significantly decrease the occurrence of atelectasis and PPCs following thoracic and abdominal procedures.[7,8]

The evaluation of PPCs relies mostly on thoracic computed tomography (CT), which is frequently limited by transport, ionizing radiation and other factors, resulting in missed diagnosis of early atelectasis. Due to its advantages of being cost-effective, radiation-free and dynamically measurable, ultrasound has emerged as an excellent imaging tool for perioperative lung aeration assessment.[9] The lung ultrasound score (LUS) is determined by identifying ultrasound signs for semi-quantitative assessment of perioperative atelectasis[10] and can dynamically assess not only global but also regional ventilation at each time point.[11] Published studies[12–14] have used ultrasound to assess the loss of lung aeration from surgery to the PACU admission, while the use of multiple postoperative dynamic assessments is limited.

Although several studies have demonstrated the benefits of driving pressure-guided individualized PEEP ventilation strategies for postoperative recovery in surgical patients, other researches[15,16] have reached contradictory conclusions. Currently, there is no unified consensus on the advantages of using driving pressure-guided individualized PEEP. Additionally, while lung ultrasound has gradually been employed for perioperative pulmonary function assessment, its application is usually limited to the early postoperative period, the longitudinal trajectory of lung aeration changes after laparoscopic surgery under individualized PEEP remains unclear. Therefore, we hypothesized that in adult laparoscopic surgery patients with medium-to-high risk of PPCs, individualized PEEP lung-protective ventilation guided by driving pressure might help prevent the postoperative atelectasis and pulmonary complications. This randomized trial therefore aimed to evaluate the impact of driving pressure-guided PEEP on aeration loss, not only immediately postoperatively but also serially over the first three postoperative days using LUS, providing a more comprehensive picture of pulmonary recovery.

Materials and Methods

Study Design and Ethics

This prospective, single-center, randomized controlled trial was approved by the Institutional Ethical Committee of Beijing Tongren Hospital, Capital Medical University (No. TREC2023- KY123; data: November 23, 2023) and registered in the Chinese Clinical Trial Registry (No. ChiCTR2300079041; principal investigator: GY Wang; data: December 25, 2023) before patient enrollment. This study adheres to the criteria of the Consolidated Standards of Reporting Trials (CONSORT) guidelines, consistent with the Declaration of Helsinki and its subsequent revisions. All participants provided written informed consent prior to inclusion.

Participants

The inclusion criteria were as follows: patients over 18 years old who were scheduled for laparoscopic procedure anticipated to last more than two hours; patients with body mass index (BMI) less than 35 $kg \cdot m^{-2}$ who were classified as American Society of Anesthesiologists (ASA) physical status I–III; and patients with Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) score $\geq$ 26 indicated a medium to high risk of PPCs.

The exclusion criteria were as follows: patients with severe acute and chronic lung diseases, including respiratory failure, pneumothorax, pulmonary bullae, acute exacerbation of chronic obstructive pulmonary disease, and poorly controlled asthma; patients with severe cardiovascular complications defined as NYHA class III–IV; patients who have undergone thoracic surgery or have a history of mechanical ventilation within 4 weeks; patients with other contraindications for PEEP, including high intracranial pressure, bronchopleural fistula and hypovolemic shock.

Randomization and Blinding

The patients were randomly assigned to receive an individualized PEEP guided by minimum driving pressure (Group D) or a fixed PEEP of 5 cmH_2O (Group C) according to the computer-generated random number list with an allocation ratio of 1:1. The group information was concealed in sequentially numbered, opaque, sealed envelopes and opened by the attending anesthetists who were not involved in subsequent procedures. Due to the different mechanical ventilation parameter settings in this study, the chief anesthesiologist was not blinded to ensure medical safety, but he or she was not involved in subsequent procedures. Lung ultrasound assessment was done by a well-trained anesthesiologist and the ultrasound images were analyzed by an independent investigator, both of whom were blinded to the interventions and not involved in the anesthesia procedure, the follow-up, and statistical analysis. Participants, ultrasound assessors, follow-up investigators and data collectors remained unaware of the group allocations.

Anesthesia Protocol

Perioperative management of all patients was performed by a relatively fixed anesthesia team (CH Xi et al) following the standard protocol (Figure 1 and The Study Protocol in Supplementary File 1).[17]

Intervention and Ventilation Protocol

All patients used LPVSs of volume-controlled ventilation during mechanical ventilation (Mindray WATO EX-65 Pro, Shenzhen, China) under general anesthesia, with tidal volume of 7 $ml \cdot kg^{-1}$ of predicted body weight, PEEP of 5 cmH_2O, inspiratory-to-expiratory ratio of 1:2, end-inspiratory pause of 10%, flow of 2 $L \cdot min^{-1}$, inspired oxygen fraction (FiO_2) ≥ 40% to maintain the pulse oxygen saturation (SpO_2) ≥ 95%, and the respiratory rate adjusted to maintain the end-expiratory carbon dioxide ($P_{ET}CO_2$) at 35~45 mmHg.

In traditional LPVS group, the PEEP was maintained at 5 cmH_2O throughout the procedure. In the driving pressure-guided individualized PEEP group, an incremental PEEP titration was performed to identify the optimal individualized PEEP that resulted in minimum driving pressure (calculate as Pplat - PEEP) after the establishment of pneumoperitoneum-Trendelenburg position and the recruitment maneuver (RM), as indicated in protocol. PEEP was gradually increased by 1 cmH_2O starting from the lowest PEEP allowed by the anesthesia machine (3 cmH_2O) to 12 cmH_2O,[18]

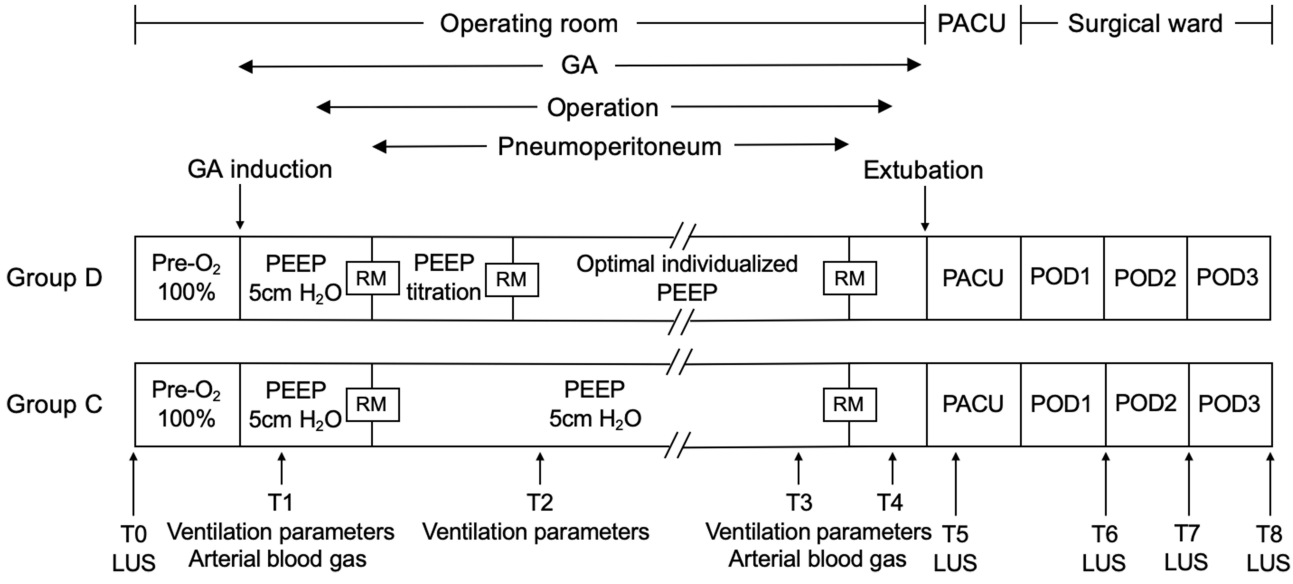

Figure 1 Schematic diagram of the study protocol and interventions.

Abbreviations: GA, general anaesthesia; Pre-O_2, preoxygenation; PEEP, positive end-expiratory pressure; RM, recruitment manoeuvre; PACU, postanesthesia care unit; POD, postoperative day; LUS, lung ultrasound score; T0, upon entering the operating room; T1, 5 min after intubation; T2, 5 min after pneumoperitoneum establishment or after individualized PEEP titration; T3, 2 h after pneumoperitoneum establishment or before the end of pneumoperitoneum; T4, the end of surgery; T5, 15 min after extubation; T6, postoperative day 1; T7, postoperative day 2; T8, postoperative day 3.

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and each PEEP level was maintained for 10 breaths. When the driving pressure decreased with increasing PEEP, downward PEEP titration was performed until the minimum driving pressure was reached. Following a subsequent RM, the ideal PEEP was sustained continuously throughout the surgery.

RMs were performed in both groups after the pneumoperitoneum-Trendelenburg position was established, the pneumoperitoneum was stopped and the supine position was resumed, and one more time in Group D after the PEEP titration was completed. RMs were performed using the incremental PEEP method in PCV mode to reach a peak airway pressure (Ppeak) of 40 cmH_2O.[19] Hemodynamic stability was ensured before the PEEP was adjusted and the RM was performed. Other details of PEEP titration and RMs are shown in the protocol (Figure 1 and The Study Protocol in Supplementary File 1).

Rescue of Hypoxemia ($SpO_2 \leq 92\%$, Lasting > 1 min)

First, eliminated diseases leading to increased airway resistance, pneumothorax, hemodynamic instability, ventilator failure, and then took intervention measures according to the groups.

Group C: First, gradually increased FiO_2, when FiO_2 increased to 100% and SpO_2 still did not reach 92%, gradually increased PEEP levels. If there was still no improvement, then increased RMs. If the blood oxygen still did not the standard, adjusted position to the supine position.

Group D: First, performed individualized PEEP titration again after RM. If SpO_2 still did not reach 92%, gradually increased FiO_2. If the blood oxygen still did not the standard, adjusted position to the supine position.

Lung Ultrasound

All lung ultrasound scans were performed by a blinded well-trained anesthetist (JY Zhu), via a Wisonic ultrasound machine (Wisonic Medical Co., Ltd., Shenzhen, China) with a 5–12 MHz linear transducer. Each hemithorax was divided into 6 regions using 3 lines (anterior axillary, posterior axillary and pectoral nipple). All intercostal spaces of twelve lung regions were scanned in sequence while patients were in supine position, as previously described[20] and protocol mentioned (The Study Protocol in Supplementary File 1). Ultrasound scans of each region were preserved for blinded evaluation by an independent investigator (Y Zhang).

Outcomes

The primary outcome was the LUS on postoperative day (POD) 1 (T6). The LUS calculation is to add the scores from 0 to 3 points of 12 regions as previously mentioned.[21] The LUSs at other time points, including while enter the operating room (T0), 15 min after extubation (T5), on POD2 (T7) and POD3 (T8), were also recorded.

The secondary outcomes included the incidence of postoperative atelectasis at T5, T6, T7 and T8, which was defined as an LUS ≥ 2 for any of the 12 regions,[3] and the incidence and specific types of PPCs within 7 days postoperatively or before discharge. The definitions of clinical outcomes for PPCs were adopted from the European Joint Taskforce guidelines published in 2015,[22] details of which can be found in the study protocol (Supplementary File 1). Postoperative recovery indicators included PACU duration, the desaturation in PACU (defined as a $SpO_2 \leq 95\%$), admission and duration of intensive care unit (ICU), postoperative analgesia assessment, duration of hospitalization and postoperative stay, and mortality during the hospital stay.

Intraoperative hemodynamics and mechanical ventilation parameters were recorded. Intraoperative hemodynamics included HR, MAP and SpO_2; mechanical ventilation parameters included the driving pressure, Ppeak, plateau pressure (Pplat), and dynamic compliance (Cdyn) at 5 min after intubation (T1), 5 min after pneumoperitoneum establishment or after individualized PEEP titration (T2), 2 h after pneumoperitoneum establishment or before the end of pneumoperitoneum (T3), and the end of surgery (T4); VT, PEEP, FiO_2, respiratory rate, and $P_{ET}CO_2$ mean values at the above time points; oxygenation indices (PaO_2/FiO_2) at T1, T3, and T4.

Other perioperative variables were recorded. Intraoperative indicators included type, position and Trendelenburg angle of surgery; duration of mechanical ventilation, operation and pneumoperitoneum; fluid balance; intraoperative adverse events; and use of vasopressors. Investigators for data collection (YF Bai and Y Zhang) had been trained before initiating the trial.

Sample Size Calculation

According to previous study,[23] an elevated LUS on POD1 is related to the higher risk of PPCs following major abdominal procedures. Consequently, the sample size determination relied on the LUS on POD1. PASS 15.0 was used for sample size calculation. On the basis of our clinical experience with the LUS at T6 (6.1±3.1 in Group C and 4.3±2.1 in Group D), the estimated sample size was 48 patients in each group, with a two-sided alpha of 0.05 and a power of 0.9. Considering a 10% dropout rate, 106 patients in total were required.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics 26.0. Distribution normality was tested using the Shapiro–Wilk test. The LUSs and other nonnormally distributed continuous variables were expressed as medians (interquartile ranges). The Friedman test was used to compare within-group differences, whereas the Mann–Whitney *U*-test was used to analyze between-group differences. Normally distributed continuous variables were reported as the means ± standard deviations (± s) and were compared via independent samples *t* tests. Repeated-measures analysis of variance (ANOVA) was used to analyze intraoperative hemodynamics, respiratory mechanics and arterial blood gas. Multiple comparisons within groups were conducted using the Bonferroni correction. The categorical variables were expressed as frequencies or percentages (%) and were analyzed using the χ^2 test or Fisher's exact test. For binary variables, the relative risk (RR) was illustrated with the 95% CI. A two-sided P value < 0.05 was considered statistically significant.

Results

Participants

A total of 135 consecutive participants were screened for enrollment, with 106 were randomized to the control or individualized PEEP group, the CONSORT flow diagram was shown in Figure 2. Two patients in Group D did not receive an entire ultrasound examination, and 2 patients in Group C had ultrasound images that were lost. Therefore, data analysis was performed for 102 patients. Table 1 shows the baseline and intraoperative characteristics of the participants, with no significant differences between the groups.

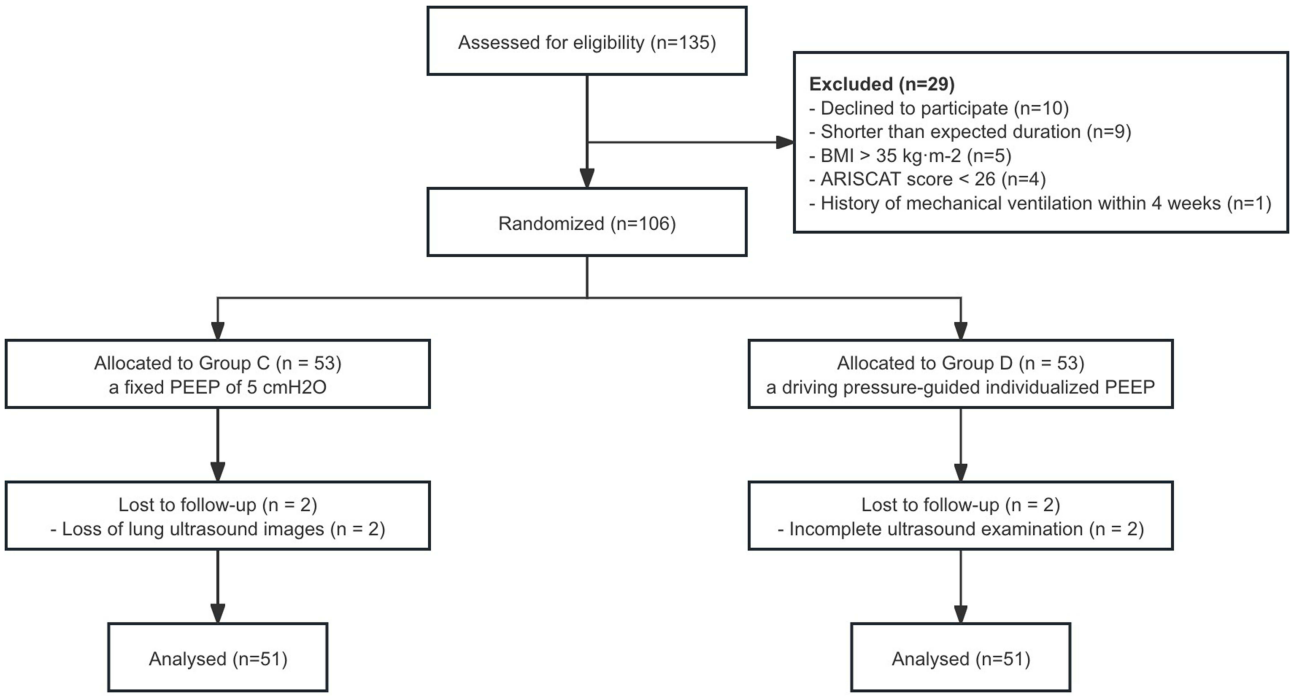

Figure 2 CONSORT flow diagram.

Abbreviations: ARISCAT, Assess Respiratory Risk in Surgical Patients in Catalonia; BMI, body mass index; CONSORT, Consolidated Standards Of Reporting Trials; PEEP, positive end-expiratory pressure.

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Table 1 Baseline of Patient Characteristics and Intraoperative Characteristics

	Group C (n=51)	Group D (n=51)	*P* value
Baseline characteristics			
Age (year)	63.2±11.2	60.6±10.7	0.225
Sex, male/female	25(49.0)/26(51.0)	27(52.9)/24(47.1)	0.692
BMI ($kg \cdot m^{-2}$)	23.8±4.2	23.2±3.1	0.481
PBW (kg)	58.5±8.7	60.5±9.3	0.251
ASA physical status, I / II / III	2(3.9)/43(84.3)/6(11.8)	1(2.0)/46(90.2)/4(7.8)	0.640
Active smoking, n (%)	7(13.7)	12(23.5)	0.432
ARISCAT risk index, medium/high	44(86.3)/7(13.7)	47(92.2)/4(7.8)	0.338
Comorbidity, n (%)			
Hypertension	21(41.2)	17(33.3)	0.413
Diabetes	13(25.5)	10(19.6)	0.477
Coronary artery disease	4(7.8)	6(11.8)	0.505
Cerebrovascular disease	4(7.8)	4(7.8)	1.000
Chronic kidney disease	3(5.9)	0(0)	0.243
Anaemia	9(17.6)	10(19.6)	0.799
Pulmonary comorbidity, n (%)	6(11.8)	4(7.8)	0.505
Pneumonia	4(7.8)	3(5.9)	
Bronchiectasis	2(3.9)	1(2.0)	
COPD	1(2.0)	0(0)	
Asthma	0(0)	1(2.0)	
Intraoperative characteristics			
Type of operation, n (%)			0.944
Gastrectomy	6(11.8)	6(11.8)	
Hepatectomy	2(3.9)	2(3.9)	
Duodenopancreatectomy	2(3.9)	0(0)	
Colectomy	10(19.6)	11(21.6)	
Radical rectectomy	10(19.6)	12(23.5)	
Gynecologic surgery	13(25.5)	12(23.5)	
Urological surgery	8(15.7)	8(15.7)	
Position, Trendelenburg/anti-Trendelenburg	41(80.4)/10(19.6)	43(84.3)/8(15.7)	0.603
Trendelenburg angle (deg)	12[9–15]	12[9–20]	0.580
Duration (min)			
Mechanical ventilation	211[184–270]	197[165–258]	0.140
Operation	180[153–240]	164[131–220]	0.145
Pneumoperitoneum	150[114–190]	128[104–156]	0.085
Crystalloid fluids (L)	2.6[1.6–3.0]	2.1[1.6–2.6]	0.172
Blood loss (mL)	150[100–275]	100[100–150]	0.400
Urine output (mL)	300[200–575]	300[200–500]	0.314
Use of vasopressor, n (%)	22(43.1)	25(49.0)	0.551

Notes: Data are presented as mean ± SD or median [IQR] or number (%).
Abbreviations: BMI, body mass index; PBW, predicted body weight; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

Effect of Driving Pressure-Guided Individualized PEEP Intervention

After individualized titration, Group D had a significantly higher PEEP than Group C did (7[6–7] cmH_2O vs 5[5–5] cmH_2O, $U = 102.000$, $P < 0.001$). Individualized PEEP resulted in lower driving pressure, higher Cdyn and oxygenation index (OI) but no intergroup differences in inspiratory peak pressure or plateau pressure (Table 2).

Primary Outcome: Serial LUSs

Preoperative LUS results were similar between the two groups (T0; Figure 3A and Table 3). Lung aeration loss was present to varying degrees at each postoperative time point, with a maximum at 15 min after extubation, but the degree in

Table 2 Intraoperative Hemodynamics and Respiratory Mechanics Parameters

	Group C (n=51)	Group D (n=51)	*U*/*t*/*F*	*P* value
Hemodynamics				
MAP (mmHg)			0.731	0.534
T1	80±10‡	79±10‡		
T2	96±10	94±9		
T3	80±9‡	80±8‡		
T4	80±9‡	81±10‡		
Heart rate (bpm)			0.789	0.470
T1	63±11‡	64±11		
T2	67±10	65±10		
T3	62±10‡	62±9		
T4	60±9‡	61±10‡		
SpO_2 (%)				
T1	100[99–100]	100[99–100]	1017.000	0.129
T2	100[99–100]	100[99–100]	1011.000	0.111
T3	100[99–100]	100[99–100]	1160.500	0.762
T4	100[99–100]	100[99–100]	1121.500	0.494
Respiratory mechanics				
PEEP (cmH_2O)	5[5–5]	7[6–7]	102.000	<0.001*
VT ($mL \cdot kg^{-1}$)	7.0±1.2	7.0±0.7	0.070	0.944
FiO_2 (%)	59[50–65]	57[50–61]	1130.000	0.618
RR (bpm)	12[12–13]	13[12–13]	1130.500	0.598
$P_{ET}CO_2$ (mmHg)	35.6±2.8	35.9±2.7	0.624	0.529
DP (cmH_2O)			12.533	<0.001*
T1	9.2±2.2	8.9±1.6	0.573	0.451
T2	16.3±2.7†	13.9±2.5†	20.919	<0.001*
T3	17.8±3.4†‡	14.5±2.3†	31.700	<0.001*
T4	11.5±2.0†‡§	9.8±1.8‡§	18.556	<0.001*
Cdyn ($mL \cdot cmH_2O^{-1}$)			4.385	0.018*
T1	56.2±13.2	56.7±10.3	0.051	0.821
T2	30.6±7.7†	35.8±6.6†	12.592	0.001*
T3	27.8±7.3†‡	32.8±6.3†‡	13.176	<0.001*
T4	48.6±12.2†‡§	53.6±9.3‡§	5.258	0.024*
P_{peak} (cmH_2O)			1.208	0.301
T1	16.5±2.2	16.3±1.7		
T2	23.7±2.9†	23.0±2.6†		
T3	25.2±3.6†‡	24.0±2.8†‡		
T4	19.0±2.3†‡§	18.5±2.8†‡§		
P_{plat} (cmH_2O)			0.954	0.385
T1	14.2±2.2	13.9±1.6		
T2	21.1±3.0†	20.2±2.5†		
T3	22.6±3.7†‡	21.5±2.4†‡		
T4	16.4±2.1†‡§	15.8±2.6†‡§		
OI (mmHg)			11.455	<0.001*
T1	431.7±66.2	435.1±68.8	0.056	0.813
T3	382.5±81.0†	431.8±81.9	8.172	0.005*
T4	391.6±69.1†	452.7±88.3§	12.957	0.001*

Notes: Data are presented as mean ± SD or median [IQR]. *compared with Group C, $P < 0.05$; †compared with T1 in the same group, $P < 0.05$; ‡compared with T2 in the same group, $P < 0.05$; §compared with T3 in the same group, $P < 0.05$.
Abbreviations: MAP, mean arterial pressure; SpO_2, peripheral oxygen saturation; PEEP, positive end-expiratory pressure; VT, tidal volume; FiO_2, inspired oxygen fraction; RR, respiratory rate; $P_{ET}CO_2$, end-expiratory carbon dioxide; DP, driving pressure; Cdyn, dynamic compliance; P_{peak}, peak inspiratory pressure; P_{plat}, plateau pressure; OI, oxygenation index; T1, 5 min after intubation; T2, 5 min after pneumoperitoneum establishment or after individualized PEEP titration; T3, 2 h after pneumoperitoneum establishment or before the end of pneumoperitoneum; T4, the end of surgery.

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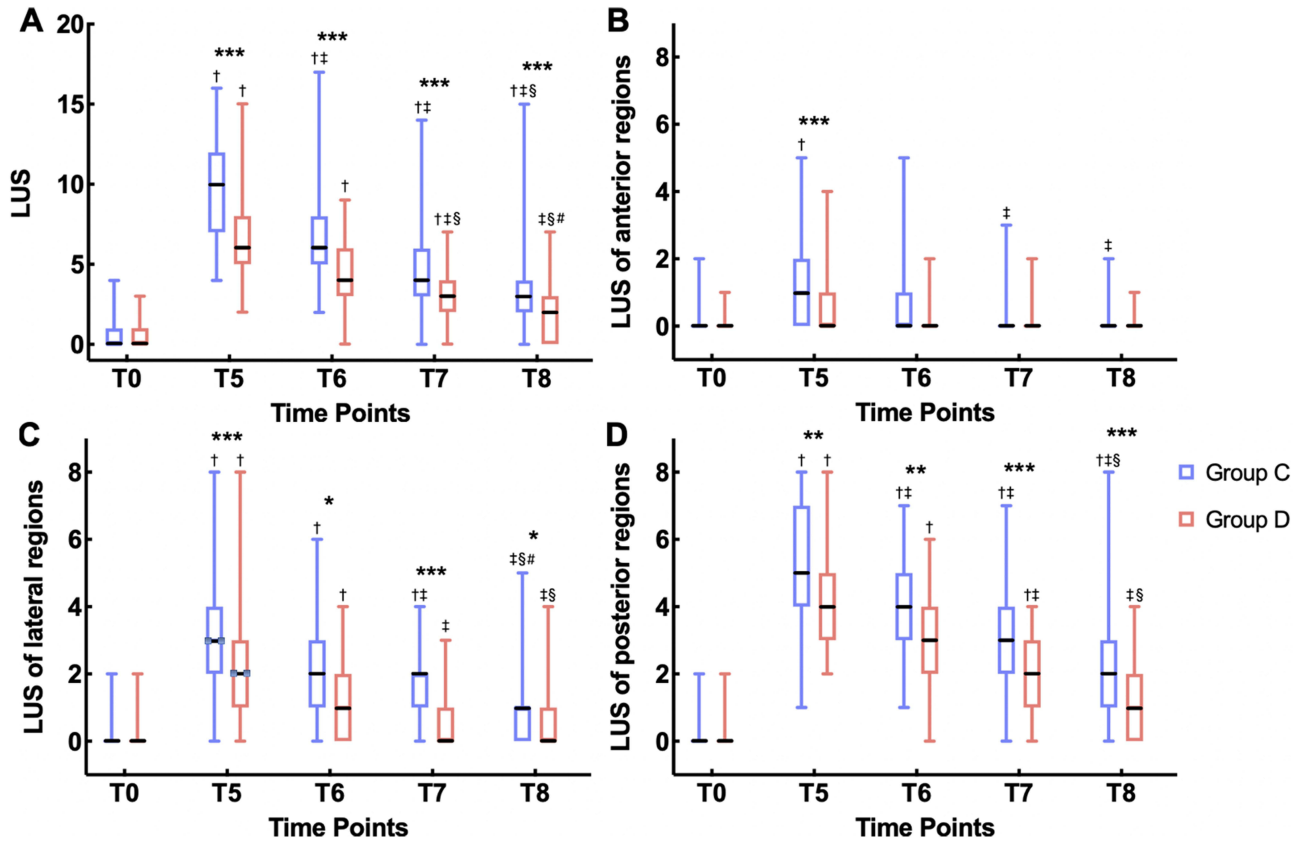

Figure 3 Temporal evolution and regional distributions of the LUSs. (**A**) Total LUS. (**B**) LUS of anterior regions. (**C**) LUS of lateral regions. (**D**) LUS of posterior regions.
Notes: The bold line represents the median, the ends of the boxes represent interquartile ranges and error bars represent min to max ranges. *** compared with Group C, $P < 0.001$; ** compared with Group C, $P < 0.01$; *compared with Group C, $P < 0.05$; †compared with T0 in the same group, $P < 0.05$; ‡compared with T5 in the same group, $P < 0.05$; §compared with T6 in the same group, $P < 0.05$; #compared with T7 in the same group, $P < 0.05$ (according to Bonferroni correction).
Abbreviations: LUS, lung ultrasound score; T0, upon entering the operating room; T5, 15 min after extubation; T6, postoperative day 1; T7, postoperative day 2; T8, postoperative day 3.

Group D was significantly better than that in Group C (T5, 6[5–8] vs 10[7–12], $U = 562.000$, $P < 0.001$). The LUS on POD1, which was the primary outcome, began to improve, and that of Group D was still significantly lower than that of Group C (T6, 4[3–6] vs 6[5–8], $U = 728.500$, $P < 0.001$). This trend was maintained until POD2 (T7, 3[2–4] vs 4[3–6], $U = 621.500$, $P < 0.001$) and POD3 (T8, 2[0–3] vs 3[2–4], $U = 703.500$, $P < 0.001$).

After Bonferroni-corrected multiple comparisons within groups (Figure 3A and Table 3), the recovery of LUS in Group D was faster, with no significant difference between T8 and T0 (2[0–3] vs 0[0–1], $P = 0.094$). However, the lung

Table 3 LUSs in Total and in Different Regions

	Group C (n=51)	Group D (n=51)	*U*	*P* value
T0				
Total LUS	0[0–1]	0[0–1]	1283.000	0.884
In the anterior regions	0[0–0]	0[0–0]	1276.500	0.668
In the lateral regions	0[0–0]	0[0–0]	1262.000	0.645
In the posterior regions	0[0–0]	0[0–0]	1262.000	0.704
T5				
Total LUS	10[7–12]†	6[5–8]†	562.000	<0.001*
In the anterior regions	1[0–2]†	0[0–1]	812.500	<0.001*
In the lateral regions	3[2–4]†	2[1–3]†	785.000	<0.001*
In the posterior regions	5[4–7]†	4[3–5]†	884.500	0.005*

(*Continued*)

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Table 3 (Continued).

	Group C (n=51)	Group D (n=51)	*U*	*P* value
T6				
Total LUS	6[5–8]†‡	4[3–6]†	728.500	<0.001*
In the anterior regions	0[0–1]	0[0–0]	1083.000	0.072
In the lateral regions	2[1–3]†	1[0–2]†	944.000	0.014*
In the posterior regions	4[3–5]†‡	3[2–4]†	866.500	0.003*
T7				
Total LUS	4[3–6]†‡	3[2–4]†‡§	621.500	<0.001*
In the anterior regions	0[0–0]‡	0[0–0]	1224.500	0.479
In the lateral regions	2[1–2]†‡	0[0–1]‡	714.500	<0.001*
In the posterior regions	3[2–4]†‡	2[1–3]†‡	773.500	<0.001*
T8				
Total LUS	3[2–4]†‡§	2[0–3]‡§#	703.500	<0.001*
In the anterior regions	0[0–0]‡	0[0–0]	1094.500	0.114
In the lateral regions	1[0–1]‡§#	0[0–1]‡§	984.500	0.018*
In the posterior regions	2[1–3] †‡§	1[0–2] ‡§	760.500	<0.001*

Notes: Data are presented as median [IQR]. *compared with Group C, $P < 0.05$; †compared with T0 in the same group, $P < 0.05$; ‡compared with T5 in the same group, $P < 0.05$; §compared with T6 in the same group, $P < 0.05$; #compared with T7 in the same group, $P < 0.05$.

Abbreviations: LUS, lung ultrasound score; T0, upon entering the operating room; T5, 15 min after extubation; T6, postoperative day 1; T7, postoperative day 2; T8, postoperative day 3.

aeration loss in Group C recovered slowly after POD1 (T6 vs T7, 6[5–8] vs 4[3–6], $P = 0.332$; T7 vs T8, 4[3–6] vs 3 [2–4], $P = 0.054$) without normalization at POD3 (T8 vs T0, 3[2–4] vs 0[0–1], $P = 0.005$).

An analysis of regional lung ventilation revealed that the lung aeration loss was more severe in gravity-dependent regions and that individualized PEEP had a protective effect. The LUS of the anterior region showed significant intergroup differences only at T5 (0[0–1] vs 1[0–2], $U = 812.500$, $P < 0.001$), whereas the LUS of the lateral and posterior regions in Group D presented significantly lower scores at each postoperative time point (Figure 3B–D and Table 3). Representative ultrasound images of one participant from each group at each time point are shown in Figure 4.

Secondary Outcomes

Atelectasis Assessed by Lung Ultrasound

Compared with that in Group C, the incidence of atelectasis evaluated by ultrasonography was lower in Group D at 15 min after extubation (58.8% vs 80.4%, RR 0.48, 95% CI 0.25–0.91, $P = 0.018$), on POD1 (35.3% vs 56.9%, RR 0.67, 95% CI 0.46–0.97, $P = 0.029$) and on POD2 (5.9% vs 25.5%, RR 0.79, 95% CI 0.67–0.94, $P = 0.006$), but it was comparable on POD3 (2.0% vs 13.7%, RR 0.88, 95% CI 0.78–1.06, $P = 0.060$; Table 4).

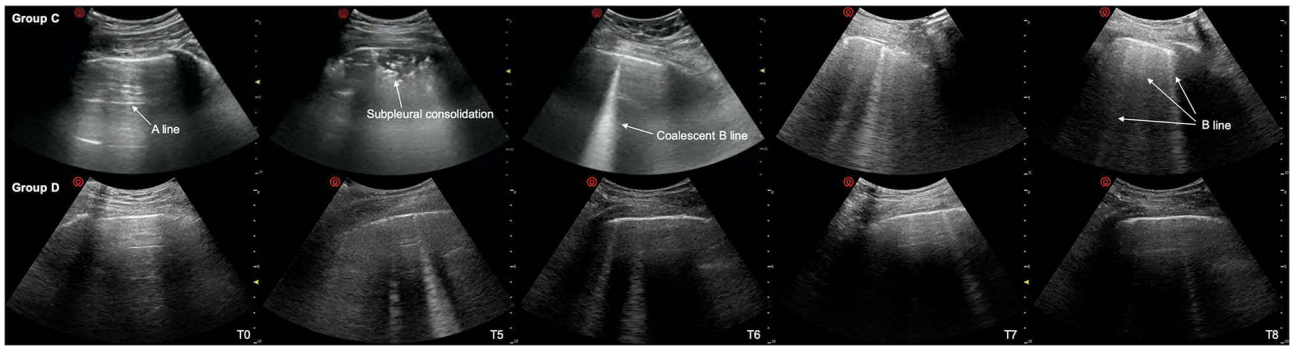

Figure 4 Lung ultrasound images in the left inferoposterior quadrant of one representative patient from each group at each time point.

Abbreviations: T0, upon entering the operating room; T5, 15 min after extubation; T6, postoperative day 1; T7, postoperative day 2; T8, postoperative day 3.

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Table 4 Incidence of Atelectasis Assessed by Ultrasound, PPCs and Other Postoperative Recovery Indicators

	Group C (n=51)	Group D (n=51)	$U/t/\chi^2$	*P* value
Atelectasis assessed by ultrasound				
T0	2(3.9)	1(2.0)	–	1.000
T5	41(80.4)	30(58.8)	5.607	0.018*
T6	29(56.9)	18(35.3)	4.774	0.029*
T7	13(25.5)	3(5.9)	7.413	0.006*
T8	7(13.7)	1(2.0)	–	0.060
PPCs	16(31.4)	7(13.7)	4.547	0.033*
Atelectasis	13(25.5)	5(9.8)	4.317	0.038*
Pleural effusion	9(17.6)	4(7.8)	2.204	0.138
Pneumonia	3(5.9)	3(5.9)	–	1.000
Respiratory failure	2(3.9)	2(3.9)	–	1.000
Pulmonary embolism	1(2.0)	0(0.0)	–	1.000
Postoperative recovery indicators				
PACU duration (min)	56[41–69]	55[44–63]	963.000	0.967
Desaturation in PACU, n (%)	10(19.6)	5(9.8)	1.954	0.162
ICU admission, n (%)	6(11.8)	7(13.7)	0.088	0.767
ICU duration (hour)	24.4±10.4	21.9±8.9	0.467	0.650
VAS score				
T6	3[2–3]	2[1–3]	907.000	0.218
T7	2[1–2]	1[1–2]	831.000	0.055
T8	1[1–1]	1[0–1]	947.000	0.319
Length of postoperative stay (day)	10.9±5.3	10.2±3.9	0.830	0.409
Length of hospital stay (day)	17.4±6.7	15.3±5.5	1.804	0.074
Mortality, n (%)	0(0.0)	0(0.0)	–	–

Notes: Atelectasis was defined as LUS ≥ 2 for any of the 12 regions. Data are presented as mean ± SD or median [IQR] or number (%). *$P < 0.05$.

Abbreviations: PPCs, postoperative pulmonary complications; LUS, lung ultrasound score; PACU, post-anesthesia care unit; ICU, intensive care unit; VAS, visual analog scale; T0, upon entering the operating room; T5, 15 min after extubation; T6, postoperative day 1; T7, postoperative day 2; T8, postoperative day 3.

Incidence of PPCs

Compared with Group C, Group D presented a significantly lower incidence of PPCs (13.7% vs 31.4%, RR 0.80, 95% CI 0.64–0.99, $P = 0.033$; Table 4). Among the PPCs, the incidence of atelectasis identified by CT was significantly lower in Group D than in Group C (9.8% vs 25.5%, RR 0.83, 95% CI 0.69–0.99, $P = 0.038$). There was no intergroup difference in the incidence of other PPCs, including pleural effusion, pneumonia, respiratory failure and pulmonary embolism ($P > 0.05$). No participants experienced other respiratory complications including pneumothorax, bronchospasm, pulmonary edema or ARDS during the study period.

Postoperative Recovery

Although 5 subjects in Group D and 10 in Group C experienced desaturation in PACU, no significant intergroup difference was observed (9.8% vs 19.6%, RR 0.89, 95% CI 0.76–1.05, $P = 0.162$). Other postoperative recovery indicators, including PACU duration, ICU admission and duration, postoperative VAS score, length of hospital stay and postoperative stay, were similar between the two groups (Table 4). No patients died during the hospital stay.

Intraoperative Hemodynamics and Respiratory Mechanics

There were no significant differences in intraoperative hemodynamics according to the intergroup comparisons ($P > 0.05$), whereas the intragroup comparisons revealed higher MAP and HR only at 5 min after pneumoperitoneum establishment than other time points (Table 2). No intraoperative adverse events, such as desaturation, occurred in either

group of patients. Individualized PEEP resulted in higher PEEP, lower driving pressure, better Cdyn and OI, but there were no intergroup differences in other respiratory mechanics parameters (Table 2). Repeated-measures ANOVA revealed time-dependent effects of the driving pressure, Cdyn, Ppeak, and Pplat, whereas PEEP titration mitigated time-dependent effects on driving pressure and Cdyn.

Discussion

Our findings indicated that the use of titrated PEEP decreased postoperative LUSs and the incidence of ultrasound-assessed atelectasis until POD3 by providing better intraoperative oxygenation and respiratory mechanics. Titrated PEEP may also lead to a possible reduction in PPCs within 7 days postoperatively without significant hemodynamic alterations.

Recently, studies have used ultrasound to guide intraoperative RMs[24,25] and evaluate perioperative lung aeration loss.[11,13] Some studies reported LUSs results in the early postoperative period, such as after extubation or before PACU discharge.[12,26,27] Although a multicenter observational study on major abdominal surgery demonstrated that LUS on POD1 was correlated with the development of PPCs within 10 days after surgery,[23] the dynamic evolution of LUSs more than 24 hours after surgery remains poorly investigated and documented. Our findings demonstrated that individualized PEEP effectively reduced the LUS on POD1, the extent of lung aeration loss, and the incidence of atelectasis assessed by ultrasound. Additionally, through dynamic measurements via lung ultrasound, we noticed that the LUSs remained better in individualized PEEP group at all measurement time points postoperatively, indicating that the improvement in individualized PEEP with respect to lung aeration loss could last at least until POD3.

Patients undergoing laparoscopic surgery under general anesthesia are prone to atelectasis,[3,25] which is considered as a mechanism leading to PPCs.[28] The use of RMs or fixed PEEP is beneficial to prevent the perioperative atelectasis and PPCS,[13,24] but the fixed PEEP is not appropriate for all populations due to significant individual differences.[12,29] In our study, the median PEEP of Group D was 7 cmH_2O after PEEP titration, which was significantly higher than 5 cmH_2O, indicating that the empirically used PEEP is not sufficient to prevent alveolar collapse during laparoscopic surgery. In addition, the individualized PEEP after titration in the intervention group varied widely (from 4 to 10 cmH_2O), which was similar to the findings of a recent study.[30] This heterogeneity highlights the need for dynamic monitoring of changes in lung aeration and individualized mechanical ventilation during the perioperative period. The individualized PEEP titration methods vary with inconsistent results,[27,29,31–33] which measured by electrical impedance tomography (EIT) and transpulmonary pressure (TPP) are not highly practical due to equipment limitations. Driving pressure reflects TPP and the entire lung strain in patients with healthy lungs, which can be measured easily during clinical mechanical ventilation.[34] Zhang C et al observed by EIT imaging that the lower driving pressure was related to the reduction in atelectasis of the dependent lung regions,[7] which confirms that driving pressure can be an effective and practical strategy to achieve individualized PEEP. Another previous reported that driving pressure-guided individualized PEEP reduced postoperative atelectasis in abdominal surgery while our study extends this benefit to patients undergoing laparoscopic surgery.[26] However, on-pump cardiac surgery and thoracic surgery dose not reduce PPCs with individualized PEEP guided by driving pressure,[15,16] possibly due to the absence of dynamic imaging to confirm the reduction of atelectasis in those studies.

Using repeated ultrasonography, we dynamically assessed lung aeration and identified atelectasis in the early post-operative phase. Intragroup comparisons revealed prolonged lung aeration loss after laparoscopy, which persisted until POD3 (Figure 3A). Comfortingly, interventions of individualized PEEP can accelerate recovery. The LUS of the individualized PEEP group normalized on POD3, whereas the LUS of the control group on POD3 was still significantly higher than preoperative ones with a slow recovery. Furthermore, our regional lung aeration analysis revealed that the individualized PEEP protected non-dependent lung regions, maintaining insignificant LUS differences even immediately after extubation (Figure 3B). The dependent regions were more susceptible to surgical procedures and mechanical ventilation, increasing the possibility of atelectasis in these regions. Our results were similar with those of Général et al[13] and Sun-Kyung et al[3] who reported that the dorsal region had the worst LUSs both during gynecological open surgery and after gynecological laparoscopic surgery. While EIT-guided individualized PEEP reduced intraoperative collapse in the dependent lung regions,[35] few studies track regional recovery beyond 24 hours postoperatively. Our serial measurements within 3 postoperative days revealed that the loss of lung aeration in lateral regions recovered on POD2,

with posterior regions recovering on POD3 in intervention group, whereas the recovery in control group was delayed by one day (Figure 3C and D). Aeration in dependent lung regions particularly benefits from the individualized PEEP, and the advantages do not disappear immediately in the early postoperative period.

Although the intergroup differences in aeration loss continued from extubation until POD3, the intergroup disparities in ultrasound-diagnosed atelectasis persisted only until POD2 (5.9% vs 25.5%, $P = 0.006$), which was essentially consistent with the incidence of CT-diagnosed atelectasis (9.8% vs 25.5%, $P = 0.038$), indicating that POD2 may be a critical time point. Without effective lung-protective ventilation interventions, up to a quarter of patients may still develop atelectasis within the first 2 postoperative days. Prolonged atelectasis leads to impaired gas exchange, reduced functional residual capacity, and hypoxemia, all of which increase the risk of PPCs.[36] Our results revealed that the control group experienced higher occurrence of atelectasis and PPCs within 7 days postoperatively, which was consistent with the LUSs and the incidence of atelectasis diagnosed by ultrasound. Zhang C et al[7] reported that severe PPCs of Grade 2 or higher were more clinically significant, as mild PPCs did not affect clinical outcomes. Our study yielded similar results, although the incidence of PPCs and atelectasis significantly decreased in intervention group, ICU-related outcomes and hospital stay did not differ significantly, which may be correlated with a higher incidence of mild PPCs that did not require additional respiratory treatments. Consequently, further research is required in the future to confirm the direct correlation between postoperative atelectasis assessed by lung ultrasound and pulmonary complications, as well as their impact on clinical outcomes.

Our study is significant in several aspects. Firstly, we did not impose excessive restrictions on age, sex, weight, and type of surgery when recruiting patients, aiming to include as many different types of individuals undergoing laparoscopic surgery as possible, with the expectation that the results would benefit a broader audience. In terms of intervention, we applied an individualized PEEP ventilation strategy based on minimum driving pressure, which is comparable in effectiveness to methods such as EIT and TPP but more practical and feasible, easier to measure and apply in clinical practice to benefit patients. Additionally, the control group also utilized lung-protective ventilation, with only differences in PEEP settings between the two groups, ensuring that all included patients received proven lung-protective measures. Furthermore, we achieved dynamic assessment of lung aeration and early identification of atelectasis by repeated measurements with ultrasound in the early postoperative phase, while avoiding radiation exposure and high costs.

There are several limitations in this study. First, dynamic individualized PEEP titration is necessary, as the optimal PEEP level varies across different types of patients and under different surgical conditions. As the pneumoperitoneum significantly affects lung aeration and respiratory mechanics,[37] we applied individualized PEEP during pneumoperitoneum to enhance the feasibility of the study. The LUSs after extubation in our findings were similar to those in previous trial that involved dynamic PEEP titration in elderly laparoscopic surgery patients,[27] which indicates that the lung protective effects of both methods are comparable. Second, lung ultrasound assessment has inherent subjectivity as the primary method in this study. To mitigate potential errors arising from equipment and operator techniques, the ultrasound machine used in our study was a specialized instrument, and the investigators who completed ultrasound examinations and image scoring were professionally trained and blinded. Considering the radiation exposure and costs, we assessed atelectasis using ultrasound but did not concurrently evaluate the extent of atelectasis with CT scans. The combined use of ultrasound as a screening and identification tool for early postoperative period and CT as a diagnostic tool for confirming PPCs and assessing their severity may be a more optimal approach for the early identification, diagnosis, and prevention of PPCs. In addition, considering the impact of driving pressure on special populations such as minors with incomplete development and patients with severe obesity, the inclusion criteria of our study had limitations. The results may not be applicable to all surgical patients, and further large-sample, multicenter trials are needed to confirm our results.

Conclusion

In conclusion, compared with the application of a fixed PEEP of 5 cmH_2O during laparoscopic surgery in adult patients, driving pressure-guided individualized PEEP lung-protective ventilation improved postoperative LUSs and reduced the occurrence of atelectasis assessed by ultrasound in the early postoperative period, which could persist until postoperative day 2, while reducing the occurrence of PPCs and atelectasis in first 7 postoperative days, which may be related to enhancements in intraoperative respiratory mechanics and oxygenation indices.

Data Sharing Statement

The de-identified participant data will be made available upon reasonable request to the corresponding author (Guyan Wang: guyanwang2006@163.com) from 6 months after publication for a period of 2 years.

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Disclosure

The authors report no conflicts of interest in this work.

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