Langenbeck's Archives of Surgery (2025) 410:99
https://doi.org/10.1007/s00423-025-03666-z

RESEARCH

Effect of controlled hyperventilation on post-laparoscopic cholecystectomy shoulder pain: a prospective randomized controlled trial

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Received: 15 November 2024 / Accepted: 3 March 2025

Abstract

Objective This study investigated whether intraoperative controlled hyperventilation could reduce the incidence and severity of post-laparoscopic shoulder pain.

Methods In this prospective, randomized, double-blind controlled trial, 150 patients undergoing elective laparoscopic cholecystectomy were randomly assigned to either controlled hyperventilation ($n=75$) or conventional ventilation ($n=75$) groups. The hyperventilation group received mechanical ventilation with a tidal volume of 10 mL/kg and respiratory rate adjusted to maintain end-tidal CO_2 between 30 and 35 mmHg, while the control group received conventional ventilation (tidal volume 8 mL/kg, end-tidal CO_2 35–45 mmHg). The primary outcome was the incidence and severity of shoulder pain during the first 48 postoperative hours. Secondary outcomes included intraoperative parameters, gas exchange values, surgical site pain, and patient satisfaction.

Results The hyperventilation group demonstrated significantly lower shoulder pain incidence (36.0% vs. 60.0%, $P=0.003$), shorter pain duration (4.13 ± 6.25 vs. 9.24 ± 7.82 h, $P<0.001$), and consistently lower pain intensity scores at all time points up to 48 h postoperatively. The intervention group also showed shorter operation time (50.01 ± 12.04 vs. 80.32 ± 34.23 min, $P<0.001$), lower pneumoperitoneum pressure requirements (11.73 ± 1.19 vs. 33.72 ± 19.47 mmHg, $P<0.001$), and improved patient satisfaction (73.33% vs. 42.67%, $P<0.001$). No significant differences were observed in postoperative complications, time to first flatus, or length of hospital stay.

Conclusion Intraoperative controlled hyperventilation effectively reduces the incidence and severity of shoulder pain following laparoscopic cholecystectomy, while improving surgical conditions and patient satisfaction. This simple intervention provides a safe and cost-effective approach to enhancing postoperative outcomes in laparoscopic surgery.

Keywords Laparoscopic cholecystectomy · Shoulder pain · Controlled hyperventilation · Pneumoperitoneum · Postoperative pain management

Introduction

Laparoscopic cholecystectomy (LC) has become the gold standard for treating symptomatic gallstone disease, offering significant advantages over open surgery, including reduced postoperative pain, shorter hospital stay, and improved cosmetic outcomes [1]. However, postoperative shoulder pain remains a common complaint, affecting 35–80% of patients following laparoscopic procedures [2]. This referred pain, typically manifesting in the right shoulder, can significantly impact patient recovery and satisfaction with the surgical experience [3].

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Published online: 15 March 2025

The pathophysiology of post-laparoscopic shoulder pain is primarily attributed to carbon dioxide (CO_2) pneumoperitoneum-induced diaphragmatic irritation and phrenic nerve stimulation [4]. During laparoscopic procedures, CO_2 gas is insufflated into the peritoneal cavity to create adequate surgical space, leading to local irritation and inflammation [5, 6]. Additionally, the residual CO_2 gas trapped under the diaphragm post-surgery can cause referred pain to the shoulder region through phrenic nerve pathways [7]. Various strategies have been investigated to reduce post-laparoscopic shoulder pain, including low-pressure pneumoperitoneum, preemptive analgesics, intraperitoneal local anesthetic installation, and passive gas drainage [8]. However, these interventions have shown variable efficacy, and there is no consensus on the optimal approach to prevent or manage this common postoperative complication.

Recent physiological studies have demonstrated that CO_2 absorption and elimination during laparoscopic procedures are significantly influenced by ventilation parameters [9]. Controlled hyperventilation, achieved through increased tidal volume and respiratory rate, may enhance CO_2 elimination and potentially reduce residual pneumoperitoneum [10]. Furthermore, maintaining lower arterial CO_2 levels through controlled hyperventilation might influence the local tissue pH and inflammatory response around the diaphragm [11].

Despite the theoretical basis for using controlled hyperventilation to reduce post-laparoscopic shoulder pain, limited research has systematically evaluated its clinical effectiveness. Previous studies have primarily focused on the impact of ventilation strategies on intraoperative gas exchange and hemodynamics, with little attention to postoperative pain outcomes [12, 13]. The relationship between ventilation parameters, CO_2 homeostasis, and post-laparoscopic shoulder pain remains incompletely understood [14].

Therefore, this prospective randomized controlled trial aimed to investigate the effect of intraoperative controlled hyperventilation on the incidence and severity of shoulder pain following laparoscopic cholecystectomy. By examining this intervention's impact on both physiological parameters and clinical outcomes, this study seeks to provide evidence-based guidance for optimizing ventilation strategies during laparoscopic procedures.

Methods

Study design and setting

This prospective, single-center, randomized controlled trial was conducted between January 2023 and October 2024. The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrollment.

Participants

Adult patients aged 18–75 years scheduled for elective laparoscopic cholecystectomy under general anesthesia were eligible for participation. Exclusion criteria included: emergency surgery, acute cholecystitis requiring urgent intervention, history of chronic shoulder pain or cervical spine disorders, previous upper abdominal surgery, pregnancy, American Society of Anesthesiologists (ASA) physical status > III, body mass index > 35 kg/m², severe cardiopulmonary disease, and refusal to participate in the study. The patients who underwent conversion to open cholecystectomy, experienced delayed recovery, or were unable to comprehend pain scales were excluded from the final statistical analysis.

Randomization and blinding

Participants were randomly assigned to either the controlled hyperventilation group (observation group) or the conventional ventilation group (control group) using a computer-generated random number sequence with a 1:1 allocation ratio. The allocation was concealed using sequentially numbered, opaque, sealed envelopes that were opened immediately before the induction of anesthesia. While the attending anesthesiologist was aware of the group assignment due to the nature of the intervention, the surgical team, post-anesthesia care unit staff, ward nurses, outcome assessors, and patients remained blinded to the group allocation throughout the study period.

Anesthetic management

All patients received standardized preoperative preparation and monitoring, including electrocardiography, non-invasive blood pressure measurement, pulse oximetry, and end-tidal carbon dioxide ($ETCO_2$) monitoring. Arterial catheterization was performed for blood gas analysis. Anesthesia was induced with etomidate ($_2$ mg/kg), propofol (0.5-1 mg/kg), sulfentanyl (0.5 μg/kg), and rocuronium (0.6 mg/kg). After tracheal intubation, anesthesia was maintained with sevoflurane (1.5–2.5%) in an oxygen-air mixture (FiO_2 0.5).

In the control group, mechanical ventilation was initiated with conventional parameters: tidal volume of 8 mL/kg of ideal body weight, respiratory rate adjusted to maintain $ETCO_2$ between 35 and 45 mmHg, and positive end-expiratory pressure (PEEP) of 4 cmH_2O. The observation group received controlled hyperventilation with a tidal volume of 10 mL/kg and an increased respiratory rate targeted to

maintain $ETCO_2$ between 30 and 35 mmHg, with the same PEEP settings.

Surgical technique

All surgical procedures were performed by experienced surgeons using a standardized four-port technique. Pneumoperitoneum was established using CO_2 insufflation through a Veress needle inserted at the umbilicus, with an initial pressure of 12 mmHg. The operation was performed using standard laparoscopic instruments and electrocautery. At the end of the procedure, CO_2 was evacuated by manual compression of the abdomen with open trocars. No intraperitoneal local anesthetic was administered.

Postoperative management

All patients received standardized postoperative care and multimodal analgesia according to institutional protocols. The analgesic regimen included regular intravenous paracetamol(1 g every 6 h), flurbiprofen axetil (50 mg ivgtt) and rescue tramadol (50–100 mg) for breakthrough pain. Postoperative nausea and vomiting were treated with ondansetron (4 mg) as needed.

Outcome measurements

The primary outcome was the incidence and severity of shoulder pain during the first 48 postoperative hours. Shoulder pain was assessed using a visual analog scale (VAS) ranging from 0 (no pain) to 10 (worst imaginable pain) at 2, 6, 12, 24, and 48 h postoperatively. Secondary outcomes included intraoperative parameters (operation time, pneumoperitoneum duration, total CO_2 consumption), arterial blood gas values (pH, $PaCO_2$), surgical site pain scores, time to first flatus, length of hospital stay, postoperative complications, and patient satisfaction.

Table 1 Baseline demographic and clinical characteristics of study participants

Characteristic	Control Group ($n=75$)	Hyperventilation Group ($n=75$)	Statistical Value	P Value
Age (years)	55.96 ± 10.70	58.35 ± 10.33	t = 1.390	0.168
Sex (Male/Female)	29/46	30/45	χ^2=0.028	0.867
BMI (kg/m²)	24.37 ± 2.23	24.41 ± 2.12	t = 0.113	0.910
ASA classification (I/II/III)	22/52/1	24/47/4	χ^2=2.543	0.280
Comorbidities, n (%)				
- Hypertension	45 (60.0)	39 (52.0)	χ^2=1.087	0.297
- Diabetes mellitus	16 (21.3)	14 (18.7)	χ^2=0.165	0.685
- Coronary heart disease	8 (10.7)	12 (16.0)	χ^2=0.917	0.338
Previous abdominal surgery (Yes/No)	8/67	7/68	χ^2=0.076	0.783
Severity of cholecystitis (Mild/Moderate/Severe)	30/34/11	30/34/11	χ^2=0.000	1.000

Values are presented as mean ± SD or number (percentage)

Sample size calculation

Based on previous studies, we estimated that the incidence of shoulder pain in the control group would be approximately 60%. Assuming a reduction to 35% in the intervention group, with an α of 0.05 and a power of 0.80, we calculated that 73 patients would be required per group. To account for potential dropouts, we planned to enroll 75 patients per group.

Statistical analysis

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation and compared using Student's t-test or Mann-Whitney U test as appropriate. Categorical variables were presented as numbers and percentages and analyzed using chi-square or Fisher's exact test. Repeated measures analysis of variance was used to compare serial measurements between groups. A two-sided P-value < 0.05 was considered statistically significant.

Results

Patient characteristics

Between January 2023 and October 2024, a total of 178 patients were initially enrolled, with 28 cases ultimately excluded from the analysis (25 due to an inability to comprehend pain scales and 3 due to delayed recovery). Consequently, 150 patients were included in the final statistical analysis, comprising the controlled hyperventilation group ($n=75$) and the conventional ventilation group ($n=75$). The baseline demographic and clinical characteristics were comparable between the two groups (Table 1).

Intraoperative parameters

Significant differences were observed in several intraoperative parameters between the groups (Table 2). The hyperventilation group demonstrated significantly shorter operation time (50.01 ± 12.04 vs. 80.32 ± 34.23 min, $P<0.001$) and lower pneumoperitoneum pressure (11.73 ± 1.19 vs. 33.72 ± 19.47 mmHg, $P<0.001$). However, the pneumoperitoneum duration was longer in the hyperventilation group

Table 2 Intraoperative parameters and ventilation characteristics

Parameter	Control Group ($n=75$)	Hyperventilation Group ($n=75$)	Statistical Value	P Value
Operation time (min)	80.32 ± 34.23	50.01 ± 12.04	t = 7.234	< 0.001
Pneumoperitoneum pressure (mmHg)	33.72 ± 19.47	11.73 ± 1.19	t = 9.658	< 0.001
Pneumoperitoneum duration (min)	24.29 ± 18.12	44.56 ± 11.56	t = 8.123	< 0.001
CO_2 consumption (L)	66.67 ± 38.72	104.88 ± 32.52	t = 6.524	< 0.001
Intraoperative blood loss (mL)	6.28 ± 2.86	6.71 ± 2.98	t = 0.912	0.363
Tidal volume (mL/kg)	8.01 ± 0.12	9.93 ± 0.25	t = 62.445	< 0.001
Respiratory rate (breaths/min)	12.12 ± 0.33	12.84 ± 1.10	t = 5.432	< 0.001
PEEP (cmH_2O)	4.24 ± 0.46	4.19 ± 0.43	t = 0.712	0.477

Table 3 Perioperative gas exchange parameters

Parameter	Control Group ($n=75$)	Hyperventilation Group ($n=75$)	Statistical Value	P Value
$ETCO_2$ (mmHg)				
- Anesthesia induction	34.91 ± 1.74	31.77 ± 1.41	t = 12.111	< 0.001
- Pneumoperitoneum start	40.83 ± 2.85	36.52 ± 2.13	t = 10.523	< 0.001
- Pneumoperitoneum end	42.15 ± 2.96	37.84 ± 2.45	t = 9.876	< 0.001
- Surgery end	37.65 ± 2.34	34.92 ± 2.12	t = 7.432	< 0.001
$PaCO_2$ (mmHg)				
- Anesthesia induction	38.64 ± 1.79	35.89 ± 1.65	t = 9.874	< 0.001
- Pneumoperitoneum start	45.12 ± 2.45	41.23 ± 2.21	t = 10.234	< 0.001
- Pneumoperitoneum end	46.35 ± 2.78	42.56 ± 2.43	t = 8.965	< 0.001
- Surgery end	40.25 ± 2.12	37.45 ± 1.98	t = 8.432	< 0.001
pH				
- Anesthesia induction	7.40 ± 0.03	7.38 ± 0.02	t = 4.832	< 0.001
- Pneumoperitoneum start	7.33 ± 0.03	7.32 ± 0.03	t = 2.234	0.027
- Pneumoperitoneum end	7.32 ± 0.03	7.31 ± 0.02	t = 2.543	0.012
- Surgery end	7.36 ± 0.03	7.35 ± 0.02	t = 2.321	0.022

(44.56 ± 11.56 vs. 24.29 ± 18.12 min, $P<0.001$), with correspondingly higher total CO_2 consumption (104.88 ± 32.52 vs. 66.67 ± 38.72 L, $P<0.001$).

Gas exchange parameters

The hyperventilation group maintained significantly lower $ETCO_2$ and $PaCO_2$ levels throughout the procedure (Table 3; Fig. 1). Both groups showed expected changes in blood pH, with slightly lower values during pneumoperitoneum, but the differences between groups remained clinically minimal though statistically significant.

Postoperative pain outcomes

The incidence of shoulder pain was significantly lower in the hyperventilation group compared to the control group (36.0% vs. 60.0%, $P=0.003$). When shoulder pain occurred, it had a shorter duration (4.13 ± 6.25 vs. 9.24 ± 7.82 h, $P<0.001$) and earlier onset (1.81 ± 3.33 vs. 3.55 ± 3.21 h, $P=0.001$) in the hyperventilation group. Shoulder pain intensity, as measured by VAS scores, was consistently lower in the hyperventilation group at all time points (Table 4; Fig. 2).

Postoperative recovery and satisfaction

No significant differences were observed between groups in the incidence of postoperative nausea and vomiting (9.33% vs. 12.00%, $P=0.599$), time to first flatus (4.56 ± 1.22 vs. 4.39 ± 1.06 h, $P=0.363$), or length of hospital stay (4.17 ± 0.84 vs. 3.97 ± 0.90 days, $P=0.154$). No postoperative complications or 30-day readmissions were reported in either group. Patient satisfaction was significantly higher in the hyperventilation group (73.33% vs. 42.67%, $P<0.001$).

Discussion

This prospective randomized controlled trial demonstrates that intraoperative controlled hyperventilation significantly reduces the incidence and severity of shoulder pain following laparoscopic cholecystectomy. The intervention group showed a 40% reduction in shoulder pain incidence, along with decreased pain intensity scores and shorter duration of symptoms. These findings suggest that optimizing ventilation strategies during laparoscopic procedures may provide a simple yet effective approach to improving postoperative outcomes.

The observed reduction in shoulder pain aligns with the physiological principles of CO_2 homeostasis during laparoscopic surgery. Recent studies have shown that increased minute ventilation enhances CO_2 elimination during

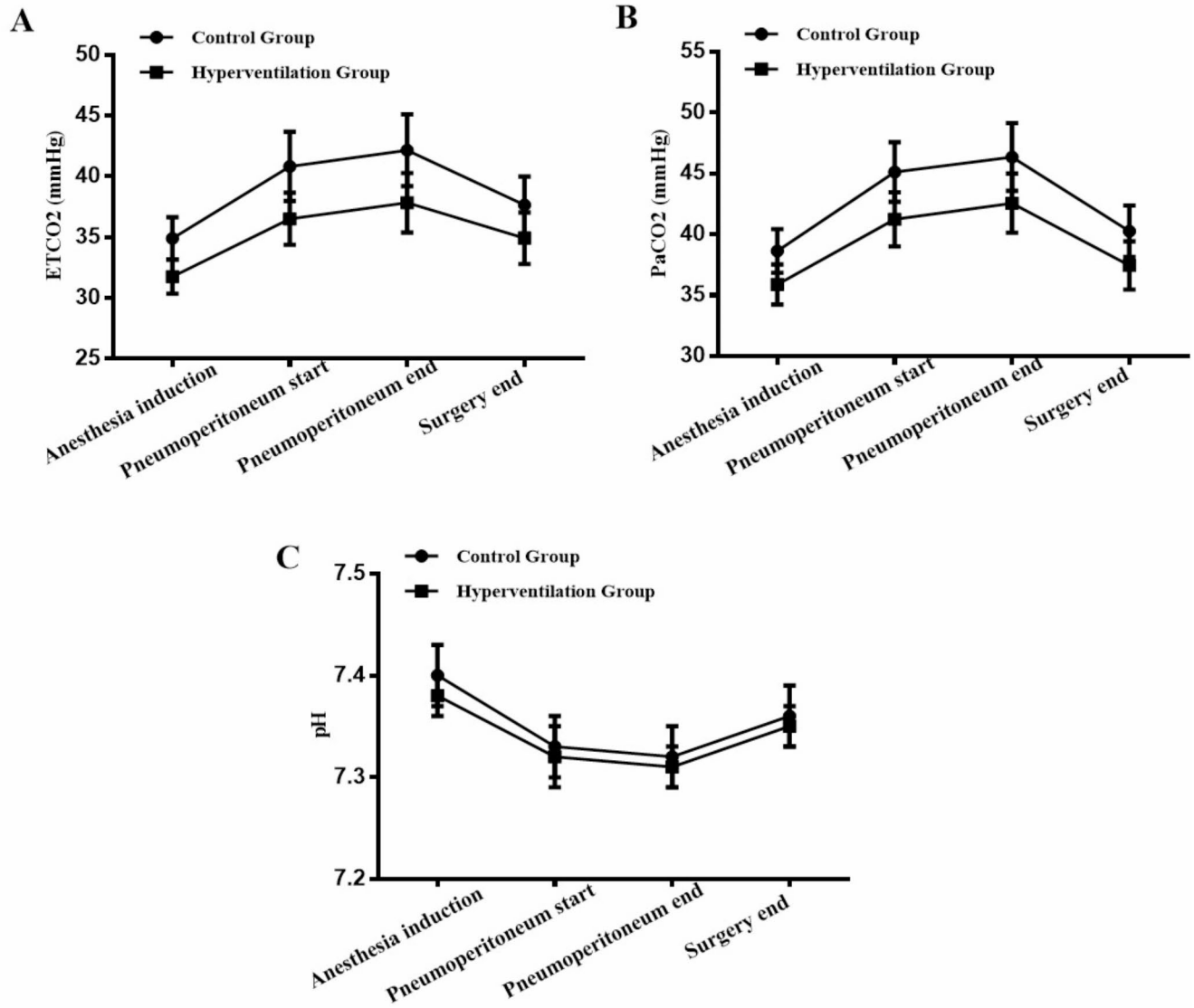

Fig. 1 Perioperative Gas Exchange Parameters between two groups. (**A**) $ETCO_2$; (**B**) $PaCO_2$; (**C**) pH

pneumoperitoneum [15]. A meta-analysis of ventilation strategies in laparoscopic surgery reported that higher tidal volumes combined with adequate PEEP could improve gas exchange and reduce postoperative complications [16]. Our results extend these findings by demonstrating a direct clinical benefit in terms of reduced shoulder pain.

Notably, our study found that the hyperventilation group required longer pneumoperitoneum duration but achieved shorter overall operation times. While it may initially seem paradoxical, this observation likely stems from the enhanced surgical field visibility and more stable pneumoperitoneum conditions afforded by the controlled hyperventilation strategy. The key mechanism behind this could be that higher tidal volumes, along with lower CO_2 levels in the hyperventilation group, help to maintain a more stable pneumoperitoneum at a lower pressure. This improved CO_2 handling can result in better intra-abdominal visibility, potentially making the procedure more efficient and leading to a reduction in operation time [17]. Previous studies have demonstrated that optimized ventilation can reduce the need for high pneumoperitoneum pressures without sacrificing surgical exposure [18]. This could allow the surgeon to perform the procedure more smoothly and, consequently, more quickly. Furthermore, by reducing residual CO_2 in the abdominal cavity, the hyperventilation technique might also decrease the need for prolonged manipulation of the abdomen to clear the gas, which may further shorten the surgery. While this finding does not directly explain the reduction in shoulder pain, the shorter operation time could contribute to a less traumatic overall surgical experience, possibly influencing postoperative pain outcomes.

Table 4 Postoperative pain outcomes

Parameter	Control Group ($n=75$)	Hyperventilation Group ($n=75$)	Statistical Value	*P* Value
Shoulder Pain Characteristics				
- Incidence, n (%)	45 (60.0)	27 (36.0)	$\chi^2=8.654$	0.003
- Duration (hours)	9.24±7.82	4.13±6.25	t=4.452	<0.001
- Time to onset (hours)	3.55±3.21	1.81±3.33	t=3.324	0.001
Shoulder Pain VAS Score				
−2 h postoperative	1.52±0.62	0.85±0.43	t=7.865	<0.001
−6 h postoperative	2.45±0.89	1.32±0.56	t=9.234	<0.001
−12 h postoperative	2.84±0.92	1.65±0.67	t=8.976	<0.001
−24 h postoperative	2.23±0.78	1.23±0.54	t=9.123	<0.001
−48 h postoperative	1.54±0.52	0.89±0.38	t=8.654	<0.001
Surgical Site Pain VAS Score				
−2 h postoperative	1.33±0.60	1.15±0.54	t=2.006	0.047
−6 h postoperative	2.01±0.85	1.42±0.63	t=4.872	<0.001
−12 h postoperative	2.03±0.66	1.52±0.58	t=5.123	<0.001
−24 h postoperative	1.53±0.56	1.21±0.49	t=3.758	<0.001
−48 h postoperative	1.08±0.34	0.98±0.32	t=1.876	0.063

In our study, despite the shorter operation time in the hyperventilation group, we observed a significant reduction in the incidence and intensity of shoulder pain. This suggests that the pain reduction is more likely attributed to the physiological benefits of controlled hyperventilation, such as enhanced CO_2 elimination and reduced postoperative inflammation, rather than solely to the shorter surgical time. The lower $PaCO_2$ levels observed in the intervention group indicate more efficient elimination of absorbed CO_2 during pneumoperitoneum [19], which may reduce local tissue acidosis around the diaphragm—an important factor in post-laparoscopic pain [20]. Furthermore, modified ventilation parameters may influence the distribution and absorption of residual pneumoperitoneum gas. Recent imaging studies using computed tomography have shown that ventilation patterns can impact the dispersion of residual CO_2 in the subdiaphragmatic space [21]. Additionally, the broader analgesic effect could be attributed to reduced systemic inflammation, as suggested by recent molecular studies indicating that CO_2 pneumoperitoneum induces a pH-dependent inflammatory response in peritoneal tissues [22].

Importantly, the implementation of controlled hyperventilation did not lead to adverse effects on acid-base balance or hemodynamic stability. The observed pH differences between groups, while statistically significant, remained within clinically acceptable ranges. This safety profile is consistent with previous studies investigating moderate hyperventilation in laparoscopic surgery [23]. Furthermore, the absence of postoperative complications in both groups suggests that the intervention can be safely integrated into standard anesthetic protocols. The economic implications of our findings warrant consideration. The reduction in postoperative pain could potentially lead to decreased analgesic requirements and earlier mobilization. Although our study did not show significant differences in length of hospital stay, a large-scale registry analysis has suggested that improved early postoperative recovery may reduce healthcare utilization and costs [24]. The simplicity of implementing controlled hyperventilation, requiring no additional equipment or medications, makes it a particularly attractive intervention from a cost-effectiveness perspective.

However, certain limitations should be acknowledged. The single-center design may limit the generalizability of our results to different surgical settings and patient populations. The standardization of postoperative analgesic protocols, while necessary for study validity, may not reflect the variability in pain management approaches across

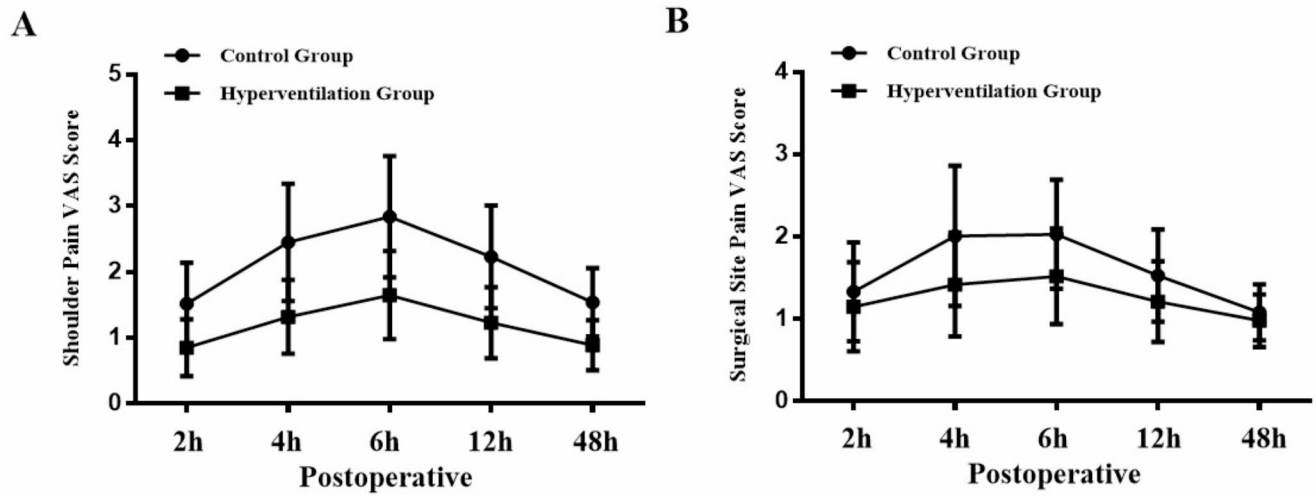

Fig. 2 Postoperative Pain Outcomes between two groups. (**A**) Shoulder Pain VAS Score; (**B**) Surgical Site Pain VAS Score

institutions. Furthermore, although we monitored patients for 48 h postoperatively, the long-term impact of the intervention remains unknown.

Conclusion

This randomized controlled trial provides strong evidence that intraoperative controlled hyperventilation effectively reduces post-laparoscopic shoulder pain without increasing complications. The intervention offers a simple, cost-effective approach to improving patient comfort after laparoscopic cholecystectomy. The demonstrated benefits in pain reduction and patient satisfaction, combined with the favorable safety profile, support the incorporation of this ventilation strategy into standard practice protocols for laparoscopic procedures.

Acknowledgements Not applicable.

Author contributions Li J and Zhao HT conceived of the study, and Sheng C, Liu YC and Zhan RJ participated in its design and data analysis and statistics. All authors helped to draft the manuscript, read and approved the final manuscript.

Funding Not applicable.

Data availability Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The Second People's Hospital of Liaocheng. We obtained signed informed consent from the participants in this study.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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