

The Effect of Permissive Hypercapnia on Postoperative Nausea and Vomiting in Patients Undergoing Gynecological Laparoscopic Surgery: A Prospective Randomized Controlled Trial

He Sun

First Affiliated Hospital of Dalian Medical University

Zhongliang Sun

First Affiliated Hospital of Dalian Medical University

Lutao Gao

First Affiliated Hospital of Dalian Medical University

Sitao Yang

First Affiliated Hospital of Dalian Medical University

Ziyu Li

First Affiliated Hospital of Dalian Medical University

Yanning Zhang

First Affiliated Hospital of Dalian Medical University

Jiayi Ban

First Affiliated Hospital of Dalian Medical University

Zhuang Miao

m18098876195@hotmail.com

First Affiliated Hospital of Dalian Medical University

Research Article

Keywords: Permissive hypercapnia, Postoperative nausea and vomiting, gynecological surgery, laparoscopic surgery, patient outcome

Posted Date: October 7th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10905952/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Postoperative nausea and vomiting is common after gynecological laparoscopic surgery despite the use of prophylactic antiemetic medication. This study investigated that whether a permissive hypercapnia ventilation strategy during surgery reduces the PONV.

Methods

In this prospective, randomized, controlled trial, 88 female patients aged 18–64 years undergoing gynecological laparoscopic surgery were randomly assigned to conventional normocapnic ventilation (control group, PaCO₂ 34–45 mmHg) or permissive hypercapnic ventilation (PHC group, PaCO₂ 45–55 mmHg). All patient received standardized general anesthesia. The primary outcome was the overall incidence of PONV within 24 h after surgery. Secondary outcomes include the incidence of nausea, retching and vomiting, rescue antiemetic use, perioperative hemodynamic variables, postoperative pain, and adverse events. The rSO₂ before anesthesia, 10 min and 60 min after pneumoperitoneum, and at the end of surgery was also measured.

Results

Eighty-three patients were included in the final analysis, comprising 42 patients in the C group and 41 patients in the PHC group. The incidence of PONV within 24 h was significantly lower in the PHC group than in the control group (39.0% vs 71.4%, 95% CI = 1.56–9.78, $P = 0.004$). The overall episodes of nausea was lower within 24 h after surgery in the PHC group (41 vs 21, 95% CI = 0.31–0.89, $P = 0.016$), and the overall episodes of vomiting was lower within 24 h after surgery in the PHC group (19 vs 9, 95% CI = 0.24–1.00, $P = 0.005$). Rescue antiemetic use and postoperative pain scores were comparable between groups. Baseline rSO₂ did not differ between groups. However, rSO₂ was significantly higher in the PHC group than in the C group 60 min after pneumoperitoneum (66.9 vs 62.1, $P < 0.001$) and at the end of surgery (64.4 vs 61.0, $P = 0.007$).

Conclusions

In patients undergoing gynecological laparoscopic surgery, a permissive hypercapnia ventilation strategy targeting PaCO₂ at 45–55 mmHg was associated with a lower incidence of PONV and higher intraoperative regional cerebral oxygen saturation. The concurrent improvement in cerebral oxygenation provides a potential physiological explanation for the observed reduction in PONV, although the underlying causal mechanisms remain uncertain.

Trail registration

The trial was retrospectively registered Chinese Clinical Trial Registry (ChiCTR2500096048, date of registration: 2025-01-16).

Background

Postoperative nausea and vomiting (PONV) remains one of the most common and distressing complications following general anesthesia [1]. Although rarely life-threatening, PONV can substantially impair postoperative recovery, delay oral intake and mobilization, and reduce patient satisfaction [2–4]. Gynecologic laparoscopic surgery is associated with a particularly high risk of PONV because several established risk factors frequently coexist, including female gender, non-smoker status, perioperative opioid administration and laparoscopic surgery [5, 6]. In addition, pneumoperitoneum and prolonged Trendelenburg positioning may further influence gastrointestinal and autonomic function, potentially contributing to postoperative nausea and vomiting.

Current approaches to reducing PONV primarily focus on identifying patients at increased risk and administering prophylactic antiemetic therapy [7–9]. Multimodal prophylaxis has substantially improved the prevention of PONV, however, nausea and vomiting continue to occur despite appropriate antiemetic treatment [10–12]. Consequently, identification of modifiable intraoperative factors that influence PONV may provide additional opportunities to improve perioperative recovery [13, 14].

Carbon dioxide pneumoperitoneum is an essential component of laparoscopic surgery and inevitably alters respiratory and hemodynamic stability. Absorption of carbon dioxide from the peritoneal cavity increases arterial and end-tidal carbon dioxide concentrations, and anesthesiologists commonly increase minute ventilation to maintain normocapnia. However, increasing evidence suggests that mild hypercapnia may have potentially beneficial physiological effects, including modulation of inflammatory responses and alterations in vascular and autonomic function [15, 16]. Consequently, permissive hypercapnia has been investigated as a component of lung-protective ventilation strategies in several clinical settings [17–19].

Whether intraoperative permissive hypercapnia influences PONV remains unclear. Changes in carbon dioxide tension may affect cerebral blood flow, autonomic activity, gastrointestinal function, and inflammatory signaling, all of which could influence the physiological pathways involved in nausea and vomiting. Nevertheless, evidence regarding the relationship between intraoperative carbon dioxide exposure and PONV, particularly in patients with a high risk of PONV, remains limited [14, 20].

Therefore, we designed this prospective randomized controlled trial to investigate the effect of a predefined permissive hypercapnia ventilation strategy on PONV in patients undergoing gynecologic laparoscopic surgery. We hypothesized that an intraoperative permissive hypercapnia ventilation strategy would reduce the incidence of PONV compared with a conventional normocapnia ventilation strategy.

Materials and methods

This study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Dalian Medical University, Approval No. PJ-KS-KY-2024-581(X) and the trial was retrospectively registered in the

Chinese Clinical Trial Registry (ChiCTR 2500096048, date of registration 2025-01-16). Written informed consent was obtained from all patients before surgery. This study adhered strictly to the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was conducted in accordance with the Declaration of Helsinki. The primary objective was to evaluate the efficacy and safety of the proposed intervention compared to standard care.

Inclusion and exclusion criteria

Enrollment eligibility included female adults aged 18–64 years undergoing gynecologic laparoscopic surgery, with a body mass index (BMI) of 18–28 kg/m², an American Society of Anesthesiologists (ASA) physical status level I or II, and non-smokers. Patients with diabetes mellitus, motion sickness, previous PONV history, and those who used opioids or steroid medication within 72 hours before surgery were excluded.

Randomization and blinding

Two researchers not involved in clinical anesthesia generated the random sequence using the random number table method. Randomization was performed in a 1:1 ratio between the two groups. Patients were randomly allocated to receive either conventional normocapnia ventilation (C group, PaCO₂ at 35–45mmHg) or permissive hypercapnia ventilation (PHC group, PaCO₂ at 45–55mmHg). To ensure patient safety and appropriate ventilation adjustments, attending anesthesiologists were aware of group assignment but did not participate in data collection, data analysis, or follow-up procedures. Patients, data collectors, and data analysts were blinded to allocation.

Anesthesia and interventions

The demographic characteristics of included patients were obtained 1 day before surgery during the pre-anesthesia visit. The PONV risk of each patient was evaluated using the Apfel scoring system.

All patients received endotracheal general anesthesia. Electrocardiogram heart rate, respiratory rate, oxygen saturation (SpO₂), noninvasive blood pressure (NIBP), body temperature, the bispectral index (BIS), and cerebral oxygenation (rSO₂) were monitored. General anesthesia was induced after a 3-min pure oxygen flush (5 L/min), and 2.0 mg/kg propofol, 0.5 µg/kg sufentanil, and 0.2 mg/kg cisatracurium were slowly administered. All patients received 0.3 mg ramosetron for prophylaxis of PONV at anesthesia induction. After the patient lost consciousness and the muscle relaxants took full effect, endotracheal intubation was performed using a video laryngoscope. Mechanical ventilation was performed using an inhaled oxygen concentration of 40%, a flow rate of 2 L/min, a tidal volume (TV) of 6–8 mL/kg, and an inhalation-to-breath ratio of 1:2. Positive end-expiratory pressure (PEEP) was set to 5 cmH₂O. Respiratory rate was adjusted to maintain target PaCO₂ during surgery: for conventional normocapnia ventilation (C group), PaCO₂ was maintained at 35–45 mmHg; for permissive hypercapnia

ventilation (PHC group), PaCO₂ was maintained at 45–55 mmHg. The difference between PaCO₂ and End-tidal CO₂ (EtCO₂) at 10 min after CO₂ pneumoperitoneum was measured by arterial blood gas analysis. PaCO₂ was calculated indirectly from corrected EtCO₂ (EtCO₂ plus the difference between PaCO₂ and EtCO₂ at 10 min after CO₂ pneumoperitoneum). Ventilation settings were adjusted to maintain the pre-determined PaCO₂ range for each group until the end of surgery.

For anesthesia maintenance, 1.5–2 mg/kg•h propofol, 0.1–0.2 µg/kg•h remifentanyl, 0.1 mg/kg•h cisatracurium, and 1%–2% sevoflurane were titrated, and BIS was maintained between 40 and 60. A balanced salt solution was infused at 8–10 ml/kg•h during surgery. Intraoperative management followed the standardized enhanced recovery after surgery (ERAS) protocol, the mean blood pressure was maintained within 20% of the pre-anesthesia baseline, and if vasopressors were required, norepinephrine or phenylephrine were administered. All patients underwent laparoscopic surgery under 12 cmH₂O pneumoperitoneum. The end of surgery was defined as completion of the final skin suture. A standardized patient-controlled intravenous analgesia (PCIA) protocol was used for postoperative pain management: 1 mg/kg esketamine, 0.1–0.2 µg/kg dexmedetomidine, and 200 mg flurbiprofen axetil diluted with 0.9% NaCl solution to 100 mL. The loading dose was 2 mL, the background infusion rate was 2 mL/h, the PCA bolus was 2 mL, and the lockout interval was 15 min. If the postoperative pain remained uncontrolled, 50 mg of tramadol was intramuscularly administered.

Study outcomes

The primary outcome of this study was the incidence of PONV within 24 h after surgery. Any episode of nausea, retching, or vomiting during the 24 h following surgery was considered a PONV occurrence. The incidence of nausea, retching, and vomiting was recorded at 0–2, 2–6, and 6–24 h follow-up after surgery or based on patients' spontaneous complaints. Patients received 10 mg metoclopramide dihydrochloride as a rescue antiemetic for PONV when they presented with any of the following indications: repeated vomiting or retching (≥ 2 times) within half an hour; persistent nausea lasting more than 15 minutes without relief; or a request for antiemetic treatment.

The secondary outcomes included intraoperative vital parameters such as mean blood pressure (MBP), heart rate (HR), body temperature, and rSO₂, which were recorded at four different time points: before anesthesia induction (T0), 10 min after pneumoperitoneum (T1), 60 min after pneumoperitoneum (T2), and the end of surgery (T3). The postoperative pain severity was assessed using the pain VAS, and postoperative adverse events were also recorded.

Statistical analysis

Based on published data and our preliminary study, the incidence of PONV following gynecologic laparoscopic surgery is approximately 70%. We hypothesized that the incidence of PONV would be 39% in the PHC group. To achieve a statistical power of 0.8 and a class I error of 0.05, the number of patients

required for each group was calculated to be 40 after considering loss to follow-up, withdrawal, and other conditions. Allowing a 10% withdrawal rate, the final number of patients required for each group was 44.

Data were analyzed using the statistic package for Social Science (SPSS) 26.0 software (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed data were presented as the mean $\pm$ standard deviation (SD) and compared with independent-samples *t* tests (Welch correction when variances were unequal); non-normally distributed data were presented as the median and interquartile range (IQR) or range and compared with Mann-Whitney U tests; qualitative data were presented as frequency *n* (%) and compared with Fisher's exact tests where estimable. We compared the incidence of PONV between the PHC and control groups using the chi-square test or Fisher's exact test, as appropriate. The treatment effect was expressed as the relative risk (RR) with its 95% confidence interval (95% CI). For secondary outcomes, multiple comparisons were not corrected; thus, these results should be interpreted as exploratory. All statistical analyses were two-sided tests, and $P < 0.05$ indicated statistical significance.

Results

Baseline demographics and perioperative characteristics

A total of 88 patients were screened from February 2025 to May 2025. Of those, 88 patients were randomly assigned to the C group or the PHC group. All participants received gynecologic laparoscopic surgery with the designated anesthesia protocols, two patients were excluded in the C group (one patient declined to participate, one patient changed to laparotomy), and 3 patients were excluded in the PHC group (declined to participate). Finally, 42 patients in the C group and 41 patients in the PHC group were analyzed. The subject flow diagram is shown in Fig. 1.

The baseline data and perioperative characteristics were well balanced between the two groups (Table 1). The median age was 46 years in the C group and 48 years in the PHC group ($P = 0.272$). The mean BMI (24.8 vs. 24.2, $P = 0.334$), ASA status ($P = 0.546$), and comorbidities status did not differ significantly between the two groups. Patients with an Apfel score of at least 2 (female, non-smoker) were included in this study, indicating that patients in both groups had a moderate risk of PONV. The duration of surgery (127.8 vs. 122.3 min, $P = 0.552$), anesthesia (143.5 vs. 136.0 min, $P = 0.155$), and pneumoperitoneum (median time 94.5 vs. 96.0 min, $P = 0.736$) did not differ significantly between groups. The use of sufentanil (median dose 45 vs. 45 μg , $P = 0.879$), remifentanil (median dose 0.9 vs. 0.9 mg, $P = 0.693$), and propofol (median dose 420 vs. 420 mg, $P = 0.603$) was comparable between groups with no statistically significant difference. Awake time (median time 11.1 vs. 12.7 min, $P = 0.491$) and intraoperative fluid therapy (1498.9 vs. 1513 mL, $P = 0.523$) also did not differ significantly between the two groups. Intraoperative vital parameters, including HR, MBP, and body temperature at each time point, showed no statistically significant difference between groups, indicating stable hemodynamics in both groups (Table 2).

Table 1

Comparison of preoperative and intraoperative baseline characteristics between the two groups

Age (years)	C group (n = 42)	PHC group (n = 41)	P value
	46.2 ± 9.4	48.5 ± 9.1	0.272
BMI (kg/m ²)	24.8 (23.0, 26.9)	24.2 (22.9, 26.0)	0.334
ASA Physical status			
I, n (%)	7 (16.7)	4 (9.8)	0.546
II, n (%)	35 (83.3)	37 (90.2)	
Comorbidities			
Hypertension	2 (4.9)	3 (7.1)	0.512
Simplified Apfel Risk Score			
2, n (%)	39 (95.1)	40 (95.2)	1.000
3, n (%)	2 (4.9)	2 (4.8)	
Surgery duration (min)	127.8 ± 30.2	122.3 ± 2.3	0.371
Anesthesia time (min)	143.5 (126.3, 169.3)	136.0 (116.0, 148.0)	0.155
Duration of pneumoperitoneum (min)	94.5 (78.8, 120.8)	96.0 (77.5, 107.5)	0.736
Opioid dosage			
Sufentanil (µg)	45 (40, 50)	45 (40, 50)	0.879
Remifentanil (mg)	0.9 ± 0.3	0.9 ± 0.2	0.693
Propofol dosage (mg)	420.0 (387.5, 462.5)	420.0 (387.0, 485.0)	0.603
Extubation time (min)	11.1 ± 4.2	12.7 ± 4.7	0.119
Intraoperative fluid volume (mL)	1498.9 ± 314.0	1513.0 ± 311.1	0.523

Normally distributed measurement data were presented as the mean (SD), whereas non-normally distributed data were presented as the median (IQR). Counting data were presented as n (%). BMI Body mass index, ASA American Society of Anesthesiologists.

Table 2
Intraoperative vital parameters between the two groups

HR (bpm)	C group (n = 42)	PHC group (n = 41)	P value
T0	76.7 ± 10.4	76.6 ± 7.7	0.939
T1	64.50 (61.75, 72.00)	64.00 (59.00, 68.00)	0.268
T2	62.00 (57.75, 68.25)	63.00 (58.00, 68.50)	0.927
T3	64.00 (58.00, 67.00)	64.00 (58.00, 69.50)	0.491
MBP (mmHg)			
T0	96.8 ± 6.3	97.4 ± 5.3	0.666
T1	93.6 ± 8.3	93.3 ± 6.6	0.843
T2	94.4 ± 6.7	92.7 ± 6.6	0.249
T3	92.9 ± 7.2	92.3 ± 6.2	0.714
Body temperature (°C)			
T0	36.6 (36.5, 36.7)	36.5 (36.5, 36.8)	0.578
T1	36.5 (36.4, 36.6)	36.5 (36.4, 36.7)	0.468
T2	36.4 (36.2, 36.5)	36.4 (36.2, 36.5)	0.750
T3	36.3 (36.1, 36.4)	36.3 (36.1, 36.4)	0.430

Normally distributed measurement data were presented as the mean (SD), whereas non-normally distributed data were presented as the median (IQR). HR Heart rate, MBP Mean blood pressure. T0: before anesthesia induction, T1: 10 min after pneumoperitoneum, T2: 60 min after pneumoperitoneum; T3: the end of surgery.

Primary outcome

The overall incidence of PONV in our study cohort was 55.4%. In total, 30 of 42 patients (71.4%) in the C group and 16 of 41 patients (39.0%) in the PHC group experienced PONV within 24 hours following surgery (95% CI = 1.56–9.78, $P = 0.004$). The number of episodes of nausea, retching, and vomiting were 15/3/9, 14/4/6, and 12/5/4 in the C group and 9/5/4, 7/2/2, and 5/0/3 in the PHC group at 0–2, 2–6, and 6–24 hours after surgery, respectively (Table 3). The incidence of nausea at each time points after surgery did not differ significantly; overall, nausea was significantly less frequent in the PHC group (41 times in the C group and 21 times in the PHC group, 95% CI = 0.31–0.89, $P = 0.016$). The incidence of retching at each time point after surgery was not statistically significant difference. The incidence of vomiting at each time point after surgery was not statistically significant difference, the total incidence

of vomiting 24 h after surgery was statistically significantly lower in the PHC group (19 times in the C group and 9 times in the PHC group, 95% CI = 0.24–1.00, $P = 0.026$). In total, 21 patients in the C group and 12 patients in the PHC group experienced multiple episodes of PONV: 3 patients in the C group and 1 patient in the PHC group experienced PONV at two different follow-up time points, and 18 patients in the C group and 11 patients in the PHC group experienced PONV at three different follow-up time points. The use of antiemetics was not significantly different between groups (5 patients in the C group, 3 patients in the PHC group, 95% CI = 0.38–7.68, $P = 0.510$).

Table 3
Incidences of PONV and rescue antiemetics between the two groups

0–2 h		C group (<i>n</i> = 42)	PHC group (<i>n</i> = 41)	Relative risk (95% CI)	<i>P</i> value
	Nausea	15	9	0.61 (0.30–1.26)	0.186
	Retching	3	5	1.71 (0.67–4.32)	0.259
	Vomiting	9	4	0.46 (0.16–1.27)	0.133
2–6 h	Nausea	14	7	0.51 (0.13–1.14)	0.102
	Retching	4	2	0.51 (0.12–2.12)	0.356
	Vomiting	6	2	0.34 (0.08–1.41)	0.138
6–24 h	Nausea	12	5	0.43 (0.17–1.08)	0.072
	Retching	5	0	4.22 (0.00-not estimable)	1.000
	Vomiting	4	3	0.77 (0.24–2.48)	0.659
0–24 h	Nausea	41	21*	0.52(0.31–0.89)	0.016
	Retching	12	7	0.60(0.27–1.33)	0.208
	Vomiting	19	9*	0.49(0.24–1.00)	0.005
PONV Frequency, <i>n</i> (%)					
0		12 (28.6)	25 (61.0)*	4.4 (1.74–11.18)	0.002
1		9 (21.4)	4 (9.8)	2.52 (0.71–8.96)	0.160
2		3 (7.1)	1 (2.4)	3.08 (0.31–30.87)	0.378
3		18 (42.9)	11 (26.8)	2.05 (0.81–5.14)	0.135
PONV (0–24 h), <i>n</i> (%)		30 (71.4)	16 (39.0)*	3.91 (1.56–9.78)	0.004
Rescue antiemetics, <i>n</i> (%)		5 (11.9)	3 (7.3)	1.71 (0.38–7.68)	0.510

Counting data were presented as *n* (%). PONV Postoperative nausea and vomiting. *The difference between the two groups was statistically significant.

Secondary outcomes

The baseline value of rSO_2 was not significantly different between the two groups (61.7 vs. 60.5, $P = 0.180$). The rSO_2 was significantly higher in the PHC group at T2 and T3 (62.1 vs. 66.9 at T2, $P < 0.001$; 61.0 vs. 64.4 at T3, $P = 0.007$). Compared with baseline, rSO_2 increased during surgery in the PHC group, with significantly higher values at T2 and T3 (Table 4). Postoperative pain VAS scores and the use of rescue analgesia showed no statistically difference between the two groups (Table 5). There were no statistically significant difference in postoperative dizziness (5 patients in the C group and 3 patients in the PHC group, $P = 0.713$), headache (3 patients in the C group and 2 patients in the PHC group, $P = 1.000$), postoperative agitation (1 patient in the C group and 1 patient in the PHC group, $P = 1.000$), chest tightness (2 patients in the C group and 4 patients in the PHC group, $P = 0.433$) between the two groups of patients (Table 5).

Table 4
Intraoperative Regional Cerebral Oxygen Saturation
between the two groups

T0	C group (<i>n</i> = 42)	PHC group (<i>n</i> = 41)	<i>P</i> value
	61.7 ± 4.30	60.5 ± 4.13	0.180
T1	63.4 ± 5.83	64.1 ± 4.53	0.501
T2	62.1 ± 4.73	66.9 ± 6.06*	<0.001
T3	61.0 ± 4.80	64.4 ± 6.06*	0.007

Data were presented as the mean (SD). T0: before anesthesia induction, T1: 10 min after pneumoperitoneum, T2: 60 min after pneumoperitoneum; T3: the end of surgery. *The difference between the two groups was statistically significant.

Table 5
Postoperative pain and adverse events between the two groups

VAS scores	C group (n = 42)	PHC group (n = 41)	P value
0–2 h	3.0 ± 0.8	3.0 ± 0.6	0.874
2–6 h	2.8 ± 0.8	2.8 ± 0.6	0.640
6–24 h	0.6 (0.0, 1.2)	1.0 (0.0, 1.3)	0.259
PCIA bolus times	69	64	0.763
Rescue analgesia, n (%)	2.0 (4.8)	2.0 (4.9)	1.000
Dizziness, n (%)	5 (11.9)	3 (7.3)	0.713
Headache, n (%)	3 (7.1)	2 (4.9)	1.000
Postoperative agitation, n (%)	1 (2.4)	1 (2.4)	1.000
Chest tightness, n (%)	2 (4.8)	4 (9.8)	0.433
Hypoxemia, n (%)	0 (0.0)	0 (0.0)	--
Laryngospasm, n (%)	0 (0.0)	0 (0.0)	--
Overall adverse events, n (%)	11 (26.2)	10 (24.4)	0.871

Normally distributed measurement data were presented as the mean (SD), whereas non-normally distributed data were presented as the median (IQR), counting data were presented as *n* (%). VAS Visual analog scale, PCIA Patient-controlled intravenous analgesia.

Discussion

In this prospective randomized controlled trial, we found that a permissive hypercapnia ventilation strategy targeting PaCO₂ at 45–55 mmHg was associated with a significantly lower incidence of PONV than a conventional normocapnic ventilation strategy targeting PaCO₂ at 35–45 mmHg within 24 h after gynecologic laparoscopic surgery. The permissive hypercapnia ventilation strategy was also associated with higher regional cerebral oxygen saturation during later stages of surgery. These findings suggest that the beneficial effect of permissive hypercapnia on PONV may be associated with alteration in cerebral oxygenation during laparoscopic surgery.

PONV remains a major challenge after gynecological laparoscopic surgery despite the implementation of ERAS protocols. The incidence of PONV is influenced by a variety of factors, including patients' characteristics, anesthesia technique, perioperative medications, and type of surgery. Previous studies have reported an incidence of PONV ranging from 40% to 80% in patients undergoing gynecological

laparoscopic surgery [21–22]. Current ERAS pathways emphasise multimodal PONV prevention, particularly in patients with moderate to high PONV risk [10–11]. The ERAS Society recommendations for gynecological surgery advocate prophylaxis with a combination of at least two antiemetics for PONV prevention. However, implementation of guideline-based PONV prevention in routine clinical practice may be inconsistent [23]. In the current study, all patients received prophylaxis according to a standardized anesthesia protocol. We reported that 71% of patients experienced PONV within 24 h after surgery in the conventional normocapnic ventilation strategy group. This finding highlights the limitations of relying exclusively on pharmacological prophylaxis and supports investigating modifiable intraoperative factors that may influence PONV.

As part of lung-protective ventilation, permissive hypercapnia has been incorporated into approaches for patients with respiratory failure, such as acute respiratory distress syndrome (ARDS). Permissive hypercapnia may reduce ventilator-induced lung injury and attenuate mechanical and inflammatory stress within the lung by accepting a controlled increase in PaCO_2 rather than increasing minute ventilation to maintain normocapnia. Furthermore, elevated PaCO_2 can induce systemic and cerebral vasodilation, thereby improving cardiovascular hemodynamics, tissue perfusion, and cerebral oxygenation. These physiological effects are particularly relevant during laparoscopic surgery, in which CO_2 pneumoperitoneum increases systemic CO_2 absorption and intra-abdominal pressure, and conventional ventilation strategies compensate by hyperventilation. Thus, a controlled increase in PaCO_2 could influence postoperative outcomes such as PONV.

Recent studies have reported conflicting findings regarding the effect of hypercapnia on PONV. Saghaei *et al.* reported that mild intraoperative hypercapnia (EtCO_2 target: 43–45 mmHg) resulted in a lower incidence and severity of PONV in patients who underwent percutaneous nephrolithotomy [14]. Conversely, another study found no significant difference in PONV between different intraoperative PaCO_2 level settings during laparoscopic surgery, with a maximum PaCO_2 range of 46–50 mmHg [20]. In our study, we used a higher PaCO_2 target of 45–55 mmHg and observed a substantial reduction in PONV. The upper PaCO_2 target in our study was higher than that used in the previous laparoscopic surgery study, potentially resulting in greater hypercapnic exposure. Differences in surgical procedures and pneumoperitoneum duration may have contributed to the discrepant findings. Therefore, the relationship between the magnitude and duration of intraoperative hypercapnia and PONV requires further investigation.

An important finding of our study was the concomitant increase in cerebral regional oxygen saturation. Our study specifically evaluated regional cerebral oxygen saturation to provide additional physiological information: baseline rSO_2 was comparable between groups, whereas rSO_2 became significantly higher in the PHC group 60 min after pneumoperitoneum and at the end of surgery. This temporal pattern is noteworthy because the difference in cerebral oxygenation emerged after exposure to pneumoperitoneum rather than before anesthesia. The finding suggests that the higher PaCO_2 target may have influenced cerebral oxygenation during the period when patients were exposed simultaneously

to pneumoperitoneum and Trendelenburg positioning [24–25]. Carbon dioxide is a potent cerebral vasodilator, and moderate increases in PaCO₂ can increase cerebral blood flow. Therefore, increased cerebral blood flow and oxygen delivery may have contributed to the higher rSO₂ observed in the permissive hypercapnia group. In this study, the higher rSO₂ observed during permissive hypercapnia provides a potential physiological link between the ventilation strategy and the observed reduction in PONV. However, this study was not designed to determine whether rSO₂ mediates the relationship between PaCO₂ and PONV, and we did not directly measure cerebral blood flow, cerebral perfusion pressure, or cerebral oxygen metabolism. Future studies incorporating more direct assessments of cerebral hemodynamics and cerebral oxygen metabolism are therefore warranted to clarify whether changes in cerebral oxygenation contribute to the effect of permissive hypercapnia on PONV.

There are several limitations in this study. First, this study was a single-centre study involving relatively healthy women undergoing gynecological laparoscopic surgery; therefore, the results may not be generalizable to older patients with substantial cardiopulmonary comorbidity. Second, the relatively small sample size limits the precision of the findings. Third, a corrected EtCO₂ value was used as PaCO₂ target to avoid multiple arterial blood gas analyses. Fourth, although patients, data collectors, and data analysts were blinded to group allocation, the attending anesthesiologists could not be blinded due to adjusting intraoperative ventilation settings. Finally, the study was not designed to investigate the mechanism between increased rSO₂ and reduced PONV. Larger, multicenter studies incorporating more direct assessments of cerebral hemodynamics are warranted to determine whether cerebral oxygenation mediates the relationship between permissive hypercapnia and PONV.

Conclusions

In patients undergoing gynaecological laparoscopic surgery, a permissive hypercapnia ventilation strategy targeting PaCO₂ at 45–55 mmHg was associated with a significantly lower incidence of PONV compared with conventional normocapnic ventilation targeting PaCO₂ at 35–45 mmHg. Permissive hypercapnia was also associated with higher intraoperative regional cerebral oxygen saturation during the later stages of surgery. This concurrent improvement in cerebral oxygenation may explain the observed reduction in PONV, although the underlying mechanisms remain uncertain.

Abbreviations

PONV

Postoperative nausea and vomiting

CONSORT

Consolidated Standards of Reporting Trials

BMI

body mass index

ASA

American society of anesthesiologists

PHC

Permissive hypercapnia

PaCO₂

Arterial carbon dioxide gas partial pressure

SpO₂

Oxygen saturation

NIBP

Noninvasive blood pressure

BIS

Bispectral index

rSO₂

Cerebral oxygenation

TV

Tidal volume

PEEP

Positive end-expiratory pressure

EtCO₂

End-tidal CO₂

ERAS

Enhanced recovery after surgery

PCIA

Patient-controlled intravenous analgesia

VAS

Visual analog scale

MAP

Mean blood pressure

HR

Heart rate

ARDS

Acute respiratory distress syndrome

Declarations

Ethics approval and consent to participate

This study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Dalian Medical University, Approval No. PJ-KS-KY-2024-581(X). Written informed consent was obtained from all patients before surgery. This study adhered strictly to the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was conducted in accordance with the Declaration of Helsinki.

Clinical trial number

This study was retrospectively registered in registered in the Chinese Clinical Trial Registry (ChiCTR2500096048, <https://www.chictr.org.cn/showproj.html?proj=255179>), date of registration 2025-01-16.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed in the study are not publicly available due to the limitations of ethical approval, which involve patient data and anonymity. However, these are available from the corresponding authors on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by Liaoning Provincial Education Science “14th Five-Year” Planning Projects (Grant No. JG24DB107) and Liaoning Provincial Department of Education 2025 Annual Basic Research Project (Grant No. LJ212510161049).

Authors’ contributions

He Sun: anesthesia, study design, manuscript drafting.

Zhongliang Sun: study design, manuscript drafting, final approval.

Lutao Gao: patient follow-up, data analysis.

Sitao Yang: anesthesia, data acquisition.

Ziyu Li: anesthesia, data acquisition.

Yanning Zhang: anesthesia, data acquisition.

Jiayi Ban: patient follow-up, data analysis.

Zhuang Miao: study design, final approval.

Acknowledgement

None.

References

1. Gress K, Urits I, Viswanath O, Urman RD. Clinical and economic burden of postoperative nausea and vomiting: Analysis of existing cost data. *Best Pract Res Clin Anaesthesiol.* 2020;34:681–6.
2. Heffernan AM, Rowbotham DJ. Postoperative nausea and vomiting-time for balanced antiemesis? *Br J Anaesth.* 2000;85(5):675–7.
3. Scuderi PE, Conlay LA. Postoperative nausea and vomiting and outcome. *Int Anesthesiol Clin.* 2003;41(4):165–74.
4. Kranke P, Schnabel A, Eberhart LH, Muellenbach R, Morin AM, Roewer N. Providing effective implementation of antiemetic strategies: the postoperative nausea and vomiting-free hospital is a laudable and realistic goal. *Eur J Anaesthesiol.* 2011;28(4):308–9.
5. Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, et al. Evidence-based analysis of risk factors for postoperative nausea and vomiting. *Br J Anaesth.* 2012;109:742–53.
6. Echeverria-Villalobos M, Fiorda-Diaz J, Uribe A, Bergese SD. Postoperative nausea and vomiting in female patients undergoing breast and gynecological surgery: A narrative review of risk factors and prophylaxis. *Front Med (Lausanne).* 2022;9:909982.
7. Tricco AC, Soobiah C, Blondal E, et al. Comparative efficacy of serotonin (5-HT₃) receptor antagonists in patients undergoing surgery: A systematic review and network meta-analysis. *BMC Med.* 2015;13:136.
8. Jin Z, Daksla N, Gan TJ. Neurokinin-1 antagonists for postoperative nausea and vomiting. *Drugs.* 2021;81:1171–9.
9. Chen W, Li G, Jiang K, et al. Dexamethasone for postoperative nausea and vomiting in papillary thyroid carcinoma patients: A randomized clinical trial. *J Am Coll Surg.* 2022;235:454–67.
10. Nelson G, Bakkum-Gamez J, Kalogera E, et al. Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations-2019 update. *Int J Gynecol Cancer.* 2019;29(4):651–68.
11. Hu J, Wang Z, Ma B, Wang T, Wang E, Yu W. Chinese Society of Anesthesiology Working Group on Clinical Practice Guidelines for the Prevention and Management of Postoperative Nausea and Vomiting (2025 Edition). *J Anesth Transl Med.* 2025;4(4):286–302.
12. Gan TJ, Belani KG, Bergese S, et al. Fourth consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg.* 2020;131:411–48.
13. Afshan R, Kundra P, Vinayagam S, Subbaiah M, Kate V, Abdulbasith KM. Effect of modified rapid sequence induction on postoperative nausea and vomiting in patients undergoing gynecologic laparoscopic surgery - A randomized controlled trial. *J Anaesthesiol Clin Pharmacol.* 2026;42(1):37–43.
14. Saghaei M, Matin G, Golparvar M. Effects of intra-operative end-tidal carbon dioxide levels on the rates of post-operative complications in adults undergoing general anesthesia for percutaneous nephrolithotomy: A clinical trial. *Adv Biomed Res.* 2014;28:3: 84.

15. Akça O, Doufas AG, Morioka N, et al. Hypercapnia improves tissue oxygenation. *Anesthesiology*. 2002;97(4):801–6.
16. Fleischmann E, Herbst F, Kugener A, et al. Mild hypercapnia increases subcutaneous and colonic oxygen tension in patients given 80% inspired oxygen during abdominal surgery. *Anesthesiology*. 2006;104(5):944–9.
17. Laffey JG, O’Croinin D, McLoughlin P, et al. Permissive hypercapnia-role in protective lung ventilatory strategies. *Intensive Care Med*. 2004;30(3):347–56.
18. Joe YE, Lee CY, Kim N, Lee K, Kang SJ, Oh YJ. Effect of permissive hypercarbia on lung oxygenation during one-lung ventilation and postoperative pulmonary complications in patients undergoing thoracic surgery: A prospective randomised controlled trial. *Eur J Anaesthesiol*. 2023;40(9):691–8.
19. Riddell JR, Jones BJ, Fernandes BM, Law DJ, Cooper JA, Wise MP. Mechanical ventilation variables associated with high pulmonary artery pressures in ARDS patients: a post hoc analysis. *Crit Care*. 2022;26(1):396.
20. Son JS, Oh JY, Ko S. Effects of hypercapnia on postoperative nausea and vomiting after laparoscopic surgery: a double-blind randomized controlled study. *Surg Endosc*. 2017;31(11):4576–82.
21. McKeen DM, Arellano R, O’Connell C. Supplemental oxygen does not prevent postoperative nausea and vomiting after gynecological laparoscopy. *Can J Anesth*. 2009;56(9):651–7.
22. Lee WS, Lee KB, Lim S, Chang YG. Comparison of palonosetron, granisetron, and ramosetron for the prevention of postoperative nausea and vomiting after laparoscopic gynecologic surgery: a prospective randomized trial. *BMC Anesthesiol*. 2015;15:121.
23. Goode V, Kang SH, Hornsby M, Reuyan R, Doughton S, Williams D, Cripps C, Richendollar K, Pelton W, Harris D, Toepp A. Anesthetic Outcomes: Postoperative Nausea and Vomiting in Laparoscopic Gynecological Surgery Patients Who Had General Anesthesia With an Enhanced Recovery After Surgery (ERAS) Technique. *J Perianesth Nurs*. 2026: S1089–9472 (26) 00080–8.
24. Li M, Li X, Gu X, He X, Wu Y, Chen Y. The effects of permissive hypercapnia on regional cerebral oxygen saturation and postoperative delirium in obese patients undergoing laparoscopic bariatric surgery: a randomized controlled trial. *Minerva Anesthesiol*. 2025;91(7–8):666–75.
25. Zhu L, Shi H, Zhu C, Liu H, Su Z, Zhao Y. Impact of permissive hypercapnia on regional cerebral oxygen saturation and postoperative cognitive function in patients undergoing cardiac valve replacement. *Ann Palliat Med*. 2020;9(6):4066–73.

Figures

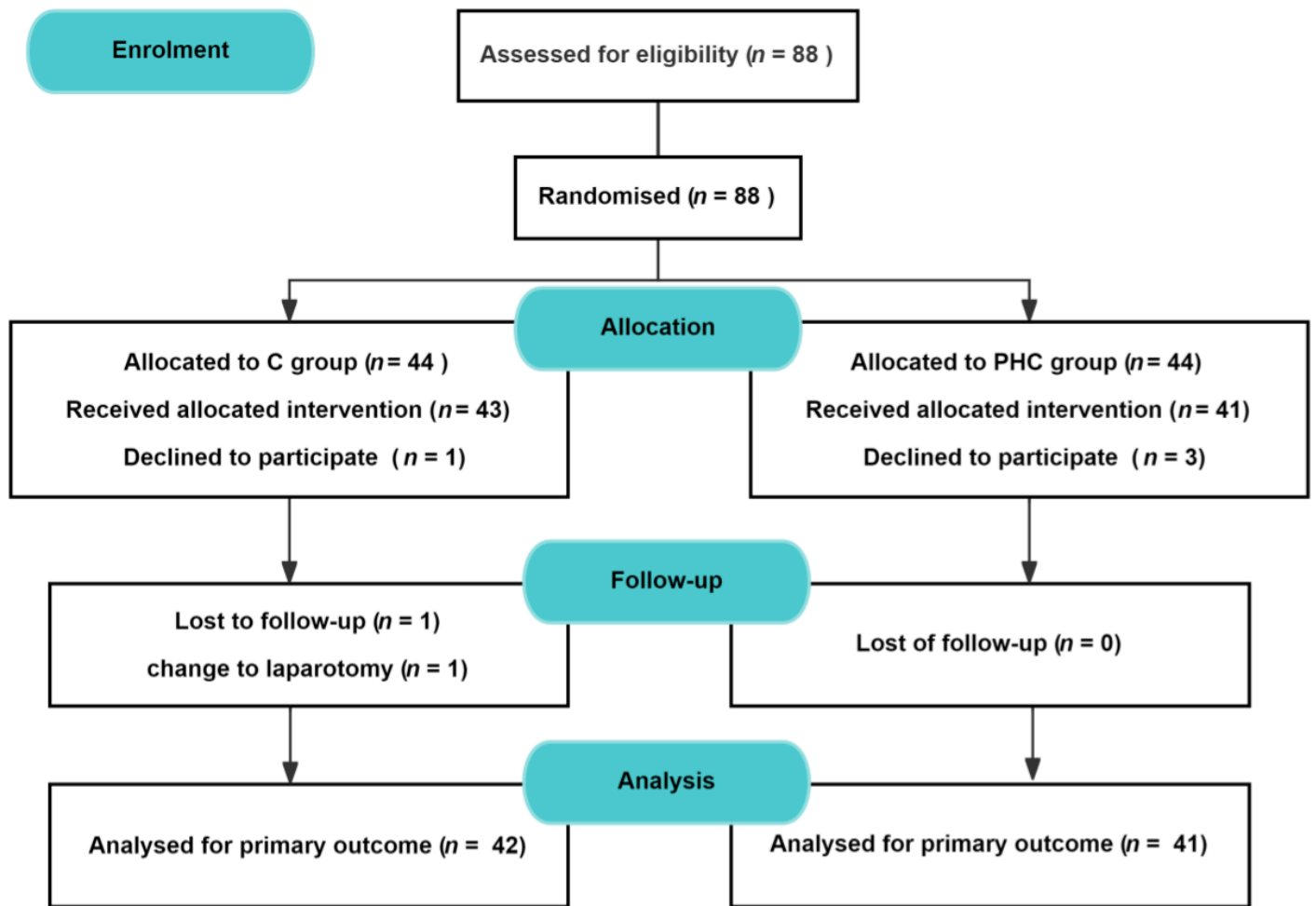


Figure 1

Flow diagram of the study.