

Original Research

## Risk Factors for Postoperative Nausea and Vomiting and the Impact of Zero-Opioid General Anesthesia in Laparoscopic Surgery for Benign Ovarian Cysts

Juan Chen<sup>1</sup>, Xiao-Yan Jiang<sup>1</sup>, Xiao-Hong Zhu<sup>1</sup>, Jie Song<sup>2</sup>,\*

Academic Editor: Maria E. Street

Submitted: 10 September 2024 Revised: 23 January 2025 Accepted: 27 January 2025 Published: 26 May 2025

#### **Abstract**

Background: Laparoscopic debulking surgery can effectively remove ovarian cysts and alleviate clinical symptoms, yet it is also associated with a high rate of postoperative nausea and vomiting (PONV). This study aimed to identify the risk factors for PONV occurrence in patients undergoing laparoscopic surgery for benign ovarian cyst debulking. Additionally, it examined the impact of zero-opioid general anesthesia on reducing PONV to improve the prognosis of patients. Methods: We retrospectively analyzed 334 patients who underwent laparoscopic ovarian cyst debulking. The patients were divided into treatment groups and control groups depending on the differences in their treatment strategies. Propensity score matching was performed in a 1:1 ratio according to age, race, and body mass index (BMI); the final number of patients in each group was 100. The clinician performed an ultrasound-guided bilateral transversus abdominis plane block in the treatment group, while the control group received fentanyl before surgery at a dose of 4 µg/kg. Differences in the clinical characteristics of patients between the groups were analyzed, and the incidence of PONV was compared. Independent risk factors for PONV occurrence were analyzed using binary logistic regression. Results: The incidence of PONV was lower in the treatment group (18%) than in the control group (47%). The use of opioid anesthetics (odds ratio (OR) = 4.258, p = 0.028), the anesthesia duration (OR = 1.098, p = 0.025), history of motion sickness (OR = 4.305, p = 0.015), history of PONV (OR = 5.314, p = 0.009), postoperative analgesic pump use (OR = 6.688, p = 0.001), preoperative fluid volume (OR = 0.967, p = 0.000), preoperative use of 5-hydroxytryptamine (OR = 0.982, p = 0.016), and postoperative use of 5-hydroxytryptamine for 12 h (OR = 1.008, p = 0.015) were independent predictive factors for PONV occurrence (p < 0.05). Conclusion: The occurrence of PONV in patients with ovarian cysts is associated with a history of PONV and a history of motion sickness. Implementing a zero-opioid general anesthesia technique can significantly reduce PONV incidence, contributing to improved patient prognoses.

Keywords: zero-opioid general anesthesia technique; PONV; benign ovarian cyst; laparoscopy

### 1. Introduction

Ovarian cysts are common gynecological diseases that can occur at any age but are most seen during the reproductive years. These cysts are mostly benign and generally do not demonstrate specific symptoms, except in cases of acute abdomen caused by torsion or rupture in some cases. The estimated global incidence of ovarian cysts is approximately 7% [1]. The current clinical treatment for ovarian cysts involves a combination of surgery, mostly laparoscopic, and medication. Laparoscopic surgery is often used as the preferred surgical procedure owing to its advantages of shorter hospital stays, faster recovery, and less postoperative pain and bleeding [2,3]. Postoperative nausea and vomiting (PONV) is more common in gynecological laparoscopic surgery under general anesthesia, and up to 80% of patients have postoperative nausea, and 30% of patients have postoperative vomiting [4-6]. It is the second most common postoperative complication after surgical pain [7].

PONV is a complex phenomenon involving the interaction of various receptors, neural pathways, and both peripheral and central nervous systems. Therefore, the incidence of PONV has a greater effect on the associated risk factors. Common risk factors for PONV include being a female, a nonsmoker, having a history of Multiple Sclerosis (MS), prolonged duration of anesthesia, younger age, and postoperative use of opioids [8,9]. As the number of risk factors increases, the incidence of PONV also increases. Apfel et al. [10] and Son and Yoon [11] reported that being a female, a nonsmoker, having a history of MS or PONV, postoperative opioid use, receiving general anesthesia and the use of nasogastric tubing are independent risk factors for PONV. Xu et al. [12] reported that the incidence of PONV in patients receiving total intravenous anesthesia was lower than that in patients receiving composite anesthesia by static inhalation. Remimazolam reduces the incidence of PONV after gynecologic laparoscopic surgery [13].

<sup>&</sup>lt;sup>1</sup>Department of Anesthesiology, Rudong Clinical College Affiliated to Yangzhou University (Rudong Hospital of Traditional Chinese Medicine), 226400 Nantong, Jiangsu, China

<sup>&</sup>lt;sup>2</sup>Department of Anesthesiology, Nantong First People's Hospital (The Second Affiliated Hospital of Nantong University), 226001 Nantong, Jiangsu, China

<sup>\*</sup>Correspondence: mz454920568@163.com (Jie Song)

Opioid-free anesthesia (OFA) is a multimodal approach for anesthesia induction and involves the use of hypnotics, N-methyl-D-aspartate receptor antagonists, local anesthetics, anti-inflammatory drugs, and  $\alpha$ -2 agonists [14]. The use of opioids during the intraoperative or postoperative period is an important factor leading to PONV, and opioids are widely used in clinical practice for inducing general anesthesia. Opioids primarily produce intestinal dysfunction and inhibit sphincter function by agonizing mu ( $\mu$ ) receptors in the intestine [15], thereby inhibiting intestinal mobility. This results in clinical symptoms such as abdominal distension, constipation, nausea, and vomiting. Opioid avoidance may exacerbate postoperative pain after laparoscopic surgery, which, in turn, may lead to or worsen PONV. Conversely, the use of opioids to alleviate pain can also contribute to or exacerbate PONV [16-21]. A metaanalysis investigating the effects of opioids versus opioid avoidance on postoperative pain and incidence of postoperative PONV showed that opioids provided better analgesia 2 h after surgery, but the incidence of postoperative PONV increased by about 20% [22]. The use of opioids is a high-risk factor for PONV in children undergoing adenotonsillectomy and strabismus repair [23]. Zero-opioid general anesthesia is administered for head and neck tumor resection and breast cancer surgery [24,25], and this approach significantly reduces postoperative Visual Analogue Scale/Score (VAS), the need for analgesics, and PONV incidence [26].

However, only a few reports are available on PONV incidence and its associated risk factors after laparoscopic benign ovarian cyst debulking, and detailed reports on the effectiveness of the zero-opioid general anesthesia technique in reducing PONV occurrence are scarce. Therefore, the present study investigated risk factors influencing PONV occurrence and the effectiveness of zero-opioid general anesthesia in reducing PONV in patients undergoing laparoscopic benign ovarian cyst debulking.

## 2. Materials and Methods

### 2.1 Research Participants

A retrospective analysis was conducted on 334 patients who underwent laparoscopic ovarian cyst debulking at Rudong Clinical College affiliated with Yangzhou University (Rudong Hospital of Traditional Chinese Medicine) from December 2021 to December 2022 were enrolled in this study. According to the different treatment methods, the patients were divided into the observation group of bilateral transversus ventral plane block under ultrasound guidance and the control group of intravenous 4  $\mu$ g/kg fentanyl before operation. There were 178 cases in the control group and 156 cases in the observation group. Propensity score matching was performed in a 1:1 ratio according to age, race, and body mass index (BMI), and the final number of patients in each group was 100.

The inclusion criteria were as follows: (I) American Society of Anesthesiologists classification score of I–II; (II) patient age between 20–60 years; (III) BMI between 18.5–24.9 kg/m<sup>2</sup>; (IV) no severe visual or hearing impairment; (V) patients undergoing elective gynecological laparoscopic surgery, and (VI) diagnosis of ovarian cysts.

The exclusion criteria were as follows: (I) pregnant women with severe preoperative hepatic or renal abnormalities; (II) presence of severe cardiac, pulmonary, or metabolic disease; (III) history of neurological or psychiatric disease or substance abuse, (III) history of radiotherapy or chemotherapy treatments within the past 4 weeks; (IV) use of other antiemetic drugs within 48 h before surgery; (V) hypersensitivity to 5-hydroxytryptamine (5-HT) receptors and their preparations; and (VI) patients with prolonged QT interval on electrocardiogram (ECG).

Informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Rudong Clinical College affiliated with Yangzhou University (Rudong Hospital of Traditional Chinese Medicine) (No. 2022105).

### 2.2 General Information Questionnaire

The general information questionnaire collected demographic data (e.g., ethnicity, age, weight, BMI, and smoking history) and clinical data (history of PONV or MS, preoperative intravenous fluid volume, postoperative analgesic pump use, and other parameters).

### 2.3 Anesthesia Method and Grouping

The operations of both groups were carried out by the same surgical team.

Upon admission to the operating room, the patient's ECG, heart rate (HR), mean arterial pressure, and pulse oximetry (SpO<sub>2</sub>) were monitored routinely. During the procedure, efforts were made to maintain the patient's normal body temperature. Ten minutes before the induction of anesthesia, dexmedetomidine was administered intravenously at a dose of 0.7 µg/kg/min. After adequate oxygen denitrogenation for three min, flurbiprofen ester (1 mg/kg), propofol (2-2.5 mg/kg), and cis-atracurium (0.2 mg/kg) were injected intravenously. A laryngeal mask was then fixed in place, and mechanical ventilation was initiated with a tidal volume of 6-8 mL/kg, a respiratory rate of 12 breaths/min, an inspiratory-to-expiratory ratio of 1:2, and a gas flow rate of 2 L/min. The partial pressure of end-expiratory carbon dioxide (PETCO<sub>2</sub>) was monitored, and the respiratory parameters were adjusted to maintain PETCO<sub>2</sub> within the normal range of 35–45 mmHg, with the ventilation index adjusted according to blood gas analysis results.

After the induction of anesthesia in the treatment group, an experienced anesthesiologist performed a bilateral transversal plane block under ultrasound guidance. The



blocking procedure began by exposing the skin area from the costal arch to the iliac crest while the patient was in a supine position. The skin around the puncture site and surrounding areas were routinely disinfected and covered. The Sono M-Turbo color ultrasound diagnostic instrument was used to perform the ultrasound-guided bilateral transversal plane blocks. The sterile linear ultrasonic scanning probe was placed at the midpoint of the line between the iliac ridge and the costal margin, perpendicular to the anterior axillary line for axial scanning. The subcutaneous tissue, external abdominal oblique muscle, internal abdominal oblique muscle, transversal abdominal muscle, and peritoneum were displayed on the screen of the ultrasonic instrument, and the areas of interest were identified successively from the shallow to deep regions. The angle of the probe was adjusted to obtain the best ultrasonic imaging. A  $22 \text{ G} \times 100 \text{ mm}$  local anesthesia needle was held in hand, and the needle tip was inserted either inside or outside the probe. Under the guidance of the ultrasonic display, 3 mL of normal saline was injected when the needle tip puncture reached the fascia between the internal oblique muscle and the transversal muscle of the abdomen, and the normal saline began to spread in the fascia under ultrasound guidance. After confirming the absence of blood and air during the extraction, 20 mL of 0.5% ropivacaine was injected into each side. The nerve block procedures and ultrasoundguided imaging analysis were performed by the same experienced anesthesiologist. The patients in the control group received an intravenous injection of fentanyl 4 µg/kg before the operation.

Intraoperative anesthesia was maintained by continuous inhalation of sevoflurane (2%–2.5%) and intermittent administration of cis-atracurium in both groups, with additional fentanyl as needed in the control group. The intraoperative blood pressure was below 90/60 mmHg or 30% below the basal value; 6 mg of ephedrine was pushed intravenously, and 0.2 mg of atropine was pushed intravenously if the HR was less than 50 beats/min. The indications for extubating were as follows: the ability to follow verbal instructions, ability to open eyes, tidal volume of  $\geq$ 300 mL, respiratory rate of 16–25 breaths/min, and SpO<sub>2</sub> of  $\geq$ 95%.

### 2.4 PONV Classification

The PONV classification used in this study adhered to World Health Organization standards categorized as follows: grade I: no nausea and vomiting; grade II: slight nausea, but no vomiting; grade III: nausea and with a sensation of vomiting feeling, but without actual vomiting; and grade IV: severe vomiting of gastric juice and other contents, needing medical intervention.

### 2.5 40-Item Quality-of-Recovery Rating Scale

The 40-item Quality of Recovery rating scale (QoR-40) rating scale was utilized to assess patients' recovery at 24 h after surgery [27]. Subjects were evaluated using the

QoR-40 rating scale, which encompasses five basic quality-of-life dimensions: emotional state, physical comfort, psychological support, and pain management. The total score of the QoR-40 rating scale ranges from 40 to 200, with higher scores indicating better recovery status.

### 2.6 Statistical Analysis

The results of each scale were entered into a computer for score conversion, and statistical analysis of the collected data was performed using SPSS 26 (IBM SPSS, Chicago, IL, USA). Measured data were expressed as means and standard deviations, while count data were reported as frequencies and percentages. Comparisons between groups were made using analysis of variance (ANOVA) and Chisquare test, and risk factors influencing PONV were identified using binary logistic regression. A two-sided p < 0.05 was considered to indicate statistical significance.

### 3. Results

### 3.1 Baseline Data

The baseline characteristics of patients are shown in Table 1. A total of 200 patients undergoing laparoscopic surgery for benign ovarian cysts were included in this study, and they were divided into treatment and control groups, with 100 cases in each group. The differences in age, weight, BMI, ethnicity, history of smoking, history of PONV, history of MS, postoperative use of an analgesic pump, and preoperative intravenous rehydration volume were not significant between the treatment and control groups (p > 0.05). In the patient with PONV, a significant difference was noted in the smoking history, history of PONV, history of MS, preoperative intravenous rehydration volume, and postoperative use of an analgesic pump (p < 0.05). One patient (1.5%) in the PONV group had a history of smoking, and 14 patients (10.4%) in the non-PONV group had a history of smoking. The history of PONV and MS was reported in 14 patients (21.5%) in the PONV group, 11 patients (8.1%) with a history of PONV in the non-PONV group, and 13 patients (9.6%) with a history of MS. Postoperative analgesic pumps were used in 19 patients (29.2%) in the PONV group and 19 patients (14.1%) in the non-PONV group. The preoperative intravenous rehydration volume was 480.04  $\pm$  22.32 mL in the non-PONV group and 462.38  $\pm$  41.09 mL in the PONV group (Table 1).

# 3.2 Comparison of Surgical Indexes between Patients with and without PONV

There was no significant difference between the treatment and control groups in surgical and anesthetic indexes such as anesthesia time, intraoperative bleeding during surgery, and first postoperative venting time. The anesthesia time in the PONV and non-PONV groups was  $112.65 \pm 8.09$  min and  $110.35 \pm 6.87$  min, respectively (Table 2), with a significant difference observed between the two groups (p < 0.05)



Table 1. Comparison of clinical features of patients.

Item N (%)	Treatment group	Control group	$t/\chi^2$	p	PONV group	Non-PONV group	$t/\chi^2$	p
Age (years)	$40.26 \pm 11.81$	$37.78 \pm 10.83$	-1.548	0.123	$38.20 \pm 11.00$	$39.41 \pm 11.57$	-0.707	0.481
Ethnicity								
Han Chinese	99 (99.0)	98 (98.0)	0.338	0.561	64 (98.5)	133 (98.5)	0.001	0.975
Other	1 (1.0)	2 (2.0)			1 (1.5)	2 (1.5)		
Body weight (kg)	$55.05 \pm 10.11$	$55.53 \pm 10.65$	0.327	0.744	$55.75\pm9.83$	$55.07 \pm 10.63$	0.439	0.661
BMI (kg/m <sup>2</sup> )	$20.06 \pm 1.11$	$19.88\pm1.15$	-1.153	0.250	$20.10\pm1.13$	$19.91 \pm 1.13$	1.105	0.271
History of smoking								
Yes	7 (7.0)	8 (8.0)	0.072	0.788	1 (1.5)	14 (10.4)	4.933	0.026
No	93 (93.0)	92 (92.0)			64 (98.5)	121 (89.6)		
History of PONV								
Yes	10 (10.0)	15 (15.0)	1.143	0.285	14 (21.5)	11 (8.1)	7.193	0.007
No	90 (90.0)	85 (85.0)			51 (78.5)	124 (91.9)		
Preoperative intravenous	$472.97 \pm 25.38$	$475.63 \pm 35.44$	-0.610	0.543	$462.38 \pm 41.09$	$480.04 \pm 22.32$	3.936	0.000
rehydration volume (mL)								
History of motion sickness								
Yes	12 (12.0)	15 (15.0)	0.385	0.535	14 (21.5)	13 (9.6)	5.329	0.021
No	88 (88.0)	85 (85.0)			51 (78.5)	122 (90.4)		
Postoperative use of								
analgesic pumps								
Yes	18 (18.0)	20 (20.0)	0.130	0.718	19 (29.2)	19 (14.1)	6.549	0.010
No	82 (82.0)	80 (80.0)			46 (70.8)	116 (85.9)		

BMI, body mass index; PONV, postoperative nausea and vomiting.

Table 2. Comparison of surgical indexes of patients in the patients with PONV or not.

T4	NI (0/)	A	On anotion time (min)	Tutus au austinus	First most marking
Item	N (%)	Anesthesia time (min)	Operation time (min)	Intraoperative	First postoperative
				bleeding (mL)	exhaustion (min)
Treatment group	100 (50.0)	$111.36 \pm 7.10$	$51.47 \pm 6.42$	$90.72 \pm 6.55$	$12.48 \pm 2.80$
Control group	100 (50.0)	$110.83 \pm 7.62$	$52.30 \pm 6.84$	$91.94 \pm 6.42$	$13.25 \pm 2.81$
t		-0.509	0.885	1.332	1.940
p		0.611	0.377	0.184	0.054
PONV group	65 (32.5)	$112.65 \pm 8.09$	$53.12 \pm 7.02$	$91.56 \pm 6.60$	$13.20 \pm 2.78$
Non-PONV group	135 (67.5)	$110.35 \pm 6.87$	$51.29\pm6.38$	$91.22 \pm 6.47$	$12.71 \pm 2.84$
t		2.089	1.844	0.350	1.143
p		0.038	0.067	0.727	0.255

PONV, postoperative nausea and vomiting.

# 3.3 Comparison of Postoperative Complications between the Treatment and Control Groups

The results of ANOVA suggested no significant differences in postoperative complications such as vomiting, bleeding, constipation, and urinary retention between the treatment and control groups and a significant difference in nausea and incisional infection (p < 0.05). Forty patients (40%) in the opioid group had postoperative nausea, and 9 patients (9%) had an incisional infection, whereas 18 patients (18%) in the non-opioid group had postoperative nausea, and 2 patients (2%) had an incisional infection (Table 3).

# 3.4 Comparison between Preoperative and Postoperative Serological Indices between Patients with and without PONV

No significant difference existed between the PONV and non-PONV groups in terms of the preoperative sero-logical indices 5-HT and substance P (SP) usage, whereas a significant difference existed in these indices at 12 h post-operatively (p < 0.05). The doses of 5-HT and PS in the PONV group were 488.79  $\pm$  62.28 nmol/L and 69.36  $\pm$  9.55 pg/mL, respectively, at 12 h postoperatively, which were significantly higher than those of 445.68  $\pm$  61.76 nmol/L and 58.90  $\pm$  11.74 pg/mL in the non-PONV group, respectively (Table 4).



Table 3. Comparison of postoperative complications between the treatment group and control group.

Item N (%)	Naus	eating	Vom	iting	Hemorrhage		
11cm 17 (70)	Yes	No	Yes	No	Yes	No	
Treatment group	18 (18.0)	82 (82.0)	18 (18.0)	82 (82.0)	4 (4.0)	96 (96.0)	
Control group	40 (40.0)	60 (60.0)	27 (27.0)	73 (73.0)	12 (12.0)	88 (88.0)	
$\chi^2$	11.753		2.3	323	4.438		
p	0.0	001	0.128		0.037		
	Incision infection		Const	ipation	Urinary retention		
	Yes	No	Yes	Yes No		No	
Treatment group	2 (2.0)	98 (98.0)	2 (2.0)	98 (98.0)	4 (4.0)	96 (96.0)	
Control group	9 (9.0)	91 (91.0)	55 (5.0) 95 (95.0)		2 (2.0)	98 (98.0)	
$\chi^2$	4.714		1.332		0.687		
p	0.0	030	0.248		0.407		

PONV, postoperative nausea and vomiting.

Table 4. Preoperative and postoperative serological indices in the patients with PONV or not.

Item	N (%)	5-HT	(nmol/L)
Tem	11 (70)	Preoperative	12 h postoperative
PONV group	65 (32.5)	$189.95 \pm 28.66$	$488.79 \pm 62.28$
Non-PONV group	135 (67.5)	$197.51 \pm 28.15$	$445.68 \pm 61.76$
t		-1.758	4.598
p		0.081	0.000
	N (%)	PS (	(pg/mL)
	11 (70)	Preoperative	12 h postoperative
PONV group	65 (32.5)	$38.29 \pm 5.93$	$69.36 \pm 9.55$
Non-PONV group	135 (67.5)	$39.31 \pm 5.89$	$58.90 \pm 11.74$
t		-1.143	6.251
p		0.253	0.000

5-HT, 5-hydroxytryptamine; PS, substance-P.

# 3.5 Comparison of PONV Classification between the Treatment and Control Groups

The incidence of PONV was lower in the treatment group (18%) compared to the control group (47%). The results of the Chi-square test analysis indicated significant differences in PONV classification between the two groups (p < 0.05). Furthermore, 82 patients (82.0%) in the treatment group and 53 patients (53.0%) in the control groups had PONV grade I, respectively; 4 patients (4.0%) in the treatment group and 5 patients (5.0%) in the control groups had grade IV, respectively (Table 5).

# 3.6 Comparison of QoR-40 between the Treatment and Control Groups

In the QoR-40 scale, the treatment group has significantly higher scores in physical comfort (54.38  $\pm$  2.98), psychological condition (41.90  $\pm$  1.83), physical independence (22.35  $\pm$  2.11) psychological support (32.46  $\pm$  1.87), pain (30.64  $\pm$  3.04), and total score (181.73  $\pm$  5.85) compared to the control group. No significant difference existed between the vomiting and non-PONV groups in terms of emotional state, physical comfort and psychological sup-

port, while these groups showed significant differences in terms of physical comfort, physical independence, pain, and total QoR-40 (p < 0.05) (Table 6).

# 3.7 Binary Logistic Regression Analysis of Risk Factors for PONV

The results of binary logistic regression analysis revealed that use of opioid anesthetics, anesthesia duration, history of PONV, history of MS, postoperative use of an analgesic pump, amount of preoperative rehydration, preoperative usage of 5-HT, and 12-h postoperative usage of 5-HT were the independent factors influencing the occurrence of nausea and vomiting occurrence after surgery (p < 0.05; Table 7; Fig. 1).

### 4. Discussion

As one of the common complications after general anesthesia, PONV usually occurs within 6 to 24 hours after surgery. It will not only aggravate the patient's discomfort and dissatisfaction with the treatment but also contribute to increased healthcare costs due to extended hospital stays. Given these implications, anesthesiologists need



Table 5. Comparison of PONV classification between the treatment group and control group.

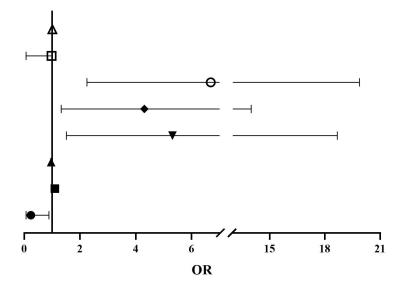
Item N (%)	Control group	Treatment group	$\chi^2$	p
Occurrence rate of PONV	47%	18%		
PONV Classification				
Grade I	53 (53.0)	82 (82.0)		
Grade II	31 (31.0)	8 (8.0)	21.375	0.000
Grade III	11 (11.0)	6 (6.0)	21.575	0.000
Grade IV	5 (5.0)	4 (4.0)		

PONV, postoperative nausea and vomiting.

Table 6. Comparison of QoR-40 between the treatment group and control group.

Item N (%)	Control group	Treatment group	t	p	PONV group	Non-PONV group	t	p
Emotional state	$40.77 \pm 2.91$	$41.90\pm1.83$	-3.283	0.001	$40.91 \pm 2.59$	$41.54 \pm 2.42$	1.690	0.093
Physical comfort	$53.30 \pm 3.94$	$54.38 \pm 2.98$	-2.186	0.030	$53.08 \pm 3.97$	$54.21 \pm 3.25$	2.001	0.048
Psychological support	$31.01\pm2.63$	$32.46 \pm 1.87$	-4.491	0.000	$31.79 \pm 2.39$	$31.63 \pm 2.40$	0.427	0.670
Physical independent	$21.20\pm2.07$	$22.35 \pm 2.11$	-3.896	0.000	$21.32\pm2.09$	$21.99 \pm 2.17$	2.070	0.040
Pain	$26.59 \pm 2.98$	$30.64 \pm 3.04$	-9.516	0.000	$27.06\pm3.21$	$29.36 \pm 3.59$	4.396	0.000
Total QoR-40	$172.87 \pm 6.76$	$181.73 \pm 5.85$	-9.913	0.000	$174.00 \pm 6.92$	$178.89 \pm 7.59$	4.388	0.000

QoR-40, quality of recovery-40; PONV, postoperative nausea and vomiting.



- Use of opioid narcotics
- Anesthesia time (min)
- ▲ Preoperative intravenous rehydration volume (mL)
- ▼ History of PONV
- History of motion sickness
- O Postoperative use of analgesic pumps
- ☐ Preoperative 5-HT (nmol/L)
- △ 12h postoperative 5-HT (nmol/L)

Fig. 1. Binary logistic regression analysis of PONV of patients. PONV, postoperative nausea and vomiting; OR, odds ratio.

to prioritize the prevention and management of PONV to enhance patient outcomes and reduce unnecessary health-care expenditures [28]. In this study, a history of PONV, history of MS, postoperative use of analgesic pumps, and insufficient amount of preoperative intravenous rehydration showed significant differences between patients with and without PONV. Apfel *et al.* [10] reported that the incidence of PONV in patients with a history of PONV and MS was relatively high, consistent with the results of the present study. Additionally, the results of this study indicated that a history of PONV, history of MS, postoperative use of analgesic pumps, preoperative intravenous fluid volume, and 5-HT usage are independent risk factors for PONV occurrence after surgery. For patients who had a history of PONV

and MS, their nausea and vomiting threshold was low, and thus, the incidence of PONV was high [28]. In addition, there is a study showing that certain patients with a previous history of MS may have the same mechanism for PONV development as that of MS [29]. Analgesic drugs slow down the peristalsis of the patient's gastrointestinal tract, inhibit gastrointestinal tract function, and may trigger vomiting by stimulating various receptors involved in the transmission of vomiting information, including 5-HT3 receptors, 5-HT4 receptors, opioid receptors, cholinergic receptors, and dopamine receptors [30], which, in turn, causes nausea, vomiting, and other side effects. The patient's anxiety and psychological stress can activate a stress response, leading to an increase in the release of catecholamines including



Table 7. Binary logistic regression analysis of PONV of patients.

Related factor	В	SE	Wald	p	OR	95% CI	
Related factor						Upper	Lower
Use of opioid narcotics	1.449	0.660	4.818	0.028	4.258	15.528	1.168
Anesthesia time (min)	0.093	0.042	5.012	0.025	1.098	1.191	1.012
Operation time (min)	-0.004	0.045	0.006	0.936	1.004	1.096	0.919
Intraoperative bleeding (min)	-0.009	0.032	0.082	0.775	0.991	1.056	0.930
Ethnicity	1.525	1.955	0.608	0.436	4.593	212.050	0.099
Body weight (kg)	0.012	0.019	0.424	0.515	1.013	1.051	0.975
BMI $(kg/m^2)$	0.170	0.185	0.840	0.359	1.185	1.703	0.824
History of smoking	-1.786	1.173	2.318	0.128	0.168	1.670	0.017
History of PONV	1.670	0.641	6.786	0.009	5.314	18.672	1.512
History of motion sickness	1.460	0.602	5.889	0.015	4.305	13.995	1.324
Postoperative use of analgesic pumps	1.900	0.556	11.694	0.001	6.688	19.877	2.250
First postoperative exhaustion (min)	-0.024	0.074	0.105	0.746	0.976	1.128	0.845
Preoperative intravenous rehydration volume (mL)	-0.034	0.009	14.448	0.000	0.967	0.984	0.950
Preoperative 5-HT (nmol/L)	-0.018	0.008	5.890	0.015	0.982	0.997	0.968
12 h postoperative 5-HT (nmol/L)	0.008	0.003	5.869	0.015	1.008	1.015	1.002
Preoperative PS (pg/mL)	-0.060	0.036	2.755	0.097	0.942	1.011	0.878
12 h postoperative PS (pg/mL)	0.010	0.032	0.096	0.757	1.010	1.076	0.948

5-HT, 5-hydroxytryptamine; PS, substance-P; PONV, postoperative nausea and vomiting; SE, standard error; OR, odds ratio; CI, confidence interval.

serotonin (5-HT) and dopamine. This, in turn, results in delayed gastric emptying, which can contribute to nausea and vomiting. Additionally, the elevated levels of these neurotransmitters may exert central emetogenic effects further exacerbating the symptoms. Additionally, the use of carbon dioxide for artificial pneumoperitoneum during laparoscopic surgery causes physical and chemical stimulation of the septal muscle and septal nerve, which induces nausea and vomiting. Furthermore, prolonged intraoperative lithotomy causes prolonged compression of the gastrointestinal mucosa, leading to ischemia of the intestinal mucosa and release of 5-HT3 and resulting in PONV [31]. The study has shown that hypoperfusion of organs is also the cause of PONV [32]. Preoperative fluid infusion can reduce the occurrence of hypotension after induction and avoid splanchnic hypoperfusion. In addition, preoperative intravenous fluid infusion can supplement the body fluid loss caused by intestinal preparation and diet prohibition, maintain the stability of the internal environment, reduce stress response, and reduce the incidence of postoperative insulin resistance. Therefore, preoperative fluid infusion can reduce the incidence of postoperative PONV [33-35].

In the current study, the use of opioids for anesthesia was identified as an independent risk factor for the occurrence of PONV in patients following surgery. Opioid agonists activate opioid-like activity at intestinal peripheral receptors, inhibit acetylcholine release from the mesenteric plexus, and stimulate  $\mu$  receptors. This combination leads to decreased muscle tone and peristaltic activity. Consequently, delayed gastric emptying and gastric dilation occur, activating visceral mechanoreceptors and chemorecep

tors. This process triggers PONV through the serotonergic signaling pathways [36]. Similarly, a recent study highlighted that remifentanil dosage and the use of neostigmine were risk factors for PONV in patients undergoing gynecologic laparoscopic surgery [37]. In this context, the use of OFA not only prolonged the time to the first dose of rescue analgesia but also decreased pain scores, minimized the need for antiemetic medications, and enhanced the quality of postoperative recovery for patients [38]. In the present study, the incidence of PONV in the treatment group was significantly lower than that in the control group, with the treatment group experiencing less than half the incidence of PONV. Moreover, the postoperative quality of life scores of patients in the treatment group were significantly higher than those of patients in the control group, consistent with the findings from previous research [38].

In addition to anesthesia, a crucial element in preventing PONV occurrence involves conducting a thorough assessment of risk factors, identifying patients with high-risk profiles, and implementing appropriate preventive measures [39,40]. For those identified as high-risk, perioperative guidelines for PONV prevention and treatment [41] recommend the combined use of multiple medications. In cases where prophylaxis has not been administered, the initial occurrence of PONV can be treated with a small dose of 5-HT3 receptor antagonists [42]. Conversely, for patients who have received prophylaxis, the first occurrence of PONV can be managed through a combination of different medications. Following treatment, it is important to evaluate the effectiveness of antiemetic drugs and monitor for any adverse reactions. Furthermore, greater emphasis



should be placed on several key areas (i) addressing the patient's psychological well-being through effective communication, which can help alleviate anxiety and depression; (ii) implementing proper postoperative dietary care, to enhance the patient's recovery; (iii) incorporating acupuncture as an adjunct to assist anesthesia [43]; (iv) ensuring completion of the surgical procedure by effectively aspirating gas and fluids from the abdominal cavity, followed by abdominal compression to facilitate the expulsion of CO<sub>2</sub> gas from the body, thereby minimizing its irritation of the septal muscle. These methods can yield significant benefits and help reduce the incidence of PONV.

This study has certain limitations that must be considered. It is a retrospective analysis, and although the indicators were sourced from the same hospital data, the time-frame for data collection was restricted. Additionally, the sample collection was confined to China, which may lead to varying results in different countries and among diverse ethnic groups. Future studies addressing these limitations are necessary to validate the findings of this study.

In conclusion, this study demonstrated that the zeroopioid general anesthesia technique significantly reduced postoperative complications. Additionally, it identified independent risk factors for nausea and vomiting after laparoscopic surgery for benign ovarian cysts by analyzing the clinical characteristics of patients in the treatment and control groups and in the PONV and non-PONV groups. These findings are expected to provide a reference for reducing PONV occurrence in patients after gynecological laparoscopy and improving their postoperative quality of life.

### 5. Conclusion

PONV occurrence in patients with ovarian cysts is associated with a history of PONV and motion sickness, and the zero-opioid general anesthesia technique can significantly reduce PONV occurrence, which will aid in improving patient prognosis.

## **Availability of Data and Materials**

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

### **Author Contributions**

Conception and design: JC; Administrative support: JS; Provision of study materials or patients: JC; Collection and assembly of data: XYJ and XHZ; Data analysis and interpretation: JC, XYJ, XHZ and JS. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## **Ethics Approval and Consent to Participate**

Informed consent was obtained from all patients. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Rudong Clinical College affiliated with Yangzhou University (Rudong Hospital of Traditional Chinese Medicine) (RDXZYY-PA-20221109).

## Acknowledgment

We would like to express our gratitude to all those who helped us during the writing of this manuscript. Thanks to all the peer reviewers for their opinions and suggestions.

## **Funding**

This study was supported by the Nantong Municipal Health Commission scientific research project (No. MSZ2022096).

## **Conflict of Interest**

The authors declare no conflict of interest.

### References

- [1] Farghaly SA. Current diagnosis and management of ovarian cysts. Clinical and Experimental Obstetrics & Gynecology. 2014; 41: 609–612.
- [2] El Khouly NI, Barr RL, Kim BB, Jeng CJ, Nagarsheth NP, Fishman DA, et al. Comparison of robotic-assisted and conventional laparoscopy in the management of adnexal masses. Journal of Minimally Invasive Gynecology. 2014; 21: 1071–1074. https://doi.org/10.1016/j.jmig.2014.05.007.
- [3] Mansouri G, Safinataj M, Shahesmaeili A, Allahqoli L, Salehiniya H, Alkatout I. Effect of laparoscopic cystectomy on ovarian reserve in patients with ovarian cyst. Frontiers in Endocrinology. 2022; 13: 964229. https://doi.org/10.3389/fendo.2022.964229.
- [4] Kawano H, Ohshita N, Katome K, Kadota T, Kinoshita M, Matsuoka Y, et al. Effects of a novel method of anesthesia combining propofol and volatile anesthesia on the incidence of postoperative nausea and vomiting in patients undergoing laparoscopic gynecological surgery. Brazilian Journal of Anesthesiology (Elsevier). 2016; 66: 12–18. https://doi.org/10.1016/j.bjane.2014.07.005.
- [5] Elvir-Lazo OL, White PF, Yumul R, Cruz Eng H. Management strategies for the treatment and prevention of postoperative/postdischarge nausea and vomiting: an updated review. F1000Research. 2020; 9: F1000 Faculty Rev-983. https://doi.org/10.12688/f1000research.21832.1.
- [6] Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesthesia and Analgesia. 2014; 118: 85– 113. https://doi.org/10.1213/ANE.0000000000000002.
- [7] Halliday TA, Sundqvist J, Hultin M, Walldén J. Post-operative nausea and vomiting in bariatric surgery patients: an observational study. Acta Anaesthesiologica Scandinavica. 2017; 61: 471–479. https://doi.org/10.1111/aas.12884.
- [8] Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999; 91: 693–700. https://doi.org/10.1097/00000542-199909000-00022.



- [9] Rashad AE, El Hefnawy E, Elmorshedi M, Abuyousif YA, Salem A, Attia M, et al. Prevalence, Risk Factors, and Management of Postoperative Nausea and Vomiting After Laparoscopic Sleeve Gastrectomy (a Retrospective Multicentric Study). Obesity Surgery. 2023; 33: 3237–3245. https://doi.org/10.1007/ s11695-023-06803-z.
- [10] Apfel CC, Heidrich FM, Jukar-Rao S, Jalota L, Hornuss C, Whelan RP, *et al.* Evidence-based analysis of risk factors for post-operative nausea and vomiting. British Journal of Anaesthesia. 2012; 109: 742–753. https://doi.org/10.1093/bja/aes276.
- [11] Son J, Yoon H. Factors Affecting Postoperative Nausea and Vomiting in Surgical Patients. Journal of Perianesthesia Nursing: Official Journal of the American Society of PeriAnesthesia Nurses. 2018; 33: 461–470. https://doi.org/10.1016/j.jopan. 2016.02.012.
- [12] Xu R, Zhou S, Yang J, Li H, Zhang Q, Zhang G, et al. Total intravenous anesthesia produces outcomes superior to those with combined intravenous-inhalation anesthesia for laparoscopic gynecological surgery at high altitude. The Journal of International Medical Research. 2017; 45: 246–253. https://doi.org/10.1177/0300060516687230.
- [13] Hari Y, Satomi S, Murakami C, Narasaki S, Morio A, Kato T, et al. Remimazolam decreased the incidence of early postoperative nausea and vomiting compared to desflurane after laparoscopic gynecological surgery. Journal of Anesthesia. 2022; 36: 265–269. https://doi.org/10.1007/s00540-022-03041-y.
- [14] Harkouk H, Fletcher D, Beloeil H. Opioid free anaesthesia: Myth or reality? Anaesthesia, Critical Care & Pain Medicine. 2019; 38: 111–112. https://doi.org/10.1016/j.accpm.2019.01. 005.
- [15] Panchal SJ, Müller-Schwefe P, Wurzelmann JI. Opioid-induced bowel dysfunction: prevalence, pathophysiology and burden. International Journal of Clinical Practice. 2007; 61: 1181–1187. https://doi.org/10.1111/j.1742-1241.2007.01415.x.
- [16] Rüsch D, Eberhart LHJ, Wallenborn J, Kranke P. Nausea and vomiting after surgery under general anesthesia: an evidencebased review concerning risk assessment, prevention, and treatment. Deutsches Arzteblatt International. 2010; 107: 733–741. https://doi.org/10.3238/arztebl.2010.0733.
- [17] Eikaas H, Raeder J. Total intravenous anaesthesia techniques for ambulatory surgery. Current Opinion in Anaesthesiology. 2009; 22: 725–729. https://doi.org/10.1097/ACO.0b013e3283310f6b.
- [18] Cruthirds D, Sims PJ, Louis PJ. Review and recommendations for the prevention, management, and treatment of postoperative and postdischarge nausea and vomiting. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2013; 115: 601– 611. https://doi.org/10.1016/j.oooo.2012.09.088.
- [19] Carcamo-Cavazos V, Cannesson M. Opioid-Free Anesthesia: The Pros and Cons. Advances in Anesthesia. 2022; 40: 149–166. https://doi.org/10.1016/j.aan.2022.07.003.
- [20] White PF, Sacan O, Nuangchamnong N, Sun T, Eng MR. The relationship between patient risk factors and early versus late post-operative emetic symptoms. Anesthesia and Analgesia. 2008; 107: 459–463. https://doi.org/10.1213/ane.0b013e31817aa6e4.
- [21] Wang JJ, Ho ST, Liu YH, Ho CM, Liu K, Chia YY. Dexamethasone decreases epidural morphine-related nausea and vomiting. Anesthesia and Analgesia. 1999; 89: 117–120. https://doi.org/10.1097/00000539-199907000-00020.
- [22] Frauenknecht J, Kirkham KR, Jacot-Guillarmod A, Albrecht E. Analgesic impact of intra-operative opioids vs. opioid-free anaesthesia: a systematic review and meta-analysis. Anaesthesia. 2019; 74: 651–662. https://doi.org/10.1111/anae.14582.
- [23] Kovac AL. Postoperative Nausea and Vomiting in Pediatric Patients. Paediatric Drugs. 2021; 23: 11–37. https://doi.org/10.1007/s40272-020-00424-0.
- [24] Balandin VV, Gorobec ES. Opioid-free anesthesia, analgesia

- and sedation in surgery of head and neck tumor. Anesteziologiia i Reanimatologiia. 2015; 60: 39–42.
- [25] Di Benedetto P, Pelli M, Loffredo C, La Regina R, Policastro F, Fiorelli S, et al. Opioidfree anesthesia versus opioid-inclusive anesthesia for breast cancer surgery: a retrospective study. Journal of Anesthesia, Analgesia and Critical Care. 2021; 1: 6. https://doi.org/10.1186/s44158-021-00008-5.
- [26] Tripathy S, Rath S, Agrawal S, Rao PB, Panda A, Mishra TS, et al. Opioid-free anesthesia for breast cancer surgery: An observational study. Journal of Anaesthesiology, Clinical Pharmacology. 2018; 34: 35–40. https://doi.org/10.4103/joacp.JOAC P 143 17.
- [27] Myles PS, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: the QoR-40. British Journal of Anaesthesia. 2000; 84: 11–15. https://doi.org/10.1093/oxfordjournals.bja.a013366.
- [28] Veiga-Gil L, Pueyo J, López-Olaondo L. Postoperative nausea and vomiting: physiopathology, risk factors, prophylaxis and treatment. Revista Espanola De Anestesiologia Y Reanimacion. 2017; 64: 223–232. https://doi.org/10.1016/j.redar.2016.10.001.
- [29] Horn CC, Meyers K, Oberlies N. Musk shrews selectively bred for motion sickness display increased anesthesia-induced vomiting. Physiology & Behavior. 2014; 124: 129–137. https://doi. org/10.1016/j.physbeh.2013.11.002.
- [30] Gan TJ. Mechanisms underlying postoperative nausea and vomiting and neurotransmitter receptor antagonist-based pharma-cotherapy. CNS Drugs. 2007; 21: 813–833. https://doi.org/10.2165/00023210-200721100-00003.
- [31] Goll V, Akça O, Greif R, Freitag H, Arkiliç CF, Scheck T, *et al.* Ondansetron is no more effective than supplemental intraoperative oxygen for prevention of postoperative nausea and vomiting. Anesthesia and Analgesia. 2001; 92: 112–117. https://doi.org/10.1097/00000539-200101000-00022.
- [32] Gan TJ, Mythen MG. Does peroperative gut-mucosa hypoperfusion cause postoperative nausea and vomiting? Lancet. 1995; 345: 1123–1124. https://doi.org/10.1016/s0140-6736(95) 90857.
- [33] Pusch F, Berger A, Wildling E, Zimpfer M, Moser M, Sam C, et al. Preoperative orthostatic dysfunction is associated with an increased incidence of postoperative nausea and vomiting. Anesthesiology. 2002; 96: 1381–1385. https://doi.org/10.1097/00000542-200206000-00017.
- [34] Pusch F, Berger A, Wildling E, Tiefenthaler W, Krafft P. The effects of systolic arterial blood pressure variations on postoperative nausea and vomiting. Anesthesia and Analgesia. 2002; 94: 1652–1655. https://doi.org/10.1097/00000539-200206000-00054.
- [35] Maharaj CH, Kallam SR, Malik A, Hassett P, Grady D, Laffey JG. Preoperative intravenous fluid therapy decreases post-operative nausea and pain in high risk patients. Anesthesia and Analgesia. 2005; 100: 675–682. https://doi.org/10.1213/01.AN E.0000148684.64286.36.
- [36] de Boer HD, Detriche O, Forget P. Opioid-related side effects: Postoperative ileus, urinary retention, nausea and vomiting, and shivering. A review of the literature. Best Practice & Research. Clinical Anaesthesiology. 2017; 31: 499–504. https://doi.org/ 10.1016/j.bpa.2017.07.002.
- [37] Luo D, Huang Z, Tang S, Cheng J, Deng Y, Zhang X, *et al.* Risk analysis of postoperative nausea and vomiting in patients after gynecologic laparoscopic surgery. BMC Anesthesiology. 2024; 24: 345. https://doi.org/10.1186/s12871-024-02727-y.
- [38] Hakim KYK, Wahba WZB. Opioid-Free Total Intravenous Anesthesia Improves Postoperative Quality of Recovery after Ambulatory Gynecologic Laparoscopy. Anesthesia, Essays and Researches. 2019; 13: 199–203. https://doi.org/10.4103/aer.AE



- R 74 19.
- [39] Kienbaum P, Schaefer MS, Weibel S, Schlesinger T, Meybohm P, Eberhart LH, *et al.* Update on PONV-What is new in prophylaxis and treatment of postoperative nausea and vomiting?: Summary of recent consensus recommendations and Cochrane reviews on prophylaxis and treatment of postoperative nausea and vomiting. Der Anaesthesist. 2022; 71: 123–128. https://doi.org/10.1007/s00101-021-01045-z.
- [40] Gan TJ, Jin Z, Meyer TA. Rescue Treatment of Postoperative Nausea and Vomiting: A Systematic Review of Current Clinical Evidence. Anesthesia and Analgesia. 2022; 135: 986–1000. ht tps://doi.org/10.1213/ANE.0000000000006126.
- [41] Hooper VD. SAMBA Consensus Guidelines for the Management of Postoperative Nausea and Vomiting: An Executive Summary for Perianesthesia Nurses. Journal of Perianesthesia

- Nursing: Official Journal of the American Society of PeriAnesthesia Nurses. 2015; 30: 377–382. https://doi.org/10.1016/j.jopan.2015.08.009
- [42] Gan TJ, Belani KG, Bergese S, Chung F, Diemunsch P, Habib AS, et al. Fourth Consensus Guidelines for the Management of Postoperative Nausea and Vomiting. Anesthesia and Analgesia. 2020; 131: 411–448. https://doi.org/10.1213/ANE. 000000000000004833.
- [43] Zhang X, Wang Q, Dong Y, Jia Y, Hou Z, Deng W, et al. Acupuncture-assisted anaesthesia for catheter ablation of atrial fibrillation to reduce the consumption of morphine hydrochloride and postoperative nausea and vomiting (PONV): study protocol for a randomised controlled trial. BMJ Open. 2022; 12: e068318. https://doi.org/10.1136/bmjopen-2022-068318.

