Impact of Intraoperative End-Tidal CO_2 Variations on Postoperative Nausea, Vomiting, and Pain

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Abstract

Aim: Patients undergoing robotic-assisted laparoscopic procedures tend to experience a higher frequency of postoperative nausea and vomiting (PONV). This study aimed explore the influence of intraoperative end-tidal carbon dioxide ($ETCO_2$) levels on the occurrence of PONV in robotic surgery.

Methods: This observational clinical study included patients undergoing robotic laparoscopic radical prostatectomy. Patients were divided into two groups based on intraoperative $ETCO_2$ levels: Group 1 (26–35 mmHg) and Group 2 (36–45 mmHg). The incidence of PONV, the use of rescue antiemetics, and pain scores were recorded at 0, 2, 4, 8, 12, and 24 hours postoperatively.

Results: We found that Group 1 exhibited lower PONV scores at both 0 ($p < 0.001$) and 2 ($p = 0.046$) hours post-surgery. Furthermore, Group 2 had a higher incidence of PONV and greater usage of rescue antiemetics within the first 24 hours following surgery. ($p<0.05$)

Conclusions: We found that lower intraoperative $ETCO_2$ levels were associated with a reduced incidence of PONV in robotic laparoscopic surgery, a procedure known to carry a high risk of PONV. PONV remains a significant clinical issue that negatively affects patient comfort and recovery. We believe that future research should continue to explore the effectiveness of both pharmacological and non-pharmacological approaches for the prevention of PONV.

***Keywords**: End-tidal carbon dioxide; Pain; Postoperative nausea and vomiting; Robotic-assisted laparoscopic radical prostatectomy*

1. Introduction

Radical prostatectomy remains a cornerstone surgical intervention for managing prostate cancer and may be carried out via open, laparoscopic, or robot-assisted approaches. Among these, robotic-assisted surgery provides distinct benefits such as tremor filtration and improved dexterity, which together help minimize intraoperative bleeding. Moreover, robotic surgery has been associated with faster return to daily activities and shorter hospital stays for patients.[1-3]

This surgery is performed in the Trendelenburg position, a head-down posture, combined with intraperitoneal carbon dioxide (CO_2) insufflation. In addition to increased intra-abdominal pressure, this technique leads to elevated intracranial and intraocular pressures due to the Trendelenburg positioning and pneumoperitoneum. Moreover, patients undergoing robotic-assisted laparoscopic procedures tend to experience a higher frequency of postoperative nausea and vomiting (PONV).[4,5] PONV can lead to dehydration, electrolyte imbalances, extended hospitalizations.[6]

The chemoreceptor trigger zone (CTZ), which is responsible for triggering the vomiting reflex, is situated outside the blood-brain barrier. Various mediators, including histamine, serotonin, neurokinin-1, and dopamine, are involved in pathophysiology of nausea and vomiting. While the precise mechanism underlying PONV is not fully understood, it has been reported that tissue hypoxia in the brain and gastrointestinal tract may stimulate the vomiting center. In laparoscopic surgeries, CO_2 insufflation due to pneumoperitoneum can increase intracranial pressure, which may in turn elevate the incidence of PONV.[7,8] Several studies have investigated the impact of varying intraoperative end-tidal carbon dioxide ($ETCO_2$) levels on occurrence of PONV. However, current literature presents inconsistent findings regarding the relationship between different $ETCO_2$ levels and PONV incidence.[9,10]

This study aimed explore the influence of intraoperative $ETCO_2$ levels on the occurrence of PONV. The primary goal was to evaluate the incidence of PONV, with secondary aims focusing on the use of antiemetic and postoperative pain assessment.

Corresponding Author: Yusuf Ozguner, y.ozguner@hotmail.com, Received: 02.05.2025, Accepted: 09.06.2025, Available Online Date: 30.06.2025 Varlık Mah., Halil Sezai Erkut Cd. No:5, 06170 Yenimahalle, Ankara Etlik City Hospital, Anesthesiology and Reanimation Clinic, Ankara, Türkiye. https://doi.org/10.36516/jocass.1689160

2. Materials and Methods

This observational clinical study included patients undergoing robotic laparoscopic radical prostatectomy. (Ethics No: 102; Date: 26/04/2023). Exclusion criteria included: refusal to participate, age under 18, history of PONV, motion sickness, abnormal fluid-electrolyte balance, hepatic or renal failure, and current use of steroids or antiemetic medications.

Patients were divided into two groups based on intraoperative $ETCO_2$ levels: Group 1; 26–35 mmHg, and Group 2: 36–45 mmHg.[9]

All patients received an identical anesthetic protocol for induction. For maintenance of anesthesia, 0.8–1.2 MAC sevoflurane and remifentanil at 0.05–0.2 mcg/kg/min were administered. Intraoperative ventilation was managed using a volume-controlled ventilation mode with 50% oxygen and 50% air, a tidal volume of 6 mL/kg, and a respiratory rate of 12 breaths per minute. Standard intraoperative monitoring included heart rate, noninvasive blood pressure, pulse oximetry (SpO_2), $ETCO_2$, bispectral index (BIS), temperature, urine output. All patients received 100 mg intravenous tramadol, 1 g paracetamol for analgesia, and 4 mg ondansetron as an antiemetic. During the first 24 hours postoperatively, all patients routinely received 100 mg intravenous tramadol and 1 g paracetamol for pain control.

PONV score and antiemetic requirements were assessed using the Verbal Descriptive Scale (VDS). (0-2-4-8-12-24 hours).[11] Individuals with an VDS of ≥2 received 4 mg ondansetron. VDS:

0=no PONV: patient reports no nausea and has had no emesis episodes;

1=mild PONV: patient reports nausea but declines antiemetic treatment;

2=moderate PONV: patient reports nausea and accepts antiemetic treatment;

3=severe PONV: nausea with any emesis episode (retching or vomiting).

Pain was assessed using the Numerical Rating Scale (NRS). Individuals with an NRS score greater than 4 were administered 50 mg dexketoprofen as rescue analgesia.

2.1. Statistical analysis

According to the results of a preliminary study in which the incidence of PONV was closed to 50%, 46 patients were required for each group to detect 40% reduction in the incidence of PONV (a=0.05, b=0.20). So 56 patients were enrolled for possible dropouts in each groups. The numerical values were expressed as the mean ± standard deviation or median (range). The Chi-square test (for categorical variables), One-way ANOVA (for continuous variables with normal distribution), and Mann-Whitney U tests (for continuous variables with non-normal distribution) were employed in this study.

3. Results

A total of 112 patients who underwent robot-assisted laparoscopic radical prostatectomy were initially enrolled in the study. However, two patients were excluded due to conversion to laparotomy during the intraoperative period, and one patient was excluded due to reoperation in the postoperative period. As a result, the final analysis included 109 patients.(Figure 1). The demographic and clinical features were similar between the two groups.(Table 1).

At postoperative hour 0, the PONV score distribution (0/1/2/3) was 46/6/2/0 in Group 1 and 26/21/8/0 in Group 2 ($p < 0.001$). At postoperative hour 2, the PONV score distribution (0/1/2/3) was 44/7/3/0 in Group 1 and 33/14/8/0 in Group 2 ($p = 0.046$).(Table 2)

Figure 1

Flow diagram of the study

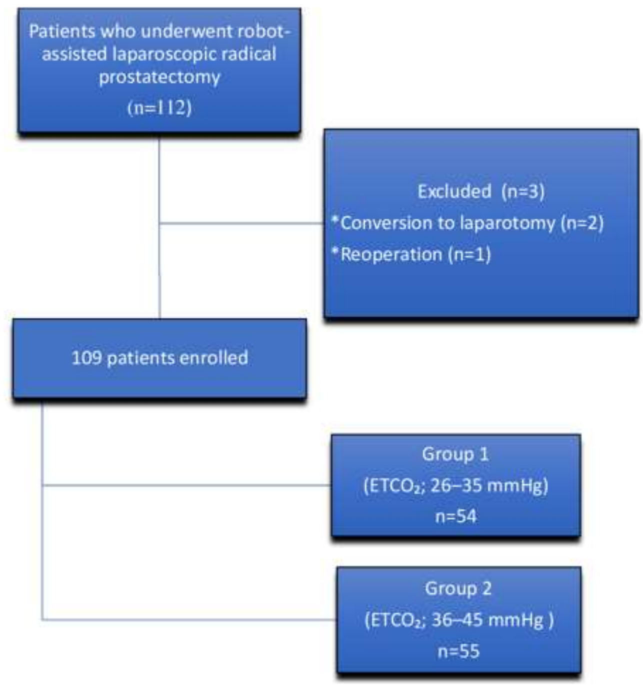

Table 1

Clinical characteristics of the patients

	Group 1 n=54	Group 2 n=55	p
Age (year)	63.63 ± 6.91	63.40 ± 5.79	0.851
BMI (kg/m²)	27.36 ± 4.42	26.58 ± 2.77	0.273
ASA Score (2/3) (n)	38/16	43/12	0.351
Duration of surgery (minute)	233.79 ± 32.15	226.73 ± 32.74	0.258
Comorbidities			
· Hypertension	22	19	0.504
· Diabetes mellitus	18	17	0.786
· CAD	16	10	0.161
· COPD	5	7	0.563
· Smoking	12	15	0.541

Values are presented as Mean ± SD and numbers. n: Number, BMI: Body Mass Index, ASA: American Society of Anesthesiologists, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease.

PONV scores at 4, 8, 12, and 24 hours postoperatively were similar between the two groups ($p > 0.05$).(Table 2)

PONV occurred within the first 24 hours postoperatively in 17 patients (31.4%) in Group 1 and in 29 patients (52.7%) in Group 2 ($p = 0.025$) Rescue antiemetic therapy was required in 5 patients in Group 1 and 14 patients in Group 2 ($p = 0.026$).(Table 2)

Postoperative pain scores assessed by the Numerical Rating Scale (NRS) at all time points were comparable between the two groups ($p > 0.05$) (Table 3).

Table 2

PONV Incidence and Severity

	Group 1 n=54	Group 2 n=55	p
PONV(n, %)	17 (31.4)	29 (52.7)	0.025*
PONV Score (n) 0/1/2/3			
0th hour	46/6/2/0	26/21/8/0	<0.001*
2nd hour	44/7/3/0	33/14/8/0	0.046*
4th hour	52/2/0/0	51/3/1/0	0.549
8th hour	51/3/0/0	51/1/3/0	0.136
12th hour	53/1/0/0	53/2/0/0	0.569
24th hour	54/0/0/0	54/1/0/0	0.320
Required antiemetic (n)	5	14	0.026*

*Values are presented as numbers. n: Number/Percentages, PONV: postoperative nausea and vomiting. p<0.05 was considered significant. *: There were significant differences between the two groups.*

Table 3

Pain scores (NRS)

	Group 1 n=54	Group 2 n=55	p
NRS 0th	5(4)	4(4)	0.207
NRS 2th	3(4)	3(2)	0.414
NRS 4th	3(3)	2(4)	0.374
NRS 8th	2(2)	2(3)	0.469
NRS 12th	2(4)	2(4)	0.929
NRS 24th	2(3)	2(3)	0.259

NRS: Numeric Rating Score. Values are given as median (range) and numbers. p<0.05 was considered significant.

4. Discussion

In this study, which examined the the effects of $ETCO_2$ variations on PONV, we found that Group 1 exhibited lower PONV scores at both 0 and 2-hours post-surgery. Furthermore, Group 2 had a higher incidence of PONV and greater usage of rescue antiemetics within the first 24 hours following surgery.

In a study by Son et al. [12], which examined different $ETCO_2$ levels (36–40 mmHg, 41–45 mmHg, and 46–50 mmHg) and PONV, it was reported that PONV incidence and the use of antiemetics were similar across all groups. In contrast, Feng et al. [13] reported a higher incidence of PONV in the hypercapnic group among patients undergoing thyroidectomy. Similarly, a study conducted in laparoscopic gynecological surgeries found a higher PONV incidence associated with elevated $ETCO_2$ levels. That study also reported a greater increase in optic nerve sheath diameter (ONSD) in the hypercapnic group compared to the normocapnic group following pneumoperitoneum.[9] Yılmaz et al. [14] also reported that in patients undergoing laparoscopic hysterectomy, those who experienced an increase in ONSD due to Trendelenburg positioning and pneumoperitoneum had a higher incidence of PONV. In accordance with the existing literature, our study found that Group 1 had a lower incidence of PONV and required less antiemetic. In the study by Son et al. [12], all $ETCO_2$ values were above 36 mmHg. In our study, we compared patients in Group 1 (26–35 mmHg) with those in Group 2 (36–45 mmHg). We believe the difference between our results and those of Son et al. may be due to the differing ranges of $ETCO_2$ values evaluated.

In another study investigating the effect of $ETCO_2$ levels (31–33 mmHg, 37–39 mmHg, and 43–45 mmHg) on PONV during percutaneous nephrolithotomy, patients with higher $ETCO_2$ levels were found to have a lower incidence of PONV than those in the other two groups, between which the incidence was similar.[15] Fujimoto et al.[10] reported that, in open gynecological surgeries, patients with $ETCO_2$ levels below 31 mmHg had a higher incidence of PONV compared to those with values above 35 mmHg. In contrast to these studies, our patient cohort consisted exclusively of those undergoing robot-assisted laparoscopic radical prostatectomy, which involves Trendelenburg positioning and intraperitoneal CO_2 insufflation. We believe the differences in surgical technique may account for the discrepancies in findings. Moreover, in the study by Fujimoto et al.[10], three different anesthetic agents—sevoflurane, desflurane, and propofol—were used for maintenance of anesthesia, which may also have influenced the outcomes.

It has been proposed that the rise in intra-abdominal pressure during laparoscopic surgery disrupts venous drainage from lumbar plexus by compressing inferior vena cava.[16] Moreover, the increased intra-abdominal pressure elevates diaphragm, leading higher intrathoracic pressure, which in turn hinders right atrial and ventricular filling and obstructs superior vena cava drainage. This increase in central venous pressure, coupled with the reduced venous return from lumbar plexus and central nervous system, is believed to play role in observed elevation of intracranial pressure (ICP) during laparoscopic procedures.[17,18] The resultant circulatory disturbances can lead to the release of mediators such as histamine and serotonin. Furthermore, serotonin release has also been reported following intestinal ischemia and reperfusion [8, 19]. Collectively, these mechanisms are thought to contribute to the increased incidence of PONV observed after laparoscopic surgeries. In our study, we believe these mechanisms played a role in the higher incidence of PONV observed in Group 2.

4.1. Limitations

This study has several limitations. First, we did not directly monitor patients using intracranial pressure (ICP) or intra-abdominal pressure (IAP) measurements. Second, the follow-up period was limited to 24 hours postoperatively, so we were unable to assess long-term outcomes in our patient population.

5. Conclusion

Despite the numerous advantages of robotic laparoscopic surgeries, they are associated with a risk of PONV. In this study, we found that lower intraoperative $ETCO_2$ levels were associated with a reduced incidence of PONV. PONV can develop due to various factors related to anesthesia, medications used, patient characteristics, and the surgical procedure itself. Particularly common in laparoscopic surgeries, PONV remains a significant clinical issue that negatively affects patient comfort and recovery. Therefore, we believe that future research should continue to explore the effectiveness of both pharmacological and non-pharmacological approaches for the prevention of PONV.

Statement of ethics

Ethics committee approval was obtained from Ankara Etlik City Hospital Ethics Committee for our study. (Ethics No: 102; Date: 26/04/2023)

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

This Data and materials are available to the researchers.

Author contributions

YO: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, supervision, visualization, writing–original draft, writing–review & editing. DG: Conceptualization, data curation, investigation, methodology, visualization, writing–original draft, writing–review & editing. CKÇ: Conceptualization, formal analysis, methodology, project administration, resources, supervision, visualization, writing–review & editing. EEH: Conceptualization, investigation, methodology, project administration, supervision, visualization, writing–review & editing. SA: Conceptualization, formal analysis, methodology, visualization. JE: Conceptualization, methodology, project administration, resources, supervision, writing–review & editing. All authors read and approved the final version of the manuscript.

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