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The characteristics and risk factors of the postoperative nausea and vomiting in female patients undergoing laparoscopic sleeve gastrectomy and laparoscopic gynecological surgeries: a propensity score matching analysis

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Abstract. – OBJECTIVE: The aim of this study was to compare the prevalence of postoperative nausea and vomiting (PONV) in matched patients undergoing laparoscopic sleeve gastrectomy (LSG) and laparoscopic gynecological surgeries (LGS) and investigate the main cause of the high occurrence of PONV in bariatric surgeries.

PATIENTS AND METHODS: Medical records of female patients with a body mass index (BMI) greater than 30 kg/m^2 undergoing LSG or LGS from January 1, 2016 to September 1, 2020 were reviewed for PONV episodes in the first postoperative 48 hours. A 1:1 propensity score matching (PSM) method was performed between cases subject to the two types of surgery, and PONV rates were compared.

RESULTS: A total of 278 patients met the inclusion criteria (LSG = 101, LGS = 177), and 74 matched subjects were selected from each group after PSM. An increased occurrence of PONV was noted in female patients with LSG compared with those undergoing LGS (66.2% vs. 23.0%; $p<0.001$). PONV severity was significantly worse in the LSG ($p<0.001$), and more frequent use of rescue antiemetics was detected in the LSG group compared with the LGS group (51.4% vs. 17.6%; $p<0.001$). The time of the first use of rescue drugs was much earlier in the LGS group ($p = 0.034$).

CONCLUSIONS: Female patients undergoing LSG are at increased risk of PONV compared with those with LGS, indicating a critical role of procedure-related alterations of gastric physiology in the high occurrence of PONV after bariatric surgery.

Key Words:

Postoperative nausea and vomiting, Laparoscopic sleeve gastrectomy, Laparoscopic gynecological surgery, Female patient.

Introduction

Postoperative nausea and vomiting (PONV) remain the most common complications despite the development of antiemetic medications and techniques. These complications can result in extended hospitalization, increased medical costs, and decreased patient satisfaction. To date, a series of risk factors of PONV has been confirmed, including younger and female patients, nonsmoking status, a history of PONV or motion sickness, use of volatile anesthetics and nitrous oxide, postoperative opioids, and prolonged duration of anesthesia[1,2]. Furthermore, abdominal surgeries, especially laparoscopy, bariatric and gynecological surgeries, were also associated with an increased prevalence of PONV[1,3].

As obesity becomes a growing problem worldwide, the number of obese patients subject to general anesthesia is also increasing. The potential relationship between obesity and enhanced risk of PONV has become a concern. Given their body weight and increased body fat content, obese patients are more likely to receive higher quantities of volatile anesthetics and opioids. Recently, there has been an increased focus on the occurrence of PONV in bariatric surgeries, which offer the greatest success in losing weight and resolving obesity-related comorbidities.

The prevalence of PONV after laparoscopic bariatric surgery has been documented in a number of studies[4-6]. Based on various risk factors for PONV in patients undergoing this procedure, multimodal antiemetic prophylaxis has been advocated in current guidelines[7]. However, the PONV rate in the bariatric surgery can still be

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as high as 65% even with prophylaxis[6]. Among the well-accepted risk factors, the female gender is considered the strongest patient-specific predictors and the occurrence of PONV in female patients can be 3 times than that of male groups[6]. Of note, patients undergoing bariatric surgeries were far more likely to be female than male, and the distribution is skewed towards younger ages[8], which could be one of the most important reasons for the high occurrence of PONV in this surgery.

Surgery type is another risk factor that may contribute to PONV susceptibility. In recent years, laparoscopic sleeve gastrectomy (LSG) has become the most commonly selected type of surgery in clinical practice, given its safety and effectiveness[9,10]. However, the decreased dispensability and compliance of gastric pouch may increase the risk of PONV. Fathy et al[11] observed that pyloric injection of a magnesium sulfate-lidocaine mixture during LSG reduced gastric intraluminal pressure and the occurrence of PONV.

It is still unclear whether patient factors or surgery-related factors play a major role in the high prevalence of PONV after bariatric surgery. We noticed that among the laparoscopic procedures, gynecologic surgery is another type of surgery that is associated with a high risk of PONV from the perspective of patients and operation characteristics[12-15]. Therefore, a comparison of the occurrence of PONV after LSG and laparoscopic gynecologic surgeries (LGS) was conducted in matched patients to evaluate the role of the surgery type on the development of PONV.

Patients and Methods

Patients

This retrospective study was approved by the Institutional Review Board of our institution, and informed consent was exempted. A retrospective evaluation of all female patients with a body mass index (BMI) ≥30 kg/m^2 of our institution scheduled for LSG or LGS was conducted from January 1, 2016 to September 1, 2020. Patient information was correctly anonymized and identified prior to analysis. We classified the patients into two groups (LSG = laparoscopic sleeve gastrectomy; LGS = laparoscopic gynecologic surgery) according to the type of surgery.

Exclusion criteria: (1) patients who were immediately transferred to Intensive Care Unit (ICU) after surgery; (2) patients who underwent LSG or LGS *via* open surgery or converted to laparotomy; (3) revision surgeries; (4) emergency procedures; (5) patients who were lost to follow-up; (6) prior participation in other randomized controlled trials. We also excluded patients over the age of 60; those with a partially or totally dependent functional status; patients with chronic oxygen dependence, therapeutic anticoagulation, or renal insufficiency; patients requiring dialysis preoperatively; and patients with an American Society of Anesthesiology (ASA) classification 4 or greater.

Antiemetic prophylaxis (i.e., 10 mg dexamethasone or 2 mg tropisetron intravenously administered) is strongly encouraged in the institution. A standardized patient-controlled intravenous analgesia (PCIA) protocol containing tramadol and flurbiprofen axetil was applied to most of the patients to relieve postoperative pain.

Study Outcomes

The primary endpoint was the overall occurrence of PONV after LSG or LGS. An episode of PONV was defined as use of rescue antiemetics or notation of nausea, vomiting, or retching (severe PONV) within 48 hours postoperatively. This study did not consider nausea or vomiting events as separate outcomes because they have identical risk factors and predictors. The severity of PONV, use and type of rescue antiemetics, and the required time to the first rescue antiemetics were secondary outcomes in this study. Through telephone follow-up, patients were asked by one of the investigators to recall the worst episode of PONV on a four-point verbal rating scale (VRS; none, mild, moderate, or severe) as the index of the severity of PONV. For comparison purposes, the time of first use of rescue antiemetics was divided into 4 periods (1: 0-3 hours after surgery; 2: 3-6 hours after surgery; 3: 6-24 hours after surgery; 4: 24-48 hours after surgery).

Data Collection

The data consisted of 16 demographic characteristics and perioperative factors known to be closely related to PONV. Specifically, we collected variables on age, BMI, ASA classification, obesity-related comorbidity (hyperlipidemia, hypertension, diabetes mellitus), smoking status, history of motion sickness or PONV, Apfel score, prophylactic antiemetics, duration of operation and PACU (post-anesthesia care unit), intraoperative infusion speed, blood loss volume,

type of volatile anesthetics (desflurane *vs.* sevoflurane), intraoperative and postoperative opioids consumption and use of PCIA. For comparison purposes, opioid consumption is calculated in the form of the morphine equivalent based on its analgesic effect relative to morphine.

Statistical Analysis

Because this was a retrospective cohort study, patients were not randomized before the statistical analysis. Therefore, we used a propensity score matching (PSM) method to reduce the bias caused by confounding factors. A patient in group LSG was matched with 1 patient in group LGS according to the similarity of their propensity scores, facilitating the use of the logistic regression model of the effect of treatment on the baseline covariates considered potential confounding factors for PONV: BMI, smoking status, and history of motion sickness or PONV. Optimal matching with a caliper size of 0.2 was used to avoid poor matches.

The two matched groups were then analyzed based on the study endpoints. Continuous variables that were abnormally distributed were displayed as medians and interquartile ranges (IQR); otherwise, variables were provided as the mean ± standard deviation. Categorical variables were summarized by counts and percentages. The Mann-Whitney U test was used for group comparisons of continuous variables when data were abnormally distributed; otherwise, Student's *t*-test was applied. Pearson's χ^2-test and Fisher's exact test were used for group comparisons of categorical variables. $p<0.05$ was considered statistically significant. Every data point was two-tailed and analyzed using SPSS for IOS, version 26 (SPSS Inc., Chicago, IL, USA).

Results

General Condition of Patients

A total of 296 female patients with a BMI ≥30 kg/m^2 receiving LSG or LGS at our institution between January 1, 2016 and September 1, 2020 were reviewed in the study. On closer examination, 3 patients had to be excluded due to direct transfer to ICU after surgery, 2 due to converted to laparotomy, 5 due to emergency procedure, 3 were over the age of 60, 1 due to revision surgery, and 4 due to prior participation into other randomized controlled trials. Ultimately, 278 patients were enrolled in the study before the matching process (LSG: n = 101; LGS: n = 177) and 74 matched subjects were selected from each group after a 1:1 PSM, effectively counterpoising the preoperative confounding factors for both groups. The demographic characteristics and perioperative factors for all patients and matched pairs are presented in Tables I and II, respectively.

Before propensity score matching, 9 of the 16 confounding variables exhibited significant differences between both groups, including age, BMI, smoking status, prophylactic antiemetics, operation duration, blood loss volume, infusion speed, type of volatile anesthetics, and intraoperative opioids consumption (Table I). However, these differences in some of the confounding variables disappeared after propensity score matching. Compared with patients following LGS, patients who underwent LSG were significantly younger ($p<0.001$), had shorter operation duration ($p<0.001$), as well as less blood loss volume ($p<0.001$), and were more likely to receive desflurane other than sevoflurane ($p = 0.02$) (Table II). There is no significant difference in Apfel score between the two matched cohorts ($p = 0.505$) (Table III).

Comparison of Occurrence and Severity of PONV

As demonstrated in Table IV, 49 of 74 patients (66.2%) and 17 of 74 patients (23%) in the LSG and LGS groups, respectively, had reported PONV within the first postoperative 48 hours. PONV was more common in the LSG group and was more than twice as likely to occur compared with that after LGS ($p<0.001$). The severity of PONV was also different in both groups ($p<0.001$). Moderate PONV events occurred in 76.5% of the patients undergoing LGS compared with 59.2% of patients with LSG. Nine patients following LSG reported severe PONV episodes, while 0 episodes were noted in the LGS group (Table IV).

Comparison of the Use of Rescue Antiemetics

With respect to the secondary outcomes, 38 patients following LSG used rescue antiemetics to relieve their symptoms of postoperative nausea or vomiting. In the LGS, this was the case in only 13 patients. Apparently, an increased usage rate of rescue antiemetics was detected in the LSG compared with that in the LGS with a significant difference ($p<0.001$). Metoclopramide was more popular in the LSG groups, whereas ondansetron

Table I. Demographic and procedure characteristics of the LSG and LGS cohorts before PSM.

Characteristic	LSG (n = 101)	LGS (n = 177)	*p*-value
Age, year	28.1 ± 8.8	45.1 ± 8.7	< 0.001
BMI, kg/m^2	38.7 ± 5.3	33.1 ± 3.2	< 0.001
ASA class, n (%)			0.07
II	72 (71.3)	107 (60.5)	
III	29 (28.7)	70 (39.5)	
Hyperlipidemia, n (%)	24 (23.8)	26 (14.7)	
Hypertension, n (%)	34 (33.3)	39 (22.0)	
Diabetes mellitus, n (%)	20 (19.0)	25 (14.1)	
Smoking status, n (%)			0.006
Yes	13 (12.9)	7 (4.0)	
No	88 (87.1)	170 (96.0)	
PONV or motion sickness history, n (%)			0.09
Yes	0 (0)	6 (3.4)	
No	101 (100)	171 (96.6)	
Prophylactic antiemetics, n (%)			0.005
None	0 (0)	6 (3.4)	
Single drug	43 (42.6)	92 (52.0)	
Double drugs	52 (51.5)	78 (44.1)	
Triple drugs	6 (5.9)	1 (0.5)	
Operation duration, min	120.9 ± 26.4	169.9 ± 67.1	< 0.001
PACU duration, min	69.3 ± 17.9	67.0 ± 18.1	0.306
Blood loss volume, ml	20 (10,50)	100 (50,135)	< 0.001
Fluid infusion speed, ml/kg/min	0.13 ± 0.05	0.14 ± 0.06	0.028
Volatile anesthetics, n (%)			< 0.001
Sevoflurane	44 (43.6)	139 (78.5)	
Desflurane	57 (56.4)	38 (21.5)	
PCA, n (%)			0.663
Yes	96 (95.2)	166 (94.5)	
No	5 (4.8)	11 (5.5)	
Intraoperative $_{iv}$MEQ	176.3 ± 39.0	196.1 ± 63.4	0.001
Postoperative $_{iv}$MEQ	77.9 ± 16.6	75.2 ± 19.2	0.23

Data are presented as Mean (M) ± Standard Deviation (SD), percentages (%) or median and interquartile range (IQR). LSG: laparoscopic sleeve gastrectomy. LGS: laparoscopic gynecologic surgery. PSM: propensity score matching. BMI: body mass index. ASA class: American Society of Anesthesiologist classification. PONV: postoperative nausea and vomiting. PCA: patient-controlled analgesia. PACU: Post-anesthesia Care Unit. $_{iv}$MEQ: intravenous morphine equivalents in milligrams. n: count of patients.

was the most commonly used rescue antiemetics in the LGS group (p<0.001). The time of first use of rescue drugs was much earlier in the LGS group (p = 0.034) (Table V).

Discussion

In the present study, the occurrence and severity of PONV were compared among 148 female obese patients undergoing LSG or LGS using a 1:1 propensity score matching method. Our results demonstrated that even with antiemetic prophylaxis, PONV episodes still occurred in 66.2% of female obese patients undergoing LSG, which is an almost three-fold higher occurrence of PONV after LGS.

PONV is a common yet serious complication of almost all types of surgery. PONV reduced well-being, delayed diet progress, prolonged hospitalization, and increased treatment cost. PONV mainly occurs in women, nonsmokers, patients with a history of PONV or motion sickness, and those taking opioids. Laparoscopy is also associated with a high risk of PONV[1]. Women receiving LGS is a particular high-risk group for PONV with a reported prevalence as high as 70-85%[16-18]. However, the PONV rate can be decreased to 30-35% using a single antiemetic drug and to even lower level in the case of multimodal prophylaxis[19-21]. Currently, the occurrence of PONV in obese patients undergoing LGS is rarely reported. The present study reported that 23% of obese females suffered from

Table II. Demographic and procedure characteristics of the LSG and LGS cohorts after PSM (n=74).

Characteristic	LSG	LGS	*p*-value
Age, year	28.6 ± 9.5	43.9 ± 8.2	< 0.001
BMI, kg/m^2	36.8 ± 4.3	35.1 ± 3.8	0.011
ASA class, n (%)			0.116
II	54 (73.0)	45 (60.8)	
III	20 (27.0)	29 (39.2)	
Hyperlipidemia, n (%)	22 (29.7)	18 (24.3)	
Hypertension, n (%)	27 (36.5)	16 (21.6)	
Diabetes, n (%)	20 (27.0)	14 (18.9)	
Smoking status, n (%)			0.439
Yes	10 (13.5)	7 (9.5)	
No	64 (86.5)	67 (90.5)	
PONV or motion sickness history, n (%)			0.497
Yes	0 (0)	2 (2.7)	
No	74 (100)	72 (97.3)	
Prophylactic antiemetics, n (%)			0.111
None	0 (0)	0 (0)	
Single drug	33 (44.6)	45 (60.8)	
Double drugs	39 (52.7)	28 (37.8)	
Triple drugs	2 (2.7)	1 (1.4)	
Operation duration, min	121.9 ± 27.7	164.9 ± 63.5	< 0.001
PACU duration, min	69.1 ± 18.5	66.5 ± 18.6	0.394
Blood loss volume, ml	20 (10,50)	100 (50,150)	< 0.001
Fluid infusion speed, ml/kg/min	0.13 ± 0.05	0.14 ± 0.04	0.043
Volatile anesthetics, n (%)			0.02
Sevoflurane	36 (48.6)	50 (67.6)	
Desflurane	38 (51.4)	24 (32.4)	
PCA, n (%)			0.547
Yes	69 (93.2)	67 (90.5)	
No	5 (6.8)	7 (9.5)	
Intraoperative $_{iv}$MEQ	179.1 ± 41.0	199.0 ± 65.4	0.029
Postoperative $_{iv}$MEQ	76.9 ± 19.3	72.6 ± 23.2	0.223

Data are presented as Mean (M) ± Standard Deviation (SD), percentages (%) or median and interquartile range (IQR). LSG: laparoscopic sleeve gastrectomy. LGS: laparoscopic gynecologic surgery. PSM: propensity score matching. BMI: body mass index. ASA class: American Society of Anesthesiologist classification. PONV: postoperative nausea and vomiting. PCA: patient-controlled analgesia. PACU: Post-anesthesia Care Unit. $_{iv}$MEQ: intravenous morphine equivalents in milligrams. n: count of patients.

PONV following LGS when antiemetics were administered alone or in combination.

In the field of bariatric surgery, only a small number of studies have focused on the occurrence and causes of PONV to date. Patients undergoing bariatric surgery exhibit several known risk factors of PONV, including the fact that the majority of the patients are young women with nonsmoking status, laparoscopy and use of volatile anesthetics and opioids. Surgery type could also have an effect on PONV rates. Among all bariatric procedures, LSG is more likely to cause PONV than other types with a reported occurrence of up to 90%[11]. In this

Table III. Apfel score[a] (n = 74).

Apfel score, n (%)	LSG	LGS	*p*-value
1	0 (0%)	0 (0%)	0.505
2	12 (16.2%)	13 (17.6%)	
3	62 (83.8%)	59 (79.7%)	
4	0 (0%)	2 (2.7%)	

[a]0-4 for female gender, non-smoker, history of PONV, and postoperative opioid use. Each point of the Apfel score indicates that the patient has a 20% RR increase of developing PONV.

Table IV. Occurrence[b] and severity[c] of PONV (n = 74).

PONV, n (%)	LSG	LGS	*p*-value
Yes	49 (66.2)	17 (23.0)	< 0.001
Mild	11 (22.4)	4 (23.5)	< 0.001
Moderate	29 (59.2)	13 (76.5)	
Severe	9 (18.4)	0 (0.0)	
No	25 (33.8)	57 (77.0)	

PONV: postoperative nausea and vomiting. [b]PONV was defined as use of rescue antiemetics or notation of nausea, vomiting, or retching (severe PONV) within 48 hours postoperatively. [c]Through telephone follow-up, patients were asked by one of the investigators to recall the worst episode of PONV on a four-point verbal rating scale(VRS) (none, mild, moderate, or severe) as the index of the severity of PONV.

study, two-thirds of female obese patients have recorded at least one episode of PONV after LSG. This rate is lower than that presented in an observational study by Halliday et al[6], which mentioned that PONV occurred in 78% of women undergoing bariatric surgery. One possible explanation for the lower occurrence is that only one patient in our study had reported a history of PONV or motion sickness, whereas greater than 40% of patients exhibited this risk in the study by Halliday et al[6]. In addition, there may be some missed diagnosis of mild PONV episodes in this study, representing an inherent limitation of retrospective studies.

The present study demonstrated greater than twice the prevalence of PONV after LSG compared with that in the LGS group, indicating a critical role of surgery type in the occurrence of PONV. Apfel score, use of antiemetic prophylaxis, and postoperative opioid consumption were comparable between the two cohorts. Perioperative factors exhibited a longer operation duration of LGS, which may increase the cumulation of volatile anesthetics and opioids. However, an increased occurrence of PONV was observed in the LSG group, and more severe PONV events and increased use of rescue antiemetics were also connected with this surgery. This susceptibility to PONV has been attributed to surgery-related alterations in gastric anatomy. The loss of gastric dispensability and compliance is common in LSG as the gastric fundus needs to be completely removed[6]. Another cause may be related to the stimulation of the vagus nerve during operation, which involves gastric manipulation and incisions through afferent branches of the vagus nerve[6,22].

To reduce the difference in the baseline characteristics between the two groups, female patients who received LSG were matched 1 to 1 with patients undergoing LGS in this study. Accordingly, the variables of BMI, ASA classifica-

Table V. Use and types of rescue antiemetics (n = 74).

Rescue antiemetics, n (%)	LSG	LGS	*p*-value
Yes	38 (51.4)	13 (17.6)	< 0.001
No	36 (48.6)	61 (82.4)	
Period of first use of recue antiemetics, n (%)[d]			0.034
0~3h after surgery	7 (9.5)	8 (10.8)	
3~6h after surgery	6 (8.1)	1 (1.4)	
6~24h after surgery	19 (25.7)	4 (5.4)	
24~48h after surgery	6 (8.1)	0 (0)	
Types of antiemetics			< 0.001
Metoclopramide	21 (55.3)	4 (30.8)	
Ondansetron	1 (2.6)	8 (61.5)	
Tropisetron	7 (18.4)	1 (7.7)	
Double combinations	8 (21.1)	0 (0.0)	
Triple combinations	1 (2.6)	0 (0.0)	

[d]The time of first use of rescue drugs was divided into 4 periods: (1) Within 3 hours after surgery; (2) 3 to 6 hours after surgery; (3) 6 to 24 hours after surgery; (4) 24 to 48 hours after surgery.

tion, smoking status, history of PONV or motion sickness, obesity-related comorbidities, Apfel score, duration of PACU, intraoperative infusion speed, and postoperative morphine equivalents exhibited homogeneity among patients with different surgeries. Because adolescents are the major group who underwent bariatric surgery and desflurane is more commonly used in LSG, there were differences in the age and the use of volatile anesthetics between the two groups in this study. For adult patients, the younger age group (<50 years) is more prone to suffer from PONV compared with those who are 50 years and older[23]. Whether the difference in the PONV rate between the two groups is age-related remains to be clarified. Desflurane exhibits a remarkable advantage in the rapid postoperative recovery of obese patients, whereas desflurane and sevoflurane have no clinically relevant differences in terms of PONV[24-27].

Although propensity score matching was used to counterpoise the confounding factors in both cohorts, several limitations still existed in this retrospective study. First, the confirmation of a PONV event was determined by the use of rescue antiemetics or notation of its manifestation in the medical records. This approach raises the possibility that the PONV frequencies in this study were underestimated as some patients may have experienced untreated PONV. However, this limitation concerned both study groups and should not have influenced the result of group comparisons. Second, this study only focused on the overall occurrence of PONV within 48 hours postoperatively, and a few details on the occurrence of PONV at various time intervals were available. Therefore, whether a difference exists in the time to peak occurrence of PONV following the two types of surgery remains unknown. However, previous studies[6,28] on bariatric surgeries have documented the highest prevalence in the first postoperative 12 hours. Finally, although the usual definition of morbid obesity is either a BMI >35 kg/m^2 or a BMI >30 kg/m^2 together with obesity-related comorbidities, the inclusion criteria of this study is BMI >30 kg/m^2. Patients in the two groups exhibited comparable BMI, which is lower than the level of bariatric surgeries in previous studies. Considering that obesity may lead to elevated intra-abdominal pressure during laparoscopic surgery, the correlation between increased BMI and the occurrence of PONV requires further research.

Conclusions

For the first time, this study valued the role of surgery type in the risk factors that may promote PONV after bariatric surgery. Our results suggested that the procedure-related alterations in gastric physiology seem to be a major factor contributing to the susceptibility to PONV in patients with LSG, which explains the much higher prevalence of PONV in female patients undergoing LSG compared to that with LGS.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Clinic Trials

ChiCTR2000037955; ClinicalTrials.gov.

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