

# The Effect of Opioid-Free Anesthesia with Transversus Abdominis Plane Block on Patients Undergoing Laparoscopic Sleeve Gastrectomy: Randomized Controlled Study

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**Purpose:** Anesthesia for metabolic–bariatric surgery is challenging due to the increased risk of opioid-related adverse events. The purpose of the investigation was to assess the feasibility and efficacy of multimodal opioid-free general anesthesia with transversus abdominis plane (TAP) block for laparoscopic sleeve gastrectomy in contrast with conventional opioid-based general anesthesia.

**Patients and Methods:** Eighty patients who underwent laparoscopic sleeve gastrectomy and eventually 71 patients included in the analysis. They were randomly divided into an opioid-based anesthesia group (control group) with sufentanil or opioid-free anesthesia (OFA) group. Esketamine, dexmedetomidine, and TAP were as part of the OFA. Sevoflurane, dexamethasone, and muscle relaxants were administered intraoperatively to all patients. The primary outcome was antiemetic rescue within 24 hours after surgery. The secondary outcomes included pain scores, analgesic needs, extubation time, complications, the hemodynamic changes, and duration of hospital stay.

**Results:** In contrast with the control group, the need for antiemetic rescue was significantly reduced ( $p=0.035$ ). Furthermore, the visual Analog Scale (VAS) for postoperative pain was considerably lower in the OFA group ( $p<0.01$ ) than it was in the control group. There was no significant difference in the need for analgesic rescue in both groups ( $p=0.155$ ). Extubation time and post-anesthesia care unit (PACU) stay duration were equal between the two groups ( $p=0.328$  and  $p=0.54$ ). At the end of the surgery and after extubation, hemodynamic changes was more pronounced in the OFA group ( $p=0.027$ ) than the control group. The length of the hospital stay was significantly shorter compared with the control group ( $p=0.002$ ).

**Conclusion:** OFA with TAP results in a significant decrease in the need for antiemetic rescue, a lower level of pain after the surgery, and a shorter hospital stay in contrast with anesthesia based on opioids.

**Keywords:** opioid-free, nerve block, esketamine, post-operative nausea and vomiting, bariatric surgery

## Introduction

Opioids have historically served as a crucial component in balanced anesthesia regimens. Opioid-related side effects such as respiratory depression, postoperative nausea and vomiting (PONV), constipation, hyperalgesia, drug addiction<sup>1,2</sup> have been troubling many anesthesiologists and surgeons. Opioid-free anesthesia (OFA) becomes the next frontier to avoid opioid-related side effects and enhance the patient's comfort and safety. The principles of OFA are to abstain from the use of  $\mu$ ( $\mu$ )receptor agonists through the use of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, dexmedetomidine, lidocaine, ketamine, and low-dose glucocorticoids.<sup>3</sup>  $\mu$  receptor agonism is associated with significant perioperative side effects, including respiratory depression, PONV, constipation, and altered immunomodulatory signaling pathways.<sup>4</sup>

Patients undergoing laparoscopic bariatric surgery have a high risk of sleep apnea(78.3%),<sup>5</sup> and PONV(80%),<sup>6</sup> which significantly affects the postoperative recovery. Even after the administration of triple PONV prophylaxis, approximately

42.7% of patients who had bariatric surgery ultimately needed additional antiemetic medication.<sup>7</sup> Anesthetic risk factors of PONV include nitrous oxide and postoperative opioids.<sup>8,9</sup> Therefore, anesthesiologists need to explore more comfortable medical strategies and precise anesthesia protocols, including reducing opioid availability, preventing PONV, providing effective analgesia with fewer side effects, and shortening hospital stays.

OFA protocols have been used in a variety of surgeries, such as laparoscopic cholecystectomy, gynaecological laparoscopy, thoracoscopic lung resection,<sup>10–12</sup> and was effective in mitigating PONV, while overdoses of opioids can lead to respiratory depression and drug addiction.<sup>2</sup> The current evidence regarding OFA is still controversial in bariatric surgery.<sup>13–15</sup> In the present research, a prospective clinical trial in metabolic–bariatric surgery was conducted to assess the feasibility and efficacy of multimodal OFA with transversus abdominis plane (TAP) block in contrast with conventional opioid-based general anesthesia. The objectives were to explore the precise solutions to prevent PONV and reduce the adverse effects of opioids.

## Materials and Methods

### Study Design and Patients

The study was designed as a randomized, assessor-blinded, and controlled clinical experiment. The protocol was conducted at the Affiliated Hospital of Qingdao University and approved by the Ethics Committee of the Affiliated Hospital of Qingdao University, China (QYFYKYLL 926211921). It was registered at the Chinese Clinical Trial Registry (ChiCTR2300069061, Mar 6, 2023, available at: <https://www.chictr.org.cn>). The study was conducted in accordance with the Declaration of Helsinki.

Adult patients undergoing an inpatient laparoscopic sleeve gastrectomy (no sexual limitation, who were aged between 18 and 65 years old, American Society of Anesthesiologists (ASA) physical status class I–III) were eligible and provided written informed consent before participation. Exclusion criteria included being allergic to any medication, being pregnant, taking analgesics before the operation for chronic pain, having chronic kidney disease (Cr>200  $\mu\text{mol/dl}$ ), having a history of motion sickness, motion sickness, mania, or depression, and participating in another interventional trial.

In the study, preoperative assessment included the risk of PONV by the Apfel risk score<sup>16</sup> and assessed obstructive sleep apnea (OSA) by this scale STOP-Bang questionnaire<sup>17</sup> in addition to basic data (age, sex, Body Mass Index (BMI), and underlying diseases, etc).

### Randomization and Blinding

Patients were classified into a control group and an OFA group at random using computer-generated random numbers that were created by an independent researcher using Microsoft Excel with a 1:1 allocation ratio and random block sizes. The participants except for the anesthesiologist were unaware of the group allocation because of significant differences between the anesthetic techniques.

### Procedures

The patients underwent preoxygenation and were positioned on a slope prior to the administration of anesthesia. Electrocardiogram, invasive arterial blood pressure, pulse oximetry, end-tidal CO<sub>2</sub> (EtCO<sub>2</sub>), and bispectral index (BIS) were used for performing routine monitoring.

In the OFA group, esketamine 0.5 mg/kg (I.V injection) was administered after a bolus of dexmedetomidine 0.5  $\mu\text{g/kg}$  was administered 10 minutes (the patients received an infusion of the same dose of normal saline in the control group). Sufentanil was given to the patients in the control group (0.2–0.3  $\mu\text{g/kg}$ ). All patients then had standardized intravenous anesthesia induction that included midazolam (0.05mg/kg), propofol (1–2 mg/kg, total body weight), and rocuronium (0.6 mg/kg) before endotracheal intubation. After endotracheal intubation, the patient in the OFA group received bilateral transversus abdominis plane (TAP) block procedures (ropivacaine 0.3%, 20mL) guided by ultrasound. The ventilator parameters were adjusted to maintain EtCO<sub>2</sub> levels between 35 and 45 mmHg.

For maintaining anesthesia, the OFA group was administered a continuous intravenous infusion containing dexmedetomidine (0.2–0.3  $\mu\text{g}/\text{kg}/\text{h}$ ), esketamine (0.3  $\text{mg}/\text{kg}/\text{h}$ ), propofol (2 to 3  $\text{mg}/\text{kg}/\text{h}$ ), and sevoflurane (with a MAC: minimum alveolar concentration, of 0.8–1), as well as cisatracurium besilate (0.04–0.05 $\text{mg}/\text{kg}/\text{h}$ ) given intravenously. The control group, on the other hand, received repetitive doses of sufentanil (0.3  $\mu\text{g}/\text{kg}$ ) and propofol (2 to 3  $\text{mg}/\text{kg}/\text{h}$ ) as needed, determined by the anesthesiologist, and the usage of sevoflurane as well as cisatracurium besilate is same to the OFA group. All anesthetic drug dosages were based on the ideal body weight (IBW). The anesthesia depth was adjusted to achieve and maintain BIS between 40 and 60 (BIS sensor, Covidien LLC, USA) with sevoflurane in an oxygen–air mixture to obtain  $\text{SpO}_2 \geq 94\%$ . Vasoactive agents were administered to maintain hemodynamic stability.

Dexmedetomidine, sufentanil, and propofol were stopped at the end of the operation, whereas esketamine was stopped 30 minutes earlier. Neostigmine (0.04–0.06  $\text{mg}/\text{kg}$ ) and atropine (0.02  $\text{mg}/\text{kg}$ ) were used to reverse any remaining neuromuscular blockade after the procedure. All patients were administered dexamethasone 5 mg, intravenous infusion, 10 min after anesthesia induction and ondansetron 8 mg, intravenous infusion, 20 min before the completion of surgery for the purpose of standardizing antiemetics. Ropivacocaine stock solution was used for local anesthesia for a surgical incision. All patients were transferred to the post-anesthesia care unit (PACU), where the visual analogue scale (VAS) was utilized to measure pain. If the VAS value was seven or above, 50 mg intravenous tramadol (rescue analgesia) was provided, and the VAS value was 4–7 or in need of analgesia, intravenous administration of 50 mg of flurbiprofen axetil was provided to patients both groups. PONV quantitative score  $\geq 5$ , ondansetron (8mg i.v) and droperidol (10–15 $\mu\text{g}/\text{kg}$  i.v) were administered, or patients have needs although the score of 1–4, ondansetron (8mg i. v) was given.

The discharge standards of the PACU were as follows: the VAS score of less than 4, respiratory rates within 12 to 22/min with  $\text{SpO}_2$  94% or higher on room air, and the heart rate and blood pressure within 15% of the baseline value.

## Outcome

A simplified PONV impact scale was used to determine the incidence and severity of PONV 24 hours following surgery.<sup>18</sup> The primary outcome included antiemetic rescue during PONV. The secondary outcomes included post-operative pain scores as measured using the VAS and analgesic needs, extubation time, complications, the hemodynamic changes at different times, the hemodynamic changes, length of hospital stay and assessment of overall patient satisfaction using a 5-point Likert scale.

At various times (2 hours, 6 hours, 12 hours, 24 hours) throughout the course of 24 hours, patients were monitored for PONV, antiemetic needs, and VAS pain levels. The hemodynamic changes were measured at different times (T1: Base value, T2: intubation, T3: during the operation, T4: at the end of the surgery, T5: after extubation, T6: From PACU to the ward) Their medical records were used to collect information regarding the medical history, surgeries, and length of hospital stay of the patients.

## Sample Size Estimation and Statistical Analysis

### Sample Size Estimation

The antiemetic rescue after PONV served as the primary outcome, and the PASS 15 software was utilized to determine the required sample size. Based on preliminary experimentation, the antiemetic rescue in the opioid-based anesthesia group was 50%, while in the OFA group was 18%. A bilateral test  $\alpha$  of 0.05 and a power of 0.80 were applied. By inputting these values into the software, it was determined that a minimum of 35 participants needed to be enrolled in each group. Considering a 10% attrition rate, 80 patients were ultimately required.

### Statistical Analysis

The data collection was done through the preoperative visit as well as the HIS system of the hospital. The data were tested for normal distribution. Nonnormally distributed data are depicted by the median and interquartile range (IQR), and categorical variables are summarized in terms of counts and percentages. The two groups of data adhering to the normal distribution were analyzed using an independent sample *t*-test, whereas the non-parametric rank sum test was employed for comparing data that did not follow a normal distribution. Categorical data were analyzed with Fishers' exact test or  $\chi^2$  test, and risk estimates were calculated using odds ratio and 95% confidence intervals (CIs). The

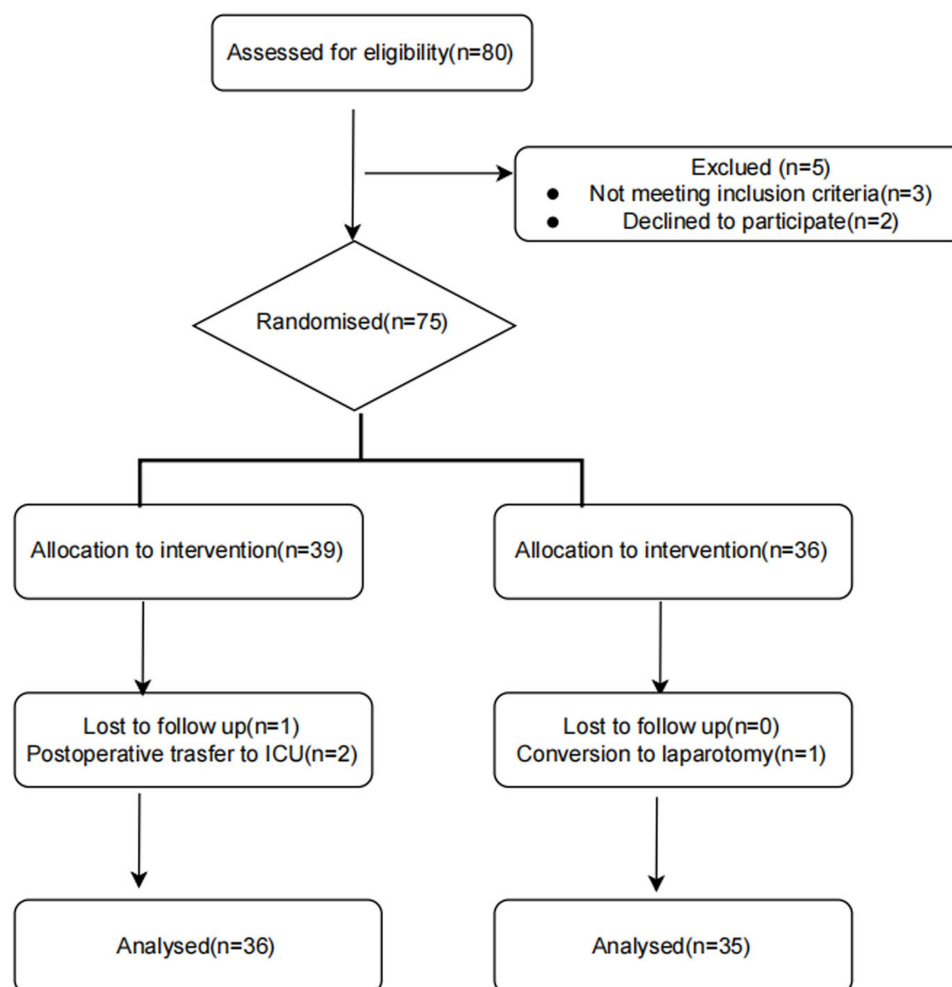
statistical software IBM SPSS 25.0 was used to examine the data. The data were expressed as the mean  $\pm$  standard deviation (SD), median, or percentage (%). Data were regarded as significant when two-sided  $p$  values were  $< 0.05$ .

## Results

In total, 80 patients underwent laparoscopic sleeve gastrectomy. Five patients were not eligible for the trial; three did not meet the requirements, and two patients declined to participate. In addition, one patient failed to follow-up visit, one patient was converted to laparotomy, and two patients were excluded as they were transferred to the ICU post-operation (Figure 1). Opioid-based anesthesia was administered in 48.64% of patients ( $n=36$ ), while OFA was used in 47.39% of patients ( $n=35$ ).

## Patient Characteristics

The study included and examined 71 patients, Table 1 depicts the clinical characteristics of the patients in both groups. The only significant difference between the baseline characteristics of the two groups was age (control group  $32.0 \pm 7.4$  vs  $28.7 \pm 6.4$  OFA group,  $p = 0.045$ ). The median age was  $30.4 \pm 7.1$ . Other clinical baseline data were similar for the two groups. Between the two groups, the preoperative PONV risk score did not differ significantly ( $p = 0.815$ ). The length of the surgery, the length of the PACU stay, and the total duration of anesthesia did not substantially differ between the two groups ( $p > 0.05$ ), as shown in (Table 1).



**Figure 1** Consort patient enrolment flow diagram.

**Table I** Baseline Patient Characteristics and Perioperative Data

	All Patients (n = 71)	Control Group (n = 36)	OFA Group (n = 35)	P-value
Sex				0.259
Male	20 (28.2%)	8 (22.2%)	12 (34.3%)	
Female	51 (71.8%)	28 (77.8%)	23 (65.7%)	
Age	30.4 ± 7.1	32.0 ± 7.4	28.7 ± 6.4	0.045
Height (cm)	170.1 ± 7.9	169.2 ± 8.6	171.0 ± 7.2	0.363
Weight (kg)	116.9 ± 19.9	113.2 ± 19.2	120.8 ± 20.0	0.108
BMI (kg/m <sup>2</sup> )	40.2 ± 5.2	39.2 ± 4.7	41.3 ± 5.6	0.097
ASA n (%)				0.673
I	21(29.6)	12(33.3)	9(25.7)	
II	27(38.0)	12(33.3)	15(42.9)	
III	23(32.4)	12(33.3)	11(31.4)	
Alcohol				0.71
No	63 (88.7%)	31 (86.1%)	32 (91.4%)	
Yes	8 (11.3%)	5 (13.9%)	3 (8.6%)	
Smoking				0.25
No	51 (77.3%)	22 (71%)	29 (82.9%)	
Yes	15 (22.7%)	9 (29%)	6 (17.1%)	
Diabetes				0.945
No	53 (74.6%)	27 (75%)	26 (74.3%)	
Yes	18 (25.4%)	9 (25%)	9 (25.7%)	
Hypertension				0.737
No	48 (67.6%)	25 (69.4%)	23 (65.7%)	
Yes	23 (32.4%)	11 (30.6%)	12 (34.3%)	
OSAS				0.626
No	28 (40.0%)	13 (37.1%)	15 (42.9%)	
Yes	42 (60.0%)	22 (62.9%)	20 (57.1%)	
PONV risk score				0.815
0	9 (12.7%)	4 (11.1%)	5 (14.3%)	
1	20 (28.2%)	9 (25%)	11 (31.4%)	
2	35 (49.3%)	20 (55.6%)	15 (42.9%)	
3	7 (9.9%)	3 (8.3%)	4 (11.4%)	
Duration of surgery (min)	136.5 ± 31.2	137.9 ± 34.7	135.0 ± 27.5	0.702
Duration of anesthesia (min)	176.4 ± 37.8	175.8 ± 45.4	177.0 ± 28.5	0.898
MAP				
T1	98.4 ± 9.6	100.0 ± 10.8	96.9 ± 8.1	0.18
T2	95.8 ± 8.6	94.4 ± 8.8	97.1 ± 8.4	0.185
T3	88.1 ± 4.9	88.0 ± 5.0	88.2 ± 4.9	0.909
T4	88.7 ± 7.6	86.7 ± 9.1	90.7 ± 5.1	0.027
T5	90.0 ± 4.9	88.8 ± 3.7	91.3 ± 5.6	0.027
T6	90.1 ± 4.2	89.5 ± 3.9	90.8 ± 4.4	0.213
HR				
T1	77.4 ± 9.3	79.1 ± 10.1	75.7 ± 8.2	0.127
T2	74.0 ± 9.1	73.5 ± 8.9	74.5 ± 9.4	0.65
T3	72.5 ± 7.3	72.2 ± 7.4	72.7 ± 7.3	0.803
T4	72.7 ± 6.9	72.8 ± 7.4	72.7 ± 6.6	0.956
T5	72.9 ± 6.4	72.9 ± 7.0	73.0 ± 5.8	0.941
T6	73.7 ± 6.8	72.9 ± 7.2	74.5 ± 6.4	0.343

**Notes:** Data are summarised by number (%), or mean (standard deviation). T1: Base value, T2: intubation, T3: during the operation, T4: at the end of the surgery, T5: after extubation, T6: From PACU to the ward.

**Abbreviations:** BMI, Body Mass Index; ASA, American Society of Anesthesiologists; OSAS, Obstructive Sleep Apnea Syndrome; MAP, mean arterial pressure; PACU, post-anesthesia care unit.

## Study Endpoints

### Postoperative Nausea and Vomiting

Patients developed different degrees of nausea and vomiting within 24 hours after surgery. In contrast with the control group, the need for antiemetic rescue was significantly reduced ( $p=0.035$ ) (Table 2). Both groups experienced a higher score of PONV within the first 6 hours following surgery, which steadily decreased after 12 hours. Two hours after surgery, the PONV score was higher in the control group, with a score of 3.5, in contrast with the OFA group, with a score of 2.1 ( $p<0.01$ ). Similarly, 6 hours following surgery, the PONV score was 3.4 in the control group and 2.6 in the OFA group (Figure 2).

### Secondary Outcomes

There were significant differences observed between the two groups in terms of pain scores throughout the study ( $p<0.001$ ). The VAS score was highest 2 hours following surgery in both groups. None of the patients in either group received any postoperative opioid analgesic medications such as tramadol. The changing trend of VAS scores recorded after surgery were similar between both groups (Figure 3). There was no significant difference in the extubation time and length of stay in the PACU between the control group ( $22.9 \pm 11.5$  minutes and  $42.5 \pm 16.4$  minutes) and the OFA group ( $20.3 \pm 10.7$  minutes and  $44.9 \pm 16.7$  minutes) ( $p>0.05$ ) (Table 2). However, the length of the hospital stay was significantly different, with the OFA group having a shorter stay ( $5.8 \pm 1.0$  days) in contrast with the control group ( $6.6 \pm 1.1$  days) ( $p=0.002$ ). By observing the hemodynamic changes in patients at different times, the variation tendency of heart rate (HR) and mean arterial pressure (MAP) was consistent in the two groups (Figure 4). However, MAP fluctuated greatly at the end of surgery and extubation in the OFA group ( $p<0.05$ ), as shown in Table 1.

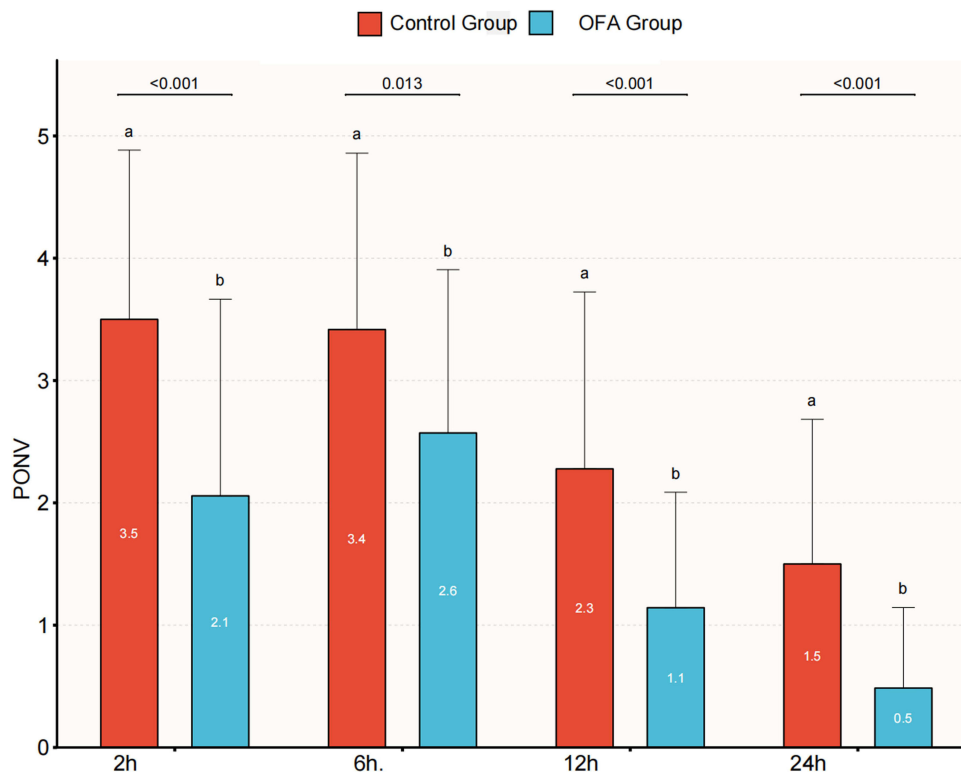
One patient in the OFA group developed postoperative delirium, which may have been caused by incomplete elimination of the anesthetic drugs but improved with treatment using dexmedetomidine. The patient satisfaction in the OFA group was higher than the control group ( $4.1 \pm 0.6$  vs  $3.4 \pm 0.6$ ) ( $p<0.001$ ), as indicated in (Table 2).

## Discussion

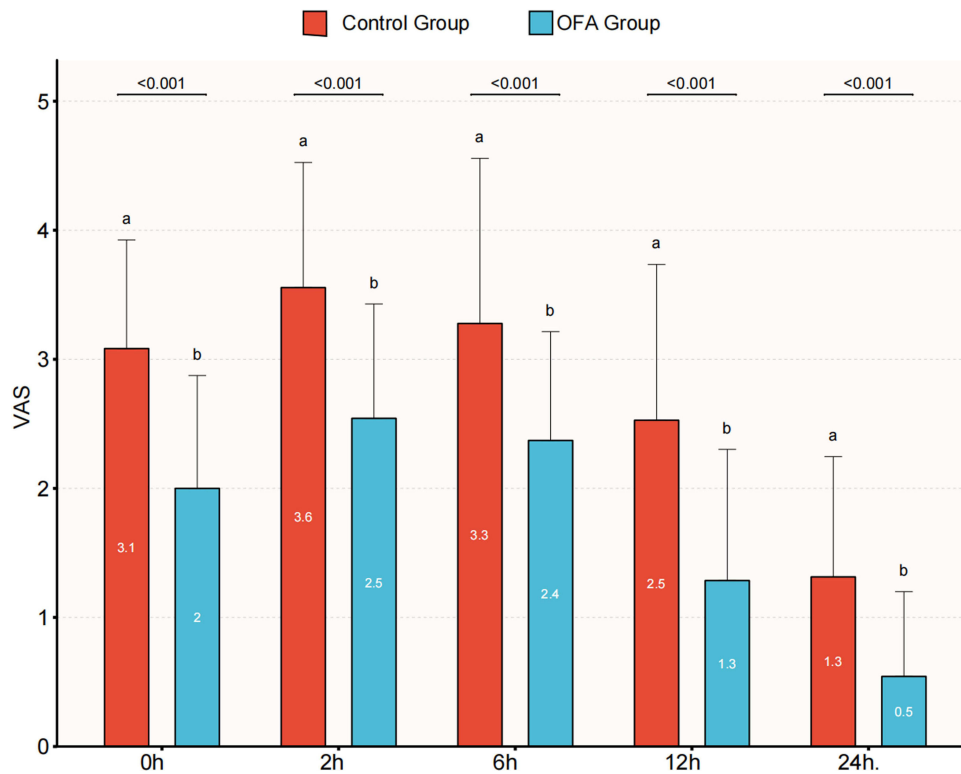
The clinical trial demonstrates the significant impact of using multimodal opioid-free anesthesia in bariatric surgery patients. TAP guided by ultrasound as well as esketamine, dexmedetomidine, and sevoflurane were the major components of multimodal opioid-free anesthesia. In comparison to conventional opioid-inclusive anesthesia, it can significantly lower the severity of PONV, alleviate postoperative pain and shorten length of hospital stay.

**Table 2** Analgesic Requirements, Complication and Recovery

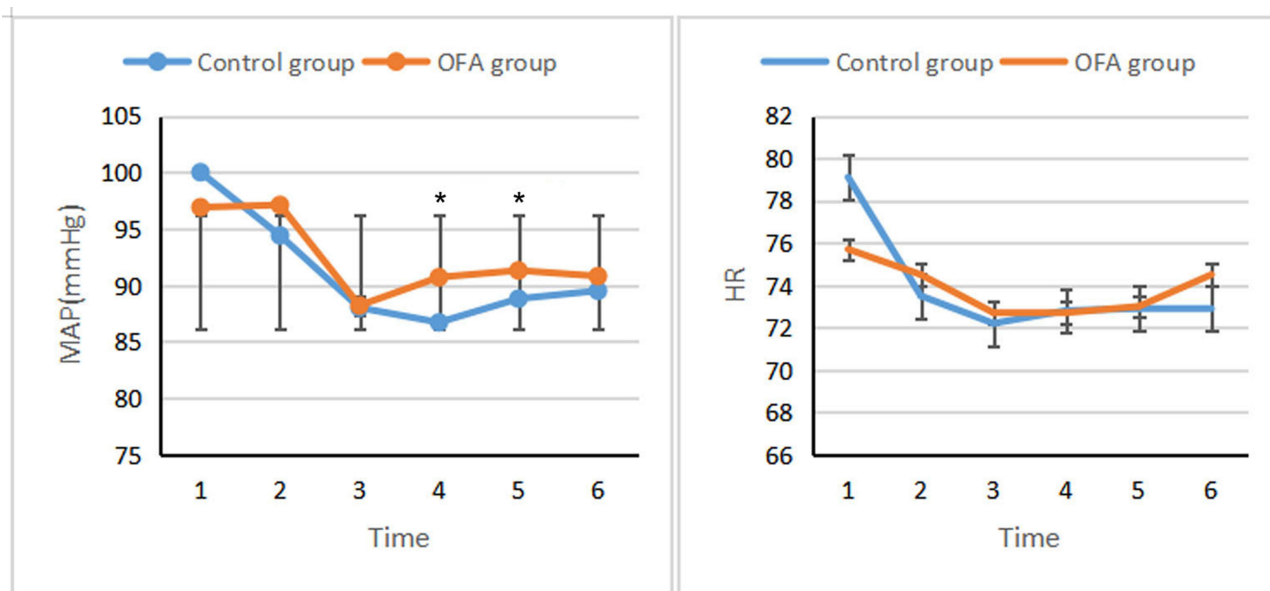
Outcome	Total (n = 71)	Control Group (n = 36)	OFA Group (n = 35)	Value
Antiemetic rescue n (%)				0.035
No	44 (62.0)	18 (50)	26 (74.3)	
Yes	27 (38.0)	18 (50)	9 (25.7)	
Length of Hospital stay(d)	$6.2 \pm 1.1$	$6.6 \pm 1.1$	$5.8 \pm 1.0$	0.002
Extubation time (min)	$21.6 \pm 11.1$	$22.9 \pm 11.5$	$20.3 \pm 10.7$	0.328
Length of stay PACU (min)	$43.7 \pm 16.5$	$42.5 \pm 16.4$	$44.9 \pm 16.7$	0.54
Satisfaction	$3.8 \pm 0.7$	$3.4 \pm 0.6$	$4.1 \pm 0.6$	< 0.001
Analgesic rescue n (%)				0.155
No	47 (66.2)	21 (58.3)	26 (74.3)	
Yes	24 (33.8)	15 (41.7)	9 (25.7)	
Postoperative irritability, n (%)				1
0	67 (94.4)	34 (94.4)	33 (94.3)	
1	4 (5.6)	2 (5.6)	2 (5.7)	
Delusion, n (%)				0.486
0	69 (98.6)	36 (100)	33 (97.1)	
1	1 (1.4)	0 (0)	1 (2.9)	



**Figure 2** The impact scale of PONV within 24h after surgery.a,b.  
**Notes:** P < 0.05, OFA vs Control group at the same time point.



**Figure 3** Visual Analogue Scale (VAS) score at different times after surgery.a,b.  
**Notes:** P < 0.05, OFA vs Control group at the same time point.



**Figure 4** Changes in the patient's vital signs.

**Notes:** \* $P < 0.05$ , OFA vs Control group. T1: Base value, T2: intubation, T3: during the operation, T4: at the end of the surgery, T5: after extubation, T6: From PACU to the ward.

PONV has multifactorial etiologies and it significantly reduces the comfort of patients undergoing laparoscopic bariatric surgery. Previous studies had shown that up to 82% of patients undergoing metabolic and bariatric surgery suffer from PONV in the PACU.<sup>6,19</sup> Our research showed that OFA with TAP is effective in reducing antiemetic rescues within 24h after surgery, that the scores of PONV were all less than four. While a PONV impact scale score of  $\geq 5$  defines clinically important PONV.<sup>18</sup> Consistent with our study, Ziemann-Gimmel P demonstrates a significant reduction in relative risk of PONV in the opioid-free group compared with balanced anaesthesia even when triple PONV prophylaxis was given to both groups undergoing elective bariatric surgery.<sup>19</sup> A Systematic Review and Network Meta-Analysis, OFA was more effective at reducing PONV (relative risks [RR], 0.6, 95% confidence interval [CI], 0.5–0.9, moderate-quality evidence) compared to opioid-sparing anaesthesia (OSA) protocols.<sup>20</sup> Notably, Massoth et al discovered that opioid-free multimodal general anaesthesia is feasible but did not decrease the incidence of PONV compared to an opioid-containing anaesthetic regimen and all patients received dexamethasone 4 mg and ondansetron 4 mg for PONV prophylaxis.<sup>11</sup> Different from the previous clinical trial, we optimized the anti-vomiting protocol by using dexamethasone (5mg intravenous infusion) 10 min after anaesthesia induction and ondansetron (8mg intravenous infusion) 20 min before the completion of surgery in the both group. Therefore, the timing of antiemetic medication during surgery may require further investigation. Moreover, we combined TAP in the OFA group, which partly reduced the pain stimulation in the abdomen, and probably reduced the severity of PONV.

To reduce opioid consumption and opioid-based adverse effects, esketamine or ketamine is an anesthetic with analgesic action that has recently been used in opioid-free anaesthesia treatment.<sup>1,3,21</sup> Esketamine, as an S-enantiomer of ketamine and twice as potent and with fewer side effects than Ketamine, and attracts much attention in treating depression.<sup>21</sup> Dexmedetomidine is a selective  $\alpha_2$ -adrenergic receptor agonist that blocks sympathetic nervous system activity by directly acting on spinal preganglionic sympathetic neurons and widely used for sedation, anxiolysis, and analgesia to reduce the requirement of anaesthetics during general anaesthesia.<sup>22</sup> Unlike dexmedetomidine, esketamine increases in sympathetic tone, hypotension and cardiac depression is less common.<sup>23</sup> Several studies have shown that as regular medication in OFA, esketamine with dexmedetomidine did not cause significant respiratory depression and postoperative pain. Zeballos et al reported that ketamine decreased postoperative pain scores and opioid consumption in bariatric surgery patients when given preoperatively.<sup>24</sup> Similarly, Yang et al found intraoperative esketamine was effective at reducing acute postoperative pain in bariatric surgery patients by a randomized control trial.<sup>25</sup> Our study showed that TAP with the above two drugs did not increase the postoperative analgesic rescue. Furthermore, TAP block

and trocar site infiltration resulted in controlled postoperative pain in laparoscopic sleeve gastrectomy due to the convenient application and fewer adverse effects.<sup>26</sup>

In another study, it was found that dexmedetomidine-inclusive anesthesia was linked to a significantly longer stay in the PACU and extubation time.<sup>27</sup> In the study, we adjusted the anesthetic dose and withdrawal duration in the trial, extubation time and length of stay PACU were not significantly longer. Notably, the MAP changed significantly after surgery and extubation, fluctuations of MAP occurred at the end of surgery and during the extubation period. It may be related to the increased sympathetic tone by esketamine,<sup>23</sup> as well as sensitivity to endotracheal intubation and bucking during the time when anesthetic patients were awakening.

## Limitations

There are several limitations to the current trial. First, the small sample size was insufficient to distinguish minute variations between the results of the two groups, with the potential for selection bias (such as ages). A postoperative delusion was found as an adverse event in OFA, which was influenced by a number of parameters. However, there is still a lack of literature on the side effects and/or complications that might be associated with it. Second, the anesthesiologists cannot be blinded due to differences in technique and anesthesia management. Third, the dose of esketamine and dexmedetomidine could be further explored. Elshazly et al discovered that bilateral erector spinae plane (ESP) block was a more practical and efficient procedure for patients undergoing laparoscopic bariatric surgery when in contrast with TAP block.<sup>28</sup> As for a multimodal analgesia plan, an erector spinae plane block can be used in overweight patients.

## Conclusion

TAP block with dexmedetomidine and esketamine in patients undergoing laparoscopic sleeve gastrectomy offers clear advantages over opioid-based anesthesia in terms of PONV. Furthermore, OFA with TAP can offer an important, very effective pain-controlling technique and a shorter hospital stay. The protocol can be tried for application to other procedures in the future.

## Data Sharing Statement

All requisite data underpinning our research have been disclosed within the manuscript. The datasets utilized and/or analyzed throughout the present study are accessible to anyone who desires to access them upon reasonable request. The data can be obtained from the corresponding author.

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The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

## Disclosure

The authors report no conflicts of interest in this work.

## References

1. James A, Williams J. Basic opioid pharmacology—an update. *Brit J Pain*. 2020;14(2):115–121. doi:10.1177/2049463720911986
2. Bhakta P, Ghosh BR, Singh U, et al. Incidence of postoperative nausea and vomiting following gynecological laparoscopy: a comparison of standard anesthetic technique and propofol infusion. *Acta Anaesth Taiwan*. 2016;54(4):108–113. doi:10.1016/j.aat.2016.10.002
3. McLott J, Stahel PF. Opioid-free anesthesia: the next frontier in surgical patient safety. *Patient Saf Surg*. 2022;16(1):38. doi:10.1186/s13037-022-00346-5
4. Pasternak GW, Pan YX. Mu opioids and their receptors: evolution of a concept. *Pharmacol Rev*. 2013;65(4):1257–1317. doi:10.1124/pr.112.007138
5. Lopez PP, Stefan B, Schulman CI, et al. Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *AM SURGEON*. 2008;74(9):834–838. doi:10.1177/000313480807400914
6. Halliday TA, Sundqvist J, Hultin M, et al. Post-operative nausea and vomiting in bariatric surgery patients: an observational study. *Acta Anaesthesiol Scand*. 2017;61(5):4719. doi:10.1111/aas.12884
7. Ziemann-Gimmel P, Hensel P, Koppman J, et al. Multimodal analgesia reduces narcotic requirements and antiemetic rescue medication in laparoscopic Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis*. 2013;9(6):975–980. doi:10.1016/j.soard.2013

8. Myles PS, Leslie K, Chan MT, et al. Avoidance of nitrous oxide for patients undergoing major surgery: a randomized controlled trial. *Anesthesio*. 2007;107(2):221–231. doi:10.1097/01.anes.0000270723.30772.da
9. Apfel CC, Kranke P, Katz MH, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Brit J Anaesth*. 2002;88(5):659–668. doi:10.1093/bja/88.5.659
10. Yu JM, Tao QY, He Y, et al. Opioid-free anesthesia for pain relief after laparoscopic cholecystectomy: a prospective randomized controlled trial. *J Pain Res*. 2023;16:3625–3632. doi:10.2147/JPR.S432601
11. Massoth C, Schwellenbach J, Saadat-Gilani K, et al. Impact of opioid-free anaesthesia on postoperative nausea, vomiting and pain after gynaecological laparoscopy - A randomised controlled trial. *J Clin Anesth*. 2021;75:110437. doi:10.1016/j.jclinane.2021.110437
12. Feng CD, Xu Y, Chen S, et al. Opioid-free anaesthesia reduces postoperative nausea and vomiting after thoracoscopic lung resection: a randomised controlled trial. *Brit J Anaesth*. 2024;132(2):267–276. doi:10.1016/j.bja.2023.11.008
13. Léger M, Pessiot-Royer S, Perrault T, et al. The effect of opioid-free anesthesia protocol on the early quality of recovery after major surgery (SOFA trial): study protocol for a prospective, monocentric, randomized, single-blinded trial. *Trials*. 2021;22(1):855. doi:10.1186/s13063-021-05829-x
14. Bohringer C, Astorga C, Liu H. The benefits of opioid free anesthesia and the precautions necessary when employing it. *Transl Perr Pain Med*. 2020;7(1):152–157.
15. Mieszczanski P, Kolacz M, Trzebicki J. Opioid-free anesthesia in bariatric surgery: is it the one and only? A comprehensive review of the current literature. *Healthcare*. 2024;12(11). doi:10.3390/healthcare12111094
16. Darvall J, Handscombe M, Maat B, et al. Interpretation of the four risk factors for postoperative nausea and vomiting in the Apfel simplified risk score: an analysis of published studies. *Can J Anesth/J Can Anesth*. 2021;68(7):1057–1063. doi:10.1007/s12630-021-01974-8
17. Zheng Z, Zhang Y, Chen M, et al. Application value of joint STOP-bang questionnaire and Epworth sleepiness scale in screening for obstructive sleep apnea. *Front Public Health*. 2022;10.
18. Myles PS, Wengritzky R. Simplified postoperative nausea and vomiting impact scale for audit and post-discharge review. *Brit J Anaesth*. 2012;108(3):423–429. doi:10.1093/bja/aer505
19. Ziemann-Gimmel P, Goldfarb AA, Koppman J, et al. Opioid-free total intravenous anaesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. *BRIT J ANAESTH*. 2014;112(5):906–911. doi:10.1093/bja/aet551
20. Ao Y, Ma J, Zheng X, et al. Opioid-sparing anesthesia versus opioid-free anesthesia for the prevention of postoperative nausea and vomiting after laparoscopic bariatric surgery: a systematic review and network meta-analysis. *ANESTH ANALG*. 2024. doi:10.1213/ANE0000000000006942
21. Kim J, Farchione T, Potter A, et al. Esketamine for treatment-resistant depression - first fda-approved antidepressant in a new class. *New Engl J Med*. 2019;381(1):1–4. doi:10.1056/NEJMp1903305
22. Ao L, Shi J, Bai Y, et al. Effectiveness and safety of intravenous application of dexmedetomidine for cesarean section under general anesthesia: a meta-analysis of randomized trials. *Drug Des Devel Ther*. 2019;13:965–974. doi:10.2147/DDDT.S197165
23. Eberl S, Koers L, van Hooft JE, et al. Sedation with propofol during ERCP: is the combination with esketamine more effective and safer than with alfentanil? Study protocol for a randomized controlled trial. *Trials*. 2017;18(1):472. doi:10.1186/s13063-017-2197-8
24. Zeballos JL, Lirk P, Rathmell JP. Low-dose ketamine for acute pain management: a timely nudge toward multimodal analgesia. *Region Anesth Pain Med*. 2018;43(5):453–455. doi:10.1097/AAP.0000000000000810
25. Yang T, Mudabbar MS, Liu B, et al. Intraoperative esketamine is effective at reducing acute postoperative pain in bariatric surgery patients: a randomized control trial. *OBES SURG*. 2023;33(8):2368–2374. doi:10.1007/s11695-023-06676-2
26. Coşkun M, Yardimci S, Arslantaş MK, et al. Subcostal transversus abdominis plane block for laparoscopic sleeve gastrectomy, is it worth the time? *OBES SURG*. 2019;29(10):3188–3194. doi:10.1007/s11695-019-03984-4
27. Grape S, Kirkham KR, Frauenknecht J, et al. Intra-operative analgesia with remifentanyl vs. dexmedetomidine: a systematic review and meta-analysis with trial sequential analysis. *Anaesthesia*. 2019;74(6):793–800. doi:10.1111/anae.14657
28. Elshazly M, El-Halafawy YM, Mohamed DZ, et al. Feasibility and efficacy of erector spinae plane block versus transversus abdominis plane block in laparoscopic bariatric surgery: a randomized comparative trial. *Korean J Anesthesiol*. 2022;75(6):502–509. doi:10.4097/kja.22169

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