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Comparison between total intravenous anesthesia and balanced anesthesia on postoperative opioid consumption in patients who underwent laparoscopic-assisted distal gastrectomy

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Abstract

Remifentanil is the most frequently prescribed opioid for total intravenous anesthesia (TIVA) or balanced anesthesia (BA), due to its favorable pharmacological properties. However, several studies have reported opioid-induced hyperalgesia and/or acute tolerance after intraoperatively using remifentanil. In addition, it is imperative to control postoperative pain with lower doses of opioid anesthetic agents. Therefore, we compared the amount of opioid consumption between TIVA with propofol-remifentanil and BA with desflurane-remifentanil, to control postoperative pain in patients who underwent laparoscopic-assisted distal gastrectomy (LADG) with gastroduodenostomy.

We retrospectively evaluated demographic variables (age, gender, height, weight, and smoking habits), the duration of general anesthesia (GA), and intraoperatively administered remifentanil consumption through the electronic medical records of patients who underwent LADG with gastroduodenostomy due to early stomach cancer. The primary outcome was postoperative opioid consumption during postoperative day (POD) 2. The secondary outcomes were the incidence of any rescue opioid analgesics administered, numeric rating scale, and various adverse effects during POD 2. We categorized the data in 2 patient groups to compare TIVA with propofol-remifentanil (TIVA group) to BA with desflurane-remifentanil (BA group) on the postoperative opioid analgesic consumption.

We divided 114 patients into the TIVA (46 patients) and BA (68 patients) groups. Opioid consumption as a primary outcome was significantly higher in the BA group than in the TIVA group during POD 2 except in the post-anesthesia care unit. The cumulative opioid consumption was significantly higher in the BA than in the TIVA group. The incidence of rescue analgesic at POD 2 was higher in the BA than in the TIVA group. In the TIVA group, remifentanil consumption was higher, and the duration of GA was shorter than that in the BA group. No statistically significant differences were observed when comparing other variables.

Our results indicated that the maintenance of GA with TIVA (propofol-remifentanil) reduces opioid consumption for postoperative pain control compared to BA (desflurane-remifentanil) in patients undergoing LADG with gastroduodenostomy.

Abbreviations: BA = balanced anesthesia, BIS = bispectral index score, GA = general anesthesia, IV = intravenous, LADG = laparoscopic-assisted distal gastrectomy, NRS = numeric rating scale, OIH = opioid-induced hyperalgesia, PACU = post-anesthesia care unit, PCA = patient-controlled analgesia, POD = postoperative day, PONV = postoperative nausea and vomiting, TCI = target-controlled infusion, TIVA = total intravenous anesthesia.

Keywords: balanced anesthesia, opioid consumption, opioid-induced hyperalgesia, tolerance, total intravenous anesthesia

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1. Introduction

Short-acting intravenous (IV) anesthetics have been increasingly used in general anesthesia (GA) to overcome the disadvantages of inhalational anesthetics such as postoperative nausea and vomiting (PONV) and air pollution in the operating room.[1–5] Typically, propofol and remifentanil are the preferred anesthetic agents for total IV anesthesia (TIVA) or balanced anesthesia (BA) due to their favorable pharmacological properties.[4,6] There are several advantages of using propofol, which includes rapid onset and offset with fewer side effects such as PONV, due to which it is considered as an important drug that plays a key role in TIVA.[3,4,6] Remifentanil is an ultra-short-acting synthetic opioid and is frequently selected as an adjuvant for TIVA with propofol or BA to aid the inhalational anesthetic agents.[4,6] However, several studies have previously reported opioid-induced hyperalgesia (OIH) and/or acute tolerance after intraoperative use of remifentanil.[7–9] Significant concerns might be required in the management of postoperative pain after surgery with remifentanil-based anesthesia.

Opioids are effective in controlling postoperative pain, but may lead to adverse outcomes such as PONV, pruritus, and dizziness. These adverse effects can delay recovery and return to normal activities of daily living, while reducing patient satisfaction. Additionally, insufficient pain control can lead to postoperative chronic pain and increased postoperative morbidity.[10] Consequently, it is imperative to control postoperative pain with lower doses of opioid anesthetic agents. Although both regimens are typically used for intraoperative anesthesia, there are no studies that compared postoperative opioid consumption for TIVA and BA in patients who underwent laparoscopic-assisted distal gastrectomy (LADG).

We aimed to compare opioid consumption in TIVA with propofol-remifentanil and BA with desflurane-remifentanil to control postoperative pain in patients who underwent LADG with gastroduodenostomy.

2. Methods

This study was conducted at Asan Medical Center, Seoul, Republic of Korea. The need for informed consent was waived considering the retrospective nature of this study. We reviewed electronic medical records of patients for all necessary data. This retrospective study was approved by the institutional review board of Asan Medical Center (approval number, 2015–0112).

2.1. Study population

We searched the information technology of service management database of our institution using the following keywords

"early malignant neoplasm of the stomach," "laparoscopic-assisted distal gastrectomy," and "gastroduodenostomy" from February 2013 to September 2014. Cases were selected based on the following inclusion criteria:

(1) patients who underwent LADG with gastroduodenostomy under the GA with TIVA (propofol-remifentanil) or BA (desflurane-remifentanil) and
(2) patients who were administered postoperative IV patient-controlled analgesia (PCA).

We excluded patients that met the following condition:

1) those who simultaneously underwent LADG with gastroduodenostomy and additional surgical interventions (such as cholecystectomy or appendectomy),
2) those who underwent LADG with d-shaped anastomosis or with anastomosis to jejunum or with gastroduodenostomy as a palliative operation,
3) those who had a history of drug abuse,
4) those who previously underwent chemotherapy and/or radiotherapy,
5) those who experienced chronic pain (>3 months),
6) those who were preoperatively administered opioids,
7) those having a history of heavy alcohol intake,
8) those who had allergies to propofol, remifentanil, fentanyl, meperidine, and oxycodone,
9) those demonstrating a systemic infection,
10) those who were pregnant,
11) those who underwent urgent or emergent surgery,
12) those who underwent re-do surgical procedures,
13) those who demonstrated unstable medical or psychiatric conditions.

The patients who stopped IV PCA caused by adverse effects before the postoperative day (POD) 2 were excluded after reviewing their data.

We categorized all data into 2 patient groups to compare TIVA with propofol-remifentanil (TIVA group) to BA with desflurane-remifentanil (BA group) in patients undergoing LADG with gastroduodenostomy due to early stomach cancer.

2.2. Methods of anesthesia and analgesia

No premedication was administered before the induction of GA. All patients were continuously monitored via electrocardiogram, pulse oximetry, non-invasive arterial pressure and bispectral index score (BIS; Bispectral index™, Aspect Medical System, Norwood, MA) monitoring, temperature, capnography (end-tidal carbon dioxide), and inspiratory oxygen concentration. GA of the TIVA group proceeded as follows: Propofol and remifentanil were administrated via target-controlled infusion (TCI) to induce and maintain GA. The Marsh model was used for propofol TCI and the Schnider model was applied for remifentanil TCI. B. Braun Perfusor Space (B. Braun Medical Inc., Bethlehem, PA) was used for TCI. The plasma concentrations of propofol and remifentanil were adjusted to meet the target BIS value of 40 to 60, without severely affecting the patient's vital signs. No additional analgesic agents, such as nitrous oxide, were administered to maintain anesthesia. GA of the BA group proceeded as follows: Propofol (1.5–2.5 mg/kg) was administrated for induction of GA. GA was maintained with 6 to 7 vol% end-tidal concentration of desflurane in 50% oxygen with air and a remifentanil TCI. All of these parameters were adjusted to maintain acceptable hemodynamic parameters and a BIS of 40 to 60. Other methods of anesthesia were similar to those used in the TIVA group.

Thirty minutes before completing the surgery, all patients received analgesic single bolus doses of fentanyl (1 μg/kg) or oxycodone (0.1 mg/kg). IV ramosetron 0.3 mg was administrated to all patients for preventing PONV before starting IV PCA. The patients were transferred to the post-anesthesia care unit (PACU) after emerging from anesthesia and their postoperative pain was assessed using the numeric rating scale (NRS). Additional doses

of fentanyl (1 μg/kg) or oxycodone (0.1 mg/kg) were administered in cases of insufficient analgesia (NRS > 4) at the PACU.

2.3. Data collection and outcome assessments

We collected the relevant information associated with each patient's demographic variables (age, gender, height, weight, and smoking), the duration of GA, and intraoperatively administered remifentanil consumption. The primary outcome was the postoperative opioid consumption during POD 2. We defined POD 1 as up to 24 hours and POD 2 as up to 48 hours after surgery. The secondary outcomes were the incidence of administering any rescue opioid analgesics, NRS ranging from 0 (no pain) to 10 (worst possible pain), and various adverse effects for POD 2. NRS was measured at 0, 0.5, 1, 8, 16, 24, 32, 40, and 48 hours postoperatively.

Oxycodone or fentanyl was used in the IV PCA device (Accumate 1100, Wooyoung Medical, Seoul/Korea). The PCA device was programmed with the following settings: 1 mL/h basal infusion rate, 1 mL bolus dose, and a lockout interval of 15 min. The maximum doses of oxycodone and fentanyl were 5 mg/h and 50 μg/h, respectively. Rescue analgesics including fentanyl, oxycodone, and meperidine were used if analgesia was not sufficient (NRS > 4) on the PACU or the ward. When the patients had pain with shivering, meperidine was injected for pain management. Total amount of opioid used in the PACU and the general ward were also recorded until POD 2. Certified nurses on the Acute Pain Service of our institution monitored all the patients thrice a day and recorded the amount of PCA solution used and the presence of any side effects. Postoperative opioid consumption was quantified via IV PCA and the amount of rescue opioid required during POD 2. PCA was discontinued if the respiratory rate was < 8 breaths/min, oxygen saturation was <95%, or when other PCA-associated adverse effects were noted. After disconnecting the IV PCA, the patients were treated with conservative treatment according to the adverse effects noted. The adverse effects of opioids were defined as nausea, vomiting, dizziness, pruritus, headache, urinary retention, respiratory depression, and tendency to fall asleep during IV PCA infusion. Nausea was defined as the sensation of having the urge to vomit. Vomiting was defined as the forceful evacuation of stomach contents. Respiratory depression was defined as a respiratory rate of < 8 breaths/min. All opioids, except remifentanil, that were administered to patients were standardized to IV morphine equivalent doses according to published conversion factors (IV morphine 1 mg = oxycodone 1 mg = fentanyl 10 μg = meperidine 10 mg).[11–14]

2.4. Statistical analysis

Categorical variables are presented as absolute numbers and percentages (%). Continuous variables are presented as means with standard deviation or medians with the interquartile range. Intra-group distributions of variables were evaluated for normality using the Kolmogorov-Smirnov and histogram tests. Fisher's exact test or χ^2 test was used to evaluate categorical variables and Student's t-test or Mann-Whitney U test was used to evaluate continuous variables. All statistical analyses were performed using the SPSS Statistics version 21 (SPSS, Inc., Chicago, IL). A 2-tailed P value of < .05 was considered to be statistically significant.

We performed a retrospective power calculation. Using cumulative morphine equivalent consumption (mg) during POD 2 as the primary outcome, the mean of the TIVA group was found to be 91.7, while the mean (SD) of the BA group was 136.9 (46.4), at 90% power and an alpha of 0.05, total 50 subjects would be required. Actual power calculated in the present data was 91.1%.

3. Results

After searching the information technology of service management database, we screened 137 patients who satisfied the inclusion criteria with elective LADG with gastroduodenostomy due to early stomach cancer from February 2013 to September 2014 at our hospital. Among these 7 were excluded from the study due to the exclusion criteria. We subsequently extracted records of 130 patients. Patients who had disconnected IV PCA (16 patients) due to side effects before POD 2 were excluded from the analysis. Finally, 114 patients were included in this study. These 114 patients were divided into the TIVA (46 patients) and BA (68 patients) groups (Fig. 1). In the TIVA group, 39 patients used oxycodone and 7 patients used fentanyl. In the BA group, all patients used fentanyl as a drug for IV PCA. Meperidine was used 4 times in the TIVA group and 5 times in the BA group.

Table 1 shows the demographic characteristics, the duration of GA, and intraoperative remifentanil consumption of the 2 groups. There was a significant difference for GA duration and intraoperative remifentanil consumption between the 2 groups. GA duration was longer in the BA group than the TIVA group (P = .030). Total intraoperative remifentanil consumption was greater in the TIVA group than in the BA group (P < .001). No statistically significant differences were observed with respect to age, gender ratio, height, weight, body mass index, and smoking habits between the 2 groups.

Morphine equivalent doses of opioid consumption, as a primary outcome, was significantly higher in the BA group than in the TIVA group during POD 2 except in the PACU (Fig. 2). On POD 1, the mean opioid consumption (mg) was 42.2 ± 17.6 in TIVA and 72.3 ± 27.7 in BA groups (*P* < .001). On POD 2, the mean opioid consumption (mg) was 37.6 ± 18.3 in TIVA and 53.0 ± 23.6 in BA groups (*P* < .001). There were no significant differences between the 2 groups in the PACU and the mean opioid consumption (mg) was 11.8 ± 4.2 in TIVA and 11.5 ± 4.3 in BA groups. The cumulative opioid consumption of POD 1 and 2 were adjusted for body mass index and are presented in Table 2. There was a significant difference between the 2 groups (*P* < .001). The incidence of rescue analgesic for postoperative pain for POD 1 and 2 is shown in Table 3. The incidence of rescue analgesic was higher in the BA group on both POD compared to the TIVA group. However, this was the only statistically significant difference on POD 2 (*P* = .029).

Postoperative pain intensity was measured using the NRS and no significant differences between the 2 groups were noted on POD 2 (Table 4). The incidence of postoperative adverse effects in patients receiving IV PCA after elective LADG with gastroduodenostomy is shown in Table 5. There was no significant difference in the incidence of postoperative adverse effects as secondary outcomes on POD 2 between the 2 groups. Additionally, other adverse effects including frequency of urinary retention, respiratory depression, and tendency to fall asleep were not observed.

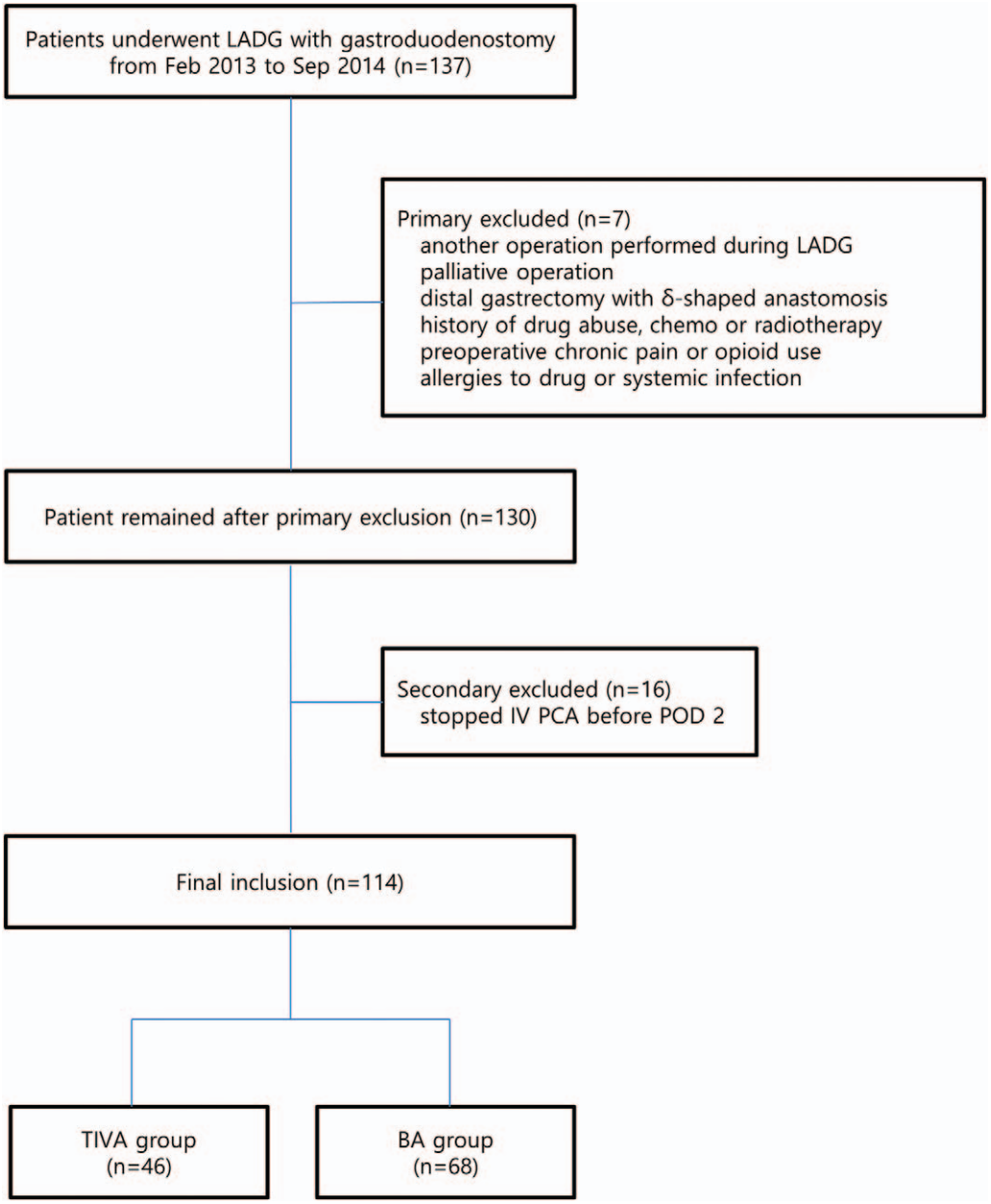

Figure 1. Flow diagram of the inclusion and exclusion criteria, along with the study design. BA = balanced anesthesia; IV = intravenous; PCA = patient-controlled analgesia; LADG = laparoscopic-assisted distal gastrectomy; TIVA = total intravenous anesthesia.

4. Discussion

Main results of this study demonstrated that the opioid consumption was significantly higher in the BA than TIVA group during POD 2 in patients who had undergone LADG with gastroduodenostomy. Additionally, the cumulative opioid consumption was significantly higher in the BA than TIVA group. However, there was no difference in the NRS or postoperative adverse effect incidence between the 2 groups. These findings suggest that similar analgesic effects can be achieved with lower doses of opioids in GA patients with TIVA than BA postoperatively.

Remifentanil use has become relatively prevalent in controlling pain associated with surgical procedures, but OIH and/or acute tolerance after surgery remains a challenge. It is understood that OIH occurs due to an opioid-mediated sensitization of the pain signaling pathway and acute tolerance is due to a desensitization of pain signaling pathways to opioids. Although OIH and acute tolerance are pharmacologically different, it is difficult to distinguish between the 2 since they are both associated with an increase in the opioid consumption to maintain the appropriate analgesic effect. An endogenous pain facilitatory system involving the N-methyl-D-aspartate (NMDA) receptor has been proposed as a mechanism of OIH.[15–18] The NMDA receptor antagonists such as ketamine and magnesium have successfully blocked opioid tolerance.[19,20] Studies have reported that clinically appropriate concentrations of remifentanil induced rapid and persistent increases in NMDA responses, associated

Table 1

Characteristics of patients who underwent laparoscopic-assisted distal gastrectomy under general anesthesia with total intravenous anesthesia or balanced anesthesia.

Parameters	TIVA (N = 46)	BA (N = 68)	*P-value*
Age (yr)	57.6 ± 11.3	57.9 ± 12.0	.898
Gender			.545
Male	30 (65.2%)	48 (70.6%)	
Female	16 (34.8%)	20 (29.4%)	
Height (m)	1.63 ± 0.08	1.63 ± 0.08	.579
Weight (kg)	61.7 ± 10.7	64.3 ± 10.7	.211
BMI (kg/m^2)	23.2 ± 3.2	23.9 ± 3.5	.247
Smoking			.766
Yes	27 (58.7%)	38 (55.9%)	
No	19 (41.3%)	30 (44.1%)	
Duration of GA (min)	171.5 (161.5–190.8)	190.0 (163.8–221.0)	.030
Intraoperative remifentanil consumption (μg)	3100.0 (2622.5–3717.5)	1208.0 (1100.0–1500.0)	<.001
BMI adjusted remifentanil* (μg/ kg/m^2)	140.4 (116.1–221.0)	53.0 (46.6–64.6)	<.001

Data are expressed as numbers (%), means ± standard deviation, or medians (interquartile range).

BA = balanced anesthesia; BMI = body mass index; GA = general anesthesia TIVA = total intravenous anesthesia.

* This value was adjusted for the total amount of administered remifentanil during the operation to BMI.

with the development of OIH and/or tolerance.[21] Interestingly, propofol plays a key role by inhibiting the NMDA subtype of glutamate receptors and might modulate postoperative hyperalgesia.[22,23] Singler et al demonstrated that propofol could delay and weaken remifentanil-induced hyperalgesia.[24] It has been reported that OIH and/or acute tolerance develop in a dose-dependent fashion.[7] However, it was interesting to note that in our results, OIH and/or acute tolerance were lower in the TIVA group with higher doses of remifentanil than in the BA group. We can assume that the effects of remifentanil and propofol on NMDA receptors were offset, resulting in lower OIH and/or acute tolerance in the TIVA group. Alternatively, maintenance of propofol with remifentanil provides better postoperative analgesia by suppression of OIH and/or acute tolerance by remifentanil, in the TIVA not the BA group.

Postoperative opioid consumption can be influenced by a range of variable factors such as gender, age, underlying disease, smoking habits, surgical characteristics, and opioid tolerance.[12] We have demonstrated that GA with TIVA reduces opioid consumption for postoperative pain control over GA with BA. Therefore, we can assume that propofol may have a more potent antagonistic effect on NMDA in OIH than that of desflurane.

Our results were supported by several studies which demonstrated that GA with TIVA was associated with less postoperative pain and opioid consumption than GA with inhalational anesthetics.[25–28] Although the effects of desflurane on OIH require further evaluation, a number of studies have demonstrated that sevoflurane and desflurane antagonized the NMDA receptor in a dose-dependent manner.[29,30]

Remifentanil dosing was significantly lower in BA than TIVA due to the fact that it plays only a supplementary role in BA. This was considered to be the reason associated with lower intraoperative consumption of remifentanil in the BA group. Additionally, the shorter durations of GA in the TIVA group was possibly because propofol is a short-acting drug and remifentanil is an ultra-short-acting drug. Ulusoy et al reported that recovery

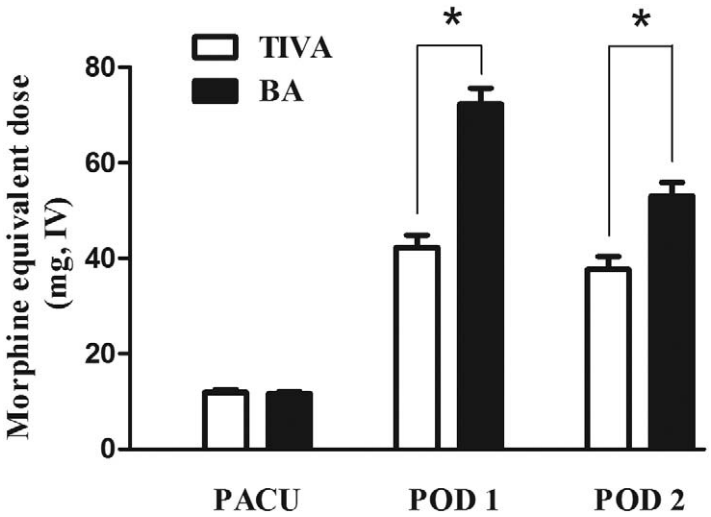

Figure 2. Postoperative opioid consumption in the post-anesthesia care unit, on postoperative day 1, and 2. *$P < .001$ in a comparison of the 2 groups. BA = balanced anesthesia; PACU = post-anesthesia care unit; POD = postoperative day; TIVA = total intravenous anesthesia.

Table 2

Postoperative opioid cumulative consumption.

Parameters	TIVA (N = 46)	BA (N = 68)	*P-value*
POD 1 cumulative (mg)	54.1 ± 19.9	83.8 ± 28.1	<.001
BMI adjusted POD 1 cumulative (mg/ kg/m^2)*	2.4 ± 0.9	3.5 ± 1.2	<.001
POD 2 cumulative (mg)	91.7 ± 32.0	136.9 ± 46.4	<.001
BMI adjusted POD 2 cumulative (mg/ kg/m^2)*	4.0 ± 1.5	5.8 ± 1.9	<.001

Data are expressed as means ± standard deviation. All opioid consumption was standardized to morphine milligram equivalents (IV morphine 1 mg = oxycodone 1 mg = fentanyl 10 μg = meperidine 10 mg).

BA = balanced anesthesia; BMI = body mass index; POD = postoperative day; TIVA = total intravenous anesthesia.

* This value was adjusted for the total amount of administered opioid to BMI.

Table 3

Incidence of rescue analgesics for postoperative pain.

POD	TIVA (N = 46)	BA (N = 68)	*P-value*
1	39 (84.8%)	62 (91.2%)	.292
2	11 (23.9%)	25.1 (45.6%)	.029

Data are presented as number (%).

BA = balanced anesthesia; POD = postoperative day; TIVA = total intravenous anesthesia.

Table 4

Numerical rating scale in the postoperative period.

Time after surgery	TIVA (N = 46)	BA (N = 68)	*P-value*
PACU 0 h	7.2 ± 1.2	7.7 ± 1.4	.062
0.5 h	6.2 ± 1.7	6.8 ± 1.6	.079
1 h	4.7 ± 1.4	4.8 ± 1.2	.563
POD1 8 h	5.8 ± 2.1	6.6 ± 2.3	.066
16 h	3.9 ± 0.9	3.6 ± 0.9	.103
24 h	3.8 ± 1.1	4.4 ± 2.0	.088
POD2 32 h	3.8 ± 1.5	4.3 ± 1.7	.137
40 h	3.5 ± 1.4	3.6 ± 1.4	.524
48 h	3.4 ± 1.3	3.7 ± 1.5	.264

Data are expressed as means ± standard deviation.

BA = balanced anesthesia; PACU = post-anesthesia care unit; POD = postoperative day; TIVA = total intravenous anesthesia.

Table 5

Incidence of postoperative adverse effects over time.

Parameters	TIVA (N = 46)	BA (N = 68)	*P-value*
POD 1			
PONV	5 (10.9%)	3 (4.4%)	.265
Dizziness	3 (6.5%)	1 (1.5%)	.301
Pruritus	1 (2.2%)	0 (0%)	.404
Headache	0 (0%)	1 (1.5%)	.409
POD2			
PONV	1 (2.2%)	1 (1.5%)	.779
Dizziness	4 (8.7%)	4 (5.9%)	.564
Pruritus	0 (0%)	1 (1.5%)	.409
Headache	0 (0%)	2 (2.9%)	.514

Data are presented as number (%). The adverse effects that did not occur in both groups were not shown.

BA = balanced anesthesia; POD = postoperative day; PONV = postoperative nausea and vomiting; TIVA = total intravenous anesthesia.

time was shorter in the TIVA group compared to BA.[31] It is our understanding that the reason could be attributed to the lower emergence time in TIVA than BA. PONV incidence was reported to be 25 to 73%, and the incidence of severe, intractable PONV was approximately 0.2 to 8% among patients that undergo surgery.[32–35] Among the various methods of controlling postoperative pain, IV-PCA has been extensively used, based on its improved pain control and minimal side effects such as PONV. Therefore, we controlled the postoperative pain with IV PCA and PONV incidence was 9%. Lower incidence of PONV could be attributed to IV ramosetron administration to all patients before starting the IV PCA.

In an effort to find the best anesthetic strategy, several studies have compared TIVA and BA or inhalational techniques in terms of the incidence of PONV, cost, recovery of cognitive function, and patient satisfaction in various surgical settings.[36–39] Adequate postoperative analgesic administration, such as of opioids, is crucial to the outcome of the surgery. Here, we first examined if there was a difference in the opioid analgesic requirements and the postoperative pain in patients undergoing LADG with gastroduodenostomy due to early stomach cancer between TIVA and BA. Typically, laparoscopic surgery offers many advantages over laparotomy, such as less pain, improved cosmetic effect, and faster recovery.[40] However, studies have reported that laparoscopic surgery may be associated with severe pain and need for higher concentrations of analgesia in the immediate postoperative period.[41] Therefore, our study is meaningful as it reveals the difference in opioid consumption for postoperative pain control according to the anesthetic method in patients who underwent LADG with gastroduodenostomy.

Our study had several limitations. First, our study had a retrospective design and a relatively small sample size. Data collection was limited because of the retrospective nature of the study. We could have improved the accuracy of the NRS by separately assessing pain while resting and moving. However, this retrospective study showed significant differences in postoperative opioid consumption dependent upon type of anesthesia. We think that several well-designed larger and/or randomized studies would be needed to reach a more definitive conclusion on the differences between TIVA and BA. Second, although multimodal analgesia is recommended for postoperative pain control,[42] the protocol followed in our institute does not permit the use of a regional block or epidural PCA to control the pain associated with laparoscopic surgery. Although the absence of multimodal analgesia contradicts the recent trend, it is our understanding that this data may successfully confirm opioid consumption for postoperative pain control in patients with total TIVA and BA. Finally, although all administrated postoperative opioids had been converted to morphine equivalent doses and analyzed, the use of multiple opioids was a limitation.

In conclusion, the outcomes of this study suggested that maintenance of GA with TIVA (propofol-remifentanil) reduces opioid consumption for postoperative pain control over BA (desflurane-remifentanil) in patients undergoing LADG with gastroduodenostomy.

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