Multimodal analgesia with thoracic paravertebral block decrease pain and side effects in mastectomy patients

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Abstract

Background: Enhanced recovery after surgery (ERAS) protocols incorporating multimodal analgesia (MMA) have become increasingly popular for breast cancer surgery. Our study evaluated an ERAS approach that combined nonintubated general anesthesia (GA) with thoracic paravertebral block (TPVB) as part of the MMA and compared it with traditional GA. Postoperative outcomes were assessed using numerical rating scale (NRS) pain scores, total analgesic consumption, and postoperative nausea and vomiting (PONV).

Methods: We reviewed the medical records of 60 female patients aged 30 to 85 years who underwent unilateral mastectomy with or without sentinel lymph node biopsy (SLNB). Thirty patients received nonintubated GA with a regional block (MMA group), whereas the remaining 30 patients received conventional GA and were matched based on their anesthesia records. Postoperative analgesics, including pethidine and tramadol, were converted into intravenous morphine equivalents. We compared the groups using paired *t* tests for age, height, weight, operation duration, NRS scores, total analgesic dosage, and the Fisher exact test for PONV rates.

Results: The MMA group showed significantly lower NRS scores ($p < 0.001$) and total analgesic consumption ($p < 0.001$) than the GA group. Although PONV rates were lower in the MMA group (0% vs 13%, $p = 0.112$), this difference was not statistically significant, likely due to the effective PONV management in the GA group with dexamethasone or 5-Hydroxytryptamine type 3 (5HT-3) antagonist. There was no significant difference in pain scores ($p = 0.722$) or the need for additional analgesics ($p = 0.419$) between double- and triple-level TPVB.

Conclusion: Nonintubated GA with total intravenous anesthesia (TIVA) and MMA using TPVB is a viable and safe alternative for breast cancer surgery. It results in reduced pain scores and analgesic needs compared with conventional GA, with PONV outcomes comparable to those managed with standard intravenous medications.

Keywords: Enhanced recovery after surgery; Intravenous anesthesia; Mastectomy; Paravertebral block; Postoperative complication

Lay Summary: This study evaluated the effectiveness and safety of nonintubated general anesthesia with total intravenous anesthesia (TIVA) combined with multimodal analgesia (MMA) using thoracic paravertebral block (TPVB) in patients undergoing mastectomy. 30 patients receiving MMA were compared to 30 patients under conventional general anesthesia (GA). The results showed that patients in the MMA group had significantly lower pain scores and required less postoperative pain medication. Furthermore, the incidence of postoperative nausea and vomiting (PONV) was comparable between the two groups, indicating that MMA with TPVB provides sufficient control over PONV, similar to standard intravenous antiemetic therapies. Overall, these findings support that nonintubated general anesthesia with TIVA and MMA utilizing TPVB is a viable, effective, and safe alternative for breast cancer surgery, offering improved pain management without compromising patient safety or increasing PONV risks.

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Conflicts of interest: Ling-Ming Tseng, an editorial board member at Journal of the Chinese Medical Association, had no role in the peer review process of or decision to publish this article. The other authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2025) 88: 486-491.

Received August 14, 2024; accepted November 12, 2024.

doi: 10.1097/JCMA.0000000000001218

1. INTRODUCTION

Enhanced recovery after surgery (ERAS) with multimodal analgesia (MMA) has recently been promoted in breast surgery.[1,2] Traditionally, breast surgery has been conducted under general anesthesia (GA) with endotracheal intubation, a method fraught with several disadvantages, including the risk of complications

<z10.1097/JCMA.0000000000001218>

related to airway management, postoperative respiratory complications, and delayed recovery.[3,4]

The concept of ERAS encompasses a range of perioperative strategies aimed at expediting recovery. Among these approaches, particular emphasis has been placed on multimodal intraoperative analgesia, including nonopioid analgesics and regional blocks, in prior studies.[2,5]

Recently, nonintubated breast surgery with a thoracic paravertebral block (TPVB) has emerged as an innovative approach in the field of breast surgery.[4] Since 2018, we have implemented the MMA protocol for breast surgery, which includes the use of nonintubated GA with TPVB under total intravenous anesthesia (TIVA). Compared with traditional GA, this technique offers several potential advantages, including reduced postoperative pain, decreased opioid consumption, faster recovery, reduced incidence of nausea and vomiting, improved patient satisfaction,[6–8] and reduced length of hospital stay.[9] Furthermore, avoiding endotracheal intubation mitigates the risk of airway-related complications, such as sore throat, hoarseness, and pulmonary complications.[7,10,11] The complication rate of TPVB is low in most previous studies (<2.6%).[4,12] Common complications include inadequate analgesia, hypotension, pneumothorax, vascular puncture, and paresthesia resulting from epidural spread of the local anesthetic agent.[13–15]

This study aimed to compare the numerical rating scale (NRS) pain score, total postoperative morphine dosage, length of hospital stay, and postoperative side effects (eg, nausea and vomiting) between GA and MMA for breast surgery.

2. METHODS

We reviewed the anesthesia records of patients who underwent breast surgery at Taipei Veterans General Hospital, Taiwan, between January 2019 and July 2021. The study was approved by the Institutional Review Board of Taipei Veterans General Hospital (approval number: 2021-10-003AC), and informed consent was obtained from all patients.

The initial sample comprised patients who underwent breast surgery, were aged between 30 and 85 years, were categorized according to American Society of Anesthesiologists (ASA) class I to II physical status, and underwent unilateral mastectomy with or without sentinel lymph node biopsy (SLNB) or modified radical mastectomy. Patients with incomplete data were excluded from the analysis. To mitigate the potential bias inherent in nonrandomized studies, propensity score matching was applied to create balanced treatment and control groups. Propensity scores were calculated using logistic regression, with age, height, weight, BMI, and type of surgical procedure as independent variables. Patients were matched 1:1 using a caliper width of 0.1 SDs of the logit of the propensity score. Nearest-neighbor matching was conducted to pair each treated patient with a control patient.

Thirty patients who received nonintubated GA with TPVB were categorized into the MMA group, and the paired groups were categorized into the GA group. Patients were allocated to the two groups after reviewing their anesthesia medical records (Fig. 1).

The MMA group (n = 30) received nonintubated GA with TPVB block and TIVA. In alignment with the ERAS protocol, patients received comprehensive education about the surgical and anesthetic processes before the operation. Patients were closely monitored using electrocardiography, noninvasive blood pressure monitoring, end-tidal carbon dioxide ($pETCO_2$) measurement via a nasal catheter, and oxygen saturation assessment using a pulse oximeter. Oxygen supplementation at a rate of 3 L/min was delivered through a standard nasal cannula, and a nasal airway was placed in all patients. To ensure a balanced anesthetic state and to promote early recovery, the bispectral index (BIS; Medtronic, Dublin, Ireland) was used to monitor the depth of anesthesia. Each patient received 0.1 mg/kg of

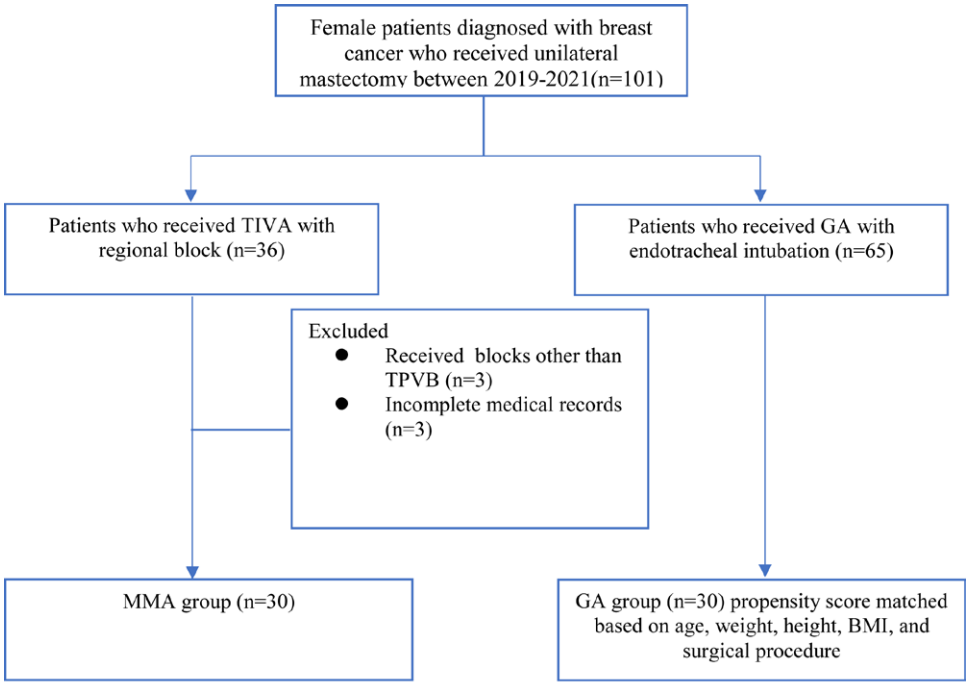

Fig. 1 Flow diagram of participant recruitment. BMI = body mass index; GA = general anesthesia; MMA = multimodal analgesia; TIVA = total intravenous anesthesia; TPVB = thoracic paravertebral block.

Table 1

Patient demographic and surgical data

Demographic	MMA group (n = 30)	GA group (n = 30)	*p*
Age (y)	60.1 ± 13.5	62.0 ± 12.8	0.58
Height (cm)	154.6 ± 16.0	156.0 ± 7.3	0.66
Weight (kg)	59.3 ± 9.2	59.9 ± 13.4	0.84
BMI ($kg \cdot m^{-2}$)	27.0 ± 17.4	24.6 ± 5.0	0.47
Operation time (min)	122.3 ± 36.8	107.8 ± 42.1	0.20
Intraoperative opioids	Remifentanil (μg)	Fentanyl (mg)	
	113.4 ± 110.8	143.3 ± 28.6	
PONV prophylaxis (n)	0 (0%)	9 (30%)	0.002*
Surgical procedure (n)			
Simple mastectomy + SLNB	24 (80%)	24 (80%)	
Modified radical mastectomy	6 (20%)	6 (20%)	

Data are expressed as mean ± SD or counts (%). BMI = body mass index; GA = general anesthesia; MMA = multimodal analgesia; PONV = postoperative nausea and vomiting; SLNB = sentinel lymph node biopsy.
*$p < 0.05$.

intravenous (IV) midazolam and was positioned in the decubitus position with the surgical side up. An experienced anesthesiologist performed the TPVB. The injection site was initially desensitized using 1 to 2 mL of 1% lidocaine, followed by 20 to 30 mL of 0.375% bupivacaine into the thoracic paravertebral space. Depending on the preference of the anesthesiologist, either two- or three-level paravertebral injections at the T1 to T6 spaces. All procedures were performed under ultrasound guidance (Sonosite X-Port; Fujifilm, Tokyo, Japan). Following the completion of the TPVB block, the patients were placed in a supine position, and propofol administration was initiated via target-controlled infusion (TCI) (Agilia, SB Medica SRL, Casalpusterlengo, Italy) at an initial rate of 1.5 μg/mL. The propofol rate was titrated to maintain the BIS target within the range of 40 to 60. Intraoperative opioids were administered with remifentanil or alfentanil TCI, with the choice left to the discretion of the anesthesiologist. Once the patient reached a sedation score of 2 on the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scale, surgery was commenced. The surgical site was cleaned and draped approximately 15 minutes after the nerve block was performed. An in-charge anesthesiologist adjusted the IV propofol TCI pump to maintain the target BIS range of 40 to 60. They also titrated opioids according to patient movement or intraoperative hemodynamic changes. Additional analgesics (parecoxib) were administered before wound closure. No prophylactic antiemetics, such as dexamethasone or granisetron, were administered during surgery. All patients received prophylactic oral acetaminophen 500 mg every 6 hours during the rest of their hospital stay. In addition, early mobilization, rehabilitation, and discharge were encouraged to adhere to the principles of the ERAS protocol.

In the GA group (n = 30), patients received GA with standard monitoring, such as electrocardiography, noninvasive blood pressure, pulse oximetry, and $pETCO_2$. All the patients were intubated using endotracheal tubes. GA was induced with propofol at a dose of 1 to 2 mg/kg IV and fentanyl at a dosage of 1 to 3 μg/kg IV. For endotracheal intubation, a muscle relaxant was administered, which included either cisatracurium (0.15-0.2 mg/kg) or rocuronium (0.5-1 mg/kg) via IV. Anesthesia was maintained with inhalational anesthetics such as desflurane or sevoflurane. Following the completion of the surgical procedure, a reversal agent, either sugammadex or neostigmine, along with atropine, was administered while the patient exhibited spontaneous breathing. All patients were extubated in the operating room after following instructions. Prophylactic antiemetics, such as 5 mg dexamethasone or 3 mg granisetron, were administered to patients with postoperative nausea and vomiting (PONV) and a history of motion sickness. All patients received prophylactic oral acetaminophen 500 mg every 6 hours for the rest of their hospital stay.

Medical records were reviewed, and the following data were recorded: age, height, weight, medical history, ASA grading, size, and location of the breast tumor, surgical procedure, maximal dose and total dose of propofol and opioids, operation time, and hospital stay. Pain scores were recorded using an NRS in the postanesthesia care unit (PACU) and postoperatively on the following day in the ward. The analgesic dosages, comprising morphine, pethidine,[16] and tramadol,[17,18] were standardized by converting them to IV morphine equivalents. PONV events were also recorded in the postoperative recovery room and ward. The experimental and control groups were paired according to age, height, weight, and surgical procedures.

Continuous baseline variables of the patients are expressed as mean ± SD and categorical variables as category counts and percentages.

The two groups were compared using paired *t* tests to measure age, height, weight, operation duration, NRS score, and total postoperative morphine dosage. The Fisher exact test was used to analyze the number of patients with PONV who required analgesics at the PACU and ward. The Mann-Whitney *U* test was used to analyze the NRS score and postoperative morphine dosage in the TPVB subgroup. Statistical significance was set at $p < 0.05$. Statistical analyses were performed using the SPSS statistical software package (version 28.0; IBM SPSS Statistics Inc., Chicago, IL).

3. RESULTS

The medical records of 60 patients were analyzed. No significant differences were observed between the two groups. In addition, there were no significant differences between the operation times. Table 1 shows that 30% of the patients in the GA group received PONV prophylaxis with either dexamethasone (n = 7, 23%) or granisetron (n = 2, 7%). No conversion to intubated GA or need for a high-flow nasal cannula was noted in the MMA group. No procedural complications, such as pneumothorax or hematoma, were observed in this study.

Patients in the MMA group exhibited a significant decrease ($p < 0.001$) in postoperative NRS scores in the PACU ($p < 0.001$) and ward ($p = 0.013$) (Fig. 2) percentage of patients requiring postoperative analgesics in the PACU and ward ($p < 0.001$ and $p = 0.010$, respectively). No significant differences were observed

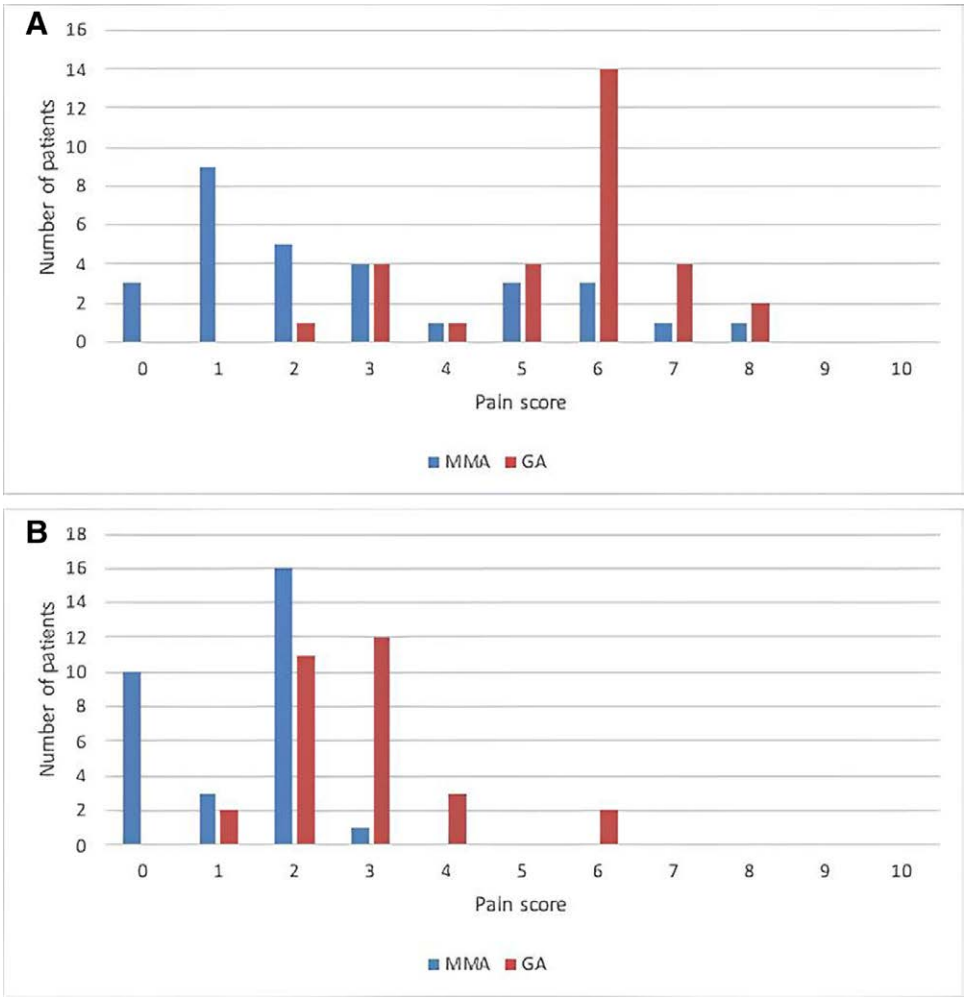

Fig. 2 Postoperative pain score at (A) PACU, (B) postoperative day 1. GA = general anesthesia; MMA = multimodal analgesia; PACU = postanesthesia care unit.

Table 2

Postoperative pain score, analgesics dosage, and PONV

	MMA group (n = 30)	GA group (n = 30)	*p*
NRS at POR (n)	2.8 ± 2.3	5.5 ± 1.5	<0.001*
NRS at postoperative day 1	1.9 ± 1.4	2.8 ± 1.6	0.013*
PONV (n)	0 (0%)	4 (13%)	0.112
Hospital stay (d)	1.7 ± 0.9	1.8 ± 1.0	0.791
Postoperative IV analgesic at POR (n)	8 (27%)	26 (87%)	<0.001*
Postoperative IV analgesic at ward (n)	4 (13%)	14 (47%)	0.010*

Data are expressed as mean ± SD or counts (%). BMI = body mass index; GA = general anesthesia; IV = intravenous; MMA = multimodal analgesia; NRS = numerical rating scale; PONV = postoperative nausea and vomiting; POR = postoperative room.
*$p < 0.05$.

between the MMA and GA groups in terms of PONV (p = 0.112) and length of hospital stay (p = 0.791) (Table 2).

Within the MMA group, we further categorized the patients into two subgroups: two-level and three-level TPVB groups. For dual vertebral level injections, T2, T4, T3, and T5 were administered. For triple-level injections, levels T1, T3, T5, or T2, T4, T6 were administered. The levels were chosen according to the anesthesiologist's preference. Our results did not reveal significant differences in postoperative pain scores (p = 0.722) or total postoperative analgesia scores (p = 0.419) (Table 3). However, there was a significant difference in the NRS score on postoperative day 1 ($p < 0.001$).

4. DISCUSSION

The findings of this study demonstrated a significant decrease in the NRS ($p < 0.001$) and a lower percentage of patients needing postoperative analgesic dose ($p < 0.001$) within the MMA group

Table 3

Postoperative pain score, analgesics dosage between single/double levels of TPVB

	Double level (n = 18)	Triple levels (n = 12)	*p*
Surgical procedure (n)			
Simple mastectomy	16 (89%)	8 (67%)	
Modified radical mastectomy	2 (11%)	4 (33%)	0.184
NRS at POR (score)	2.9 ± 2.4	2.6 ± 2.0	0.722
NRS at postoperative day 1 (score)	2.6 ± 1.0	0.9 ± 1.3	<0.001
Postoperative analgesic at POR (n)	6 (33%)	2 (17%)	0.419
Postoperative analgesic at ward (n)	8 (44%)	2 (17%)	0.235

Data are expressed as mean ± SD or counts (%). NRS = numerical rating scale; POR = postoperative room; TPVB = thoracic paravertebral block.

than in the GA group, even after accounting for age, height, weight, and BMI matching. These results highlight the potential benefits of implementing an MMA protocol for the perioperative management of patients undergoing surgery.

Pain management is an integral component of perioperative care, and optimizing analgesia is paramount to enhancing patient comfort, satisfaction, and overall recovery. Conventional GA techniques often rely on systemic opioids for pain management, which can lead to various side effects, including respiratory depression, sedation, nausea, and constipation. Moreover, opioid use can prolong the postoperative ileus and delay recovery.[2,3]

The significant decrease in the NRS pain score in the PACU observed in the MMA group signifies a heightened level of pain control in these patients. This finding is consistent with those of previous studies that have shown the effectiveness of multimodal analgesic techniques, such as local anesthetics, nonsteroidal anti-inflammatory drugs (NSAIDs), and regional anesthesia, in mitigating postoperative pain.[14,19,20] In addition, this decrease in the NRS pain score and need for analgesia in the ward continues to 1 day following the surgery, suggesting that the impact of pain management is not primarily observed immediately after the procedure but continues even beyond the duration of local anesthesia.

In the MMA group, only parecoxib, a COX-II inhibitor, was administered as an intraoperative adjuvant. At the PACU, pethidine or tramadol was administered as rescue analgesics if requested by the patient. By combining different analgesic modalities, MMA protocols can target multiple pain pathways and provide synergistic effects to improve pain management. The minimal dosage of opioids in the MMA regimen also contributed to reduced PONV and patient comfort. The outcomes of this study affirm the concept that the focus on MMA and regional anesthesia reduces the reliance on opioids during the postoperative phase.

The incidence of PONV was 0% in the MMA group and 13% in the GA group. However, it was not significantly different, which may be due to the small sample size. In the MMA group, no preventive PONV medications were administered, and no patients experienced PONV, which required additional nausea medications. In the GA group, nine patients (30%) received either dexamethasone or granisetron as preventive measures against PONV. In previous studies, prophylaxis with dexamethasone has been reported to reduce the risk of PONV. Compared with placebo, the number needed to treat to prevent PONV with dexamethasone was 7.1. In addition, when dexamethasone was used in combination with a 5-Hydroxytryptamine type 3 (5HT-3) receptor antagonist, the risk of PONV decreased from 33% to 3.9%.[21] Joo and Perks[22] reported a lower incidence of PONV in the propofol group than in the sevoflurane group. Similarly, Kumar et al[23] demonstrated comparable findings when comparing TIVA with propofol to GA inhalation using either sevoflurane or desflurane. In our study, PONV incidence using the MMA protocol was as effective as dexamethasone or 5HT-3 receptor antagonists in the GA group. This further supports the notion that TIVA and TPVB may be more comfortable protocols for patients undergoing breast surgery.

There was no significant difference in the length of hospital stay between the MMA and GA groups (1.8 ± 1.0 in the GA group vs 1.7 ± 0.2 in the MMA group, $p = 0.8$). Due to hospital policy and routine clinical practice, all patients were routinely discharged 1 or 2 days after surgery. This short hospital stay suggests that neither group experienced complications that necessitated extended admission.

The paravertebral space, a continuous area situated between the intercostal and epidural spaces, is cranially and caudally connected. Karmakar[4,24] reported that a single injection of 15 mL of 0.5% bupivacaine provided a mean coverage of five dermatomes for the somatic block and eight dermatomes for the sympathetic block. Cheema et al[25] found that the mean sensory level deficit extended by 2.2 segments above and 1.4 segments below the injection site. In a cadaveric study, Cowie et al[26] demonstrated that contrast dye spread to 4.5 segments in single-level TPVB injection and to six segments in double-level injection.

In our study, either two-level or three-level injections were administered. There were no significant differences in the postoperative pain score and postoperative analgesic dosage between the double-level (n = 18) or triple-level (n = 12) TPVB injections (Table 3). The significant numerical disparity between the two groups arises from the preferences of the anesthesiologists. However, a lower NRS score was noted on postoperative day 1 for those who received triple-level block. Kasimahanti et al[27] observed no discrepancy in the NRS score between the double- and single-level groups within the initial 24 hours postoperatively during total mastectomy and axillary clearance surgery. Also, the mean time to the first request for analgesics was delayed in the double-level group. Terkawi et al[14] noted that there was no significant difference in acute pain at rest between the single and multiple injection techniques. However, when evaluating pain during movement, multilevel block provides superior analgesia at 2, 48, and 72 hours postoperatively. It is plausible that during movement and with more severe pain, the enhanced anesthetic spread resulted in a significant pain reduction. Based on the comprehensive results of the above studies, we propose that triple-level injection may further prolong the efficacy of TPVB due to the greater spread of the medication and expanded area of analgesia. However, further studies are required to confirm this.

Although the results of this study provide valuable insights into the benefits of implementing the MMA protocol for pain management, there are several limitations. First, this was a single-center study that was conducted in Taiwan; the patients were all female Asians, and the results of the Asian population may not apply to all ethnicities. Second, our study was retrospective, which may have introduced inherent bias and limited our ability to establish causality. Although propensity score matching was used to create a comparable group, the lack of randomization may still introduce potential biases. Prospective randomized controlled trials are required to validate these findings and to provide stronger evidence for the benefits of the MMA protocol. However, it is important to note that age, height, weight, and BMI matches between the MMA and GA groups strengthened the validity of the observed differences in the pain scale and analgesic dose. By controlling for these factors, this study reduced the confounding effects of patient characteristics on pain perception and opioid requirements, thereby allowing a

more accurate assessment of the impact of the MMA protocol on pain management. Third, there were two intraoperative opioids, remifentanil, and alfentanil, chosen by anesthesiologists according to their practice. This could have affected the postoperative pain. Fourth, the study focused on the NRS pain score and postoperative analgesic dose as outcome measures; however, additional subjective measures such as patient-reported pain scores and satisfaction should also be considered to provide a more comprehensive assessment of pain management. These limitations should be addressed in future research.

In conclusion, the results of this study demonstrated that non-intubated GA using a TIVA and MMA protocol with TPVB is feasible and safe for breast surgery. It provides a significant decrease in the NRS score and the need for postoperative analgesics in the PACU. The PONV prevention ability was equivalent to that of IV PONV prevention medications such as dexamethasone and 5HT-3 antagonists. These findings support the notion that implementing an MMA protocol, with an emphasis on multimodal and regional anesthesia techniques, can improve pain management and reduce reliance on opioids in the postoperative period. Further research, including prospective randomized controlled trials, is warranted to confirm these results and explore additional subjective outcome measures to fully evaluate the impact of ERAS protocols on pain control and patient satisfaction.

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