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ORIGINAL RESEARCH

Effects of TTP-PECS Block Under Opioid-Sparing General Anesthesia on Postoperative Analgesia and Early Recovery Quality in Patients Undergoing Modified Radical Mastectomy

Yu Ma · Chunpei Wu · Zhengxia Sun · Lin Zhang · Miao Zhou · Jiaqi Chang · Hui Liu · Qingming Bian

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ABSTRACT

***Introduction*:** Potent analgesics such as sufentanil and remifentanil play a pivotal role in general anesthesia, but these medications have disadvantages, including respiratory depression, nausea, vomiting, immune system suppression, and gastrointestinal function inhibition. This study aimed to evaluate the effects of the transversus thoracic muscle plane–pectoral nerves (TTP-PECS) block on postoperative analgesia, immune function and early postoperative recovery quality in patients undergoing modified radical mastectomy under opioid-sparing general anesthesia.

***Methods*:** A total of 100 patients scheduled for modified radical mastectomy under general anesthesia were randomly divided into the TTP-PECS block combined with opioid-sparing general anesthesia group (TO group, $n = 50$) or the conventional general anesthesia group (GA group, $n = 50$). The TO group underwent TTP-PECS block prior to induction, using oxycodone as the analgesic during induction instead of sufentanil, no additional continuous infusion of analgesic was performed intra-operatively. Visual analogue scale (VAS) scores at rest and during movement at different time points were recorded in both groups, and the levels of T cell subsets, natural killer (NK) cells were measured before the surgery and at 24 h and 48 h after the surgery. Quality of Recovery-40 (QoR-40) scores were assessed at 24 h postoperatively, and the incidence of peri-operative adverse reactions was also observed in both groups.

***Results*:** Except for 48 h postoperatively, patients in the TO group had significantly lower VAS scores than those in the GA group at 2 h, 6 h, 12 h, and 24 h postoperatively at rest and during movement ($P < 0.05$). At 24 h and 48 h postoperatively, the expression of $CD4^+$ T cells and the $CD4^+/CD8^+$ ratio were significantly higher in the TO group than in the GA group ($P < 0.05$). The QoR-40 scale, assessed at 24 h postoperatively, showed that the TO group

Yu Ma, Chunpei Wu, and Zhengxia Sun have contributed equally to the manuscript: co-first authorship.

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Y. Ma · C. Wu · L. Zhang · M. Zhou · J. Chang · H. Liu (✉) · Q. Bian (✉)
Department of Anesthesiology, The Affiliated Cancer Hospital of Nanjing Medical University & Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research, Nanjing 210009, Jiangsu, China
e-mail: huilium@163.com

Q. Bian
e-mail: bqm2518@njmu.edu.cn

Z. Sun
School of Anesthesiology, Xuzhou Medical University, Xuzhou 221002, Jiangsu, China

significantly outperformed the GA group in total scores as well as in sub-scores for emotional state, physical comfort, physical independence, psychological support, and pain ($P < 0.05$). In addition, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were lower at time points T1–T4 than at T0 in both groups ($P < 0.05$), but the differences between the two groups were not statistically significant($P > 0.05$). The incidence of cough reflex during induction and postoperative nausea and vomiting were significantly lower in the TO group than in the GA group ($P < 0.05$). There was no statistically significant difference between the two groups in the incidence of other adverse reactions ($P > 0.05$).

Conclusions: The combination of TTP—PECS block and oxycodone–propofol opioid-sparing general anesthesia can provide superior postoperative analgesia and reduce the incidence of postoperative nausea and vomiting. It also alleviated the suppression of cellular immune function and improves the quality of early recovery in breast cancer patients. At the same time, opioid-sparing general anesthesia is a safe strategy for modified radical mastectomy.

Trial Registration: Chinese Clinical Trial Registry; ChiCTR2200066753.

Keywords: Transversus thoracic muscle plane; Pectoral nerves block; Oxycodone; Breast cancer; Quality of recovery-40 score

Key Summary Points

Opioid-sparing anesthesia is the combined with multimodal analgesic drugs and techniques that aim to reduce the use of opioids and the occurrence of associated adverse reactions, thereby facilitating rapid recovery of the patient.

Transversus thoracic muscle plane–pectoral nerves (TTP-PECS) block can provide effective analgesia for patients undergoing breast surgery, meeting the requirements for opioid-sparing anesthesia.

Oxycodone-propofol opioid-sparing general anesthesia with TTP-PECS block can be safely applied in modified radical mastectomy for breast cancer with its superior analgesia effect and a lower incidence of nausea and vomiting.

In patients undergoing modified radical mastectomy, the TTP-PECS block combined with oxycodone–propofol opioid-sparing general anesthesia not only enhances the quality of early recovery but also mitigates the immunosuppression induced by stress responses.

INTRODUCTION

Breast cancer, as the most prevalent malignant tumor among women, has become the second most common malignant tumor in the world, with its incidence rates escalating every year [1]. Modified radical mastectomy under general anesthesia remains a crucial surgical intervention for breast cancer. In general anesthesia, strong opioids with potent analgesic effects (e.g., sufentanil, remifentanil, etc.) are indispensable. However, these drugs have disadvantages, such as respiratory depression, postoperative nausea and vomiting, and suppression of immune and gastrointestinal function, which hinder the rapid recovery of patients in the early postoperative period.

Oxycodone as a μ, κ dual opioid receptor agonist, providing strong analgesic effects with a prolonged duration of action. Moreover, it exhibits mild respiratory depression and significantly less suppression of immune function than morphine, fentanyl, and remifentanil, among other advantages [2–4]. Theoretically, combining oxycodone with propofol for general anesthesia to minimize the use of opioids during modified radical mastectomy, without the need for sufentanil, remifentanil, or other potent opioids, can potentially diminish opioid-related adverse reactions, alleviate immunosuppression, and expedite patients' early recovery. However, concerns persist regarding whether this opioid-sparing general anesthesia approach

can adequately provide intra-operative analgesic efficacy.

In recent years, the proposed opioid-sparing anesthesia approach, which combined low-dose opioids with regional nerve blocks and non-opioid analgesics during the peri-operative period, has been gradually implemented in clinical practice. Multiple studies have consistently confirmed that peri-operative opioid-sparing anesthesia enhances surgical outcomes [5, 6]. Recent studies have demonstrated that the transversus thoracic muscle plane–pectoral nerves (TTP-PECS) block offers precise and effective analgesia for patients undergoing breast cancer surgery. This approach not only reduces the need for opioids but also maintains stable hemodynamic effects [7].

Hence, the present study employed TTP-PECS block along with oxycodone–propofol opioid-sparing general anesthesia for modified radical mastectomy. The primary objective was to assess its impact on postoperative analgesia, immune function, and the quality of early postoperative recovery.

METHODS

Study Design

This single-center, prospective, randomized controlled clinical trial investigated the advantages of TTP-PECS block under opioid-sparing general anesthesia. This study received approval from the Ethics Committee of Jiangsu Cancer Hospital (Approval number: 2022–043) and registered with the Chinese Clinical Trial Registry (https://www.chictr.org.cn, Registration number: ChiCTR2200066753). Informed consent forms were signed by all patients (or their families) prior to enrollment. This study included 100 female patients who underwent modified radical mastectomy under general anesthesia at Jiangsu Cancer Hospital from February 2023 to March 2024. The research was conducted in accordance with the Declaration of Helsinki and adhered to the applicable Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Patients

Inclusion criteria: patients scheduled for modified radical mastectomy; American Society of Anesthesiologists (ASA) physical status grade I or II; aged from 18 to 64 years old; body mass index (BMI) between 18.5 and 27.5 kg/m^2. Exclusion criteria: patients with severe cardiovascular and cerebrovascular diseases; significant hepatic and renal dysfunction; preoperative radiotherapy or chemotherapy; history of long-term opioid analgesic use; allergy to local anesthetics or opioids; infection at the puncture site; coagulation disorders; patients undergoing bilateral breast surgery; and refusal to participate by the patient or family members.

Randomization and Blinding

The participants were randomly assigned to two groups: TTP-PECS block combined with opioid-sparing general anesthesia group (TO group) and the conventional general anesthesia group (GA group). Randomization was performed by computer-generated random numbers with a fixed block size and a 1:1 ratio, each participant was allocated a unique randomization number, and all the allocations were sealed in an opaque envelope. A person not involved in the study opened this sealed envelope just before anesthesia. The anesthesiologist who attending general anesthesia was aware of the group assignments, and therefore was not blinded. Follow-up and data collection were performed by an anesthesiologist nurse who was unaware of the patient group assignments. The surgeons and patients were all blinded.

Anesthesia Protocol

Before surgery, all patients routinely underwent fasting. Upon entering the operating room, we established intravenous access in the

upper limbs, noninvasive blood pressure (NBP), SpO_2 and ECG were monitored, and they were connected to a Sedline brain function monitor. In the GA group, induction of anesthesia consisted of sequential intravenous administration of sufentanil 0.2 μg/kg, midazolam 0.04 mg/kg, propofol 1–1.5 mg/kg ,and cisatracurium 0.2 mg/kg. For the induction of anesthesia in the TO group, oxycodone 0.2 mg/kg, midazolam 0.04 mg/kg, propofol 1–1.5 mg/kg, and cisatracurium 0.2 mg/kg were injected intravenously in a sequential manner. After 3 min of mask ventilation, an appropriate type of laryngeal mask was inserted and connected to the anesthesia machine for mechanical ventilation. When the procedure began with skin incision, patients in the GA group received intravenous sufentanil 0.1 μg/kg, while those in the TO group received intravenous oxycodone 0.1 mg/kg for analgesia. Both groups of patients received a continuous intravenous infusion of propofol at a rate of 4–8 mg kg^{-1} h^{-1} during surgery. This maintained the Patient State Index (PSI) between 25 and 50, with adjustments made to the infusion rate based on the PSI values. The GA group was maintained with a continuous intravenous infusion of remifentanil (0.1–0.25 mg kg^{-1} h^{-1}), while the TO group did not receive any. Continuous intravenous infusion of cisatracurium (0.1–0.15 mg kg^{-1} h^{-1}) was chosen for intra-operative maintenance of muscle relaxation in both groups and was discontinued 30 min before the end of surgery. During the surgery, maintain NBP within 20% of the baseline value. If intra-operative NBP was less than 20% of the baseline, ephedrine (6 mg) or phenylephrine (40 μg) was given to elevate NBP as appropriate. When the heart rate (HR) was below 50 bpm, then intravenous atropine 0.5 mg was given to elevate it. Both groups of patients were weaned from all anesthetics at the end of surgery and transferred to the post-anesthesia care unit (PACU) for recovery. Pain was assessed using a visual analogue scale (VAS) and a rescue analgesic of 5 mg intravenous dezocine was administered if the VAS score was ≥ 4.

Transversus Thoracic Muscle Plane–Pectoral Nerves Block

Patients in the TO group underwent an ultrasound-guided TTP-PECS block prior to anesthesia induction. The patient was placed in the supine position with the surgical side arm abducted. After the standard disinfection and draping procedure, a sterile ultrasound sheath was wrapped around the ultrasound probe, and an ultrasound-guided pectoral nerve block(PECS) was performed first: at the junction of the medial and lateral thirds of the clavicle, the ultrasound probe was swept obliquely from inwardly superior to outwardly inferior, and the pectoralis major, pectoralis minor, and serratus anterior were identified at the level of the 3rd–4th intercostal space in the anterior axillary line. Using an in-plane approach, when the tip of the needle entered the space between the pectoralis minor and the serratus anterior muscle, it was aspirated to confirm the absence of gas and blood. Then, 20 ml of 0.3% ropivacaine was injected. The needle was retracted to the space between the pectoralis major and pectoralis minor muscles and 10 ml of 0.3% ropivacaine was injected after aspiration. Subsequently, a transversus thoracic muscle plane (TTP) block was performed: the ultrasound probe was placed between the 4th and 5th intercostal spaces, and the probe moved up and down in the coronal position to identify the pectoralis major, internal intercostal muscles, transverse thoracic muscles, and the intrathoracic arteries and veins. The same in-plane approach was used after determining the location of the transversus thoracis interspace (between the internal intercostal muscles and the transverse thoracic muscles). When the needle tip reached the plane of the transverse pectoralis, if no gas or blood was found upon aspiration, 1–2 ml of saline was injected first. Once the fluid was seen to be diffusing into the intermuscular space, an additional 15 ml of 0.3% ropivacaine was injected. All the above TTP-PECS blocks were performed by the same senior associate chief anesthesiologist. The level of pain block was tested using acupuncture method and the scoring criteria were as

follows [8]: 2 points for normal pain sensation; 1 point for decreased pain sensation; and 0 points for absent pain sensation. A score of ≤ 1 on the acupuncture method was considered a successful block, and those who failed the block were excluded from the group. General anesthesia induction began after completing the block plane test.

Outcome Assessment

Primary Outcomes

The primary outcome indicator were the VAS scores at rest and during movement at 2 h (T5), 6 h (T6), 12 h (T7), 24 h (T8), and 48 h (T9) postoperatively.

Secondary Outcomes

1. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR were recorded before anesthesia induction (T0), immediately before intubation (T1), at the time of skin incision (T2), at the time of excision of the breast specimen (T3), and at the end of the surgery (T4).
2. The expression levels of T cell subsets and natural killer (NK) cells were measured at time points T0, T8, and T9.
3. The Quality of Recovery-40(QoR-40) score was accessed at T8.
4. Occurrence of peri-operative adverse reactions, such as cough reflex during induction, intra-operative awareness, hypotension, postoperative agitation, nausea and vomiting, and pruritus, were also recorded.
5. The time of first eye opening (the duration from the cessation of anesthetic drugs to the first opening of the eyes) and the time of extubation (the time between the end of the surgery and the removal of the laryngeal mask) were recorded.

Sample Size

According to the results of the pilot test, it was found that the VAS scores during movement of the two groups were 3.2 ± 0.7 and 2.7 ± 0.6 in the postoperative 24 h, respectively. A two-sided test was used to formulate the significance level of 0.05 and the power of 0.9, allowing for a dropout rate of 20%. This calculation indicated that each group required a sample size of at least 47 cases. In this study, we finally included 50 patients in each group.

Statistical Analysis

All data were statistically analyzed using SPSS version 22.0 software. Data normality was tested using the Shapiro–Wilk test. For continuous variables that conformed to normal distribution, expressed as mean ± standard deviation. Comparisons between groups were made using the independent Student's *t* test. Continuous variables with skewed distributions were expressed as median (interquartile range) [M(IQR)]. The Mann–Whitney *U* test was used to compare differences between groups. Different time point comparisons within groups were analyzed using repeated measures ANOVA. Categorical variables were expressed as *n* (%), and analyzed using the Chi-square test or Fisher's exact test. A P value < 0.05 was considered a statistically significant difference.

RESULTS

General Information and Intraoperative Conditions

The nerve blocks in the TO group were all successful, and there were no complications related to the nerve blocks. This trial ultimately included 100 patients, with 50 patients in each group (Fig. 1). No patients withdrew from the trial. The comparison of general information and intra-operative conditions between the two groups of patients showed no statistically significant differences ($P > 0.05$; Table 1).

Primary Outcomes

The TO group exhibited significantly lower VAS scores than the GA group at the T5–T8 time points, both at rest and during movement

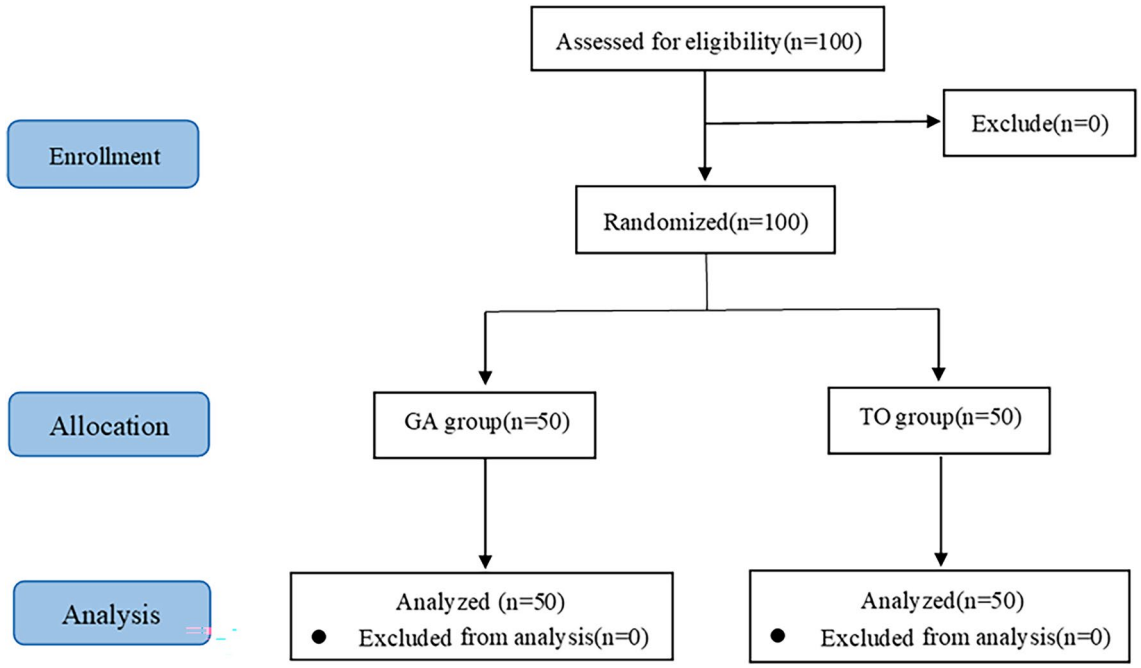

Fig. 1 CONSORT flow diagram of the study. *GA group* conventional general anesthesia group, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group

Table 1 Comparison of general and intra-operative conditions between the two groups

	GA group (n = 50)	TO group (n = 50)	P value
Age (years)	49.67 ± 7.17	49.28 ± 7.50	0.833
Height (cm)	161.00 ± 5.11	159.47 ± 5.29	0.249
Weight (kg)	55.61 ± 5.95	57.72 ± 7.48	0.509
ASA			0.677
ASA I	19 (38)	17 (34)	
ASA II	31 (62)	33 (66)	
Surgery time (min)	89.30 ± 13.73	90.75 ± 11.87	0.651
Propofol dosage (mg)	438.48 ± 62.22	423.59 ± 55.10	0.311
Eye opening time (min)	13.67 ± 2.79	12.88 ± 2.87	0.262
Extubation time (min)	16.91 ± 2. 80	15.85 ± 2.43	0.105

Continuous variables are expressed as mean ± standard deviation, categorical variables are expressed as n (%)

ASA American Society of Anesthesiologists, *GA group* conventional general anesthesia group, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group,

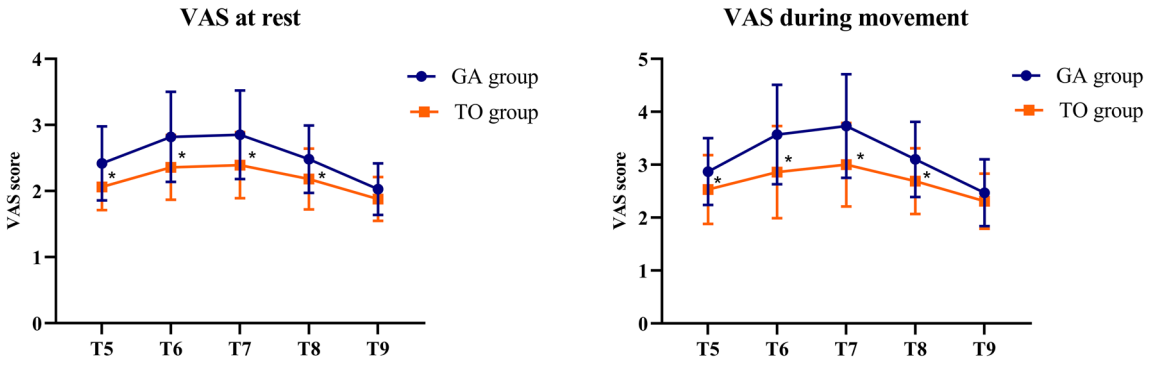

Fig. 2 VAS scores at rest and during movement during the 48 h postoperatively. Between the two groups at 2 h, 6 h, 12 h and 24 h postoperatively $^{*}P < 0.05$. T5, 2 h after surgery; T6, 6 h after surgery; T7, 12 h after surgery; T8, 24 h after surgery; T9, 48 h after surgery. *GA group* conventional general anesthesia group, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group, *VAS* visual analogue scale

($P < 0.05$). In contrast, the comparison of VAS scores between the two groups at the T9 time point, both at rest and during movement, showed no statistically significant difference ($P > 0.05$) (Fig. 2).

Secondary Outcomes

Intraoperative Variations in BP and HR

Compared with T0, both groups of patients showed significant reductions in SBP, DBP, and HR at the T1–T4 time points ($P < 0.05$). However, the comparison of SBP, DBP, and HR at each time point between the two groups showed no statistically significant difference ($P > 0.05$) (Fig. 3).

Indicators of Immunity

Compared with T0, the expression of $CD3^+$ T cells and NK cells was significantly reduced in both groups at T8 and T9 ($P < 0.05$). The GA group showed a significant decrease in $CD4^+$ T cells and $CD4^+/CD8^+$ at T8 and T9, while $CD8^+$ T cell expression significantly increased at T8 ($P < 0.05$). In the TO group, although $CD4^+$ T cells and the $CD4^+/CD8^+$ were significantly decreased at T8, they returned to levels close to T0 by T9 ($P > 0.05$). In addition, the TO group exhibited significantly higher of $CD4^+$ T cell expression and $CD4^+/CD8^+$ at T8 and T9 compared to the GA group ($P < 0.05$). There was no statistically significant difference between the two groups when comparing the expression levels of $CD3^+$, $CD8^+$ and NK cells ($P > 0.05$) (Fig. 4).

Quality of Recovery-40 Score

The total score of the QoR-40 scale and the scores for emotional state, physical comfort, physical independence, psychological support, and pain of the patients in the TO group were significantly higher than those in the GA group at the T8 time point ($P < 0.05$) (Fig. 5).

Perioperative Adverse Reactions

Neither group had intra-operative awareness. The incidence of cough reflex during induction and postoperative nausea and vomiting was significantly higher in patients in the GA group than in the TO group ($P < 0.05$). The difference in the incidence of intra-operative hypotension, postoperative agitation and other adverse reactions between the two groups was not statistically significant ($P > 0.05$) (Table 2).

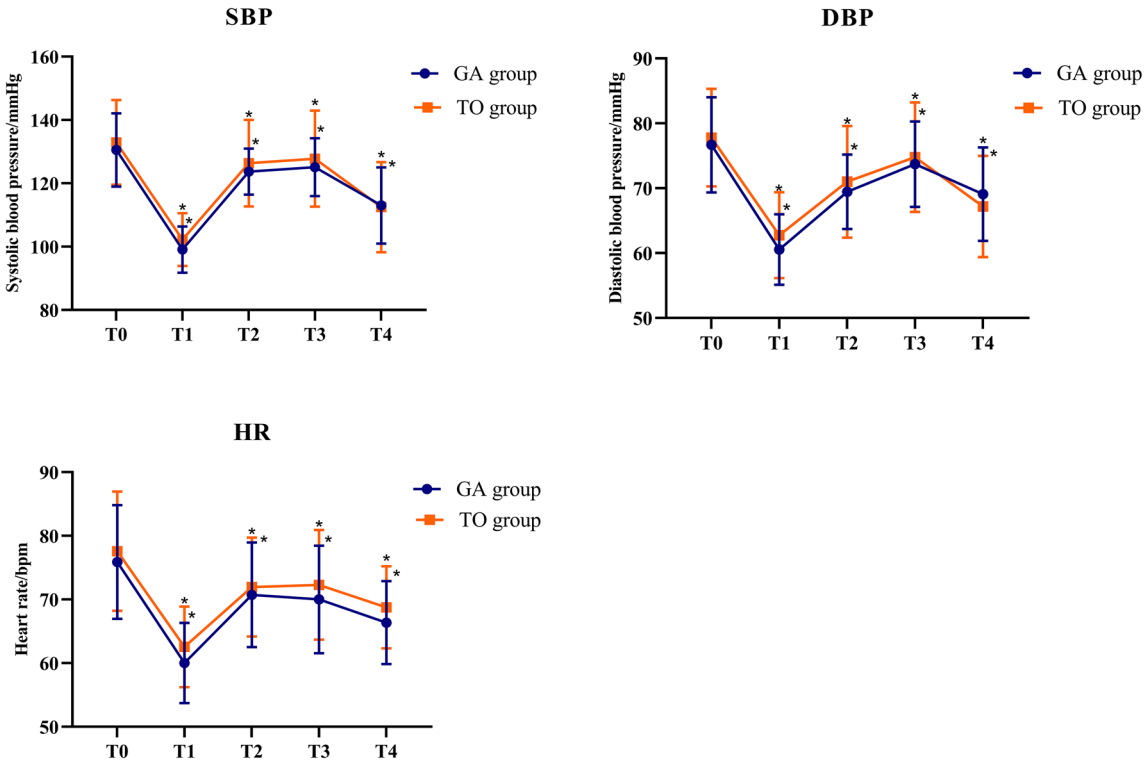

Fig. 3 SBP, DBP and HR at different intra-operative time points. Comparison with at T0, $^{*}P < 0.05$ vs. T0. *T0*, before anesthesia induction; *T1* immediately before intubation, *T2* at the time of skin incision, *T3* at the time of excision of the breast specimen, *T4* at the end of the surgery. *GA group* conventional general anesthesia group, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group

DISCUSSION

Our study demonstrated that oxycodone–propofol opioid-sparing general anesthesia assisted by TTP-PECS block applied in modified radical mastectomy for breast cancer reduced VAS scores at 2 h, 6 h, 12 h, and 24 h postoperatively, both at rest and during movement. In addition, this anesthesia protocol alleviated immunosuppression and improved the total score of QoR-40 scale and sub-scores. These results suggest that the TTP-PECS block under opioid-sparing general anesthesia could provide effective peri-operative analgesia and promote the early recovery quality of patients with breast cancer.

The rapid recovery of patients undergoing modified radical mastectomy for breast cancer is influenced by a numerous of factors, including surgical trauma, intra-operative stress responses, nausea and vomiting induced by potent opioid analgesics, suppressed gastrointestinal and immune function, and postoperative pain. Recent updates to the enhanced recovery after surgery (ERAS) guidelines for breast surgery have confirmed that a combination of intra-operative application of regional nerve blocks and a multimodal pain management strategy with minimizes opioid use peri-operatively can significantly alleviate pain, reduce opioid consumption, shorten hospital stays, and promote early recovery in patients following surgery [9, 10]. Oxycodone can simultaneously activate both μ and κ receptors, demonstrating effective analgesic properties for both incisional pain and visceral pain. Previous studies have confirmed that oxycodone not only provides superior analgesia compared to sufentanil, but also facilitates faster patient recovery with a lower incidence of adverse effects such as nausea and vomiting,

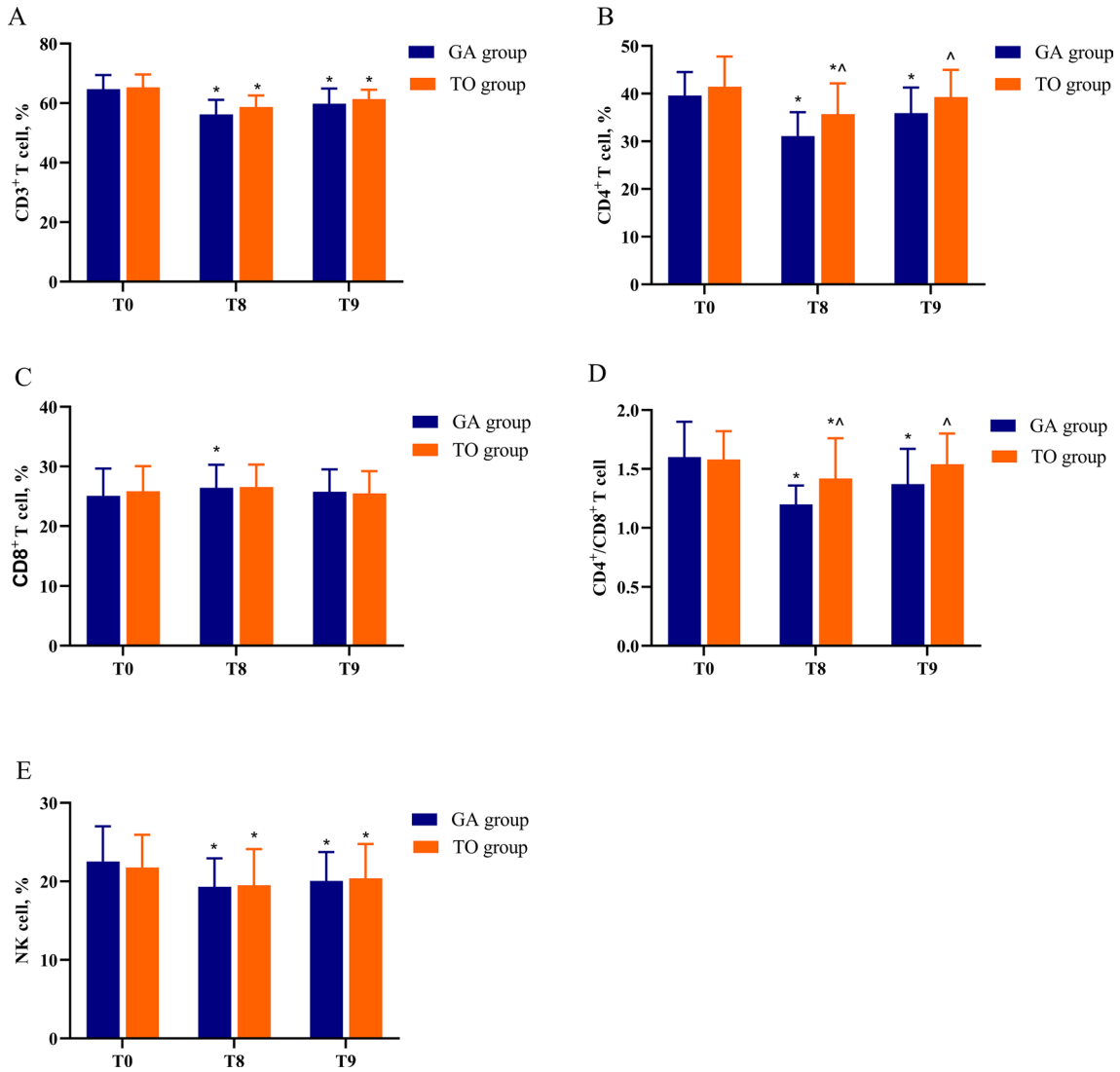

Fig. 4 Expression levels of $CD3^+$(A), $CD4^+$(B), $CD8^+$(C), $CD4^+/CD8^+$(D) and NK cells(E) at T0, T8, and T9. Comparison with at T0, $^*P < 0.05$. Compared with the GA group, $^\wedge P < 0.05$. *T0* before anesthesia induction, *T8* 24 h after surgery, *T9* 48 h after surgery. *GA group* conventional general anesthesia group, *NK* natural killer, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group

pruritus [11, 12], immunosuppression [2, 13], and postoperative cognitive dysfunction [14], which are in line with the ERAS surgical medication philosophy. However, total intravenous anesthesia with oxycodone–propofol alone may not be sufficient for surgical and anesthetic analgesia in modified radical breast cancer surgery. The combined application of regional nerve blocks (such as paravertebral nerve block, thoracic nerve block, and serratus anterior plane block) can not only meet the requirements for reduced opioid use but also provide adequate analgesia, thereby facilitating rapid recovery for patients.

In this study, we have investigated the analgesic effects of TTP-PECS blockade combined with oxycodone–propofol general anesthesia in patients undergoing radical mastectomy for

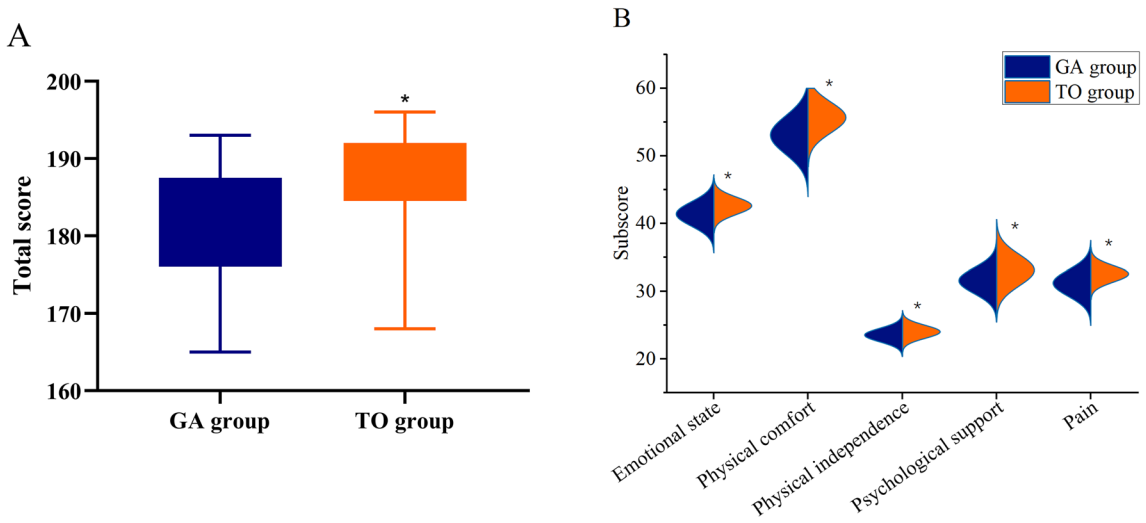

Fig. 5 Postoperative 24 h QoR-40 scale total score (**A**) and sub-scores (**B**). Compared with the GA group, $^{*}P < 0.05$. *GA group* conventional general anesthesia group, *QoR-40* Quality of Recovery-40, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group

Table 2 Comparison of the incidence of peri-operative adverse reactions between the two groups

	GA group ($n = 50$)	TO group ($n = 50$)	*P* value
Cough reflex during induction	9 (18.00)	0 (0.00)*	0.005
Intraoperative awareness	0 (0.00)	0 (0.00)	1.000
Hypotension	6 (12.00)	4 (8.00)	0.741
Postoperative agitation	3 (6.00)	0 (0.00)	0.241
Nausea and vomiting	10 (20.00)	2 (4.00)*	0.028
Pruritus	1 (2.00)	0 (0.00)	1.000

Categorical variables are expressed as *n* (%)

Compared with the GA group, $^{*}P < 0.05$. *GA group* conventional general anesthesia group, *TO group* transversus thoracic muscle plane–pectoral nerves block combined with opioid-sparing general anesthesia group

breast cancer, while also assessing its feasibility and safety. The TTP-PECS block provides adequate analgesia to the medial and lateral regions of the breast by combining PECS block and the TTP block. This approach addresses the limitations of the PECS block, which fails to provide adequate analgesia for the medial region of the breast, as well as the insufficient analgesic effect of the TTP block in the lateral region of the breast. It has been found that, compared with thoracic paravertebral block, the use of the TTP-PECS block during modified radical mastectomy for breast cancer provides superior postoperative analgesia, reduces inflammatory response, and promotes early recovery [8]. Nakanishi et al. [15] reported a case of a patient undergoing local extended mastectomy with sentinel lymph node biopsy of the breast, in which a satisfactory analgesic effect was achieved using a combination of TTP-PECS block and dexmedetomidine sedation during the procedure.

The results of this study showed that both groups of patients exhibited significantly lower SBP, DBP, and HR levels at the time points of

T1–T4 compared to T0. There were no significant differences in these parameters between the two groups at any given time point, indicating that both anesthesia methods provide effective analgesia and inhibit stress responses caused by anesthetic procedures and surgical stimuli. Importantly, no patients in our study experienced intra-operative awareness. Similarly, none of the patients were found to have nerve block-related complications such as pneumothorax, hemorrhage, infection at the puncture site, or toxic reaction to local anesthetic. These results strongly suggest that the use of oxycodone–propofol opioid-sparing general anesthesia regimen, supported by the TTP-PECS block, is both feasible and safe for modified radical mastectomy procedures.

In this study, we found that the TO group had significantly lower VAS scores than the GA group in both rest and movement states at T5–T8 time points by postoperative analgesic follow-up. This suggests that, compared with conventional general anesthesia, the TTP-PECS block combined with oxycodone provides better analgesia in patients undergoing modified radical mastectomy for breast cancer and lasts up to 24 h. Meanwhile, the incidence of postoperative nausea and vomiting was significantly lower in the TO group than in the GA group, which may be related to the fact that strong opioids such as sufentanil and remifentanil were not used in the TO group, coupled with oxycodone's inherently lower risk of these side effects. Furthermore, in the present study, we observed that patients in the GA group with sufentanil during the induction period had an 18% occurrence of developing a cough reflex, whereas no induction period cough reflex occurred in the TO group with oxycodone induction. Small doses of oxycodone were also found, in a study by Dai et al., to be effective in suppressing the fentanyl-induced cough reflex [16]. These findings suggest that the use of TTP-PECS block combined with oxycodone-propofol total intravenous anesthesia for modified radical mastectomy for breast cancer not only provides effective postoperative analgesia but also prevents opioid-induced cough reflexes during the induction period and reduces the incidence of postoperative nausea and vomiting by eliminating the need for potent opioid analgesics (such as fentanyl, sufentanil, and remifentanil), and thus reducing the occurrence of postoperative complications.

The findings of our study also revealed a notable decrease in $CD3^+$ T cells, $CD4^+$ T cells, $CD4^+/CD8^+$ ratio, and NK cells in both groups at 24 h and 48 h after surgery compared to pre-anesthesia induction ($P < 0.05$). This indicates that various factors, including surgical trauma, stress responses, anesthesia, and drugs, can lead to postoperative immunosuppression in patients. Previous studies have shown that suppression of immune function in the perioperative period may promote the growth of small residual lesions and circulating tumor cells after malignant tumor surgery, leading to tumor recurrence and metastasis [17, 18]. Therefore, enhancing the immune function of patients during the peri-operative period would be beneficial in reducing the risk of tumor recurrence and metastasis. Our study further demonstrated that, while both groups experienced some degree of immunosuppression postoperatively, the TO group exhibited significantly higher expression of $CD4^+$ T cells and a higher $CD4^+/CD8^+$ratio compared to the GA group at 24 h and 48 h after surgery ($P < 0.05$). Furthermore, the recovery of cellular immune function was accelerated in the TO group, with CD4 + T cell expression gradually returning to preoperative levels by 48 h after surgery. The findings of this study suggest that combining the TTP-PECS block with oxycodone–propofol opioid-sparing general anesthesia can reduce immunosuppression in the body. It may affect immune function through the following mechanisms. Pure μ receptor agonists, including sufentanil and remifentanil, activate the μ-opioid receptors in the central nervous system, stimulating the hypothalamic–pituitary–adrenal axis and the sympathetic-adrenal medullary system. This activation leads to the release of glucocorticoids and catecholamines, which indirectly suppress cellular immune function [19, 20]. On the other hand, it can also directly act on the μ receptors on the surface of immune cells, thereby reducing the proliferation of these immune cells [21]. However, the affinity of oxycodone for μ receptors is only 1/5 to 1/10 that of morphine [22],

resulting in a comparatively weaker immunosuppressive effect mediated by μ receptor activation. In contrast, in the TO group, the combination of TTP-PECS and oxycodone was applied intra-operatively, and sufentanil and remifentanil were not used, thus attenuating the immunosuppressive effects of these drugs. At the same time, the TO group also offers improved postoperative analgesic effects, which may mitigate the immunosuppressive effects of stress responses. Relevant studies indicate that high levels of the $CD4^+$, $CD8^+$ T cells, and $CD4^+/CD8^+$ ratio in tumor infiltration are favorable prognostic indicators for breast cancer [23]. In our study, the TO group exhibited significantly higher expression levels of $CD4^+$ T cells and $CD4^+/CD8^+$ ratios at 24 h and 48 h after surgery compared to the GA group. Although this research focused on serum T cell expression levels, the increase in serum T cell levels may correlate with an increase in tumor-infiltrating T cells, thereby providing a better prognosis.

The QoR-40 is one of the key scales used to assess the quality of postoperative recovery and health status in patients. It primarily evaluates five dimensions: emotional state, physical comfort, ability to perform self-care, psychological support, and pain, providing a comprehensive reflection of the patient's recovery quality following surgery. The QoR-40 scale scores are closely related to the quality of early postoperative recovery in patients [24]. The validity and reliability of the QoR-40 scale have been confirmed through various language versions [25–29]. Our study revealed that the total score on the QoR-40 scale, as well as the individual scores for emotional state, self-care ability, physical comfort, psychological support, and pain, were notably higher in the TO group compared to the GA group. This indicates that the TTP-PECS block combined with oxycodone–propofol total intravenous anesthesia can enhance the quality of early postoperative recovery for patients undergoing breast cancer surgery, facilitating a swifter recovery process.

There are certain limitations in this study: firstly, this study is a single-center, small-sample study, and further multi-center, large-sample clinical trials are still needed for validation in the future. Secondly, the follow-up period in this study was short, and a longer-term follow-up assessment would help to provide a comprehensive understanding of the long-term effects on patients. Thirdly, only the 24 h postoperative QoR-40 scale scores were assessed in this study, and additional implementation of the QoR-40 scale scores preoperatively and at 48 h and 72 h postoperatively may provide more compelling evidence. Finally, only the expression levels of T cell subsets and NK cells were measured, while the levels of stress hormones (such as plasma catecholamines and cortisol) and cytokine profiles were not measured.

CONCLUSIONS

The use of oxycodone–propofol opioid-sparing general anesthesia assisted by the TTP-PECS block can provide satisfactory intra-operative anesthesia, precise postoperative analgesia, reduce the incidence of postoperative nausea and vomiting, alleviate the suppression of cellular immune function, and enhance the quality of patients' early recovery. Meanwhile, this approach can be safely applied in modified radical mastectomy for patients with breast cancer.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Yu Ma, Chunpei Wu, Zhengxia Sun, Lin Zhang, Miao Zhou, Jiaqi Chang, Hui Liu, and Qingming Bian declare that they have no conflict of interest.

Ethical Approval. This study (2022–043) received approval from the Ethics Committee of Jiangsu Cancer Hospital. This trial was registered before patient enrollment at the Chinese Clinical Trial Registry (https://www.chictr.org.cn, ChiCTR2200066753). Written informed consent was obtained from all participants. This manuscript was conducted in accordance with the Declaration of Helsinki.

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