Randomized Trial

Ultrasound-Guided Pectoral Nerve Block I and Serratus-Intercostal Plane Block Alleviate Postoperative Pain in Patients Undergoing Modified Radical Mastectomy

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Background: Simultaneous application of pectoral nerve block and serratus-intercostal plane block (SPB) is one of the most desirable multimodal analgesic strategies, with wide implementation of the enhanced recovery after surgery pathway for modified radical mastectomy (MRM).

Objectives: The aim of the present study was to investigate the efficacy and safety of ultrasound-guided pectoral nerve block I (PECS I) and SPB for postoperative analgesia following MRM.

Study Design: A randomized, prospective study.

Setting: An academic medical center.

Methods: A total of 61 women undergoing MRM were randomly divided into 2 groups. The control group (group C, n = 32) received general anesthesia only, whereas the PECS I + SPB treated group (group PS, n = 29) received a combination of pectoral nerve block and SPB in addition to general anesthesia.

Results: Pain scores on a visual analog scale, opioid consumption, the duration at the postanesthesia care unit, and the incidence of adverse events were lower in group PS, compared with that of the group C. Moreover, PECS I together with SPB contributed to better sleep quality and higher patient satisfaction of pain relief.

Limitations: This study was limited by its sample size.

Conclusions: These results suggest that the combination of PECS I and SPB provide superior perioperative pain relief in breast cancer surgery.

Key words: Pectoral nerve block, serratus-intercostal plane block, postoperative analgesia, modified radical mastectomy

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Modified radical mastectomy (MRM), the surgical removal of the entire breast and axillary lymph nodes (1), is the most common surgical treatment for breast cancer, but results in severe acute postoperative pain (2) and is regarded as a risk factor for the development and persistence of postmastectomy pain syndrome (3,4). Another notable problem is a relatively high incidence of breast cancer-associated postoperative nausea and vomiting (PONV) (5). These unpleasant experiences may cause

critical impairments for postoperative recovery, such as poor sleep and delayed spontaneous ambulation (6). Therefore, there is an urgency to find a new approach to address these issues. Over the past few decades, a great deal of research has been conducted to pursue better analgesia in patients receiving MRM. Generally speaking, there are 4 main therapeutic options for patients undergoing MRM: thoracic epidural anesthesia (7), thoracic paravertebral block (8), intercostal nerve block (9), and pectoral nerve block (10).

Pectoral nerve block is a new approach of perioperative pain management of breast surgery (11) that has arisen along with the development and application of visualization technology. The pectoral nerve block I (PECS I) is a reliable superficial block that targets the medial and lateral pectoralis nerves originating from brachial plexuses, which can also be described as the innervation of major and minor pectoralis muscles (12). Serratus-intercostal plane block (SPB) is believed to be a viable alternative to paravertebral blockade and thoracic epidural analgesia (13). Fernández et al (14) have reported that all patients who had received an open nephrectomy had recorded a value of < 3 on the Numeric Rating Scale and a value of not more than 5 for dynamic pain. The results from Blanco et al (15) have demonstrated coverage from T2-T9 after deep serratus plane block performed at anterior axillary line. Until now, the most commonly used combined block for breast surgery was PECS I and pectoral nerve block II (PECS II) (16,17). The latter block, an interfascial approach between the pectoralis minor muscle and serratus anterior muscle, or virtually superficial to the serratus anterior muscle, provides analgesia of the lateral mammary region, intercostobrachial nerve, the long thoracic and thoracodorsal nerves, and lateral cutaneous branches of the intercostal nerves (T2-6) (11,18). The findings from Blanco et al (15) suggest that SPB helps to engender a better spread of local anesthetic, based on the occasional failure to produce adequate spread in the PECS II. In the current study, the issue of SPB being used for breast cancer has been shelved, because an in-depth randomized controlled trial was not conducted.

In this study, we only evaluate the efficacy and safety of an ultrasound-guided PECS I along with SPB for postoperative analgesia after MRM, and then validate the hypothesis that the combined nerve block procedure provides better pain management for patients with breast cancer.

Methods

Study Design

This was a prospective, randomized and double-blind clinical trial conducted at Renmin Hospital of Wuhan University, that was conducted after receiving approval from the research ethics board and registering with the Chinese Clinical Trial Registry (registration number: ChiCTR1800016331).

Inclusion and Exclusion Criteria of Study Subjects

We enrolled women aged between 18 and 55 years who had undergone MRM under general anesthesia, who were of the American Society of Anesthesiologists (ASA) physical classification I or II, and a body mass index (BMI) of 35 kg/m^2 or less. Patients with a long history of opioid or nonsteroidal anti-inflammatory drug use, skin infections at the puncture site, coagulation disorders, morbid obesity (BMI > 35 kg/m^2), allergic to local anesthetic, severe cardiopulmonary disease, renal and liver dysfunction, known or suspected neurologic deficits and mental illness, as well as those who rejected the pectoral nerve blocks and the follow-up survey after 48 hours were excluded.

Randomization and Blinding

All patients gave written informed consent to participate. Through an online computer-generated randomization service, we assigned the patients into 2 groups: a general anesthesia group (group C) and a general anesthesia plus pectoral nerve block and SPB group (group PS). The results of group assignment were concealed in sequentially numbered envelopes and deposited with the research coordinator for keeping. Before surgery, the research coordinator handed an envelope to staff anesthesiologists in the block procedure room. Postanesthesia care unit (PACU) nurses, follow-up personnel, and the patients of the study were unaware of randomization.

Nerve Block Procedure

On the day of surgery, only patients of group PS received pectoral nerve block. For the PECS I procedure, patients were placed in the supine position with standard ASA monitors including electrocardiogram, pulse oximetry, and noninvasive blood pressure. After skin sterilization was performed with 1% povidone-iodine (Yunzuo, China), a high-frequency linear array probe (6-13 MHz; Acclarix AX8 Compact Ultrasound System,

Edan, China) was placed in the transverse position on the medial aspect of the coracoid process, underneath the clavicle. We then obtained a view of the third rib and identified the thoracoacromial artery, the pectoralis major and minor muscles. A 22-G atraumatic needle, used for the peripheral nerve blocks (B. Braun Medical Industries Sdn Bhd, Penang, Malaysia), was inserted using a lateral to medial in-plane approach, and 10 mL of 0.3% ropivacaine was injected into the fascia between the pectoralis major and minor muscles.

For the SPB procedure, patients were placed in a lateral decubitus position. Furthermore, we moved the probe inferiorly and vertically down to the fifth rib for recognition of the serratus anterior muscles at the midaxillary level. Finally, the needle was punctured in-plane and advanced to a caudal-to-rostral orientation until the needle tip was beneath the serratus muscles, and subsequently 20 mL of 0.3% ropivacaine was injected into the fascia under the serratus muscles.

Block Evaluation

The blinded investigator performed the post-block assessment of sensation to temperature and pain. Sensory blockade was assessed for up to 30 minutes and compared with the nonoperative chest wall. Heat sensation assessment was implemented every 5 minutes using an alcohol-dipped cotton bud applied to the thoracic cutaneous areas, in contrast with the contralateral breast. Analgesia assessment was executed every 5 minutes using a pinprick with a 20 mL syringe applied to the skin above, in comparation with the other side of the chest. A block was regarded as successful if a loss of sensation to the pinprick was achieved within 30 minutes of the end of local anesthetic injection. The anesthesia level of ultrasound-guided SPB was recorded.

Intraoperative Management

General anesthesia was induced using propofol (2 mg/kg, intravenous [IV]), cisatracurium (0.3 mg/kg, IV), and sufentanil (0.3-0.5 mcg/kg, IV), for the application of endotracheal intubation. A continuous infusion of propofol and remifentanil acted as a supplemental analgesia, if necessary, to maintain anesthesia. A Narcotrend monitor was used for appropriate depth of anesthesia with a Narcotrend (MonitorTechnik, Bad Bramstedt, Germany) index between 20 and 46, or Narcotrend phase from E1 to D2. A 5 mg IV dose of dexamethasone and 5 mg IV dose of metoclopramide was administered for PONV.

Postoperative Management

All patients were delivered to the PACU after extubation, and scheduled to be discharged from the PACU when their Steward score was ≥ 4. The patients were treated with morphine that was equivalent to 2-5 mg IV when they complained of moderate and severe incision pain (visual analog scale [VAS]) that was recorded as ≥ 4 on a VAS (0-10 cm; 0 = no pain and 10 = worst pain imaginable). PONV in the PACU was treated with a 5 mg IV dose of tropisetron administered by blinded PACU nursing staff.

Outcomes

Preoperatively, we gathered common clinical data such as age, weight, and the ASA physical classification. Intraoperatively, we recorded the side of incision, the duration of surgery, the dosage of opioid analgesics, and whether a supplemental analgesic was required. The postoperative outcome assessment included 1) time to first analgesic request (minutes); 2) time to PACU discharge (minutes); 3) postoperative pain severity (rest-activity) at 1, 3, 6, 12, 24, and 48 hours; 4) patient satisfaction with pain relief; 5) sleep quality within 48 hours of surgery; and 6) incidence of adverse events, such as nausea, vomiting, pruritus, serious respiratory depression, pneumothorax, and dizziness.

Statistical Analysis

According to our pilot data, an estimated 15 cases per group would be needed to provide 90% power for independent populations, assuming a different opioid consumption of 5 mg (corresponding to a median opioid consumption of 24.8 mg, with a standard deviation of 3.9), with a unilateral α of 0.05. Through the use of SPSS Version 16.0 software (SPSS Inc., Chicago, IL), data were presented as mean and standard deviation for continuous factors or numerical variables, and as frequencies or proportions for categorical factors. Continuous variables were analyzed using the Student independent 2-sample t test followed by the test for homogeneity of variance, whereas categorical data were analyzed using the chi-square test. A P value of < 0.05 was considered as significant difference.

Results

Patient Characteristics

This study was performed conforming to Consolidated Standards of Reporting Trials (CONSORT) guidelines on reporting parallel group randomized

trials (19). Seventy eligible patients were enrolled in the study, of which 5 did not meet the inclusion criteria and 4 refused, resulting in 61 being recruited. Figure 1 shows the CONSORT diagram for recruitment to the trial. The 2 cohorts were well matched for demographic data and showed no statistical difference (Table 1).

Levels of Regional Analgesia

Figure 2 shows ultrasound images of PECS I and SPB. Sensory assessment of the level of anesthesia was performed at 2 time points: 30 minutes after regional nerve blockade, and in the PACU. Our findings show that SPB had been successfully implemented on all patients for pain control ranging from T2 to T5 within 30 minutes after nerve blockade, whereas it ranged from T2 to T7 in the PACU. At the first time point, segmental nerves T6, T7, T8, and T9 were involved in 89.7% (26), 72.4% (21), 41.4% (12), and 24.1% (7), respectively, of the 29 cases. The PACU assessment revealed that the thoracic nerves T6, T7, T8, and T9 were subsequently identified in 100%, 100%, 79.3% (23), 55.2% (16), and 10.3% (3) of patients, respectively. In addition, we noticed that in 3 cases the local anesthetic had spread from T2 to T10 (Fig. 3).

Postoperative Pain and Opioid Consumption

To determine the impact of PECS I and SPB on postoperative pain, we observed VAS scores 1, 3, 6, 12, 24, and 48 hours after surgery between group C and group PS. Patients undergoing PECS I and SPB

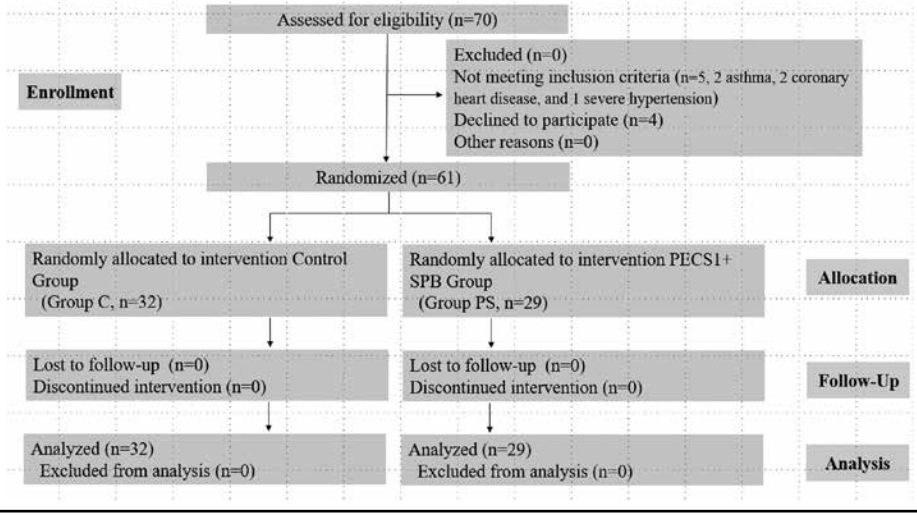

Fig. 1. *CONSORT flow diagram of patients.*

Table 1. *Demographic characteristics of study patients*

	Group C (n = 32)	Group PS (n = 29)	*P*
Age (years)*	55.38 ± 11.47	51.34 ± 8.20	0.123
Height (cm)*	161.06 ± 4.07	162.52 ± 3.71	0.151
Weight (kg)*	57.61 ± 6.98	58.74 ± 7.39	0.541
ASA status (I/II)&	10/22	9/20	0.986
Surgical side (left/right)& Duration of surgery (min)*	14/16 118.59 ± 34.53	15/14 120.24 ± 29.55	0.698 0.843
Duration of anesthesia(min)*	146.88 ± 40.28	147.48 ±2 9.04	0.947

*Values are presented as mean ± SD (unequal variance assumption, independent-samples t test). & Results are shown as numbers (chi-square tests)
ASA indicates American Society of Anesthesiologists.

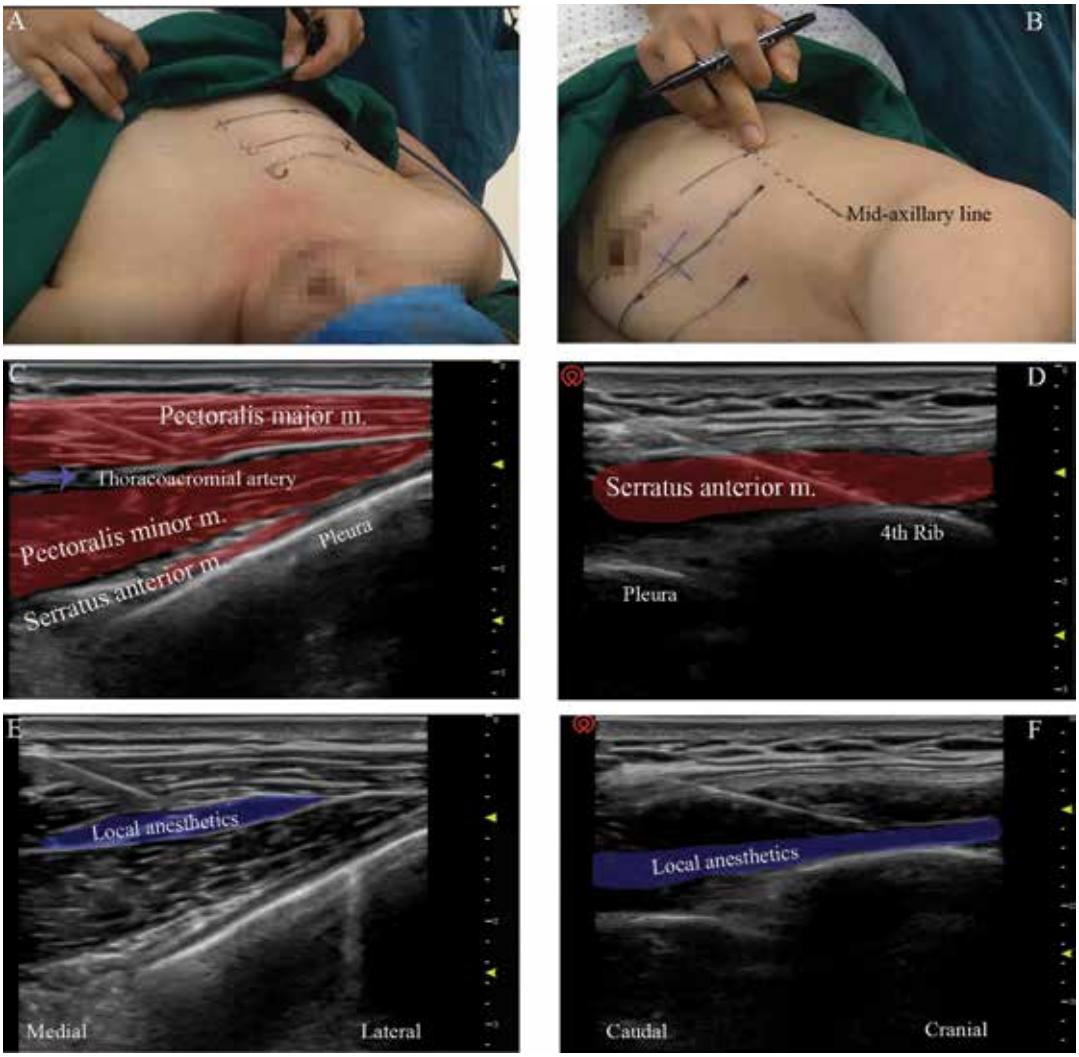

Fig. 2. *Sonographic anatomy of ultrasound-guided PECS I (A,C,E) and SPB (B,D,F). (A-B) Position of the ultrasound transducer and needle. (C-D) Ultrasound images of the muscles forming the anterior and lateral chest wall, and puncture route of the linear ultrasound transducer. (E-F) The spread of local anesthetics in the interval fascia between the pectoralis major and minor muscles for PECS I, and under serratus anterior muscles for SPB.*

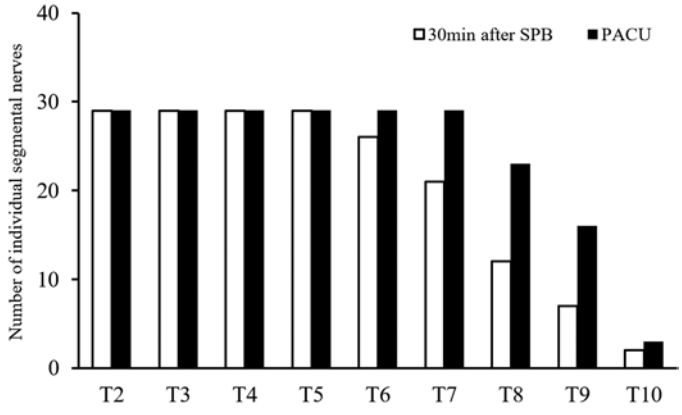

Fig. 3. *Dermatomal sensory distribution of the SPB. T2-T10 thoracic nerve roots.*

recorded decreased VAS scores at these 6 time points during quiet and active periods, compared with that of the group C (Fig. 4). Intraoperative consumption of IV morphine equivalence was significantly less for patients in the PECS I + SPB treatment group (18.10 ± 4.76 mg) compared with that of the group C (21.22 ± 4.17 mg) (P = 0.008) (Table 2). Furthermore, patients who received the nerve block anesthesia were discharged from the PACU approximately 14 minutes earlier than those in the group C (66 ± 18.7 vs. 52.28 ± 13.43; P = 0.002; Table 2). However, the nerve block therapy did not affect the mean time to the first request of an analgesic (Table 2).

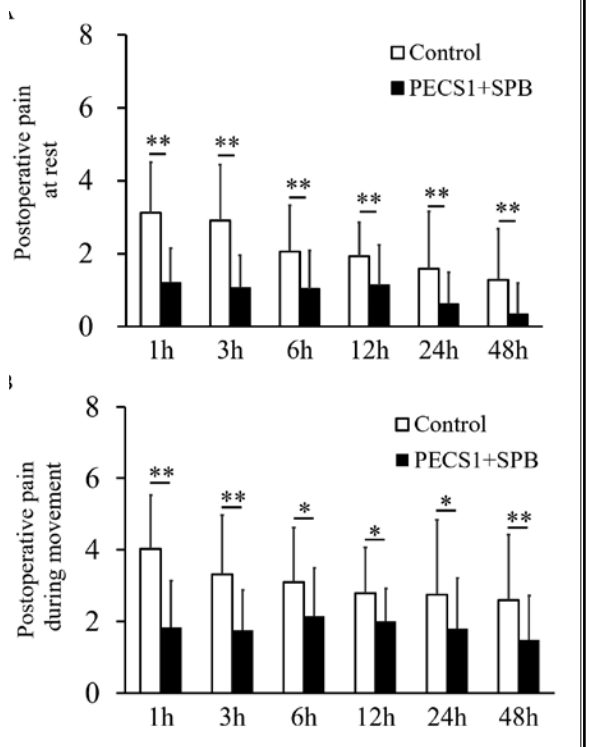

Fig. 4. *Favorable effects of PECS I and SPB on postoperative pain during quiet (A) and movement (B) stages. Data are expressed as mean ± SD. **P < 0.01 versus group C, *P < 0.05 versus group C, by independent sample t test.*

Patient Satisfaction, Sleep Quality, and Side Effects

Patients were requested to score their satisfaction using either Yes or No. The patients with breast cancer administered with an ultrasound-guided regional anesthesia felt more satisfied with pain relief, compared with those who were under general anesthesia alone (46.9% vs. 79.3%; P = 0.009; Table 2). Moreover, analysis of sleep quality between the control and the pectoral nerve block group revealed a statistical difference only in the first night after mastectomy (Table 2). The incidence of subjective nausea, vomiting, pruritus, and dizziness was exhibited significantly less in the group PS compared with that of the group C (Table 3). No other side effects such as serious respiratory depression or pneumothorax were observed in either study group (Table 3).

Discussion

In the present study, we have illustrated a typical probe position, needle-probe orientation, and the corresponding ultrasonography with the needle tip of PECS I and SPB. The follow-up results indicate that the addition of SPB to PECS I provides superior postoperative analgesia for patients undergoing MRM, because it results in a lower VAS score, less intraoperative opioid consumption, fewer postoperative adverse events,

Table 2. *Analgesic, satisfaction and quality of sleep.*

	Group C (n = 32)	Group PS (n = 29)	*P*
Intraoperative IV morphine equivalent consumption (mg)*	21.22 ± 4.17	18.10 ± 4.76	0.008
Time to first analgesic request (min) *	107.72 ± 33.37	119.76 ± 29.87	0.145
Time to PACU discharge (min) *	66 ± 18.7	52.28 ± 13.43	0.002
Patient satisfaction with pain relief+	15 (46.9%)	23 (79.3%)	0.009
High quality of sleep+			
The first night after operation	6 (18.8%)	17 (58.6%)	0.001
The second night after operation	20 (62.5%)	25 (86.2%)	0.07

*Data are presented as mean ± SD (unequal variance assumption, independent-samples t test). +Results are shown as numbers (proportion) (chi-square tests).

Table 3. *Postoperative Adverse Events of Patients between the group C and the PECS+SPIB-treated group.*

	Group C (n = 32)	Group PS (n = 29)	*P*
Nausea	17 (53.1%)	8 (27.6%)	0.043
Vomiting	15 (46.9%)	6 (20.7%)	0.032
Pruritus	13 (40.6%)	5 (17.2%)	0.046
Serious respiratory depression	0	0	1
Pneumothorax	0	0	1
Dizziness	8 (25.0%)	1 (3.4%)	0.045

Data are presented as numbers (proportion) (chi-square tests).

higher satisfaction, and better sleep quality during the first night after operation, compared with those who received only general anesthesia.

After the development of pectoral nerve blocks, a randomized controlled trial by Cros et al (20) has shown that PECS I does not improve postoperative analgesia after breast cancer surgery, whereas several other studies have provided evidence that PECS II is an effective pain management strategy for patients undergoing mastectomy (16,21-23). Likewise, an increasing number of experiments have focused on the efficacy and safety of PECS I combined with PECS II applied to MRM (17,24). In contrast, there are no reports evaluating the effect of SPB used for patients with breast cancer. To our knowledge, the current study is the first to observe the efficacy of PECS I and SPB for patients undergoing mastectomy. Blanco et al (15) found that sensory loss ranged from T2 to T9 after injection of 0.4 mL/kg of 0.125% levobupivacaine for SPB. Researchers in Japan detected that the area of sensory loss measured using a skin prick extended to 5 to 6 intercostal spaces (25). Fernández et al (26) have suggested that SPBs can lead to the blockage of the last few intercostal nerves (T7-T11). Evidence from a pig model indicated that the administration of 10 mL of iopamidol showed a mean spreading of 2.28 ± 0.31 (95% CI: 2.01-2.54) to intercostal spaces, whereas the administration of 20 mL showed a spreading of 3 ± 0.25 to intercostal spaces (27). In our findings, we also demonstrated that the spread of the local anesthetic for 10.3% of the patients ranged from segmental nerves T2 to T9. It is noteworthy that almost all patients exhibited insensitivity to skin pricks in the area located from T2 to T6, whereas 3 of the 29 patients even recorded sensory deficit in the anterolateral abdominal wall of umbilicus plane (T10). Kulhari et al (28) have observed consistent dermatomal spread in T2-T5 segments, which extended up to T6 with a probability of 25%. As is well known, the lateral aspect of the breast is innervated by lateral cutaneous branches of the second to sixth thoracic intercostal nerves (4). It is apparent that SPB can paralyze a larger number of intercostal nerves than PECS II is able to, which may innervate the mammary gland and the lateral and anterior cutaneous branches of the second to sixth thoracic intercostal nerves (29,30), and present a potential substitute for PECS II.

Consistent with the advantages of other regional anesthetic techniques suitable for breast cancer surgery (7,31-33), we have also provided insights into the beneficial effect of the simultaneous application of PECS I and SPB for postoperative pain relief, opioid consumption, patient satisfaction, and complications of anesthesia that include PONV, pruritus, and dizziness. However, unlike other studies, there was no difference found in the time taken for the first request of supplemental analgesic between the PECS I + SPB group and the group C. This phenomenon may be explained by the routine use of opioid agonist-antagonists or nonsteroidal anti-inflammatory drugs in the surgical ward. Moreover, we demonstrated that during the first night after surgery, more than half of the patients who were treated with a regional block slept very well, and also showed lower incidence of PONV, itchiness, and dizziness. It is widely accepted that severe PONV is associated with postoperative fever, poor quality of recovery, and prolonged hospitalization (34,35).

However, our study has a few limitations. The absence of outcomes from other centers resulted in few comparative samples. Sensory dermatome examination was performed using a pinprick test that has low reliability. The appropriate opportunity of postoperative rescue analgesic administration was incompletely controlled, and the consumption of postoperative additional anodyne was not calculated. Ultimately, pain intensity was only assessed up to 48 hours and levels of plasma stress-associated proteins were not measured.

Conclusions

In summary, the present study emphasizes the positive effect of combined PECS I and SPB for patients undergoing MRM, because the new technique provides more effective perioperative pain relief. However, the efficacy of combined PECS I and SPB in the prevention of chronic pain after MRM still requires further study, with the exception of a comparison of PECS II and SPB approaches for breast cancer surgery.

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