RESEARCH ARTICLE

Comparison of serratus plane block alone and in combination with pectoral type 1 block for breast cancer surgery: a randomized controlled study

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Abstract

Background/Aim: Concurrent application of ultrasound-guided pectoral type 1 (PECS I) and serratus plane block (SPB) is one of the most appropriate multimodal analgesic strategies for reducing acute post-mastectomy pain. The purpose of the present study was to compare the analgesic efficacy of SPB alone, or in combination with PECS I block for post-mastectomy pain following breast cancer surgery.

Materials and Methods: Sixty participants undergoing breast cancer surgery were randomly assigned to two groups. After anesthesia induction, group S (n =30) received SPB alone, whereas the SPECS group (n =30) received a combination of PECS I and SPB. Pain scores at 0, 1, 2, 6, 12, 24 h postoperatively, intra-operative fentanyl consumption, postoperative time to first rescue analgesia, nausea, vomiting, patient satisfaction, and anesthesia-related complications were recorded.

Results: Pain scores in the SPECS group were significantly lower than group S throughout the follow-up period ($p < 0.001$). A significant reduction in postoperative rescue morphine consumption ($p = 0.01$, median difference 7 mg, 95 % confidence interval: 5.1-7.9 mg) and intraoperative fentanyl consumption ($p = 0.01$) in the SPECS group compared with group S. Moreover, postoperative nausea and vomiting were lower, and patient satisfaction was higher in the SPECS group compared with that of the group S.

Conclusions: These results suggest that SPB application and PECS I provide more effective and reliable perioperative analgesia and increase patient satisfaction in breast cancer surgery. HIPPOKRATIA 2021, 25 (1):8-14.

Trial registration number: NCT03899545.

Keywords: Acute pain management, breast cancer surgery, bupivacaine, pectoral type 1 block, serratus plane block

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Introduction

Breast cancer ranks first among the most common malignant neoplasms in women[1]. Breast cancer surgery procedures are characterized by moderate and severe pain[2]. Insufficient postoperative acute pain control is associated with increased morbidity, delayed wound healing, lengthened hospital stay, increased side effects secondary to opioid use, chronic pain, and high care costs[3-6]. Postoperative chronic pain and long-term opioid addiction risks after breast cancer surgery are reported to be 29 % and 11 %, respectively[7-8]. Multimodal analgesia is recommended for controlling acute postoperative pain after breast surgery, and regional analgesia techniques are an essential component of this management[9].

Thoracic epidural analgesia (TEA), intercostal, intrapleural, paravertebral blocks (PVB), and local wound infiltration have been used to control the acute postoperative pain after breast surgery effectively[10-17].

The PVB is defined as the gold standard analgesic method for breast surgeries. However, the failure rate of PVB is high, and block distribution cannot be assured with a single injection[18]. The neuraxial techniques have inherent limitations due to their anatomical proximity to the pleura and central nervous structures. Additionally, these techniques do not appear to be applicable or cost-effective for outpatient breast surgeries in terms of possible complications and difficulty in administration[19].

In the last decade, various ultrasound (US) guided thoracic wall blocks [pectoralis (PECS I, PECS II) nerve block, modified PECS II block, serratus plane block (SPB)] have been developed to provide reliable analgesia in patients undergoing breast surgery[19-22].

In PECS I block technique, the local anesthetic injection is performed between the pectoralis major and minor muscles at the level of the midclavicular second and third ribs to block the medial and lateral pectoral nerves[19].

The SPB, applied at the fifth rib level in the midaxillary line above or below the serratus anterior muscle, was first described for anterolateral thoracic wall analgesia via its action on the lateral cutaneous branch of the T2-T9 thoracic intercostals, thoracicus longus, and thoracodorsal nerves[22].

Some recent studies suggest that these blocks may be alternative methods of TEA and PVB application due to their ease of application, low side effect profile, and provision of adequate analgesia for breast surgeries[18-20,22,23]. Although none of these techniques anesthetizes the entire breast and axilla alone, their effects may be more comprehensive when applied together.

It is reported in the literature that methods like the combination of pectoral blocks with SPB may increase analgesic efficacy[24-26]. A few clinical studies report that the combination of SPB and PECS I (SPECS) block provides adequate perioperative analgesia compared to general anesthesia alone[24-25]. There is no clinical study comparing the SPECS with the SPB in the literature to the best of our knowledge.

This study compared the SPB and SPECS combination in terms of perioperative analgesic efficacy. The present study hypothesizes that simultaneous ultrasound-guided SPECS block has a higher analgesic efficacy than SPB alone. The primary endpoint was the second postoperative hour pain intensity score after administration of SPB and SPECS in patients undergoing breast cancer surgery. The secondary outcomes were intra-operative fentanyl consumption, postoperative rescue morphine requirement, time to first rescue analgesia, postoperative nausea-vomiting, patient satisfaction, and block-related complication.

Methods

This prospective, randomized, double-blind study was conducted at Bezmialem Vakıf University, Turkey, from April to September 2019 after receiving permission from Bezmialem Vakıf University Institutional Ethics Committee (Approval No 1802, date: 06/03/2019) and registration at ClinicalTrials.gov (NCT03899545, registration date: 02/04/2019). The participant enrollment period started on 06/04/2019 and continued until 05/09/2019.

Our pilot study with ten participants in each group found that the numeric rating scale at the second postoperative hour was 3.6 ± 1.3 (mean ± standard deviation) in group S and 2.5 ± 0.9 in SPECS. According to our power analysis (α =0.05 and β =0.2), the sample size per group should include at least 27 participants. We enrolled 60 patients to allow for a 10 % dropout rate.

Sixty female participants scheduled for elective unilateral oncological breast surgery were evaluated for study eligibility. Written informed consent was obtained from all subjects. The inclusion criteria were age 20-75 years, the American Society of Anesthesiologists (ASA) physical status I-III and patients with elective unilateral breast cancer surgery involving the axillary region. The exclusion criteria were ASA IV patients, previous neurologic disease symptoms (TIA, syncope, dementia, etc.), allergic history to local anesthetics used, major heart disease, liver, and renal failure, psychiatric disease, patients with contraindications to medications used during the surgery and patients who refused to participate in the study.

During preoperative visits, patient data were recorded, and the numeric rating scale (NRS; 0-10: 0 =no pain, ten =worst pain imaginable) was explained to the patients. Participants were randomly assigned (1:1) to receive US-guided SPB (group S) or SPECS block (group SPECS). Patients were divided into two random groups using random numbers produced by a computer. Group allocation numbers were hidden in sealed opaque envelopes that were opened after patient registration procedures.

Patients were taken to the operating room and had venous access opened on the contralateral arm with a 20 G intravenous (iv) cannula and were monitored noninvasively using a multiparameter monitor for basal electrocardiogram (ECG), heart rate, non-invasive blood pressure (GE Healthcare, Chicago, Illinois, USA), peripheral oxygen saturation and bispectral index module (BIS module, GE Healthcare, Helsinki, Finland). Standard general anesthesia protocol was applied to all participants. General anesthesia was induced with midazolam 0.03 mg/kg iv, fentanyl one mcg/kg iv, and then propofol 1.5-2 mg/kg iv until eyelash reflex was lost. After administering rocuronium bromide 0.5 mg/kg, tracheal intubation was completed. Anesthesia maintenance was provided with 1-3 % sevoflurane in oxygen/medical air mixture to keep BIS value 40-60 with a semi-closed cycle. We observed and recorded ECG, blood pressure, oxygen saturation, end-tidal carbon dioxide, and BIS during the surgery. All patients had 3-6 ml/kg/h isotonic saline infusion during the operation.

Should a 20 % increase occur in the mean arterial blood pressure or heart rate during the operation compared to the baseline values, 50 μg/kg fentanyl was administered to the patient. Hypotension (mean arterial pressure <65 mmHg) was treated with 250 mL isotonic saline infusion. If necessary, an increased dose of iv ephedrine 5 mg was administered to the patient. When symptomatic bradycardia (heart rate <40 bpm) developed, 0.5 mg atropine intravenously was given.

We performed thoracic wall block procedures in both groups after anesthesia induction. The investigator (S.Y.), familiar with ultrasound (US)-guided truncal blocks, performed all block procedures via a 22 G, 50 mm echogenic needle (Stimuplex D, BBraun, Melsung, Germany) and an L12-4 MHz linear probe of the B. Braun and Philips Xperius™ US System (GE Healthcare, Tokyo, Japan).

The PECS I block technic: under a sterile condition with the patient in the supine position, the US probe was placed mid-clavicular to view the oblique's pectoral major and minor muscles sagittal plane at the second-third costal level. Then via in-plane technique, the needle was advanced with craniocaudal and mediolateral approaches to the fascial plane between the pectoral major and minor muscles and confirmed with hydrodissection. One-third of the prepared local anesthetic drug [0.5 ml/kg of 0.25 % bupivacaine/1 % lidocaine mixture (1:1)] was used to complete the PECS I block procedure (Figure 1).

The SPB technic: with the patient in the supine position and arm in 90° abduction, the US probe was placed in the oblique sagittal plane at the fifth costal level on the mid-axillary line. We identified the fascial plane between the latissimus dorsi and the serratus anterior muscles. Then

via the in-plane technique, the needle was advanced to the fascial plane with the mediolateral in-plane technique, and the block procedure was completed by administering a local anesthetic drug into the interfascial space (Figure 1).

In both groups, 0.5 ml/kg of 0.25 % bupivacaine/1 % lidocaine mixture (1:1) was used. In group SPECS, 2/3 of the total local anesthetic drug was used for SPB and 1/3 for PECS I block. The total local anesthetic drug volume was completed in the SPECS group to 30 mL with isotonic saline in patients with a bodyweight below 60 kg. As is known, the time onset of lidocaine action is considerably faster than bupivacaine. Bupivacaine is often preferred in peripheral blocks due to its long duration of action. Since thoracic wall blocks were performed after anesthesia induction, we preferred to use a mixture of bupivacaine and lidocaine to accelerate the onset of action.

Within the scope of multimodal analgesia, paracetamol 1 g, tenoxicam 20 mg, and dexamethasone 4 mg iv were administered to both groups 30 minutes before the end of the operation as a standard. At the end of the surgery, the neuromuscular block was antagonized with sugammadex (Bridion; Schering-Plough Corporation, Oss, Netherlands) 2 mg/kg iv and fully awake tracheal extubation was performed.

Age, body mass index, operation duration, operation type, intra-operative fentanyl (μg), and first rescue analgesic requirements were recorded. In the postoperative period, at 0 (immediately after recovery from anesthesia), 1, 2, 6, 12, and 24 hours pain intensity was assessed with an NRS (0 =no pain, 10 =pain as bad as possible), and nausea-vomiting were assessed with postoperative nausea and vomiting scale (PONV) (0 =no PONV, 1 =mild nausea, 2 =severe nausea or vomiting once, 3 =vomiting more than once). Side effect formation (itching, apnea, urine retention, or paralytic ileus) and complications related to block were recorded in the first 24 hours after surgery. The satisfaction levels were recorded as very bad, bad, mediocre, good, or very good. Also, intravenous paracetamol 1 g every eight hours was ordered in both groups. If participants complained of moderate or severe pain (NRS ≥4), they were treated with morphine 0.1 mg/kg iv as rescue analgesia. The nausea-vomiting was treated with metoclopramide 10 mg IV. The outcome assessor (attending anesthesiologist) for perioperative data was different from the investigator and was not informed of the group assignment. The attending anesthesiologist administering the opioid was not admitted to the operating room during the standard time required for the block. Participants were blind to the group allocation as blocks were applied after anesthesia induction.

Statistical Analysis

Descriptive statistics for the data obtained were calculated as the arithmetic mean, standard deviation, quartiles (first, second and third quartiles), number, and percentage frequency according to type and are presented in the Tables/Figures.

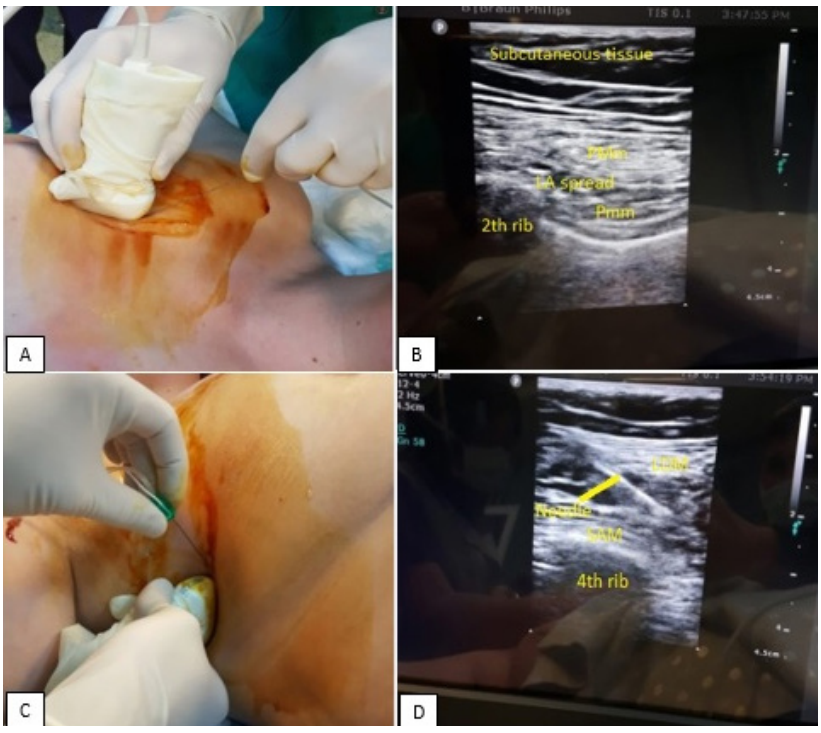

Figure 1: Pectoral 1 block and serratus plane block. A) Position of the needle before performing the pectoralis 1 block. B) Ultrasound images of the pectoral 1 block application of local anesthetic drug between pectoral major and minor muscle. C) Position of the needle before performing the serratus plane block. D) Ultrasound images of the serratus plane block application of local anesthetic drug superior to the serratus muscle.
PMm: pectoralis major muscle, Pmm: pectoralis minor muscle; SAM: serratus anterior muscle.

Linked to the distribution of features, comparison of two groups in terms of measurements at different times used the independent samples t-test and Mann-Whitney U test. Correlations between groups with traits with categoric variables were assessed with the Fisher-Freeman-Halton test. Statistical significance was taken at $p < 0.05$ level, and calculations used the IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp., Armonk, NY, USA).

Results

The flow chart is summarized in Figure 2 according to the CONSORT statement. Data from 30 patients in each group were analyzed. The group S and group SPECS were similar concerning baseline demographic characteristics, ASA physical status, anesthesia duration, surgery duration, and type of surgery (Table 1). The perioperative hemodynamic parameters were also comparable.

Compared to group S, postoperative NRS pain scores in group SPECS were statistically significantly lower up to 24 h ($p < 0.001$; Figure 3). The addition of PECS I to SPB attenuated pain intensity compared to the SPB alone. Intraoperative fentanyl was required by 18 patients (60 %) of group S compared to two patients (6.7 %) of group SPECS ($p = 0.01$). Compared with the SPB, SPECS decreased cumulative rescue morphine consumption for the first 24 h (median difference 7 mg, 95 % confidence interval: 5.1-7.9 mg, $p < 0.001$) post-operatively. Postoperative rescue morphine was required by 22 patients (73.3 %) of group S compared to five patients (16.7 %) of group SPECS ($p = 0.01$). In group SPECS, only five participants required rescue analgesia, and all were administered immediately after recovery (0 hours). In group S, a total of 15 participants had rescue analgesia. In group S, 13 participants had rescue analgesic at 0 hours. Additionally, there were three participants at 0 and 6th hours, three participants at 0 and 12th hours, one participant at 0, 6th, and 12th hours, one participant at 1st and 12th hours, and one participant only at the 12th hour, who required rescue analgesia.

There was significant reduction in the PONV scale in group SPECS compared with group S at 0 hours ($p = 0.003$); at 1 hour ($p = 0.017$); at 2 hours ($p = 0.008$), and at 12 hours ($p = 0.010$) (Table 2). At the same time, vomiting was observed in three patients in group SPECS and seven patients in group S. Also, the patient satisfaction indices in group SPECS were significantly higher than group S ($p = 0.001$) (Table 2). No side effects and complications related to the block procedure were reported in either group.

Discussion

The present study demonstrated that the SPECS combination's application significantly reduces postoperative NRS pain scores up to 24 hours postoperatively compared to the SPB. The SPECS combination results in less intra-operative fentanyl consumption, lower postoperative rescue morphine requirement, and higher patient satisfaction than those who received only SPB.

The analgesic efficacy of PECS I block for breast cancer surgery is controversial. Cros et al[27] reported that PECS I did not improve postoperative analgesia after oncologic breast surgery. Contrary to this, some authors demonstrate the PECS I block effectiveness with simultaneous administration with the PVB or PECS II block[28,29]. In their retrospective cohort study, Abdallah et al[30] reported that PECS I and SPB were similarly effective in reducing postoperative opioid consumption and postoperative nausea and vomiting after ambulatory breast cancer surgery. Some studies in the literature about PECS I block possibly provide adequate analgesia for axillary dissection[31,32]. A cadaver study showed that PECS I spreads better to the axillary region than the modified PECS II block (without PECS I component)[33]. Our study observed that the combination of the SPECS significantly reduced pain

Table 1: Baseline characteristics of the sixty patients undergoing breast cancer surgery, who were included in this prospective, randomized study, and received serratus plane block alone (Group S) or a combination of pectoral type 1 and serratus plane block (Group SPECS).

	Group S (n =30)	Group SPECS (n =30)	p-value
Age (years)	58.2 (11.6)	54.7 (13.1)	0.292
BMI (kg/m^2)	29.1 (4.6)	29.9 (4.9)	0.549
Duration of Anesthesia (min)	146.1 (27.0)	148.6 (40.4)	0.785
Duration of Surgery (min)	120.4 (26.4)	120.8 (41.3)	0.962
ASA score			
1	14 (46.7)	10 (33.3)	
2	15 (50.0)	20 (66.7)	0.304
3	1 (3.3)	0 (0.0)	
Type of surgery			
Mastectomy + Axillary dissection	4 (13.3)	6 (20.0)	
Mastectomy + Sentinel Lymph Node Biopsy	20 (66.7)	18 (60.0)	0.777
Modified Radical Mastectomy	6 (20.0)	6 (20.0)	

Values are presented as mean with standard deviation in brackets or count with percentage in brackets, n: number, ASA: American Society of Anesthesiologists physical status, BMI: body mass index.

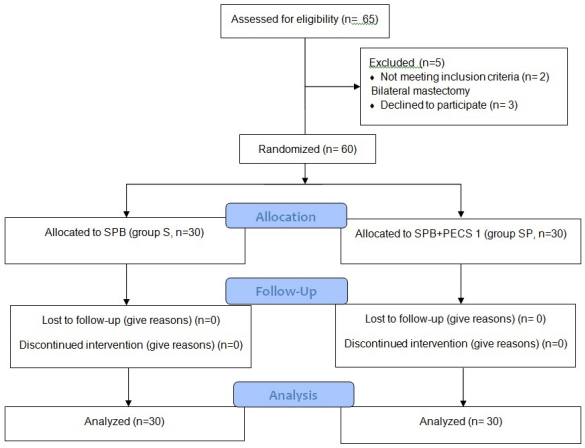

Figure 2: Flow diagram of participant recruitment according to the CONSORT statement.

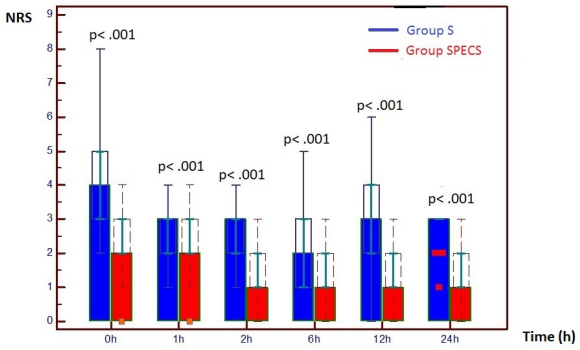

Figure 3: Box plots of postoperative numeric rating scale (NRS) pain scores in each group over the first 24 postoperative hours. The horizontal color line in each box represents the median value, the outer margins of the box represent the interquartile range, and the whiskers represent the 10th and 90th percentile for each time point.
NRS: numeric rating scale (0 to 10 scale), Group S: patients received serratus plane block alone, Group SPECS: patients received a combination of pectoral type 1 and serratus plane block

intensity score up to 24 hours postoperatively compared to SPB alone.

According to the current literature, SPB should be supported by additional analgesic methods during axillary dissection because SPB rarely ensures T1 sensory loss[31]. Hetta and Rezk[34] detected sufficient sensory blockade at T1-T7 dermatomal levels for 100 % of patients after PVB, and this rate remained at 40 % after SPB. Kunigo et al[35] performed SPB with 20 mL and 40 mL local anesthetic drugs at the 4th rib level in their study's midaxillary line. They performed dermatomal examination with the pinprick test and found T1 involvements in 0 patients in the 20 mL group and three patients in the 40 mL group, with T2 involvement in three patients in the 20 mL group and five patients in the 40 mL group. As a

Table 2: Descriptive values for postoperative nausea-vomiting scale (PONV) score and patients' satisfaction results according to group.

		Group S		Group SPECS		p-value
		n	%	n	%	
PONV 0 (h)	0	10	33.3	23	76.7	**0.003**
	1	16	53.3	5	16.7	
	2	4	13.3	2	6.7	
PONV 1 (h)	0	10	33.3	21	70.0	**0.017**
	1	17	56.7	8	26.7	
	2	3	10.0	1	3.3	
PONV 2 (h)	0	15	50.0	26	86.7	**0.008**
	1	13	43.3	4	13.3	
	2	2	6.7	0	0.0	
PONV 6 (h)	0	24	80.0	27	90.0	0.278
	1	6	20.0	3	10.0	
PONV 12 (h)	0	24	80.0	30	100.0	**0.010**
	1	6	20.0	0	0.0	
PONV 24 (h)	0	27	90.0	30	100.0	0.076
	1	3	10.0	0	0.0	
Patient Satisfaction	very bad	2	6.7	0	0.0	**0.001**
	mediocre	18	60.0	2	6.7	
	good	7	23.3	5	16.7	
	very good	3	10.0	23	76.7	

Group S: patients received serratus plane block alone, Group SPECS: patients received a combination of pectoral type 1 and serratus plane block, n: number, PONV: postoperative nausea and vomiting scale (0 to 3 scale).

result, Group S patients may have required more rescue analgesia due to pain caused by axillary dissection that SPB cannot control.

A few theories can explain the analgesic mechanism of PECS I block. Firstly, PECS I may reduce pectoralis major and minor muscle spasms after surgery[36,37]. Secondly, the medial and lateral pectoral nerves may contain sensory innervations[38]. Thirdly, medial and lateral pectoral nerves can merge with the intercostal nerves' anterior cutaneous branches and have an analgesic effect[39].

A few case reports show that the SPECS block combination is an effective method for perioperative analgesia in breast cancer surgery[40,41]. A randomized controlled study from recent times reported that the SPB and PECS I block combination did not affect first rescue analgesia requirement time compared to general anesthesia[25]. In our study, five participants in the group SPECS required rescue analgesia immediately after recovery from anesthesia. The inadequate spread of the SPECS can explain these results to the anterior cutaneous branches of intercostal nerves that innervate the parasternal part of the breast region, depending on the type of surgery.

In recent years, some reports suggest that the addition of parasternal intercostal or transversus thoracic muscle plane blocks to PECS blocks to achieve anesthesia in the whole breast (blocking the anterior cutaneous branches of intercostal nerves) in patients undergoing breast surgery[26,42]. In a report, it is argued that the addition of a parasternal intercostal block to a combination of SPB and PECS I blocks does not make a difference in rest NRS scores but significantly reduces NRS scores during movement[43]. In our opinion, future studies should also explore whether the addition of a parasternal block to the SPECS combination can provide surgical anesthesia for breast surgery.

Recently, some authors have proposed combining the PECS I, PECS II, and SPB techniques under the SAP block from a single injection point around the fourth rib[44]. They have explained in detail that the upper intercostal nerves' branches provide the anterolateral chest wall's sensory innervation without any contribution from the brachial plexus. Contrary to this, in the study by Sopena-Zubiria et al[45], it was concluded that the addition of the pectoral nerve block to the thoracic paravertebral block in reconstructive breast surgery improves the results obtained, provides better analgesia in the early postoperative period and lower sedation requirement. Therefore, further studies are needed on this subject.

This study is the first to compare the SPECS efficacy with SPB for patients undergoing breast cancer surgery to the best of our knowledge. In this study, the hypothesis was supported that SPECS administration has a beneficial effect on perioperative analgesia, opioid consumption, and patient satisfaction for breast cancer surgeries. Group S had a significantly higher requirement for both intra-operative fentanyl and postoperative morphine. Patients in group S had higher pain scores during the follow-up period, despite receiving a higher postoperative rescue dose of morphine.

Innervation of the breast is complex and is supplied by multiple nerve branches. We think that more effective analgesia can be achieved with combined thoracic wall blocks instead of a single block for breast cancer surgeries involving axillary dissection.

The current trial has some limitations. The fact that the study was single-centered, the absence of results from other centers resulted in few comparative samples. Another limitation of our study is that we choose intermittent analgesic use instead of patient-controlled analgesia, which may have affected the difference in opioid requirements. Since block procedures are performed after anesthesia induction, we could not assess block onset or sensory dermatomal level. However, all blocks were performed by a single experienced anesthesiologist via US guidance. As a result, we believe that the majority of the applied blocks were successfully managed. Despite this, there is a limitation that the operator performing the blocks could not be blinded, and conscious or unconscious bias in block performance may have occurred.

Conclusion

In summary, this study emphasizes the positive effect of the SPECS block combination for patients undergoing breast cancer surgery because this technique provides more effective perioperative analgesia. Further studies are needed to compare the efficacy of SPECS block combination with PECS II block to prevent acute pain after breast cancer surgery.

Acknowledgment

Patients gave their written informed consent before the study enrollment.

Conflict of interest

The authors have no conflicts of interest to declare.

References

1. Cancer Research UK. Breast cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer, date accessed: 20/12/2020.
2. Vadivelu N, Schreck M, Lopez J, Kodumudi G, Narayan D. Pain after mastectomy and breast reconstruction. Am Surg. 2008; 74: 285-296.
3. Abdallah FW, Morgan PJ, Cil T, McNaught A, Escallon JM, Semple JL, et al. Ultrasound-guided multilevel paravertebral blocks, and total intravenous anesthesia improve the quality of recovery after ambulatory breast tumor resection. Anesthesiology. 2014; 120: 703-713.
4. Andersen KG, Kehlet H. Persistent pain after breast cancer treatment. a critical review of risk factors and strategies for prevention. J Pain. 2011; 12: 725-746.
5. Hussain N, Shastri U, McCartney CJL, Gilron I, Fillingim RB, Clarke H, et al. Should thoracic paravertebral blocks be used to prevent chronic postsurgical pain after breast cancer surgery? A systematic analysis of evidence in light of IMMPACT recommendations. Pain. 2018; 159: 1955-1971.
6. Gärtner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery. JAMA. 2009; 302: 1985-1992.
7. Peuckmann V, Ekholm O, Rasmussen NK, Groenvold M, Christiansen P, Møller S, et al. Chronic pain and other sequelae in

long-term breast cancer survivors: nationwide survey in Denmark. Eur J Pain. 2009; 13: 478-485.
8. Lee JS, Hu HM, Edelman AL, Brummett CM, Englesbe MJ, Waljee JF, et al. New Persistent Opioid Use Among Patients With Cancer After Curative-Intent Surgery. J Clin Oncol. 2017; 35: 4042-4049.
9. Wick EC, Grant MC, Wu CL. Postoperative Multimodal Analgesia Pain Management With Nonopioid Analgesics and Techniques: A Review. JAMA Surg. 2017; 152: 691-697.
10. Lynch EP, Welch KJ, Carabuena JM, Eberlein TJ. Thoracic epidural anesthesia improves outcome after breast surgery. Ann Surg. 1995; 222: 663-669.
11. Atanassoff PG, Alon E, Weiss BM. Intercostal nerve block for lumpectomy: superior postoperative pain relief with bupivacaine. J Clin Anesth. 1994; 6: 47-51.
12. Dravid RM, Paul RE. Interpleural block - part 1. Anaesthesia. 2007; 62: 1039-1049.
13. Dravid RM, Paul RE. Interpleural block - part 2. Anaesthesia. 2007; 62: 1143-1153.
14. Schnabel A, Reichl SU, Kranke P, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of paravertebral blocks in breast surgery: a meta-analysis of randomized controlled trials. Br J Anaesth. 2010; 105: 842-852.
15. Karmakar MK. Thoracic paravertebral block. Anesthesiology. 2001; 95: 771-780.
16. Marret E, Vigneau A, Salengro A, Noirot A, Bonnet F. Efficacité des techniques d'analgésie locorégionale après chirurgie du sein: une méta-analyse [Effectiveness of analgesic techniques after breast surgery: a meta-analysis]. Ann Fr Anesth Reanim. 2006; 25: 947-954.
17. Bansal P, Saxena KN, Taneja B, Sareen B. A comparative randomized study of paravertebral block versus wound infiltration of bupivacaine in modified radical mastectomy. J Anaesthesiol Clin Pharmacol. 2012; 28: 76-80.
18. Tighe SQ, Karmakar MK. Serratus plane block: do we need to learn another technique for thoracic wall blockade? Anaesthesia. 2013; 68: 1103-1106.
19. Blanco R. The 'pecs block': a novel technique for providing analgesia after breast surgery Anaesthesia. 2011; 66: 847-848.
20. Blanco R, Fajardo M, Parras Maldonado T. Ultrasound description of Pecs II (modified Pecs I): a novel approach to breast surgery. Rev Esp Anestesiol Reanim. 2012; 59: 470-475.
21. Goswami S, Kundra P, Bhattacharyya J. Pectoral nerve block1 versus modified pectoral nerve block2 for postoperative pain relief in patients undergoing modified radical mastectomy: a randomized clinical trial. Br J Anaesth. 2017; 119: 830-835.
22. Blanco R, Parras T, McDonnell JG, Prats-Galino A. Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia. 2013; 68: 1107-1113.
23. Pérez MF, Miguel JG, de la Torre PA. A new approach to pectoralis block. Anaesthesia. 2013; 68: 430.
24. Wang W, Song W, Yang C, Sun Q, Chen H, Zhang L, et al. Ultrasound-Guided Pectoral Nerve Block I and Serratus-Intercostal Plane Block Alleviate Postoperative Pain in Patients Undergoing Modified Radical Mastectomy. Pain Physician. 2019; 22: E315-E323.
25. Najeeb HN, Mehdi SR, Siddiqui AM, Batool SK. Pectoral Nerves I, II and Serratus Plane Blocks in Multimodal Analgesia for Mastectomy: A Randomised Clinical Trial. J Coll Physicians Surg Pak. 2019; 29: 910-914.
26. Ueshima H, Otake H. Addition of transversus thoracic muscle plane block to pectoral nerves block provides more effective perioperative pain relief than pectoral nerves block alone for breast cancer surgery. Br J Anaesth. 2017; 118: 439-443.
27. Cros J, Sengès P, Kaprelian S, Desroches J, Gagnon C, Labrunie A, et al. Pectoral I Block Does Not Improve Postoperative Analgesia After Breast Cancer Surgery: A Randomized, Double-Blind, Dual-Centered Controlled Trial. Reg Anesth Pain Med. 2018; 43: 596-604.
28. Bouzinac A, Tournier JJ, Delbos A, Bérot JE. Intérêt de l'association du bloc échoguidé du nerf pectoral latéral à un bloc paravertébral pour l'analgésie lors d'une mastectomie complète [Interest of ultrasound-guided lateral pectoral nerve block associated with paravertebral block for complete mastectomy pain management]. Ann Fr Anesth Reanim. 2014; 33: 548-550.
29. Bashandy GM, Abbas DN. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery: a randomized clinical trial. Reg Anesth Pain Med. 2015; 40: 68-74.
30. Abdallah FW, MacLean D, Madjdpour C, Cil T, Bhatia A, Brull R. Pectoralis and Serratus Fascial Plane Blocks Each Provide Early Analgesic Benefits Following Ambulatory Breast Cancer Surgery: A Retrospective Propensity-Matched Cohort Study. Anesth Analg. 2017; 125: 294-302.
31. Ohgoshi Y, Yokozuka M, Terajima K. [Serratus-Intercostal Plane Block for Brest Surgery]. Masui. 2015; 64: 610-614.
32. O'Scanaill P, Keane S, Wall V, Flood G, Buggy DJ. Single-shot pectoral plane (PECs I and PECs II) blocks versus continuous local anaesthetic infusion analgesia or both after non-ambulatory breast-cancer surgery: a prospective, randomised, double-blind trial. Br J Anaesth. 2018; 120: 846-853.
33. Kikuchi M, Takaki S, Nomura T, Goto T. [Difference in the Spread of Injectate between Ultrasound Guided Pectoral Nerve Block I and II. A Cadaver Study]. Masui. 2016; 65: 314-317.
34. Hetta DF, Rezk KM. Pectoralis-serratus interfascial plane block vs thoracic paravertebral block for unilateral radical mastectomy with axillary evacuation. J Clin Anesth. 2016; 34: 91-97.
35. Kunigo T, Murouchi T, Yamamoto S, Yamakage M. Injection Volume and Anesthetic Effect in Serratus Plane Block. Reg Anesth Pain Med. 2017; 42: 737-740.
36. Hoffman GW, Elliott LF. The anatomy of the pectoral nerves and its significance to the general and plastic surgeon. Ann Surg. 1987; 205: 504-507.
37. Govshievich A, Kirkham K, Brull R, Brown MH. Novel approach to intractable pectoralis major muscles spasm following sub-muscular expander-implant breast reconstruction. Plast Surg Case Studies. 2015; 1: 68-70.
38. Brermner-Smith AT, Umvin AJ, Williams WW. Sensory pathways in the spinal accessory nerve. J Bone Joint Surg Br. 1999; 81: 226-228.
39. Akita K, Kawashima T, Shimokawa T, Sato K, Sato T. Cutaneous nerve to the subacromial region originating from the lateral pectoral nerve. Ann Anat. 2002; 184: 15-19.
40. Bouzinac A, Brenier G, Dao M, Delbos A. Bilateral association of pecs I block and serratus plane block for postoperative analgesia after double modified radical mastectomy. Minerva Anestesiol. 2015; 81: 589-590.
41. Fusco P, Scimia P, Marinangeli F, Pozone T, Petrucci E. The association between the ultrasound-guided Serratus Plane Block and PECS I Block can represent a valid alternative to conventional anesthesia in breast surgery in a seriously ill patient. Minerva Anestesiol. 2016; 82: 241-242.
42. Ohgoshi Y, Ino K, Matsukawa M. Ultrasound-guided parasternal intercostal nerve block. J Anesth. 2016; 30: 916.
43. Song WQ, Wang W, Yang YC, Sun Q, Chen H, Zhang L et al. Parasternal Intercostal Block Complementation Contributes to Postoperative Pain Relief in Modified Radical Mastectomy Employing Pectoral Nerve Block I and Serratus-Intercostal Block: A Randomized Trial. J Pain Res. 2020; 13: 865-871.
44. Franco CD, Inozemtsev K. Refining a great idea: the consolidation of PECS I, PECS II and serratus blocks into a single thoracic fascial plane block, the SAP block. Reg Anesth Pain Med. 2019; rapm-2019-100745.
45. Sopena-Zubiria LA, Fernández-Meré LA, Valdés Arias C, Muñoz González F, Sánchez Asheras J, Ibáñez Ernández C. Bloqueo paravertebral torácico frente al bloqueopararavertebral torácico más bloqueo de nervios pectoralesen cirugía reconstructiva de mama [Thoracic paravertebral block compared to thoracic paravertebral block plus pectoral nerve block in reconstructive breast surgery]. Rev Esp Anestesiol Reanim. 2012; 59: 12-17.