Effect of combination between serratus anterior plane block and transversus thoracis plane block on the management of acute postmastectomy pain: a prospective randomized clinical trial

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Abstract:

Background: The serratus anterior plane (SAP) block cannot block the most internal mammary region, whereas, the transversus thoracis plane (TTP) block can. Hence, we studied patients undergoing mastectomy to determine whether the combination of these two blocks provides better pain control than the serratus anterior plane block alone.

Methods: Fifty-four adult female patients scheduled for modified radical mastectomy were randomly allocated to one of two groups. Group (A) (n = 27) received the serratus anterior plane block alone, and group (B) (n = 27) received the transversus thoracis plane block combined with the serratus anterior plane block. The primary outcome measure was post-operative opioid consumption. Secondary outcome measures were visual analogue scale (VAS), duration till request of the first analgesia, and total sum of intra-operative fentanyl consumption.

Results: the cumulative 24-hour postoperative opioid consumption, VAS score both at rest and movement, time of request of the first analgesia, and intraoperative fentanyl consumption showed no significant difference between the two groups.

Conclusion: The combination of transversus thoracis plane block and serratus anterior plane block has no additional analgesic effect than serratus anterior plane block alone for the management of acute postmastectomy pain.

Clinical trial registration: registered at "www.clinicaltrial.gov" under number: (NCT04375111).

Keywords: breast cancer, mastectomy, analgesia, regional block, serratus anterior plane block, transversus thoracis plane block.

Introduction:

In 2019, regarding the estimations performed by the World Health Organization (WHO), cancer comes first or second as a leading cause of death in people below 70 years old in about 113 countries with a total of 183 and comes third or fourth in other 23 countries. Female breast cancer has taken the lead as the most commonly diagnosed cancer from lung cancer with about 2.3 million new cases (11.9% of total new cases in 2019). [1]

Perioperative pain after breast surgeries remains to be taken lightly due to the minimal invasiveness of breast surgeries [2]. However, it is estimated that 25-60% of patients undergoing breast cancer-related surgeries develop chronic pain [3].

Acute postoperative pain remains an important risk factor in developing chronic post-mastectomy pain;

about 40% of women would have acute postoperative pain, on the other hand, 50% would have chronic pain[4].

Different regional anaesthesia techniques have achieved better management of post-breast surgery acute pain and subsequently less frequent chronic pain[5,6]. Add to that, effective regional anaesthesia would decrease both the surgical stress response and the requirements of general anaesthetics and opioids, which would keep the function of the immune system intact[7]. A lot of regional anaesthesia techniques have been used to control anterior chest wall pain as the pectoral nerves (PECs) block, paravertebral block, intercostal nerve blocks, thoracic epidural analgesia, serratus anterior plane block[8-13].

The breast receives its innervation through the anterior and lateral cutaneous branches of the 2nd to the 6th intercostal nerves [14]. Targeting the serratus plane is a safer and simpler procedure than multiple intercostal or paravertebral blocks [15]. As a setback for the serratus anterior plane block, it only blocks the lateral cutaneous branches of the intercostal nerves with minimal if any effect on the anterior cutaneous branches [15, 16].

The serratus anterior plane block, being unable to block the anterior cutaneous branches of the intercostal nerves, has to be combined with another technique, transversus thoracic plane block in which the local anaesthetic is injected between the transversus thoracic muscle and the internal intercostal muscle, blocking those anterior cutaneous branches of the intercostal nerves [16].

We hypothesized that the combination of transversus thoracis plane block to serratus anterior plane block would improve the quality of perioperative and decrease side effects of postoperative opioid use. In this study, we tried to compare the analgesic efficacy of combined transversus thoracis plane block and serratus anterior plane block to serratus anterior plane block alone on the management of acute postmastectomy pain.

Patients and Methods:

Enrollment and eligibility:

This randomized prospective Assessor-blinded clinical trial was conducted on patients in surgical oncology department and post anesthesia care unit (PACU) in South Egypt Cancer Institute (SECI), Assiut University, Egypt, after obtaining medical ethics committee, Institutional review board approval under number (17101174); it was prospectively registered at "www.clinicaltrial.gov" under number: (NCT04375111). Fifty-four ASA "American Society of Anesthesiologists" I-II female patients aged 30-60 years, weighed 50-90 Kg and scheduled for modified radical mastectomy (MRM) breast cancer with axillary dissection for breast carcinoma were enrolled after obtaining written informed consents. Excluded from the study were patients with known allergy to the study drugs, skin infection at the site of needle puncture, significant organ dysfunction, Coagulopathy, drug or alcohol abuse, epilepsy, and psychiatric illness that would interfere with perception and assessment of pain.

Randomization and blindness:

The participating females were randomly allocated using computer-generated randomizer program (http://www.randomizer.org) into one of 2 groups.

Group (A): Patients in this group have undergone Serraturs anterior plane block.

Group (B): Patients in this group have undergone combined Serraturs anterior plane block and Transversus thoracic plane block.

Postoperative patients' assessment in the post anesthesia care unit (PACU) was done by a doctor who was blind to patient group allocation.

Preoperative protocol:

All patients preoperatively were instructed how to evaluate their own pain using VAS (Visual Analog Scale) score from zero to ten, where 0 = no pain and 10 = the worst pain imaginable for acute postoperative pain.

Anesthetic procedure

Upon patient's entering the operation theatre, after appropriate fasting hours, standard monitoring (noninvasive blood pressure, pulse oximetery. ECG, temperature, and capnography) was applied. Then, an intravenous cannula was placed and secured on the opposite side of surgery.

All patients have undergone general anaesthesia. Induction was performed by intravenous injection of propofol 1-2.5 mg/kg, lidocaine 1.5 mg/kg, and fentanyl 1-2 µg /kg. Neuromuscular blockade was achieved with atracurium 0.5 mg/kg, and then maintained by 0.1 mg/kg at anaesthetist discretion. Then tracheal intubation was performed. Anaesthesia was maintained using the inhalational anaesthetic Isoflurane 1.2-2.5%. Additional boluses of fentanyl 1-2 ug/kg could be used to maintain heart rate and blood pressure within 20% of basal vital signs measured one night before the surgery at a relaxing comfortable environment.

After induction of anaesthesia, ultrasound-guided plane blocks were performed using the linear probe of Sonosite M-Turbo c ultrasound machine, and with a 22 gauge Sonoplex STIM needle.

After surgery completion, muscle relaxation was reversed by neostigmine 50 µg/kg and atropine 10 µg/kg. After the patient's response to verbal commands, the trachea was extubated and the patient was transferred to the PACU where the patient's blood pressure, heart rate, oxygen saturation, and pain level were monitored.

Ultrasound-guided plane blocks:

Serratus anterior plane block was carried out with the patient lying in the lateral position. On the ipsilateral side of surgery after skin disinfection, a high-frequency linear ultrasound probe was applied parallel to and between the 5th and 6th ribs in the mid-axillary region, for identification of the superficial latissimus dorsi muscles and deep anterior serratus muscles. Then,

25 ml of isobaric bupivacaine 0.25% was injected above the serratus anterior muscle. Figure (1)

Transversus thoracis plane block was carried out with the patient lying in the supine position. On the ipsilateral side of surgery after skin disinfection, a high-frequency linear ultrasound probe was applied parallel to and between the 3rd and 4th ribs connecting at the sternum. Then, 15 ml of isobaric bupivacaine 0.25% was injected between the transversus thoracic muscle and the internal intercostal muscle. Figure (2)

Postoperative monitoring:

In the PACU, data including heart rate, mean blood pressure, oxygen saturation and VAS scores (at rest and at movement in the form of abduction of the ipsilateral arm) at baseline, 2, 4, 6, 12, and 24 hours postoperatively to evaluate acute pain were observed, by blinded trained doctors for pain evaluation, were recorded and managed as the following:

If VAS score ≥ 3, rescue postoperative analgesia in the form of morphine Patient-controlled analgesia (PCA) using (B.Braun Melsungen AG type "8713030" PCA device) with an initial bolus of 0.1 mg/ kg morphine once pain was expressed followed by 1mg bolus with a locked period of 15 minutes, the first request of analgesia and the total analgesic consumption in the 1st 24 hours were observed and recorded. Postoperative adverse effects such as nausea, vomiting, and itching were recorded and treated with ondansetron 8 mg IV, and dexamethasone 8 mg IV.

Outcome assessment:

Our primary outcome was total sum of morphine consumption. Secondary outcomes were postoperative pain score, intraoperative fentanyl consumption, time of request of first analgesia, and side effects.

Statistical analysis:

Based on a previous research comparing pectoral plane block to pectoral plane block combined with transversus thoracic plane block with an expected background standard deviation of 1.0, an alpha error not exceeding 0.05, and power of 80%, we estimated that 27 patients in each group would be required.

(Effect size = 1.0, Power = 0.80, α-error = 0.05)

Data entry and analysis were performed using SPSS version 20 (Statistical Package for Social Science). Data were presented as number, percentage, mean, and standard deviation. Chi-square test was used to compare qualitative variables. Independent samples t-test was used to compare quantitative variables between two groups. P-value is considered statistically significant when $P < 0.05$.

Results:

Sixty-four patients were assessed for eligibility to participate in the study. Six patients refused to participate and four patients withdrew from the study. Those four patients refused to state a definite reason for their withdrawal, it was most likely due to uncomfortableness and anxiety. A final fifty-four patients were scheduled for modified radical mastectomy surgery for cancer breast completed this study and were equally distributed in two groups (n = 27 patients per group), Group (A) representing patients who have undergone serratus anterior plane (SAP) block, and group (B) representing patients who have undergone combined serratus anterior plane block and transversus thoracis plane (TTP) block as described in the study flow diagram. Figure (3).

Patients' characteristics and demographic data have been compared between the two groups. Regarding age, height, weight, and BMI, the two groups showed no significant difference. Also, anaesthesia duration and surgical duration showed no significant differences between the two studied groups as shown in Table [1].

There was no significant difference between the two groups regarding intraoperative non-invasive mean blood pressure measurements with p-value > 0.05. Similarly, intraoperative heart rate showed no significant difference between the two groups with p-value > 0.05, except at 90th minute of surgery with group (A) mean ± SD of (77.55 ± 6.23) BPM, and group (B) mean ± SD of (80.96 ± 3.46) with a p-value of 0.016. Table (2)

Postoperative heart rate showed no significant difference between the two groups with p-value > 0.05. However, postoperative non-invasive mean blood pressure showed significant differences at 4th, 6th, 12th, and 24th postoperative hours with a p-value < 0.05. Table (3)

Total morphine consumption during the postoperative 24 hours showed no significant difference between the two groups (group A: 4.5 ± 3.61 mg, group B: 4.3 ± 3.71 mg). Table (4)

Both VAS scores at rest and movement showed no significant difference between the two groups as shown in Table (5).

Intraoperative fentanyl consumption to keep blood pressure and heart rate within ± 20% of baseline measurements showed no difference between the two groups. Table (4)

Regarding postoperative rescue analgesia, there was no significant difference between the two groups in neither need for analgesia (group A: 17(63%), group B: 16(59.3%))], nor time of request of the first analgesia (group A: 14.24 ± 6.078 hours, group B: 18.75 ± 6.148 hours). Table (4) Figure (4).

No patients in both groups have experienced pneumothorax, vascular puncture, nerve injury, inadvertent intravascular injection, respiratory depression, hypotension, or local anesthetic systemic toxicity. Nausea, vomiting, headache, and itching have been experienced by patients in both groups with no significant differences with a p-value > 0.05. Table (6)

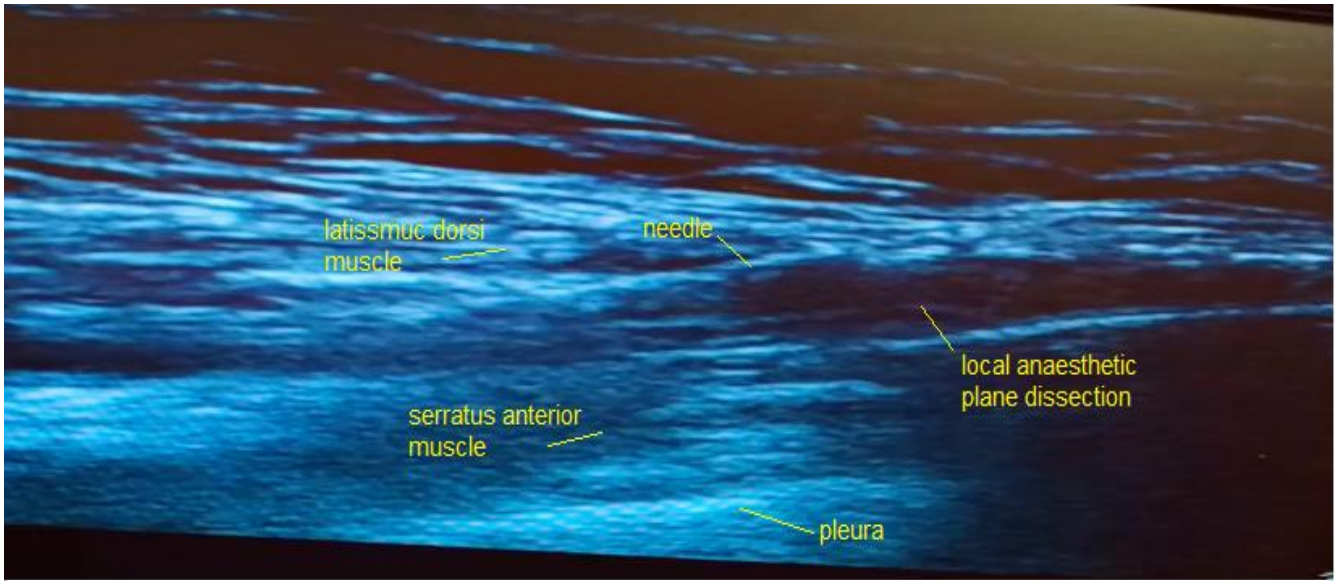

Figure (1): Serratus anterior plane (SAP) block during injection of the local anaesthetic

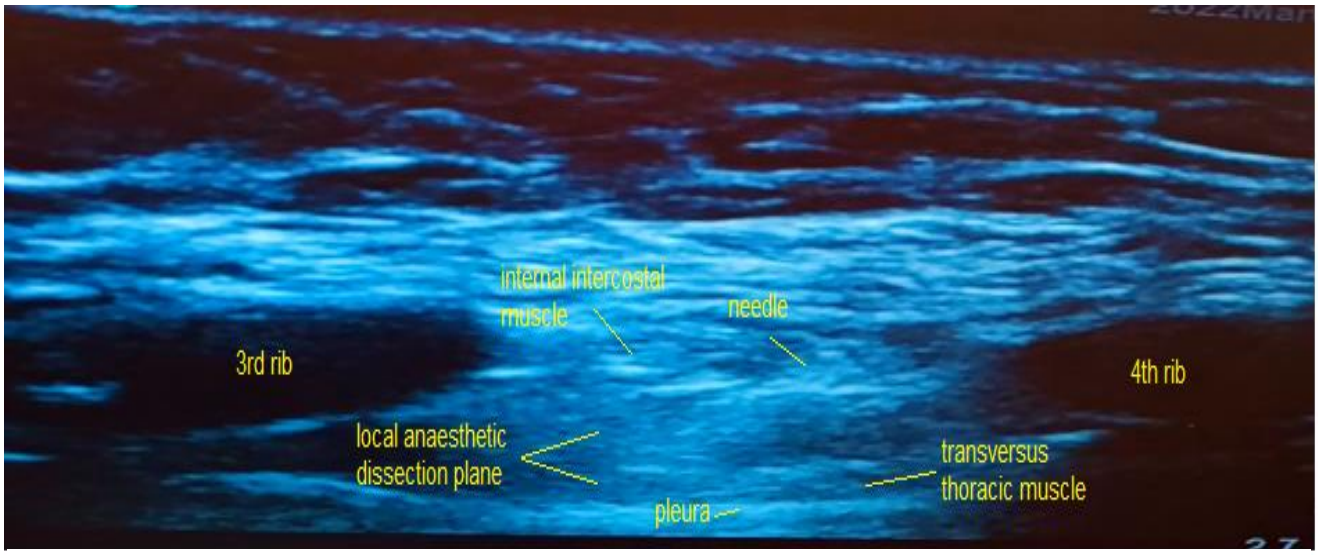

Figure (2): Transverus thoracis plane (TTP) block during injection of the local anaesthetic

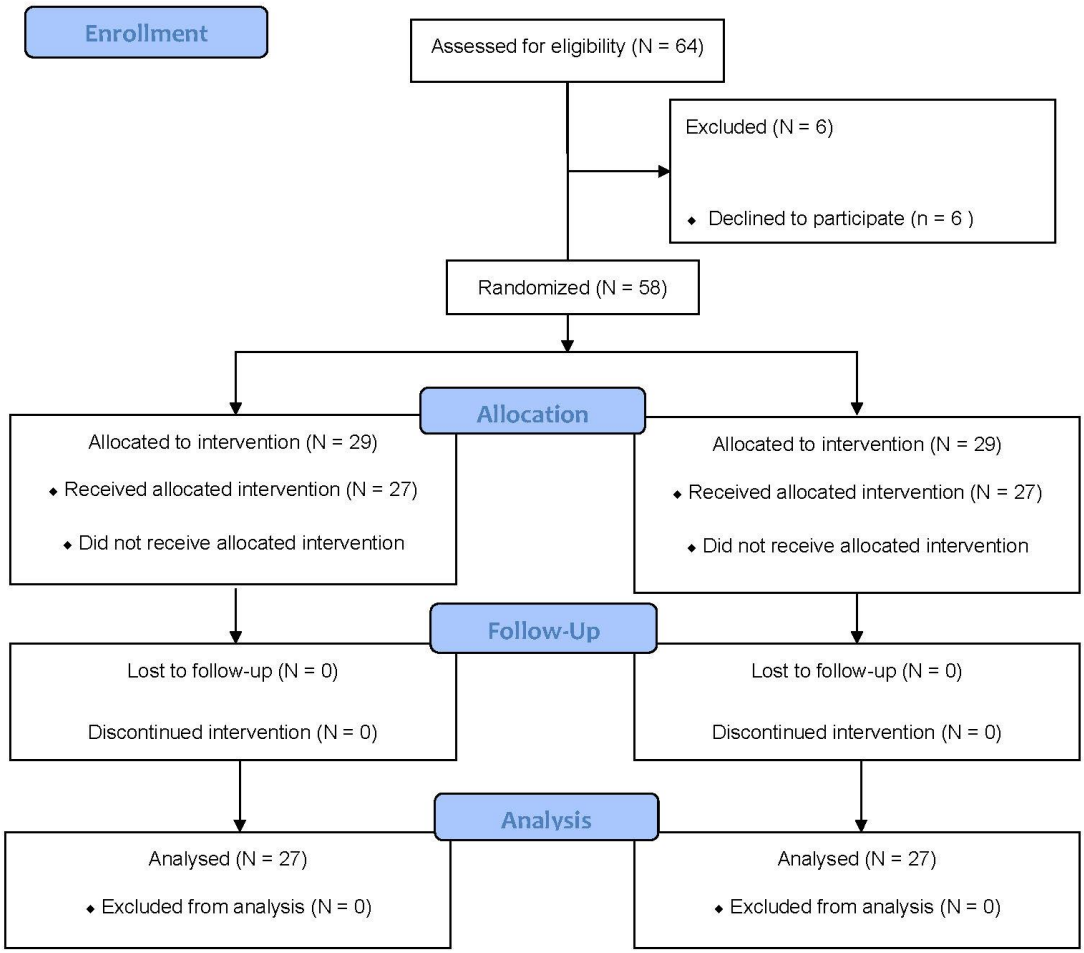

Figure (3): flowchart of the study

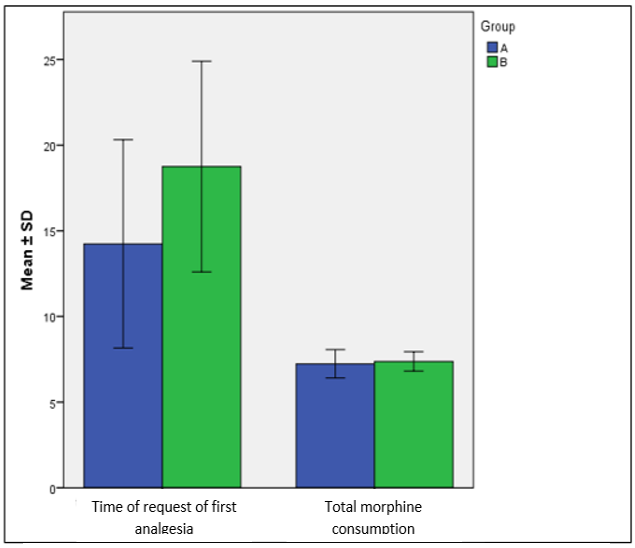

Figure (4): post-operative rescue analgesia comparison between the two groups

Table (1): Comparison of the demographic data of the studied two groups

Baseline data	Group A (N = 27) (Mean ± SD)	Group B (N = 27) (Mean ± SD)	P-value
Age	46.74 ± 8.6	45.00 ± 8.54	0.459
Height (cm)	165.88 ± 2.95	166.37 ± 3.78	0.604
Weight	73.18 ± 7.86	74.26 ± 5.47	0.563
BMI	26.62 ± 3.08	26.85 ± 2.19	0.749
ASA			
-I	12 (44.4%)	13 (48.1%)	0.785^
-II	15 (55.6%)	14 (59.9%)	
Anaesthesia duration (minutes)	104.81 ± 7.53	106.66 ± 7.84	0.380
Surgery duration (minutes)	98.62 ± 8.00	99.77 ± 8.22	0.605

Data expressed as mean ± SD, and number and percentage.
Group A: serratus anterior plane block group
Group B: combined serratus anterior plane block, and transversus thoracis plane block group.
Independent t-test was used to compare the means among groups
^ **Chi-square analysis** was used to compare the frequency among group

Table (2): intra-operative heart rate differences of the two studied groups

HR	Group (A) (N = 27) Mean ± SD	Group (B) (N = 27) Mean ± SD	P – value
HR at baseline	81.29 ± 7.58	79.48 ± 4.35	0.286
HR at 10th minute	76.15 ± 8.17	74.03 ± 6.59	0.301
HR at 20th minute	72.41 ± 7.04	70.22 ± 5.87	0.221
HR at 30th minute	73.18 ± 7.87	71.11 ± 6.83	0.306
HR at 40th minute	76.15 ± 7.62	75.81 ± 5.65	0.856
HR at 50th minute	77.78 ± 8.01	77.41 ± 5.13	0.840
HR at 60th minute	77.26 ± 6.98	79.00 ± 4.54	0.282
HR at 70th minute	77.30 ± 6.98	79.59 ± 3.98	0.141
HR at 80th minute	77.44 ± 6.86	80.07 ± 3.53	0.082
HR at 90th minute	77.55 ± 6.23	80.96 ± 3.46	0.016*
HR at 100th minute	78.54 ± 6.56	80.41 ± 4.57	0.233
HR at 110th minute	78.09 ± 6.98	80.30 ± 4.61	0.361
HR at 120th minute	76.33 ± 6.35	81.80 ± 2.49	0.124

Data expressed as mean ± SD
HR stands for heart rate
Group A: serratus anterior plane block group
Group B: combined serratus anterior plane block, and transversus thoracis plane block group.
Independent t-test was used to compare the means among groups.
(*) significant results

Table (3): Post-operative mean arterial blood pressure (MABP) comparison of the two studied groups.

MABP	Group (A) (N = 27) Mean ± SD	Group (B) (N = 27) Mean ± SD	P – value
MABP baseline	86.29 ± 4.05	86.92 ± 3.98	0.567
MABP at 2nd hr	92.11 ± 3.66	90.92 ± 1.77	0.136
MABP at 4th hr	92.85 ± 2.47	90.88 ±1.45	0.001*
MABP at 6th hr	93.44 ± 3.00	91.55 ± 2.01	0.009*
MABP at 8th hr	92.96 ± 2.59	92.37 ± 1.80	0.334
MABP at 12th hr	94.14 ± 3.13	91.77 ± 2.12	0.002*
MABP at 24th hr	93.70 ± 2.97	92.14 ± 1.77	0.023*

Data expressed as mean ± SD.
MABP stands for mean arterial blood pressure
Group A: serratus anterior plane block group
Group B: combined serratus anterior plane block, and transversus thoracis plane block group.
Independent t-test was used to compare the means among groups**.**
(*) significant results

Table (4): Rescue analgesia differences between the two studied groups

	Group (A) N = 27 Mean ± SD	Group (B) N = 27 Mean ± SD	P-value
	Intraoperative		
Intraoperative fentanyl consumption	111.11 ± 32.02	107.40 ± 26.68	0.646
	Postoperative		
Postoperative need for analgesia	17 (63%)	16 (59.3%)	0.780^
Time of request of first postoperative analgesia (hours)	14.24 ± 6.078	18.75 ± 6.148	0.293
Postoperative total morphine consumption	4.5 ± 3.61	4.3 ± 3.71	0.854

Data expressed as mean ± SD, and number and percentage.
Group A: serratus anterior plane block group
Group B: combined serratus anterior plane block, and transversus thoracis plane block group.
Independent t-test was used to compare the means among groups
^ Chi-square analysis was used to compare the frequency among group

Table (5): Post-operative Visual Analogue Score (VAS) at rest and at movement comparison between the two studied groups

VAS at rest	Group (A) (N = 27) Median (range)	Group (B) (N = 27) Median (range)	P – value
VAS at rest baseline	0 (0 - 1)	0 (0 - 1)	0.254
VAS at rest at 2nd hour	1 (0 - 2)	1 (0 - 2)	0.603
VAS at rest at 4th hour	1 (0 - 2)	1 (0 - 2)	0.398
VAS at rest at 6th hour	1 (0 - 4)	1 (0 - 2)	0.203
VAS at rest at 8th hour	1 (0 - 5)	1 (0 - 4)	0.784
VAS at rest at 12th hour	1 (0 - 5)	1 (0 - 5)	0.406
VAS at rest at 24th hour	1 (0 - 4)	1 (0 - 4)	0.352
VAS during movement baseline	1 (0 - 1)	1 (0 - 1)	0.293
VAS during movement at 2nd hour	1 (0 - 2)	1 (0 - 2)	0.327
VAS during movement at 4th hour	2 (0 - 2)	2 (0 - 2)	0.215
VAS during movement at 6th hour	2 (0 - 4)	2 (0 - 2)	0.326
VAS during movement at 8th hour	1 (0 - 5)	2 (0 - 4)	0.126
VAS during movement at 12th hour	2 (0 - 4)	2 (1 - 5)	0.361
VAS during movement at 24th hour	2 (0 - 4)	1 (1 - 5)	0.285

Data expressed as median (range).
Group A: serratus anterior plane block group
Group B: combined serratus anterior plane block and transversus thoracis plane block group.
Mann Whitney U test was used to compare the medians between groups**.**

Table (6): side effects differences between the two studied groups

Side effects	Group (A) N (%)	Group (B) N (%)	P-value
Nausea/Vomiting	4 (14.8 %)	7 (25.9 %)	0.311
Headache	2 (7.4 %)	3 (11.11 %)	0.299
Itching	4 (14.8 %)	2 (7.4 %)	0.386

Chi-square analysis was used to compare the frequency per group.

Discussion:

To the best of our knowledge, no other researchers has tested how efficacious is the addition of transversus thoracis plane block to serratus anterior plane block for better analgesic effect for the management of post-mastectomy pain.

Our study showed no additional benefit from the combination of transversus thoracis plane block and the serratus anterior plane block for better management of postmastectomy pain.

Different regional anaesthesia techniques have achieved good management of post-breast surgery acute pain and subsequently less frequent chronic pain[5,6]. Add to that, effective regional anaesthesia would decrease both the surgical stress response and the requirements of general anaesthetics and opioids, which would keep the function of the immune system intact[7].

A lot of regional anaesthesia techniques have been used to control anterior chest wall pain. However, an optimal method has not yet been identified and each of these blocks has many drawbacks.[8-13]

The TTP block has been found to provide adequate surgical analgesia for patients requiring breast resection when combined with the Pecs II block in 3 cases. The TTP blocks were performed under US guidance by injecting levobupivacaine between the third and fourth ribs. The Pecs II block was performed by administering levobupivacaine between the pectoralis major and minor muscles at the third rib. All 3 cases of breast cancer resection were then successfully completed under propofol or dexmedetomidine sedation. These patients had uneventful postoperative courses and were

discharged home without any analgesic drugs. For breast surgery, the TTP block is insufficient as a sole technique, and the addition of the Pecs II block is necessary. [17]

Yao et al., studied the use of serratus anterior plane block to enhance the postoperative pain relief following breast cancer surgeries. They found that preoperative administration of SAP block with ropivacaine improved the quality of recovery, postoperative analgesia, and patient satisfaction following breast cancer surgery. They found a significant difference in cumulative opioid consumption between SAP block group and the control group with mean ± SD of 50.1 ± 2.8 and 69.8 ± 7.0 respectively with a p-value of < 0.001. [18]

Chong et al., compared serratus anterior plane block vs. paravertebral block vs. control group for the management of acute pain in breast and thoracic surgeries. They found that serratus anterior plane block was likely as efficacious as paravertebral blocks in reducing post-operative morphine total consumption and in providing better pain control post-operatively.[19]

Ohgoshi et al. studied the use of serratus intercostal plane block, where the local analgesic is instilled between the serratus anterior muscle and the external intercostal muscle at the mid-axillary line at the fifth intercostal space. They found that providing the local anaesthetic in the area previously mentioned provided analgesia in the ipsilateral upper and lower lateral quadrants of the breast and/or subareolar region. However, they found that it should be administered with other additional analgesic agents when axillary dissection is performed because sensory loss of T1 is difficult to achieve.[20]

Study limitations:

This study has some limitations. The small sample size might have obscured the additional benefit of the TTP block. Also, the TTP block was carried out as a single level injection whereas multiple level injections may be more efficacious for local anesthetic spread. Results weren't corrected regarding Socioeconomic and educational levels of the patients as different socioeconomic statuses and educational levels of the patients might have confounded the interpretation of the same level of pain.

Conclusion:

The combination of transversus thoracis plane block and serratus anterior plane block has no additional analgesic effect than serratus anterior plane block alone for the management of acute postmastectomy pain.

Authors' contributions:

AH crafted the study design, and taught and performed the aforementioned regional blocks. MA helped draft the manuscript. ZZ revised and approved the study design, and helped draft the manuscript. AW performed the statistical analysis, and helped perform the aforementioned regional blocks. All authors have read and approved the final manuscript.

List of abbreviations:

ASA: American Society of Anaesthesiologists
BPM: Beat Per Minute
CDC: Centers for Disease Control and Prevention
ECG: Electrocardiogram
ICU: Intensive Care Unit
PACU: Post Anaesthesia Care Unit
PCA: Patient-Controlled Analgesia
PECs: Pectoral Nerves
SAP: Serratus Anterior Plane
SECI: South Egypt Cancer Institute
SPSS: Statistical Package for Social Science
TTP: Transversus Thoracis Plane
VAS: Visual Analogue Scale
WHO: World Health Organization

Competing interests:

There were no competing interests regarding any of the authors.

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