

ORIGINAL RESEARCH

PAIN MANAGEMENT

Ultrasound-guided serratus anterior plane block versus thoracic epidural analgesia for acute post-thoracotomy pain: a prospective randomized controlled study

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Abstract

Background: Post-thoracotomy pain can result not only in discomfort to the patient but also in pulmonary complications, due to ineffective coughing, which leads to retention of secretions. It can result into chronic post-thoracotomy pain in the long term. Many analgesic techniques are in use to control it, including continuous serratus anterior plane block (SAPB) and thoracic epidural analgesia (TEA). We compared the efficacy and safety of SAPB with continuous TEA in patients undergoing open lung resection.

Methodology: This randomized, open-labeled, parallel-controlled trial was done in 60 patients aged 20 to 60 y with American Society of Anesthesiologists physical status II–III, who underwent elective thoracotomy for lung cancer surgery. Patients were randomly allocated according to analgesia either via a thoracic epidural catheter (10 ml levobupivacaine 0.25%, followed by 5 ml/h of 0.125%) or an ultrasound-guided SAPB (30 ml levobupivacaine 0.25% followed by 5 ml/h of 0.125%). Mean arterial pressure and heart rate were recorded during and after the surgery. Inj. fentanyl was used as rescue analgesia. Postoperatively VAS at rest and on coughing was used to assess the pain. Any complications were noted.

Results: After excluding five patients, 27 and 28 patients were allocated to the TEA and SAPB groups, respectively. Intraoperatively and until 24 h after the end of surgery, the mean arterial pressure and heart rate were higher in the SAPB group than in the TEA group. Intraoperatively, the requirement for fentanyl was more in the SAPB group. Postoperatively, VAS at rest and cough were significantly higher in the SAPB group. The occurrence of nausea and vomiting, hypotension, and bradycardia were similar in the groups.

Conclusions: In patients undergoing open lung resection for cancer, continuous serratus anterior plane block was less effective than thoracic epidural analgesia in controlling postoperative pain and presented similar adverse events.

Key words: Serratus anterior plane block; Thoracic epidural, Continuous; Thoracotomy pain, Acute

Abbreviations: PTP – Post-thoracotomy pain; TEA – Thoracic epidural analgesia; VAS – Visual analog scale; SAPB – Serratus anterior plane block; MAP – Mean arterial blood pressure; LA – Local anesthetics

Preregistration: The study was registered in the institutional board ethical committee (201617026) and on www.clinicaltrials.gov (NCT03933592)

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1. Introduction

Post–thoracotomy pain (PTP) is one of the most severe, debilitating pain and occurs as a result of skin incision, rib retraction, intercostal nerve injury, and intercostal and serratus anterior muscle damage.¹ PTP may result in some serious complications such as pulmonary complications, due to ineffective coughing, which leads to retention of secretion, in the short term; and chronic PTP in the long term.²

Chronic PTP prevalence varies from 25 to 91%, and this high range may be due to variabilities in the pathophysiology, trial design, and the clinical context. There are many predisposing factors that lead to the development of chronic PTP, such as age, sex, comorbid conditions, and the level of preoperative and acute postoperative pain.³

The main techniques for controlling pain in thoracic surgeries are regional blocks and the administration of opioids.⁴ However, thoracic epidural analgesia (TEA) and regional standard analgesic techniques used for open thoracotomy (e.g., paravertebral block) are associated with many risks (e.g., inadvertent intravascular injection, total spinal anesthesia, and pneumothorax etc.). Additionally, some of them (e.g., intercostal and intrapleural blocks) do not provide the desired analgesia. TEA is one of the gold standard techniques used for thoracotomy.^{5–9}

Additionally, opioids have many side effects, such as respiratory depression, constipation, and increased risk of postoperative nausea and vomiting.¹⁰ Weaker analgesics, such as nonsteroidal anti–inflammatory analgesics, are not sufficient to treat the severe pain that accompanies thoracotomy and these also have many side effects, such as risk of peptic ulcers, gastrointestinal bleeding, and renal impairment.¹¹ Similarly, opioids with intermediate potency (e.g., tramadol) are do not manage PTP adequately in most of the cases.¹²

Serratus anterior plane block (SAPB) is one of the interfascial plane blocks that acts by diffusion of local anesthetics (LA) between fascial planes to reach the lateral cutaneous branches of the intercostal nerves.¹³ Unlike TEA, SAPB does not block the autonomic nervous system or lead to adverse events such as epidural hematoma and spinal cord injury. Moreover, identification of SAPB sonoanatomy is not difficult, especially with the shallow needle angle allowing easy administration of the block.¹⁴

We hypothesized that SAPB might be an alternative to TEA with fewer adverse effects or in cases with contraindications for TEA. Therefore, we evaluated the efficacy and safety of continuous SAPB compared with continuous TEA in patients undergoing open lung resection.

2. Methodology

2.1. Patient population and eligibility criteria

This randomized controlled parallel study included 60 patients ages, between 20 and 60 y, ASA physical status II or III, and BMI < 40 kg/m², underwent elective thoracic surgery for lung cancer. After approval of the institutional board ethical committee, written informed consent was obtained from the patients. The study was performed from June 2019 to May 2020 at the National Cancer Institute, Cairo, Egypt. The study was open labelled, as blinding was not practical due to the different techniques and different volumes.

The exclusion criteria were coagulation defects, patient refusal, local infection at the site of injection, chronic opioid use, bone metastases, and known allergy to any of the drugs used.

2.2. Randomization

Patients were randomly allocated according to receive analgesia, either via a thoracic epidural catheter, with a bolus of 10 ml levobupivacaine 0.25%, followed by an infusion of 5 ml/h of levobupivacaine 0.125%, or an ultrasound–guided SAPB with a bolus of 30 ml levobupivacaine 0.25% followed by an infusion of 5 ml/h of levobupivacaine 0.125%.

Randomization was performed in the anesthesia clinic by computer–generated random numbers and closed opaque envelopes. Envelopes were used and opened after enrollment by another anesthesiologist who was not included in the other steps of the study.

Routine preoperative assessment was conducted as standard protocol. Investigations included complete blood count, liver and kidney function tests, coagulation profile, and chest X–ray, in addition to pulmonary function tests. The visual analog scale (VAS) (0 indicates no pain and 10 indicates the worst imaginable pain) was explained to all patients preoperatively. A VAS score at rest greater than 3 required additional analgesia.¹⁵

2.3. Interventions

Upon arrival at the holding area, all the patients were monitored by standard monitoring, including ECG, pulse oximetry, and noninvasive automated arterial blood pressure. Then 3–5 mg midazolam IV was given as premedication after fixation of the 20 G cannula. After sedation, patients were put on oxygen through a nasal cannula at 2 L/min. All blocks were performed by the same anesthesia consultant who was fully experienced in regional anesthesia. All operations were done by the same surgeon. Complete aseptic techniques were observed in both groups. The point of needle entry was infiltrated by lidocaine 1%.

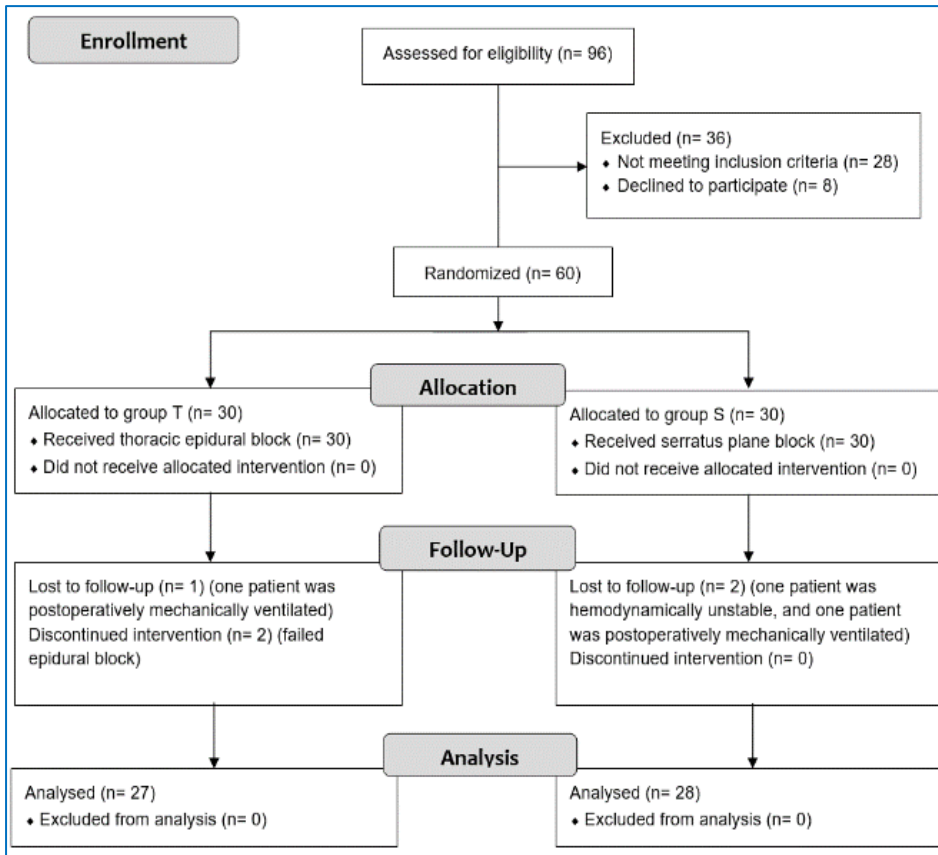


Figure 1: CONSORT flow diagram of both groups

In the TEA group before the induction of anesthesia, patients were in a sitting position. An 18G epidural Tuohy needle (Perifix™, B-Braun, Melsungen AG, Germany) was used. Insertion of a 20G thoracic epidural catheter was done at T6/T7 space; a test dose was given to exclude intrathecal or intravascular catheter insertion. A bolus of 10 ml levobupivacaine 0.25% was given 30 min before skin incision, and then levobupivacaine 0.125% infusion was continued @ 5 ml/h after surgery. Before induction of anesthesia, the sensory block was assessed by pinprick, and failed cases were excluded.

In the SAPB group, after induction of anesthesia and in the lateral position with the surgery side up, a linear probe (10–12 MHz) was placed in a sagittal plane over the mid-axillary region of the chest wall, and the 5th rib was identified. The following muscles were identified: teres major (superior), latissimus dorsi (superficial and posterior), and serratus anterior muscle (deep and inferior). A 22G spinal needle was inserted in-plane to target the fascial plane superficial to the serratus anterior muscle. Thirty minutes before the skin incision, a bolus of 30 ml levobupivacaine 0.25% was injected under continuous US guidance. At the end of the surgery, the

surgeon placed a catheter deep in the serratus anterior muscle, fixed it with a chest tube, and then administered an infusion of 0.125% levobupivacaine at a rate of 5 ml/h. Sensory block was assessed by skin incision, and failed cases by an increase in heart rate (HR) or mean arterial blood pressure (MAP) by 20% above the baseline after induction. All of these cases were excluded.

Induction of anesthesia was performed by inj. fentanyl 2 µg/kg, propofol 2 mg/kg, and cisatracurium 0.5 mg/kg IV. Intubation and mechanical ventilation were performed for all patients using volume-controlled ventilation. Monitoring included pulse oximetry, electrocardiogram (5

leads), noninvasive blood pressure, temperature probe, and capnogram. The maintenance of anesthesia was achieved by 1–1.5% isoflurane in 50–60% oxygen and with 0.1 mg/kg cisatracurium IV. A standard posterolateral incision was made in all thoracotomies. Reversal of muscle relaxant and extubation were performed at the end of the surgery. Then, patients were transferred to the post-anesthesia care unit (PACU).

2.4. Pain Management:

Pain was managed intraoperatively by bolus dose for both groups. To ensure adequate analgesia throughout the operation, all patients were carefully observed, and upon the appearance of signs of inadequate analgesia, e.g., an increase in HR or MAP 20% above baseline (before induction), fentanyl rescue doses of 0.5 µg/kg were supplemented and recorded.

Postoperatively pain was managed by continuous epidural or nerve block infusion. After arriving at the ward, all patients received IV paracetamol every 8 h. In morphine 5 mg IV was given as rescue analgesia when the VAS score at rest was more than 3.

2.5. Measurements

Table 1: Patient characteristics of both groups

Variable		TEA group (n = 27)	SAPB group (n = 28)	P value
Age (y)		50.3 ± 6.2	52.3 ± 5.7	0.229
Sex	Male	13 (48.1%)	16 (57.1%)	0.504
	Female	14 (51.9%)	12 (42.9%)	
BMI (kg/m ²)		24.7 ± 5.3	26.9 ± 5.1	0.135
ASA physical status	II	20 (74.1%)	19 (67.9%)	0.77
	III	7 (25.9%)	9 (32.1%)	
Type of surgery	Metastatectomy	10 (37%)	15 (53.6%)	0.218
	Pleuro–pneumonectomy	7 (25.9%)	9 (32.1%)	0.612
	Segmentectomy	7 (25.9%)	3 (10.7%)	0.177
	Lobectomy	3 (11.1%)	1 (3.6%)	0.352
Duration of surgery (minutes)		151.2 ± 22.5	149 ± 21.0	0.701

Data are presented as mean ± SD or number (percentage). ASA: American Society of Anesthesiologists, BMI: body mass index

Table 2: Intraoperative and postoperative required analgesia in both groups.

Analgesia data	TEA group (n = 27)	SAPB group (n = 28)	p-value
Patients required intraoperative analgesia	7 (25.9%)	28 (100%)	<0.001
Total intraoperative fentanyl consumption (µg)	0 (0–15)	120 (120–160)	
Patients required rescue analgesia at first 24h postoperative	6 (22.2%)	28 (100%)	
Total morphine consumption at first 24h postoperative (mg)	0 (0–0)	25 (20–25)	

Data are presented as median (IQR) or number (percent)

The primary outcome was the percentage of patients who required postoperative rescue analgesia in the first 24 h. The secondary outcomes were postoperative assessment of VAS at rest and cough over the first 24 h postoperatively, cumulative opiate consumption, hemodynamics, and occurrence of adverse events.

MAP and HR were recorded every 10 min for the first hour of the blockade, every 30 min for the next 2 h, and every 2 h for the next 12 h.

Total intraoperative rescue fentanyl consumption was measured. VAS at rest and coughing were recorded in the PACU every 2 h as soon as the patient was alert enough until 24 h. Time to the first rescue analgesia and total morphine consumption during the first 24 h postoperatively were recorded.

Adverse effects were also noted, such as postoperative nausea and vomiting (PONV), hypotension (MAP < 65 mmHg), bradycardia (HR < 60 beats/min), and any arrhythmia. PONV was treated by ondansetron 4 mg IV. Hypotension was treated with incremental doses of ephedrine 5–10 mg. Bradycardia was treated with atropine 0.1 mg/kg IV.

2.6. Sample size calculation:

The sample size calculation was performed by G*Power 3.1.9.2 (Universität Kiel, Germany). It was calculated based on the assumption (based on a pilot study done on

10 patients in each group) that the percentage of patients who required postoperative analgesia in TEA is 50% compared to 100% with SAPB. Using 90% power and a 5% significance level, 26 patients in each group were sufficient to reject the null hypothesis. This number was increased to 30 in each group to overcome dropout.

2.7. Statistical analysis:

Statistical analysis was performed using SPSS v25 (IBM®, Chicago, IL, USA). The Shapiro–Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data are presented as the mean and standard deviation (SD) and were analyzed by unpaired Student's t-test and repeated-measures ANOVA (for repeated measures). Quantitative nonparametric data are presented as the median and interquartile range (IQR) and were analyzed by the Mann–Whitney U test and the Friedman test (for repeated measures). Qualitative data are presented as numbers and percentages and were compared by chi-square (χ^2) or Fisher's exact test when appropriate. Kaplan–Meier curves were used to show the time to first postoperative analgesic requirement. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

We enrolled 96 patients and allocated 60 patients (30 patients in each group), but the final analysis was on 55 patients only: 27 patients in the TEA group and 28 patients in the SAPB group, as shown in the flowchart (Figure 1).

There were insignificant differences in age, sex, BMI, ASA physical status, and type and duration of surgery between the groups (Table 1). Metastatectomy was palliative or performed for single metastases.

The proportion of patients who required intraoperative analgesia and total intraoperative rescue fentanyl consumption was significantly lower in the TEA group than in the SAPB group ($p < 0.001$) (Table 2). There were 6 (22.2%) patients in the TEA group and all patients of

Table 3: Visual analogue scale (VAS) at rest and at cough in both groups

		PACU	2h	4h	6h	8h	10h	12h	18h	24h
VAS at rest										
TEA group (n = 27)	Median	2	2	2	2	2	2	2	2	2
	IQR	1–2	1–3	1–3	1.5–3	1.5–3	1–2.5	1–2.5	2–3	1.5–3
SAPB group (n = 28)	Median	3	3.5	3	3	3	4	3.5	4.5	5
	IQR	2–4.25	1.75–5	2–5	2–5	2–4	3–4.25	2–5	3–5	4–7
p value		< 0.001	0.003	0.007	0.009	0.004	< 0.001	< 0.001	< 0.001	< 0.001
VAS on coughing										
TEA group (n = 27)	Median	2	2	3	3	2	3	2	3	3
	IQR	2–3	2–3	2–4	2–4	2–3	2–3	2–3	2–4	2–4
SAPB group (n = 28)	Median	3.5	4	4	4	4	4	4	5	5.5
	IQR	3–5	2–5.25	2.75–5	3–5	3–4	3–5	3–5	3.75–6	4–7
p value		< 0.001	0.003	0.007	0.009	0.004	< 0.001	< 0.001	< 0.001	< 0.001

IQR: interquartile range, PACU: Post-anesthesia care unit

the SAPB group, who required rescue analgesia, being significantly less patients in the TEA group ($p < 0.001$). The median value (IQR) of total postoperative morphine consumption at 24 h was nil in the TEA group and 25 mg (20–25 mg) in the SAPB group, being significantly less in the TEA group ($p < 0.001$) (Table 2).

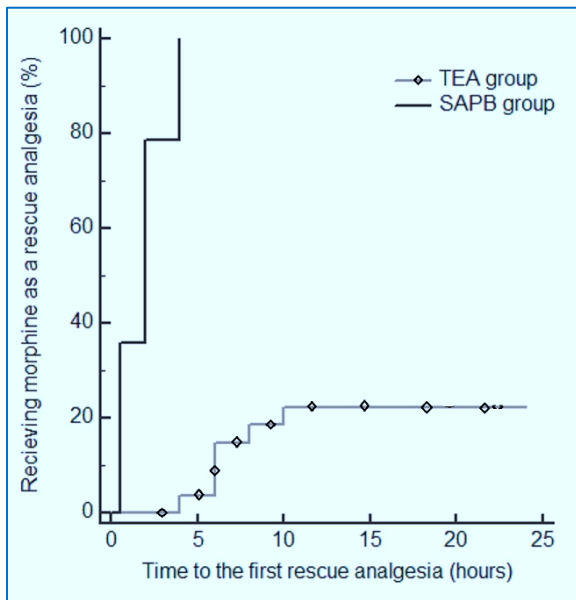


Figure 2: Kaplan Meier curve of time to the first rescue analgesia in both groups

Time to the first rescue analgesia was significantly higher in the TEA group than in the SAPB group ($p < 0.001$); the median value (IQR) was 6 (6–7.5) h in the TEA group and 2 (0.5–2) h in the SAPB group (Figure 2).

HR and MAP were significantly increased in the SAPB group compared to the TEA group at skin incision and intraoperative and postoperative measurements. In the TEA group, the MAP decreased significantly intraoperatively compared to baseline values. In the SAPB group, intraoperative and postoperative HR and MAP were significantly increased compared to baseline values. Repeated measures analysis showed that both group and time factors were significant ($p < 0.001$) (Figure 3 and 4).

VAS at rest and VAS on coughing were significantly lower in the TEA group than in the SAPB group at all postoperative measurements (Table 3). There were significantly fewer patients who required rescue analgesia ($VAS > 3$) in the TEA group than in the SAPB group at all postoperative measurements ($p < 0.05$).

Regarding adverse events, the occurrence of PONV, hypotension ($MAP < 65$ mmHg), and bradycardia ($HR < 60$ beats/min) were not significantly different between the groups. (Table 4)

Table 4: Adverse events in both groups.

Adverse events	TEA group (n = 27)	SAPB group (n = 28)	p value
PONV	3 (11.1%)	5 (17.9%)	0.705
Hypotension	5 (18.5%)	2 (7.1%)	0.252
Bradycardia	2 (7.4%)	2 (7.1%)	1

*Data are presented as number (percent).
PONV: postoperative nausea and vomiting*

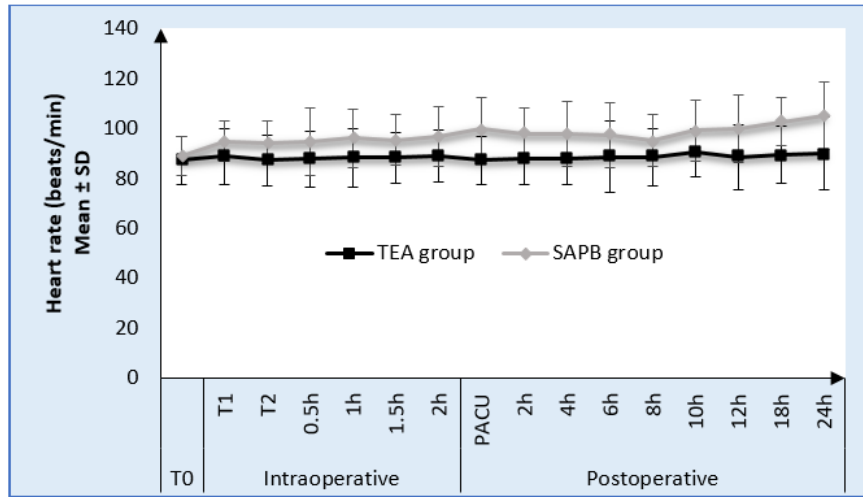


Figure 3: Heart rate changes in both groups (T0: Baseline value, T1: after induction, T2: at skin incision, PACU: Post-anesthesia care unit)

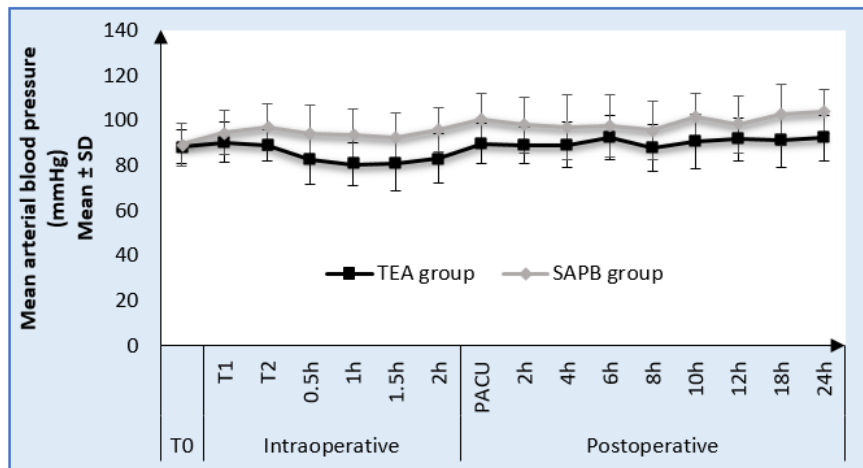


Figure 4: Mean arterial blood pressure changes in both groups (T0: Baseline value, T1: after induction, T2: at skin incision, PACU: Post-anesthesia care unit)

4. Discussion

In our study, TEA provided better intraoperative and postoperative analgesia. This was shown in the lower VAS scores at rest and on coughing, by a low percent of patients requiring intraoperative and postoperative analgesia, total intraoperative rescue fentanyl consumption, and total postoperative morphine consumption. The TEA group had a lower MAP than the SAPB group, but the occurrence of hypotension (MAP < 65 mmHg) and bradycardia was comparable between the two groups. Adverse events were minimal and minor in both TEA and SAPB groups.

In our study, the catheter of SAPB was placed surgically, as a previous study demonstrated the effectiveness of SAPB performed under direct vision on controlling

postoperative pain in breast surgeries.¹⁶ We also used the idea of preemptive analgesia by performing blocks (TEA and SAPB) before surgical incision, which prevents central sensitization and the development of chronic neuropathic pain.^{17, 18} This concept is essential in operations with thoracotomy, as in 25 to 60% of those patients develop chronic pain.¹⁹

In SAPB, the solution of LA is given either superficially or deep to the facial plane of the serratus anterior.²⁰ Blanco et al. found that when contrast dye was injected above the serratus anterior muscle, it showed a more full spread than when it was injected below, as demonstrated by MRI in volunteers.²⁰ Therefore, we injected the anesthetic solution superficial to the serratus anterior muscle.

The reasons for insufficient pain control with SAPB are a large surgical posterior incision (different from VATS), insufficient diffusion of LA at the incisional site, pleural innervation, and rib spreading, which is not covered by blocking the more superficial cutaneous branches. In thoracotomy, SAPB blocks the

anterior part of the incision (innervated by anterior cutaneous branches), but it does not block the posterior part of the incision (posterior cutaneous branches).²¹ SAPB is superior to opioids alone, as shown in a recent meta-analysis,²² but SAPB is inferior to TEA.

Blanco et al. first described SAPB in volunteers and showed its efficacy in blocking the lateral branches of T2–T9 intercostal nerves. They showed that this plane has less vascularity and therefore, less absorption and less toxicity of LAs^[20].

In agreement with our results, Semyonov et al.^[23] showed that patients in SAPB received rescue analgesia in the PACU, indicating the incomplete effectiveness of SAPB. VAS in the first 8 h postoperatively and morphine usage in the first 30 minutes in the PACU and the total

usage were significantly decreased with single-shot SAPB compared to the opioid pain control. Additionally, VAS was insignificantly different between injections of LA solutions either superficially or deep to the serratus anterior muscle.

Additionally, Elsabeeny et al. demonstrated that MAP and the percentage of patients who required intraoperative rescue fentanyl in cancer patients undergoing thoracotomy were significantly higher with SAPB than with TEA intraoperatively.²⁴ Additionally, postoperative analgesia was better with TEA, which was evident by a lower percentage of patients who required postoperative morphine, prolonged first time to receive morphine, lower total postoperative morphine consumption, and lower postoperative VAS values in the first 24 h at rest.

In contrast to our results, Khalil et al. demonstrated that SAPB was effective in managing acute PTP. The VAS score was higher with continuous SAPB than with continuous TEA only at 14, 16, and 22 h postoperatively but was insignificantly different at the other measurement times.¹⁴ Twenty percent of patients with SAPB compared to 15% with TEA required rescue analgesics, and the total 24 h morphine consumption was not significantly different. Hypotension occurred more frequently with TEA (20%) than with SAPB (0%), with $p = 0.02$. However, our results are in agreement with some of their results; MAP was significantly lower with TEA than with SAPB during the whole study period, nausea was insignificantly different between the two groups, and the adverse effects were not serious.

The explanation for the different hemodynamic changes in the two groups is that continuous TEA provides better analgesia and causes sympathetic blockade and in turn vasodilatation and predominant cardiac vagal tone. The autonomic block that accompanies epidural block is not found in SAPB, explaining the hemodynamic stability associated with SAPB.²¹

5. Limitations

The follow-up of acute pain in our study was for 24 h only. Additionally, chronic pain was not monitored in follow up. The research was open-label and performed at a single center. Moreover, we excluded patients with ASA physical status >III and BMI > 40 kg/m². Different criteria were used to determine failed blocks for each group; in particular, MAP and HR, which were also part of the outcome measures and were used to determine failed blocks in SAPB but not in TEA.

6. Conclusions

In patients undergoing open lung resection for cancer, continuous serratus anterior plane block is less effective than continuous thoracic epidural analgesia in

controlling postoperative pain and presented similar adverse events. Further studies are needed to compare thoracic epidural analgesia and serratus anterior plane block with narcotic-based postoperative analgesia for longer follow-up periods for both acute and chronic pain, especially in obese and risky patients. Other techniques, such as erector spinae block as a safer alternative to TEA, should be investigated.

5. Conflict of interests

None declared by the authors

6. Authors' contribution

MMM: Study design, manuscript writing, data collection

AHB: Manuscript writing, data collection

RMG: Manuscript editing, review

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