DOI: https://doi.org/10.17816/RA645367 EDN: LPTGPP

Assessment of the effectiveness of continuous erector spinae plane block versus continuous thoracic epidural analgesia following major thoracic surgery

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ABSTRACT

BACKGROUND: Acute postoperative pain results from the physiological response to surgical stress. Without adequate management, it may not only contribute to early negative outcomes but also increase the risk of chronic postoperative pain. Despite numerous studies, the optimal postoperative analgesic strategy in thoracic surgery remains undefined.

AIM: To perform a comparative assessment of the analgesic effectiveness of continuous erector spinae plane block as part of multimodal analgesia versus continuous thoracic epidural analgesia within a multimodal pain management protocol in patients undergoing extensive thoracic surgery.

METHODS: This prospective randomized study was based on the analysis of analgesia quality and intensity in the early postoperative period in 66 patients who underwent thoracic surgery. Patients received either continuous ultrasound-guided erector spinae plane block (ESPB) in combination with nonsteroidal anti-inflammatory drugs (NSAIDs) and paracetamol, or continuous thoracic epidural analgesia combined with NSAIDs and paracetamol. Pain intensity was assessed using the visual analog scale (VAS) at rest, during movement, and while coughing at 24 h, 72 h, and postoperative day 7. Vital capacity (VC) and peak expiratory flow were assessed at all stages of the study. The study evaluated the impact of the analgesic techniques on blood levels of C-reactive protein, substance P, interleukin-6, and tumor necrosis factor alpha as indirect markers of analgesic effectiveness.

RESULTS: On postoperative day 1, VAS scores for pain during movement and coughing were significantly lower in the study group (30 mm) compared to the control group (30 mm during movement and 40 mm during coughing; p=0.0004). No significant between-group differences in pain intensity during movement and coughing were found at 72 h or day 7 after operation. No significant between-group differences in inflammatory markers were observed at any time point. VC values decreased to 2.9 L on day 1 in both groups ($p < 0.01$). By postoperative day 7, VC values returned to baseline in both groups: 3.6 L in the study group and 3.6 L in the control group ($p < 0.01$).

CONCLUSION: Continuous ESPB ensures effective analgesia in the early postoperative period in patients after open thoracic surgery, comparable in efficacy to thoracic epidural analgesia, and may be used as an alternative.

Keywords: analgesia; thoracic epidural analgesia; nerve block; postoperative pain.

To cite this article:
Drobotova EF, Antipin EE, Svirskii DA, Paromov KV, Volkov DA, Bochkareva NA, Koroleva NI, Yakovenko MP, Zagoskin NS, Bogatyreva MA, Gladkov KA, Zvezdina YuM., Kirov MYu. Assessment of the effectiveness of continuous erector spinae plane block versus continuous thoracic epidural analgesia following major thoracic surgery. *Regional anesthesia and acute pain management.* 2025;19(1):71–83. DOI: 10.17816/RA645367 EDN: LPTGPP

Received: 09.01.2025 **Accepted:** 18.03.2025 **Published:** 25.03.2025

DOI: https://doi.org/10.17816/RA645367 EDN: LPTGPP

Оценка эффективности продлённой блокады нервов нейрофасциального пространства мышц, выпрямляющих позвоночник, в сравнении с продлённой эпидуральной анальгезией после обширных торакальных вмешательств

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АННОТАЦИЯ

Обоснование. Острая послеоперационная боль формируется в результате физиологического ответа на хирургический стресс, но, кроме ранних патогенетических негативных эффектов, при отсутствии адекватной терапии она может трансформироваться в хроническую послеоперационную боль. Несмотря на большое количество проведённых исследований, оптимальная стратегия послеоперационного обезболивания в торакальной хирургии не определена.

Цель. Сравнительная оценка анальгетической эффективности непрерывной блокады нервов нейрофасциального пространства мышц, выпрямляющих позвоночник, как компонента мультимодальной анальгезии и непрерывной эпидуральной блокады на грудном уровне в комплексе мультимодального обезболивания при обширных торакальных операциях.

Материалы и методы. В основу проспективного рандомизированного исследования положены результаты анализа качества и уровня обезболивания в раннем послеоперационном периоде у 66 пациентов, перенёсших торакальные вмешательства, которым проводилась анальгезия методом продлённой блокады нервов нейрофасциального пространства мышц, выпрямляющих позвоночник (erector spinae muscle plane block — ESPB), под контролем ультразвука в сочетании с нестероидными противовоспалительными препаратами (НСПВП) и парацетамолом, или методом продлённой грудной эпидуральной анальгезии в сочетании с НСПВП и парацетамолом. Исследование включает оценку болевого синдрома по визуально-аналоговой шкале (ВАШ) в покое, при движении и кашле через 24, 72 часа и на седьмые сутки после операции. Оценивали жизненную ёмкость лёгких (ЖЕЛ) и пиковую скорость выдоха на всех этапах исследования. Проведён анализ влияния исследуемых методов на динамику концентрации в крови С-реактивного белка, субстанции Р, интерлейкина-6 и фактора некроза опухоли α как косвенных показателей уровня анальгезии.

Результаты. На первые сутки в группе исследования уровень боли по ВАШ при движении и кашле составил 30 мм, в контрольной группе — 30 мм при движении, 40 мм при кашле, что является статистически значимым межгрупповым различием (p=0,0004). При анализе показателей выраженности боли в покое, при движении и кашле через 72 часа и на седьмые сутки после операции не было получено межгрупповых различий. При оценке лабораторных показателей статистически значимых межгрупповых различий на всех этапах исследования получено не было. Показатель ЖЕЛ снизился через сутки после операции в обеих группах (2,9 литра, p <0,01). К седьмым суткам послеоперационного периода показатели ЖЕЛ вернулись к дооперационным параметрам в обеих группах: 3,6 литра в группе исследования и 3,6 литра в группе сравнения (p <0,01).

Заключение. ESPB обеспечивает эффективную анальгезию в раннем послеоперационном периоде у пациентов после открытых торакальных вмешательств, сопоставимую с эпидуральной блокадой, и может использоваться как её альтернатива.

Ключевые слова: обезболивание; грудная эпидуральная анальгезия; блокада нервов; послеоперационная боль.

Как цитировать:
Дроботова Е.Ф., Антипин Э.Э., Свирский Д.А., Паромов К.В., Волков Д.А., Бочкарёва Н.А., Королёва Н.И., Яковенко М.П., Загоскин Н.С., Богатырёва М.А., Гладков К.А., Звездина Ю.М., Киров М.Ю. Оценка эффективности продлённой блокады нервов нейрофасциального пространства мышц, выпрямляющих позвоночник, в сравнении с продлённой эпидуральной анальгезией после обширных торакальных вмешательств // Регионарная анестезия и лечение острой боли. 2025. Т. 19, № 1. С. 71–83. DOI: 10.17816/RA645367 EDN: LPTGPP

Рукопись получена: 09.01.2025 **Рукопись одобрена:** 18.03.2025 **Опубликована:** 25.03.2025

BACKGROUND

Thoracic surgery is considered as one of the most traumatic surgical procedures, thus requiring a multidisciplinary approach to reduce perioperative stress, which has a negative effect on the immune and endocrine systems [1]. Over the past decades, surgical techniques have been significantly optimized. Most surgical interventions are performed using minimally invasive methods, by videothoracoscopy and robot-assisted surgery, but open surgeries cannot be avoided completely. Modern approaches allow speeding up recovery after surgical interventions and shortening patient hospital stay by reducing the severity of postoperative pain and blood loss [2, 3]. Pain control is especially important in the early postoperative period because less than 50% of patients consider analgesia to be adequate. According to the recommendations of the Society for Enhanced Recovery after Surgery and the European Society of Thoracic Surgeons, use of short-acting anesthetics and regional anesthesia techniques as part of the opioid-sparing analgesia strategy is one of the fundamental factors for early rehabilitation and mobilization in the postoperative period [4]. Thoracic epidural anesthesia is a gold standard of analgesia. It significantly reduces the risk of complications in the early postoperative period and effectively prevents the development of chronic post-thoracotomy pain syndrome (PTPS) [5].

However, this technique has some serious drawbacks, including the risk of complications, such as epidural hematoma, epidural space infections, and unintentional puncture of the dura mater [6].

Performing a thoracic epidural anesthesia requires certain skills from the anesthesiologist. Due to patient anatomical characteristics (spinal deformities, overweight), technical difficulties may arise during the blocks, thus increasing the risk of potential complications [7]. Paravertebral block can be a valuable alternative to epidural analgesia; paravertebral block has a lower effect on systemic hemodynamics, provides a high level of analgesia, reduces the usage of narcotic analgesics, and prevents the development of chronic PTPS [8].

In recent years, interest in fascial plane blocks (FPBs) has increased in various areas of surgery, including thoracic interventions [9]. This method consists in ultrasound visualization of the block area and injecting a local anesthetic into the plane between two fascial layers. These blocks can be used as an alternative to paravertebral or epidural analgesia due to their relative simplicity and safety. However, these methods have not been fully studied yet. In particular, the pattern of local anesthetic distribution in FPBs is still unknown. However, evidence is available that FPBs significantly reduced the severity of pain syndrome and the need for narcotic analgesics in thoracic surgery [2, 9]. According to the multimodal anesthesia concept, FPBs are best employed as part of multimodal analgesia with other systemic analgesics, rather than as a sole anesthetic technique [10]. For analgesia during thoracotomy, anesthesiologists can use pectoralis nerve plane block (PECS 2), serratus anterior plane block (SABP), erector spinae muscle plane block (ESPB), and retrolaminar block (RLB) with different effectiveness [11]. The effectiveness of FPBs is explained by three different mechanisms: their direct effect on nerves within the space of the fascial plane, muscle relaxation due to diffusion into adjacent muscles, and systemic effects of adsorbed local anesthetic (LA) [12]. ESPB was described by Forero et al. in 2016, although its history began in 1994, when Rachkov and Kustov received a patent called “Method for managing pain in disorders of the spinal cord and spinal column” [13]. The technique proposed by Forero is practically identical to the Rachkov–Kustov method in terms of the direction of needle insertion and the injection site of the local anesthetic solution.

When an LA is injected posterior to the transverse process of the corresponding vertebra, it spreads through the intercostal neurofascial space and results in ipsilateral blockade of the ventral and dorsal rami of the spinal nerve. When the LA penetrates the anterior and posterior epidural space through the intervertebral foramen, it causes effective sensory blockade [11]. However, it has not been fully studied how LAs spread during ESPB, what the main mechanism of action is during a thoracic block, and whether LA spread differs in an awake patient and in a patient receiving mechanical ventilation with muscle relaxants. In most studies of LA spread in ESPB in cadavers, methylene blue dye penetrated in the cranial, caudal, and lateral directions; however, this spread differed from that in living patients because cadavers do not have any dynamic changes in intrathoracic pressure, and their fascia does not perform its functions as a three-dimensional matrix due to the lack of tone [14].

Although ESPB was shown to be a safe and effective analgesic option for various types of surgery [15, 16], its effectiveness in thoracic surgery remains debatable.

Another problem that has not been solved yet is pain objectification. Often we have to rely only on subjective descriptions of patients. Available data substantiate the use of biochemical markers, including C-reactive protein (CRP), tumor necrosis factor alpha (TNF-α), substance P, and interleukins (IL) 1β, 6, 10, and 12 [17, 18], as indirect indicators of analgesia.

This **study aimed to** assess and compare the analgesic effectiveness of continuous erector spinae plane block as part of multimodal analgesia versus continuous thoracic epidural analgesia as part of a

DOI: https://doi.org/10.17816/RA645367

multimodal pain management protocol in patients undergoing extensive thoracic surgery.

METHODS

Study design

An interventional, single-center, prospective, selective, controlled, blind, randomized study was conducted.

Eligibility criteria

Inclusion criteria: elective surgery, age over 18 years; no history of mental disorders; signed informed consent to participate in the study; no purulent and septic diseases in the area of the intended puncture; no blood-clotting disorders, use of systemic anticoagulant therapy, or allergy to local anesthetics.

Exclusion criteria: refusal to participate in the study; use of systemic steroids; failure to meet the inclusion criteria.

Withdrawal criteria: need for long-term vasopressor support; infectious complications in the postoperative period; repeated surgical intervention.

Randomization

Randomization for postoperative analgesia was performed using envelopes. Sealed envelopes were kept in a safe box and handed out by the head of the department on the morning of the surgery before the preoperative examination by the anesthesiologist. Before opening the envelopes, neither the doctor nor the patient knew what method of analgesia would be used in the postoperative period.

Study setting

This study was conducted as part of the state assignment named "Studying regional morbidity in the population of reproductive age in the Arctic region of the Russian Federation with identifying factors affecting the key functional body systems and developing comprehensive methods for reducing the negative impact of extreme environmental conditions" (reg. No. 122022200516-5).

The study was conducted at the thoracic center of the Arkhangelsk Regional Clinical Hospital (Arkhangelsk, Russia).

Study duration

The study was conducted from November 2022 to November 2024.

Intervention

The randomized study included 66 patients who underwent the following elective thoracic interventions: extended pneumonectomy (n = 10), extended bilobectomy (n = 5), extended lobectomy (n = 39), diaphragm repair surgery (n = 5), total pleurectomy with resection of bullae (n = 5), or transverse lung resection (n = 1). The study group included 33 patients (20 men and 13 women) with a mean age of 64 years. The control group included 33 patients (21 men and 12 women) with a mean age of 62 years.

The study design is shown in Fig. 1. Besides standard examinations and consultations, the preoperative examination included pain assessment before surgery, respiratory function parameters such as vital capacity (VC) and peak expiratory flow (PEF), laboratory markers such as CRP, substance P, IL-6, and TNF-α, as indirect indicators of analgesia.

For all surgical interventions, anterolateral thoracotomy in the fifth intercostal space was used as a surgical approach.

Depending on randomization, the following catheterization techniques were included in anesthetic management: continuous unilateral ultrasound-guided ESPB in the study group (group 1) and continuous thoracic epidural analgesia (TEA) at Th4–Th5 in the control group (group 2). In both groups, catheters for analgesia were placed in the operating room before general anesthesia was induced. An eZono 3000 system (Germany) was used for ultrasound navigation in the study group. The study group patients received a block with 30 mL of ropivacaine 0.33% in the fascial plane; 15 minutes after that, the sensory block was assessed by the pin prick method.

Surgical interventions were performed with multimodal anesthesia with mechanical ventilation. After preoxygenation, all patients were administered propofol 1.5 mg/kg, fentanyl 100–200 μg, and rocuronium bromide 0.6 mg/kg. The trachea was intubated with a single-lumen endotracheal tube. Lung ventilation was performed following the principles of protective mechanical ventilation. Anesthesia was maintained with propofol, fentanyl, and diazepam; muscle relaxation was achieved with rocuronium 0.15 mg/kg. The mean duration of surgery was 155 minutes in group 1 and 150 minutes in group 2. The mean volume of blood loss was 540 mL in the study group and 560 mL the control group; the mean volume of infusions was 1850 and 1900 mL, respectively.

After their surgery, patients received therapy in the intensive care unit for the first 24 hours and were then transferred to the thoracic department.

In the study group, analgesia was performed according to the principle of multimodal analgesia: ESPB (30 mL of ropivacaine 0.33% bolus followed by ropivacaine 0.2% injected into the catheter at

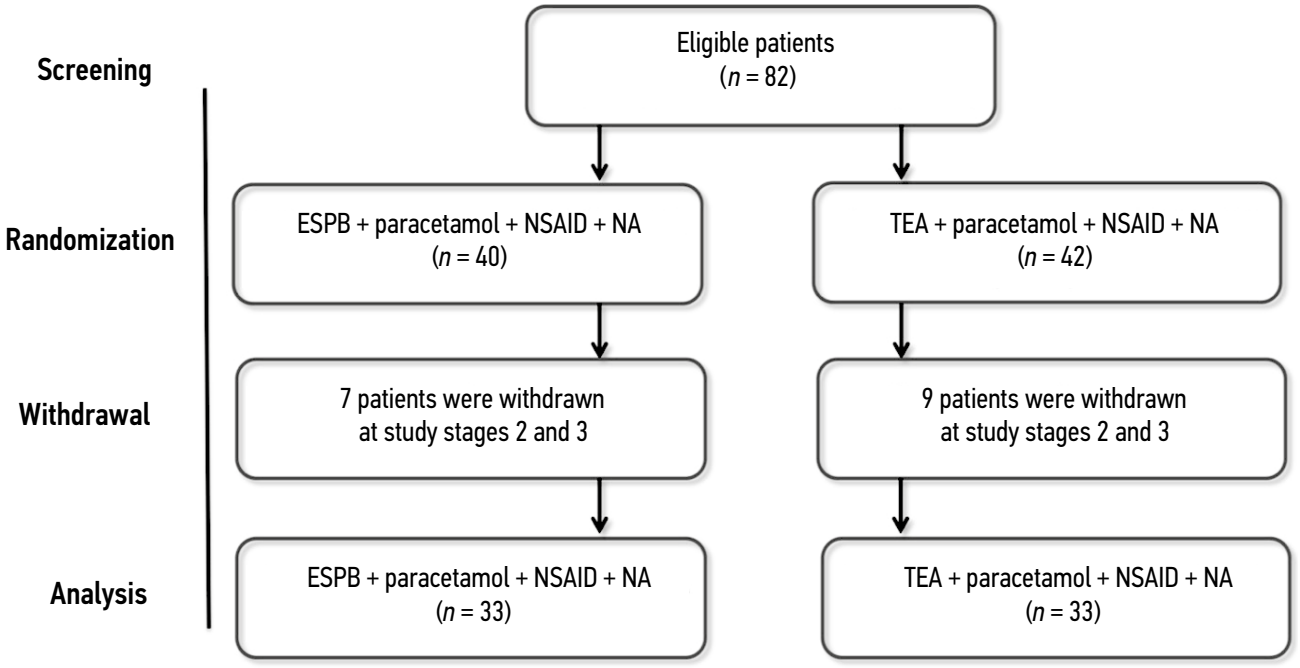

Fig. 1. Study flow-chart. ESPB, erector spinae plane block; TEA, thoracic epidural analgesia; NSAID, non-steroidal anti-inflammatory drug; NA, narcotic analgesic.

a rate of 6–7 mL/h for three days) in combination with a non-steroidal anti-inflammatory drug (NSAID) (ketoprofen 100 mg 2 times a day), paracetamol (4 g/day), and a narcotic analgesic (tramadol 100 mg, single dose) on demand.

In the control group, patients received a standard analgesia regimen: TEA (7–8 mL of ropivacaine 0.5% bolus followed by ropivacaine 0.2% 6–7 mL/h) in combination with a NSAID (ketoprofen 100 mg 2 times a day), paracetamol (4 g/day), and a narcotic analgesic (tramadol 100 mg, single dose) on demand.

Main study outcome

Pain intensity was assessed using the visual analog scale (VAS) at rest, during movement, and during cough at 24 hours, 72 hours, and day 7 after surgery. Blood pressure, heart rate, and respiration rate were also measured at these time points. Twelve months later, a telephone survey was conducted, and two questions were asked: 1) “Do you have pain in the area of your postoperative wound?”; 2) “Can you say that postoperative pain interferes with your quality of life?”

The quality of postoperative analgesia and patient satisfaction were assessed using a 100 mm VAS.

Pulmonary function tests (VC and PEF) were evaluated at control time points. Laboratory markers (CRP, IL-6, TNF-α, substance P) were evaluated as indirect indicators of postoperative analgesia.

Additional study outcomes

The incidence and severity of adverse effects due to narcotic analgesics (sedation, skin itching, nausea and vomiting, urinary retention) were assessed. The need for narcotic analgesics was considered.

Subgroup analysis

The study prospectively included 66 patients (ASA II–III) who underwent elective thoracic interventions for various reasons (tumor lesions, diaphragm elevation, bullous emphysema, or pulmonary sequestration). Distribution of patients by disease entities according to ICD-10 was the following: malignant neoplasms of respiratory and intrathoracic organs (n = 44), benign neoplasms of the respiratory organs (n = 12), chronic lower respiratory diseases, emphysema (n = 5), and disorders of the diaphragm (n = 5). The mean age of patients in the study group (n = 33; 20 men and 13 women) was 64 years. The following types of surgery were performed: extended pneumonectomy (n = 5), extended bilobectomy (n = 3), extended lobectomy (n = 21), diaphragm repair surgery (n = 2), and total pleurectomy with bullae repair (n = 2). The mean age of patients in the control group (n = 33; 21 men and 12 women) was 62 years. The following types of surgery were performed: extended pneumonectomy (n = 5), extended bilobectomy (n = 2), extended lobectomy (n = 18), transverse lung resection (n = 1), diaphragm repair surgery (n = 4), and total pleurectomy with bullae repair (n = 3).

Outcomes registration

Pain intensity was assessed using the visual analog scale at rest, during movement, and during cough at 24 hours, 72 hours, and day 7 after surgery. At these time points, external respiration parameters (VC and PEF) and serum laboratory markers (CRP, IL-6, TNF-α, substance P) were also evaluated.

Patients were asked to place a mark on a 100 mm scale corresponding to their subjective sensation of pain. Pain intensity corresponded to the distance from the beginning of the scale in millimeters. During the preoperative examination, the doctor explained the meaning of the extreme values of the scale, with 0 corresponding to no pain and 10 to unbearable pain, and gave examples of different types of pain and their position on the scale. A score of 1–30 mm corresponded to mild pain, 31–70 mm to moderate pain, and >70 mm to severe pain.

Patients assessed the intensity of their pain using VAS at rest, during movement (sitting up in bed), and during cough. VC was measured using a dry portable spirometer. PEF was measured using a Philips Personal Best portable automatic peak flow meter (USA).

At all time points of the study, venous blood was collected, whole blood was centrifuged (Liston C 2201 laboratory centrifuge, Russia) for 10 minutes at 3000 rpm, and the resulting serum was frozen at –20°C until future testing.

The following laboratory parameters were evaluated:

- Serum CRP by the latex agglutination method using reagents from Vector-Best (reference values 0–5 mg/L) on a BioSystems A-15 biochemical analyzer (Spain);
- TNF-α, IL-6, and substance P by the enzyme immunoassay using a semi-automated microplate photometer Multiskan FC (Thermo Fisher Scientific) with reagents from Vector-Best (TNF-α and IL-6) and Elabscience Bionovation Inc. (substance P). The reference ranges for TNF-α and IL-6 were established according to the manufacturer's instructions (0–6 and 0–10 pg/mL, respectively). The reference range for substance P was 40–270 pg/mL.

Ethics approval

The clinical study was conducted with an approval from the Ethics Committee of the Northern State Medical University (08/10-21 dated October 27, 2021).

Statistical analysis

Sample size was not calculated because the study was a pilot one. Statistical analysis was performed using SPSS for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA) and R statistical software package (ver. 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). Quantitative data were presented as mean and standard deviation for variables with normal distribution and as median with interquartile range for variables with skewed distribution. Qualitative data were presented as absolute values and percentages. In statistical analysis, the Shapiro–Wilk test was used to test parameters for normality of distribution. The Mann–Whitney U test was used for between-group comparisons. The Wilcoxon test and Friedman test were used for within-group comparisons; the Bonferroni correction was used for multiple comparisons. Results were considered statistically significant at $p < 0.05$.

RESULTS

Participants

Baseline data were recorded during preoperative preparation. Clinical and demographic characteristics of patients are presented in Table 1.

Primary results

No clinically significant between-group differences were found in VAS scores for the quality of postoperative analgesia (Fig. 2, 3). Analgesia was adequate in both groups. On day 1 after surgery, VAS scores for pain during movement and cough were significantly lower in the study group (both 30 mm) compared with the control group (30 mm during movement and 40 mm during cough; $p = 0.0004$). Pain intensity on days 3 and 7 did not differ between the groups. Within-group changes over time were statistically significant at all time points.

With within-group differences at all time points, pulmonary function tests did not show any between-group differences at any time points (Fig. 4).

In 24 hours after surgery, vital capacity decreased in both groups without any statistically significant differences, while remaining within the minimum average values for adults (2.9 L). However, by day 7 after surgery, vital capacity returned to preoperative levels in both groups (i.e. 3.6 L in both the ESPB group and the TEA group, which is consistent with the normal average values for adults).

Changes in the laboratory markers (CRP, IL-6, TNF-α, substance P) over time are presented in Fig. 5. The figure shows that changes were consistent with changes in pain intensity over time, thus demonstrating similar pain and stress responses to the surgery trauma in both groups. No statistically significant between-group differences in laboratory parameters were seen at any time point. Statistically significant within-group differences were seen in CRP and IL-6 levels at all time

Table 1. Clinical and demographic characteristics of the study participants

Parameter	Study group (*n* = 33)	Control group (*n* = 33)
ASA II/III	18/15	18/15
Sex, male/female	20/13	21/12
Mean age, years	64 ± 4.2	62 ± 3.8
Height, cm	170.5 ± 6.5	172.4 ± 8.3
Body weight, kg	84 ± 18	83 ± 17.2
VAS before surgery, cm	0	0
VC before surgery, liters	3.6 ± 0.8	3.6 ± 0.7
PEF before surgery, L/min	380.0 ± 35.0	375.0 ± 38.0

Note: ASA, American Society of Anesthesiologists; VAS, visual analog scale; VC, vital capacity; PEF, peak expiratory flow.

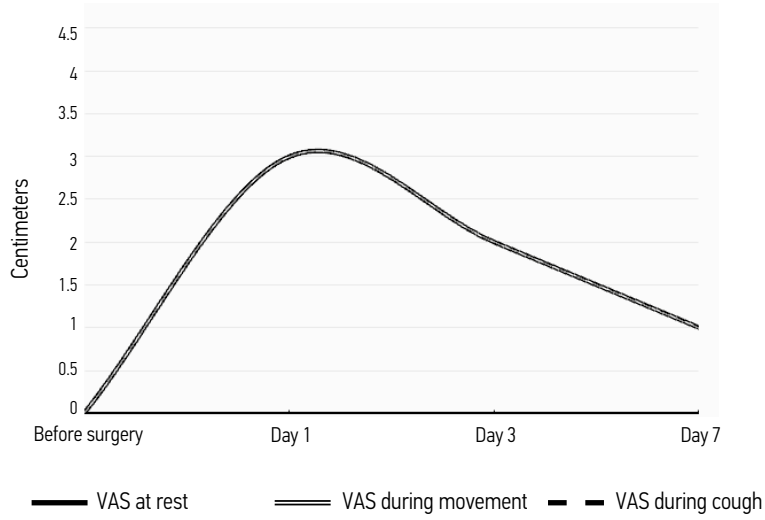

Fig. 2. Changes in VAS score (cm) for pain intensity at different time points in the study group. VAS, visual analog scale.

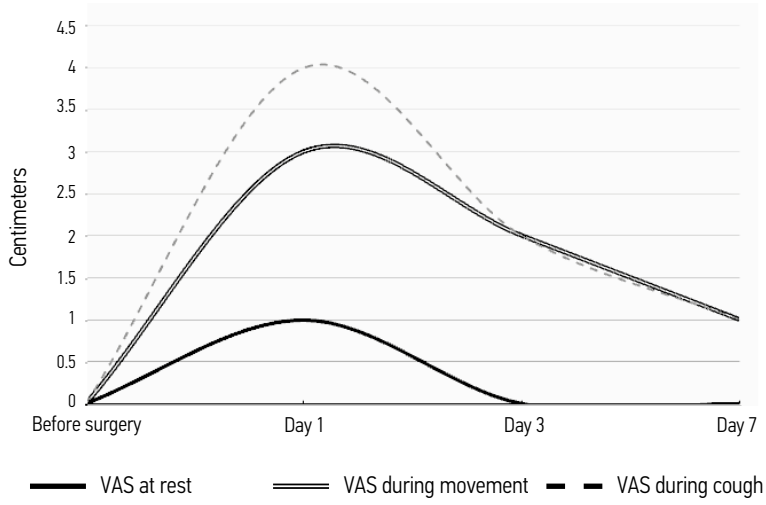

Fig. 3. Changes in VAS score (cm) for pain intensity at different time points in the control group. VAS, visual analog scale.

points; changes in substance P levels were significant in the study group on day 3 after surgery; within-group differences were seen by day 1 in the control group; TNF-α levels did not show any significant within-group differences. The data are presented in Table 2.

Telephone survey results are presented in Table 3. Of 66 patients included in the study, four patients were dead at the time of the survey, two patients refused to answer questions, and five patients were lost to follow-up. Four patients had repeat surgeries, and none of them reported pain after the first intervention. Survey results did not show any significant differences between the groups.

Secondary results

No side effects due to narcotic analgesics (sedation, skin itching, nausea and vomiting, urinary retention) were recorded in either group. The need for opioids was significantly lower in the study group (tramadol 300 mg/day) than in the control group (tramadol 400 mg/day) (p = 0.006). Eight patients in the ESPB group did not require any narcotic analgesics during the first 24 hours after surgery.

Adverse events

In the control group, three patients required vasopressor support (norepinephrine 0.36–0.28 μg/kg/

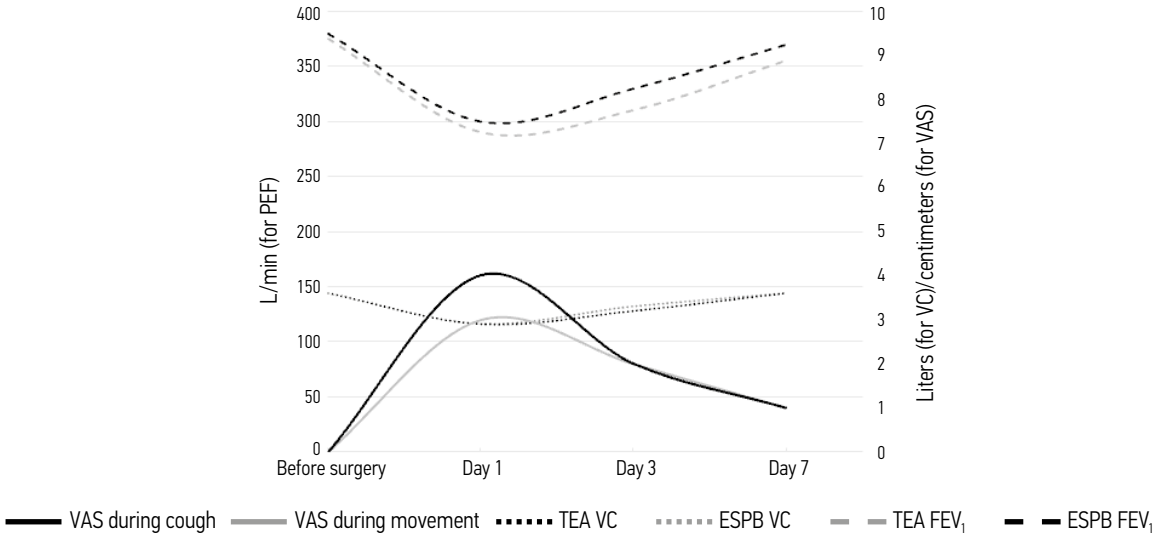

Fig. 4. Changes in pulmonary function tests over time. VC, vital capacity; VAS, visual analog scale; FEV_1, forced expiratory volume in one second; ESPB, erector spinae plane block; TEA, thoracic epidural analgesia.

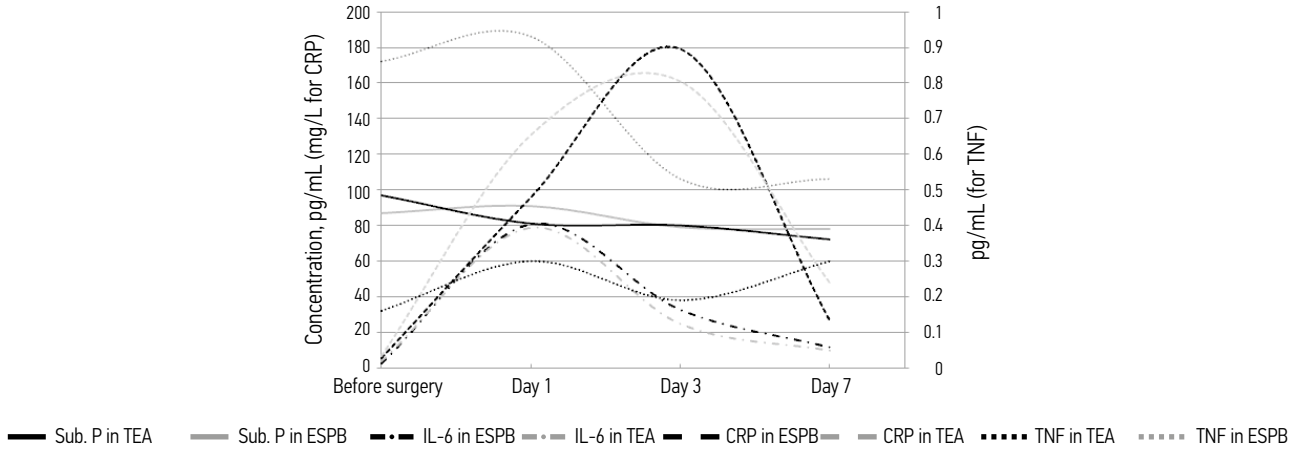

Fig. 5. Changes in laboratory parameters over time. Sub. P, substance P (pg/mL); IL-6, interleukin 6 (pg/mL); CRP, C-reactive protein, TNF, tumor necrosis factor (pg/mL); ESPB, erector spinae plane block; TEA, thoracic epidural analgesia. For TNF, an additional logarithmic scale is used on the right.

min) intraoperatively and during the first four hours of the early postoperative period.

DISCUSSION

Summary of primary results

During the first three days after thoracic interventions, continuous ultrasound-guided ESPB provided adequate analgesia, which was similar in its effect to continuous epidural analgesia, and reduced the usage of narcotic analgesics.

Interpretation

Although TEA is considered the gold standard of analgesia in thoracic surgery, ESPB has a broader safety profile (because there are no discrete nerves, large vessels, or pleura in the area of interest) and provides greater hemodynamic stability [19]. The ultrasound-guided block has better safety because the tip of the needle can be visualized [20], which reduces the risk of block failure. However, the effectiveness of ESPB in thoracic surgery compared with other regional techniques remains debatable. According to a meta-analysis by Koo et al., ESPB was inferior to thoracic

Table 2. Within-group differences in laboratory parameters.

Laboratory parameter	Groups		Before surgery	Day 1	Day 3	Day 7	Within-group differences
CRP	ESPB	Me (IQR)	6.0 (5.4)	96.3 (89.5)*	179.0 (184.3)*	27.7 (62.5)*	Chi = 71.2; p = 0.000000000000002 (2.3e-015)
	TEA	Me (IQR)	7.4 (7.9)	131.0 (100)*	161.8 (194.0)*	48.7 (39.5)*	Chi = 55.671; p = 0.00000000001 (4.9e-012)
TNF	ESPB	Me (IQR)	0.0 (0.5)	0.0 (0.9)	0.0 (0.5)	0.0 (0.3)	Chi = 2.15; p = 0.54
	TEA	Me (IQR)	0.0 (0.0)	0.0 (0.0)	0.0 (0.2)	0.0 (0.25)	Chi = 4.71; p = 0.19
IL-6	ESPB	Me (IQR)	3.0 (4.7)	81.2 (64.4)*	32.9 (41.1)*	12.4 (26.8)*	Chi = 69.05; p = 0.00000000000001 (6.8e-015)
	TEA	Me (IQR)	3.6 (5.9)	57.9 (48.9)*	25.1 (29.0)*	10.1 (12.0)*	Chi = 65.014; p = 0.0000000000001 (4.98e-014)
Substance P	ESPB	Me (IQR)	87.3 (24.3)	91.2 (41.5)	79.1 (40.3)*	78.3 (35.1)	Chi = 4.41; p = 0.22
	TEA	Me (IQR)	96.7 (45.9)	81.8 (44.7)*	80.2 (53.6)	72.3 (37.7)	Chi = 15.67; p = 0.001

Note: CRP, C-reactive protein; TNF, tumor necrosis factor; IL-6, interleukin-6; ESPB, erector spinae plane block; TEA, thoracic epidural analgesia. *Within-group differences over time. Comparison: before surgery vs. day 1; day 1 vs. day 3; day 3 vs. day 7. Critical p = 0.05/3 = 0.17.

Table 3. Results of 12-month follow-up after surgery

Groups	Number of patients	No pain	Impaired quality of life (discomfort)	Pain
ESPB	26	16	9	1
TEA	24	15	8	1

Note: ESPB, erector spinae plane block; TEA, thoracic epidural analgesia.

paravertebral block but superior to serratus anterior plane block and intercostal nerve block in postoperative analgesia [21].

In our opinion, ultrasound-guided ESPB, despite its relative simplicity, requires thorough performance to ensure analgesia quality. It is necessary to ensure its technical correctness, as evidenced by visible hydrodissection of tissues below the plane of the erector spinae muscles when the local anesthetic is injected. The block is considered successful if the anesthetic has diffused from Th5 to Th8–9 with a corresponding sensory deficit.

In our study, vital capacity decreased 24 hours after surgery in both groups without any statistically significant between-group differences, while remaining within the minimum average values for adults (2.9 L in both the study group and the control group). However, by day 7 after surgery, vital capacity returned to preoperative levels in both groups (i.e. 3.6 L in both the ESPB group and the TEA group, which is consistent with the normal average values for adults). Our data were consistent with other studies where ESPB was effective for both somatic and visceral pain with positive effects on patient respiratory function. Syal et al. [22] also showed that ESPB not only provided adequate analgesia but also improved respiratory function in a patient with respiratory dysfunction.

Among the perioperative stress markers that we studied, substance P is a key factor in responding to most stimuli that may compromise the biological integrity of the body. Substance P initiates the expression of almost all known cytokines [23]. In their turn, most cytokines induce substance P and NK1 receptors. Substance P is a key element of pain perception; it modulates the transmission of pain information to the central nervous system. Substance P exerts antinociceptive activity by initiating the enhancement of opioid activity after painful stimuli. Therefore, spinal tachykinin and opioid systems are in a direct functional interaction in the dual modulation of nociceptive responses [24].

Our study showed that substance P levels did not exceed the reference values either before surgery or at any time point in any group. Our data showed the high quality and equal analgesic effectiveness of both methods.

In a study by Gaddam et al. [25], plasma levels of substance P correlated with the levels of proinflammatory mediators such as procalcitonin, CRP, and IL-6. As regulators of immune and inflammatory processes, cytokines are key molecules in the modulation of pain pathways. Some of them, like IL-6, are both pro- and anti-inflammatory. Proinflammatory cytokines are associated with postoperative pain through activation of nerve endings, which may contribute to the maintenance of hyperalgesia [26]. Among them, IL-6 is the most representative cytokine of tissue damage. IL-6 also acts as an indicator of inflammatory response after surgical trauma and stimulates the synthesis of acute phase proteins in the liver, including CRP. According to our data, IL-6 levels, after a short-term increase 24 hours after surgery in both groups, returned to preoperative values by day 3, while no statistically significant differences were found between the groups at any time point. Similar results were obtained for TNF-α.

C-reactive protein is a well-studied inflammatory mediator involved in the clearance of damaged cells. Its levels increase immediately after tissue damage with a relatively short half-life of approximately 19 hours. Therefore, CRP significantly reflects the severity of postoperative inflammation. Increased CRP levels 3–4 days after surgery were associated with postoperative complications [27]. We did not find any statistically significant between-group differences in CRP levels over time at any time point. After an expected increase in CRP levels on day 3 after thoracotomy, they returned to reference values by day 7.

Therefore, clinical and laboratory data did not show any differences in the efficacy of ESPB and TEA in the groups. Both techniques provided high-quality postoperative analgesia.

Study limitations

Quantitative limitations of the study include small sample size. Qualitative limitations are determined by the current field of knowledge about the stress response and its influence on the formation and maintenance of pain. Subject and semantic limitations consist of the difficulty of objectifying pain characteristics.

CONCLUSION

Continuous ESPB provided effective analgesia in the early postoperative period in patients after open thoracic surgery, which was similar in effectiveness to continuous epidural block, and may be used as its alternative.

The use of ESPB as a component of multimodal analgesia allowed reducing the consumption of narcotic analgesics and avoiding the development of their side effects.

ADDITIONAL INFORMATION

Author contributions: E.F. Drobotova: conceptualization, investigation, formal analysis, writing—original draft, writing—review & editing; E.E. Antipin: conceptualization, formal analysis, writing—review & editing; D.A. Svirsky: conceptualization, formal analysis, writing—original draft, writing—review & editing; K.V. Paromov: writing—review & editing; D.A. Volkov: formal analysis; N.A. Bochkareva: investigation, formal analysis; N.I. Koroleva: investigation, formal analysis; M.P. Yakovenko: formal analysis, writing—review & editing; N.S. Zagoskin, M.A. Bogatyreva, K.A. Gladkov, Yu.M. Zvezdina: investigation; M.Yu. Kirov: formal analysis,

writing—review & editing. All the authors approved the final version before publication and agreed to be accountable for all aspects of the paper, ensuring that questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Ethics approval. The study was approved by the Ethics Committee of the Northern State Medical University, protocol No. 08/10-21 dated October 27, 2021.

Funding sources: This study was conducted as part of the state assignment named "Studying regional morbidity in the population of reproductive age in the Arctic region of the Russian Federation with identifying factors affecting the key functional body systems and developing comprehensive methods for reducing the negative impact of extreme environmental conditions" (reg. No. 122022200516-5).

Disclosure of interests: The authors have no relationships, activities, or interests for the last three years related to for-profit or not-for-profit third parties whose interests may be affected by the content of the article.

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