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Erector Spinae Plane Block Modulates Immune Function in Minimally Invasive Lung Surgery

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ABSTRACT

Minimally invasive lung surgery still triggers significant inflammatory and immunosuppressive responses. This retrospective cohort study (January 2021–December 2023) assessed whether erector spinae plane block (ESPB) improves perioperative immune/cytokine balance in lung cancer patients undergoing elective minimally invasive surgery (ESPB, n=58; control, n=65).

Compared with controls, the ESPB group demonstrated superior perioperative outcomes. Hemodynamics at incision were more stable (MAP: 103.24±9.85 vs 112.40±11.23 mm Hg, HR: 86.17±7.91 vs 94.74±9.05 beats/min), and opioid consumption was significantly lower (intraoperative sufentanil: 33.12±3.93 vs 36.75±5.08 μg). Postoperative pain scores were reduced (resting VAS at 1 hour: median 2 vs 4), comfort scores higher (BCS at 1 hour: median 2 vs 1), and patient-controlled analgesia use less frequent (total PCA demands at 48 hours: 18.55±5.14 vs 23.45±5.97).

Immunologically, the ESPB group showed significantly attenuated suppression of cellular immunity, with higher CD3+ (60.92±4.74% vs 56.53±3.27% at 48 hours), CD4+ (38.16±4.29% vs 34.18±4.06% at 48 hours), CD4+/CD8+ ratio (1.23±0.17 vs 1.02±0.23 at 48 hours), and NK cells (21.03±3.45% vs 18.27±2.78% at 48 hours). The cytokine response was also modulated favorably: the rise in proinflammatory IL-6 (26.82±4.65 vs 32.55±5.21 pg/mL at 24 hours) and TNF-α (54.86±7.12 vs 61.55±6.01 pg/mL at 24 hours) was lower, while the anti-inflammatory IL-10 was higher in the ESPB group (28.12±4.43 vs 24.55±5.44 pg/mL at 24 hours).

Clinically, the ESPB group experienced a lower incidence of postoperative dizziness (3.45% vs 13.85%), earlier ambulation (24.36±4.24 vs 27.55±5.17 hours), and a shorter hospital stay (15.16±1.83 vs 17.54±2.39 days).

Keywords: Cellular; Cytokines; Immunity, Inflammation; Nerve block; Perioperative care

INTRODUCTION

Lung cancer is the leading cause of cancer-related deaths worldwide, and surgical resection is an effective treatment for early-stage lung cancer.[1] While traditional thoracotomy has been the historical standard, it involves considerable trauma, significant postoperative pain, and extended recovery, adversely affecting patient quality of life.[2] Advances in minimally invasive techniques have established video-assisted thoracoscopic surgery (VATS) for lobectomy or segmentectomy as the current standard of care for early-stage disease.[3] This shift is

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attributed to the demonstrated benefits of VATS, including reduced surgical trauma, lower blood loss, fewer complications, better preservation of pulmonary function, and accelerated postoperative recovery. However, "minimally invasive" does not equate to "non-invasive." Despite significant reductions in surgical incisions and tissue damage, minimally invasive lung surgery itself still constitutes a traumatic insult.[4] Intraoperative one-lung ventilation, traction and resection of lung tissue, and postoperative indwelling thoracic drainage tubes inevitably activate the body's stress system, triggering a series of complex physiological and pathophysiological changes.[5] This stress response not only enhances pain perception but also leads to an imbalance in immune and inflammatory responses. This is driven by 3 key mechanisms: a surge in proinflammatory cytokines, dysregulation of anti-inflammatory cytokine expression, and suppression of cellular immune function.[6]

Surgical trauma triggers an inflammatory response where excessive proinflammatory mediators can exacerbate tissue damage and induce systemic inflammation, potentially progressing to multiple organ dysfunction. Concurrently, impaired anti-inflammatory regulation, exemplified by abnormal IL-10 expression, disrupts immune homeostasis and elevates the risk of postoperative complications, including infections and tumor recurrence.[7] Furthermore, T-lymphocyte subsets and NK cells constitute the body's core defense against pathogen invasion and tumor cell proliferation.[8] Studies have shown that following major surgery, the numbers of T-lymphocyte subsets in patients' peripheral blood significantly decrease. Specifically, the reduction in $CD4^+$ T cells and the $CD4^+/CD8^+$ ratio reflects disturbances and suppression of the body's cellular immune function.[9,10] The number and activity of NK cells are also suppressed, thereby weakening the body's ability to clear residual tumor cells and prevent postoperative infections. Consequently, how to effectively regulate the perioperative inflammatory storm and mitigate surgery-induced immunosuppression has become an important challenge for both thoracic surgeons and anesthesiologists.

Pain, as one of the most prominent stressors in the perioperative period, exhibits a close interaction with immune-inflammatory responses.[11] Traditional postoperative analgesia primarily relies on opioid drugs. However, their widespread use after thoracic surgery is limited by dose-dependent side effects, which may even exacerbate immunosuppression.[12] Multimodal analgesia represents the core concept of modern pain management. Its essence is to combine drugs and techniques with differing mechanisms to optimize analgesia while minimizing opioid dosage and associated adverse effects.[13] Regional nerve blockade serves as a crucial component of multimodal analgesia. By precisely injecting local anesthetics into specific nerves or fascial planes to block the transmission of nociceptive signals, it provides effective analgesia and reduces opioid consumption.[14] More importantly, by mitigating the stress response and decreasing opioid use, regional blockade can positively modulate perioperative immune function.[15] In 2016, Foreo et al first described erector spinae plane block (ESPB). This is a technique that injects local anesthetics into the fascia plane between the erector spinae muscle and the thoracic transverse process under ultrasound guidance.[16] ESPB is performed at a site farther from the spinal cord and pleura, offering a simpler, safer approach with a reduced risk of complications. Consequently, it has rapidly gained widespread application in various surgeries, including thoracic, abdominal, spinal, and breast procedures.[17–20] ESPB provides safe, effective postoperative analgesia for VATS, as evidenced by reduced pain scores, decreased opioid consumption, and a lower incidence of side effects such as nausea and vomiting.[21] ESPB may exert its immunomodulatory effects through multiple interconnected mechanisms. First, by blocking afferent nociceptive signals at the fascial plane, it reduces activation of the hypothalamic-pituitary-adrenal axis and sympathetic outflow, thereby limiting stress-induced glucocorticoid and catecholamine release, both of which suppress lymphocyte function. Second, the reduced opioid consumption associated with ESPB minimizes opioid-induced immunosuppression, which is known to impair NK cell activity and cytokine production. Third, by improving pain control, ESPB may indirectly support immune function through better postoperative recovery, including early ambulation and reduced inflammatory burden. However, most current studies on ESPB focus primarily on evaluating its analgesic efficacy. We therefore hypothesize that ESPB, by attenuating nociceptive transmission and reducing perioperative opioid consumption, may limit the surgery-induced surge of proinflammatory cytokines and preserve cellular immune function, thereby contributing to improved immune homeostasis.

Based on the aforementioned research background and the current gaps in knowledge, this study aims to employ a retrospective cohort design. We will collect clinical data from patients undergoing elective minimally invasive lung surgery to investigate the impact of ESPB on their perioperative cytokine network and cellular immune function. By integrating outcomes including pain scores, opioid consumption, complications, and hospital stay, we will comprehensively evaluate ESPB's clinical value in perioperative management. The findings of this study are intended to provide more robust evidence-based medical support for the application of ESPB in thoracic surgery. Additionally, it aims to offer new insights and a theoretical foundation for optimizing perioperative immune management strategies.

MATERIALS AND METHODS

Study Subjects

This study retrospectively analyzed consecutive clinical records of adult lung cancer patients who underwent elective unilateral video-assisted thoracoscopic surgery (VATS) lobectomy or segmentectomy under general anesthesia in our hospital's Department of Thoracic Surgery between January 2021 and December 2023. All procedures were performed using a standardized 3-port VATS technique without robotic assistance. Surgeries were conducted by a team of experienced thoracic surgeons (each with >5 years of VATS experience) using uniform surgical protocols to minimize variability in surgical stress and technique. Patients were identified through the hospital's electronic medical record system and were included based on the predefined criteria. The study flow is detailed in Figure 1.

Inclusion and Exclusion Criteria

Inclusion Criteria:

(1) American Society of Anesthesiologists (ASA) physical status I–III;

(2) Scheduled for elective unilateral video-assisted thoracoscopic lobectomy or segmentectomy under general anesthesia;

(3) Normal preoperative function of major organs;

(4) Complete medical records, laboratory data, and follow-up information.

Exclusion Criteria:

(1) Contraindications to ESPB, such as skin infection at the puncture site, coagulation disorders, or history of local anesthetic allergy;

(2) History of chronic pain requiring long-term use of opioids or other analgesic medications;

(3) Presence of severe neurological or psychiatric disorders impairing effective communication;

(4) Immunocompromised status or current use of immunosuppressive therapy;

(5) Pre-existing active infection;

(6) Pregnancy or lactation.

Ultrasound-guided ESPB Procedure

Prior to anesthetic induction, ESPB was performed at the T5 level. With the patient in the lateral decubitus position (surgical side up), the T5 spinous process was identified by palpation and anatomical landmarks. Using a sterile high-frequency linear ultrasound probe (Mindray M9, Shenzhen Mindray Bio-Medical Electronics Co., Ltd., 6–13 MHz) placed longitudinally 3 cm lateral to the midline, the transverse process tip was located and marked. Following standard aseptic preparation and local infiltration with lidocaine, a sterile 22-gauge 80-mm needle was advanced under real-time ultrasound guidance using an in-plane technique from a cranial-to-caudal direction. Upon confirming the needle tip position at the deep fascia of the erector spinae muscle with saline hydrodissection, 30 mL of 0.5% ropivacaine (batch No. 93B05101, Yichang Humanwell Pharmaceutical Co., Ltd.) was injected after negative aspiration, with clear visual spread of the local anesthetic along the fascial plane. Twenty minutes later, a pinprick test was performed to assess the extent and efficacy of the nerve block. Successful ESPB was confirmed by loss of sensation to pinprick in the dermatomes corresponding to the ipsilateral T3 to T9 spinal nerves.

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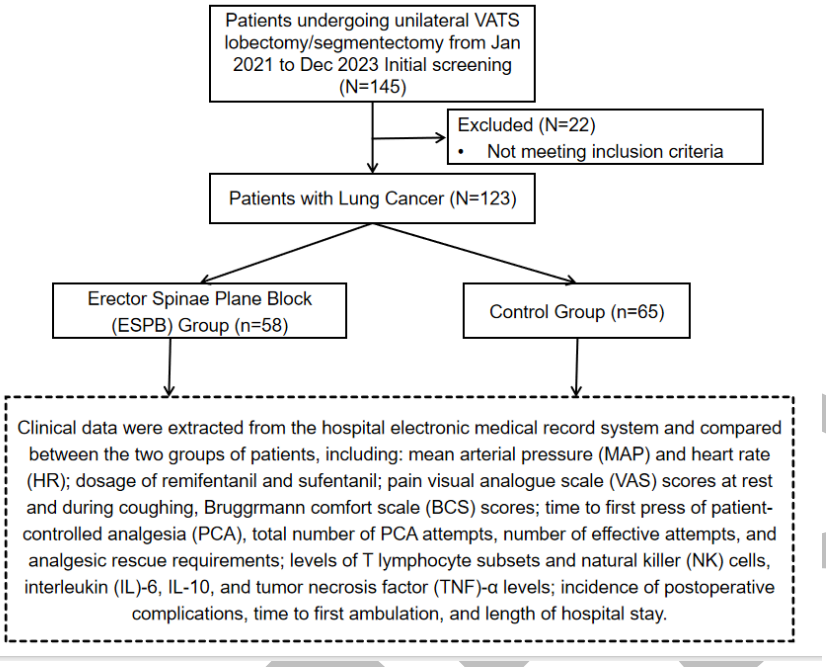

Figure 1. Study flow.

Anesthetic Management

With the patient supine, preoxygenation was performed for 3 minutes. Anesthesia was induced intravenously with midazolam (0.05 mg/kg), etomidate (0.2 mg/kg), sufentanil (0.4 μg/kg), and rocuronium (0.6 mg/kg). Following a 5-minute interval, double-lumen endotracheal intubation was performed. Correct tube position was confirmed via fiberoptic bronchoscopy, and mechanical ventilation was initiated. During two-lung ventilation, tidal volume was set at 8–10 mL/kg; during one-lung ventilation, it was reduced to 6–8 mL/kg. Respiratory rate was maintained at 14–16 breaths per minute in both phases. Anesthesia was maintained with continuous infusions of propofol (4–5 $mg \cdot kg^{-1} \cdot h^{-1}$), remifentanil (0.2–0.3 $\mu g \cdot kg^{-1} \cdot min^{-1}$), and cisatracurium (1–2 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Thirty minutes prior to the anticipated end of surgery, the cisatracurium infusion was discontinued. Additional analgesia was provided with intravenous sufentanil (0.1 μg/kg) and parecoxib sodium (40 mg) 20 minutes before conclusion. Remifentanil and propofol infusions were stopped 5 minutes prior to the end of surgery. Upon completion, the lungs were suctioned and recruited. After regaining consciousness and meeting extubation criteria, the double-lumen tube was removed.

All patients were managed under a standardized Enhanced Recovery After Surgery (ERAS) protocol, which included multimodal analgesia, early mobilization, nutritional optimization, and goal-directed fluid therapy. Postoperative analgesia was provided using a patient-controlled analgesia (PCA) device with sufentanil (2 μg/mL) and ondansetron (0.16 mg/mL), programmed as a bolus dose of 2 mL with a lockout interval of 15 minutes and no continuous background infusion. Rescue analgesia (intravenous flurbiprofen axetil 50 mg or tramadol 50 mg) was administered at the discretion of the attending anesthesiologist if the patient's VAS score at rest was ≥4 or if the patient requested additional analgesia.

Observation Indicators

The following indicators were collected and recorded via the hospital electronic medical record system and the anesthesia clinical information system. The selected time points (pre-anesthesia, end of surgery, 24 hours, and 48 hours postoperatively) were chosen to capture the acute surgical stress response, the immediate postoperative immune nadir, and the early recovery phase, which are critical windows for immune dysregulation and potential intervention.

(1) General Data: Age, sex, BMI, ASA status, type of surgery, etc.

(2) Hemodynamic Parameters: MAP and HR measured at 4 time points: before anesthesia induction, immediately after tracheal intubation, immediately after skin incision, and immediately after tracheal extubation.

(3) Anesthetic and Analgesic Drug Consumption: Total intraoperative consumption of remifentanil and sufentanil; cumulative postoperative consumption of sufentanil at 24 hours and 48 hours.

(4) PCA Usage: Time to first PCA demand postoperatively, total number of PCA demands and effective demands within 24 hours and 48 hours postoperatively; and the proportion of patients requiring rescue analgesia.

(5) Postoperative Pain and Comfort Assessment: Visual Analog Scale (VAS) for Pain: Pain intensity was assessed using the 0 to 10 scale at rest and during coughing at 1 hour, 6 hours, 24 hours, and 48 hours postoperatively. Comfort Score: Comfort level was assessed using the Bruggrmann Comfort Scale (BCS) at the same time points as the VAS assessments.

(6) Postoperative Recovery Indicators: Time to extubation, time to first ambulation, and postoperative length of hospital stay.

(7) Immune and Cytokine Indicators: A 5 mL sample of venous blood was collected from the median cubital vein at 4 time points: before anesthesia induction, immediately after surgery, 24 hours postoperatively, and 48 hours postoperatively. T Lymphocyte Subsets and NK Cells: The percentages of peripheral blood $CD3^+$, $CD4^+$, and $CD8^+$ T cells, as well as NK cell ($CD3^-CD16^+CD56^+$) levels, were detected using flow cytometry (FACSCalibur, BD, USA) with matched reagents. Serum Cytokines: Serum concentrations of IL-6, IL-10, and TNF-α were measured using an automated chemiluminescence immunoassay analyzer (Immulite 1000, Siemens, Germany) with matched reagent kits. The intra-assay and inter-assay coefficients of variation for the chemiluminescence immunoassay were <5% and <8% for IL-6, <6% and <9% for TNF-α, and <5% and <8% for IL-10, respectively, according to the manufacturer's specifications. In this study, "immune suppression" refers to a statistically significant postoperative reduction in $CD3^+$ and $CD4^+$ T-cell percentages, a decline in the $CD4^+/CD8^+$ ratio, and decreased NK cell levels relative to preoperative baseline, accompanied by functional implications as supported by prior literature. Laboratory investigators performing flow cytometry and chemiluminescence immunoassay analyses were blinded to group allocation.

(8) Postoperative Complications: The incidence of adverse reactions such as nausea and vomiting, dizziness, and somnolence was recorded. In addition, postoperative complications such as pneumonia, prolonged air leak (>5 days), atelectasis requiring bronchoscopy, and wound infection were documented from the electronic medical records.

Sample Size Calculation

This study was a retrospective analysis that included all eligible patient medical records from January 2021 to December 2023 based on the predefined inclusion and exclusion criteria. To evaluate the statistical power of the study, a post hoc sample size estimation was performed. The calculation was based on the effect size range reported in the literature concerning immune responses after VATS with ESPB.[22] An effect size of 0.6 (medium to large) was specified. Setting a 2-sided α level of 0.05 and a power (1-β) of 0.80, the sample size was estimated using the formula for comparing means between 2 independent groups. This calculation indicated a requirement of at least 45 patients per group. Ultimately, the study included a total of 123 patients (58 in the ESPB group and 65 in the control group), exceeding the minimum requirement and fulfilling the statistical power requirements for the primary immunological outcome analyses.

Statistical Analysis

Data were analyzed using SPSS version 25.0 software. During the data collection process, a detailed review of all patient electronic medical records was conducted to ensure data completeness and accuracy. For any missing data, attempts were first made to retrieve the information by reviewing additional records or consulting the attending physician. If the data could not be supplemented, the corresponding case was excluded from the study. Continuous data are presented as mean±SD or M (Q_1, Q_3), and categorical data as counts (%). Between-group comparisons utilized the independent samples t test or the Mann-Whitney U test for continuous variables, and the χ^2 test for categorical variables, as appropriate. For repeated measures (eg, hemodynamic, immune, and cytokine parameters), normally distributed data were analyzed with Repeated-Measures ANOVA; otherwise, a Generalized Estimating Equations (GEE) model was applied. Post

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hoc multiple comparisons employed the Bonferroni correction. A 2-sided $p<0.05$ defined statistical significance.

RESULTS

Comparison of Baseline Data

No statistically significant differences were observed in age, sex, BMI, ASA classification, surgical type, operative time, intraoperative fluid volume, or intraoperative blood loss between the two groups ($p>0.05$), as shown in Table 1.

Comparison of Hemodynamic Parameters

Compared with pre-anesthesia levels, MAP and HR were significantly elevated in both groups at the following time points: immediately after endotracheal intubation, immediately after skin incision, and immediately after tracheal extubation ($p<0.05$). However, compared with the control group, the ESPB group exhibited significantly smaller changes in both MAP and HR. This difference was most pronounced immediately after skin incision ($p<0.05$).

Comparison of Remifentanil and Sufentanil Dosage

Compared with the control group, the intraoperative doses of remifentanil and sufentanil, as well as the postoperative doses of sufentanil at 24 hours and 48 hours in the ESPB group were reduced ($p<0.05$). See Table 3.

Comparison of Initial Compression Time, Total Compression Count, and Effective Compression Count After PCA

Compared with the control group, the time to the first PCA demand was significantly later in the ESPB group ($p<0.05$). Additionally, the total number of PCA demands and the number of effective PCA demands within 24 hours and 48 hours postoperatively were significantly lower in the ESPB group than in the control group ($p<0.05$). See Table 4.

Table 1. Comparison of baseline data.

Variables	Control group (n=65)	ESPB group (n=58)	$t/\chi^2/Z$	*p*
Age, years	58.66±8.16	60.24±9.20	-1.009	0.315
Gender			0.652	0.419
Female	30 (46.15)	31 (53.45)		
Male	35 (53.85)	27 (46.55)		
BMI, kg/m²	23.45±3.15	23.89±3.48	-0.720	0.473
Surgery type			0.234	0.629
VATS lobectomy	41 (63.08)	39 (67.24)		
VATS segmentectomy	24 (36.92)	19 (32.76)		
ASA classification			0.508	0.476
II	17 (26.15)	12 (20.69)		
III	48 (73.85)	46 (79.31)		
Surgery time, hours	4.00 (3.00, 5.00)	3.50 (3.00, 5.00)	-0.559	0.576
Intraoperative fluid infusion volume, mL	1263.52±129.44	1254.26±132.11	0.392	0.695
Intraoperative blood loss, mL	304.18±63.78	313.24±57.73	-0.822	0.413

ASA: American Society of Anesthesiologists; BMI: body mass index; ESPB: erector spinae plane block; VATS: video-assisted thoracoscopic surgery.

Table 2. Comparison of intraoperative MAP and HR.

Variables	Time	Control group (n=65)	ESPB group (n=58)	t	*p*
MAP, mm Hg	Before anesthesia	91.86±7.91	92.33±8.14	-0.322	1.000
	Immediately after endotracheal intubation	105.71±10.39	98.53±9.23	4.028	<0.001
	Immediately after skin incision	112.40±11.23	103.24±9.85	4.782	<0.001
	Immediately after tracheal extubation	103.52±10.15	96.86±8.97	3.836	<0.001
Group		F=37.197, η^2=0.235			<0.001
Time		F=359.458, η^2=0.329			<0.001
Time × Group		F=6.212, η^2=0.049			<0.001
HR, beats/min	Before anesthesia	75.78±6.45	76.43±6.23	-0.564	1.000
	Immediately after endotracheal intubation	88.55±8.81	82.12±7.25	4.393	<0.001
	Immediately after skin incision	94.74±9.05	86.17±7.91	5.558	<0.001
	Immediately after tracheal extubation	87.26±8.39	80.68±7.08	4.677	<0.001
Group		F=50.315, η^2=0.294			<0.001
Time		F=74.978, η^2=0.383			<0.001
Time × Group		F=8.678, η^2=0.067			<0.001

ESPB: erector spinae plane block; HR: heart rate; MAP: mean arterial pressure.

Table 3. Comparison of remifentanil and sufentanil dosage.

Variables	Time	Control group (n=65)	ESPB group (n=58)	t	*p*
Remifentanil, mg	Intraoperative	2.31±0.54	2.15±0.58	1.487	0.140
Sufentanil, μg	Intraoperative	36.75±5.08	33.12±3.93	4.457	<0.001
	24 hours after surgery	60.85±6.58	55.84±6.05	4.982	<0.001
	48 hours after surgery	111.02±12.37	101.24±11.92	4.451	<0.001
Group			F=49.168, η^2=0.289		<0.001
Time			F=2497.932, η^2=0.954		<0.001
Time × Group			F=4.930, η^2=0.039		0.008

ESPB: erector spinae plane block.

Table 4. Comparison of initial compression time, total compression count, and effective compression count after PCA.

Time	Variables	Control group (n=65)	ESPB group (n=58)	t	*p*
First compression time, hours		3.00 (2.00, 5.00)	7.50 (6.00, 9.75)	-7.613	<0.001
24 hours after surgery	Total number of PCA	13.52±3.44	10.22±3.92	4.976	<0.001
	Effective times of PCA	7.83±3.24	6.02±2.25	3.633	<0.001
48 hours after surgery	Total number of PCA	23.45±5.97	18.55±5.14	4.845	<0.001
	Effective times of PCA	14.66±4.20	9.97±2.64	7.508	<0.001

ESPB: erector spinae plane block; PCA: patient-controlled analgesia.

Comparison of VAS and BCS Scores

Compared with the control group, the ESPB group exhibited significantly lower resting and coughing VAS pain scores and significantly higher BCS scores at all observation time points within 48 hours postoperatively (p<0.05). See Table 5.

Postoperative Recovery Outcomes

Time to extubation did not differ significantly between the groups (p>0.05). However, patients in the ESPB group demonstrated a shorter time to first ambulation and a reduced postoperative hospital stay compared with the control group (p<0.05). See Table 6.

Comparison of T Lymphocyte Subsets and NK Cells in Perioperative Patients

At the end of surgery and at 24 hours and 48 hours postoperatively, the ESPB group exhibited significantly higher $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ ratio, and NK cell levels, alongside lower $CD8^+$ levels, compared with controls (p<0.05). All measured parameters also showed significant within-group variation over time (p<0.05). See Table 7 and Figure 2.

Table 5. Comparison of VAS and BCS scores after the surgery.

Variables	Time	Control group (n=65)	ESPB group (n=58)	Z	*p*
Resting VAS	1 hour	4 (3, 5)	2 (2, 3)	-6.974	<0.001
	6 hours	4 (3, 4)	3 (2, 3)	-5.719	<0.001
	24 hours	3 (3, 4)	3 (2, 4)	-4.015	<0.001
	48 hours	4 (3, 4)	3 (2, 3)	-5.116	<0.001
Group		Wald χ^2=175.392			<0.001
Time		Wald χ^2=2.133			0.545
Time × Group		Wald χ^2=8.344			0.039
Cough VAS	1 hour	6 (5, 8)	5 (4, 6)	-2.922	0.012
	6 hours	6 (4, 7)	5 (3, 6)	-2.746	0.018
	24 hours	5 (4, 7)	4 (3, 5)	-3.020	0.012
	48 hours	6 (4, 7)	4 (3, 6)	-3.447	<0.001
Group		Wald χ^2=49.829			<0.001
Time		Wald χ^2=6.938			0.074
Time × Group		Wald χ^2=0.219			0.974
BCS score	1 hour	1 (1, 1)	2 (1, 2)	-4.281	<0.001
	6 hours	2 (1, 2)[a]	2 (2, 2)[a]	-4.509	<0.001
	24 hours	2 (2, 2)[ab]	2 (2, 3)[ab]	-4.712	<0.001
	48 hours	2 (2, 3)	3 (2, 3)	-4.176	<0.001
Group		Wald χ^2=83.488			<0.001
Time		Wald χ^2=247.495			<0.001
Time × Group		Wald χ^2=0.236			0.972

BCS: Bruggrmann Comfort Scale; ESPB: erector spinae plane block; VAS: Visual Analog Scale.

Table 6. Comparison of postoperative recovery outcomes.

Variables	Control group (n=65)	ESPB group (n=58)	t	*p*
Time of tracheal extubation, min	8.95±0.94	8.76±0.80	1.230	0.221
Time of first ambulation after surgery, hours	27.55±5.17	24.36±4.24	3.719	<0.001
Postoperative hospital stay, days	17.54±2.39	15.16±1.83	6.248	<0.001

ESPB: erector spinae plane block.

Table 7. Comparison of T-lymphocyte subsets and NK cells.

Variables	Time	Control group (n=65)	ESPB group (n=58)	t	*p*
$CD3^+$, %	Before anesthesia	64.48±4.19	65.28±5.37	-0.913	1.000
	At the end of surgery	54.27±5.37	58.83±4.46	-5.131	<0.001
	24 hours	50.19±4.39	55.16±4.39	-6.255	<0.001
	48 hours	56.53±3.27	60.92±4.74	-5.895	<0.001
Group		F=79.953, η^2=0.398			<0.001
Time		F=153.570, η^2=0.559			<0.001
Time × Group		F=5.500, η^2=0.043			<0.001
$CD4^+$, %	Before anesthesia	42.83±3.44	42.48±3.47	0.578	1.000
	At the end of surgery	30.87±2.01	36.21±3.40	-10.438	<0.001
	24 hours	27.82±3.07	32.89±3.55	-8.505	<0.001
	48 hours	34.18±4.06	38.16±4.29	-5.277	<0.001
Group		F=128.729, η^2=0.515			<0.001
Time		F=278.464, η^2=0.697			<0.001
Time × Group		F=17.853, η^2=0.129			<0.001
$CD8^+$, %	Before anesthesia	29.97±4.18	28.62±5.86	1.484	0.560
	At the end of surgery	39.56±3.44	35.91±3.87	5.523	<0.001
	24 hours	46.78±6.54	42.88±3.23	4.267	<0.001
	48 hours	34.41±5.67	31.41±3.72	3.503	<0.001
Group		F=51.579, η^2=0.299			<0.001
Time		F=241.471, η^2=0.666			<0.001
Time × Group		F=1.764, η^2=0.014			0.154
$CD4^+/CD8^+$	Before anesthesia	1.46±0.23	1.55±0.38	-1.715	0.360
	At the end of surgery	0.79±0.09	1.02±0.15	-10.089	<0.001
	24 hours	0.61±0.10	0.77±0.10	-8.868	<0.001
	48 hours	1.02±0.23	1.23±0.17	-5.545	<0.001
Group		F=94.938, η^2=0.440			<0.001
Time		F=365.397, η^2=0.751			<0.001
Time × Group		F=2.575, η^2=0.021			0.054
NK cell, %	Before anesthesia	22.92±3.85	23.02±3.01	-0.177	1.000
	At the end of surgery	15.33±2.37	18.45±1.77	-8.199	<0.001
	24 hours	13.83±1.46	16.82±2.12	-9.010	<0.001
	48 hours	18.27±2.78	21.03±3.45	-4.932	<0.001
Group		F=92.130, η^2=0.432			<0.001
Time		F=182.061, η^2=0.601			<0.001
Time × Group		F=8.319, η^2=0.064			<0.001

ESPB: erector spinae plane block; NK: natural killer.

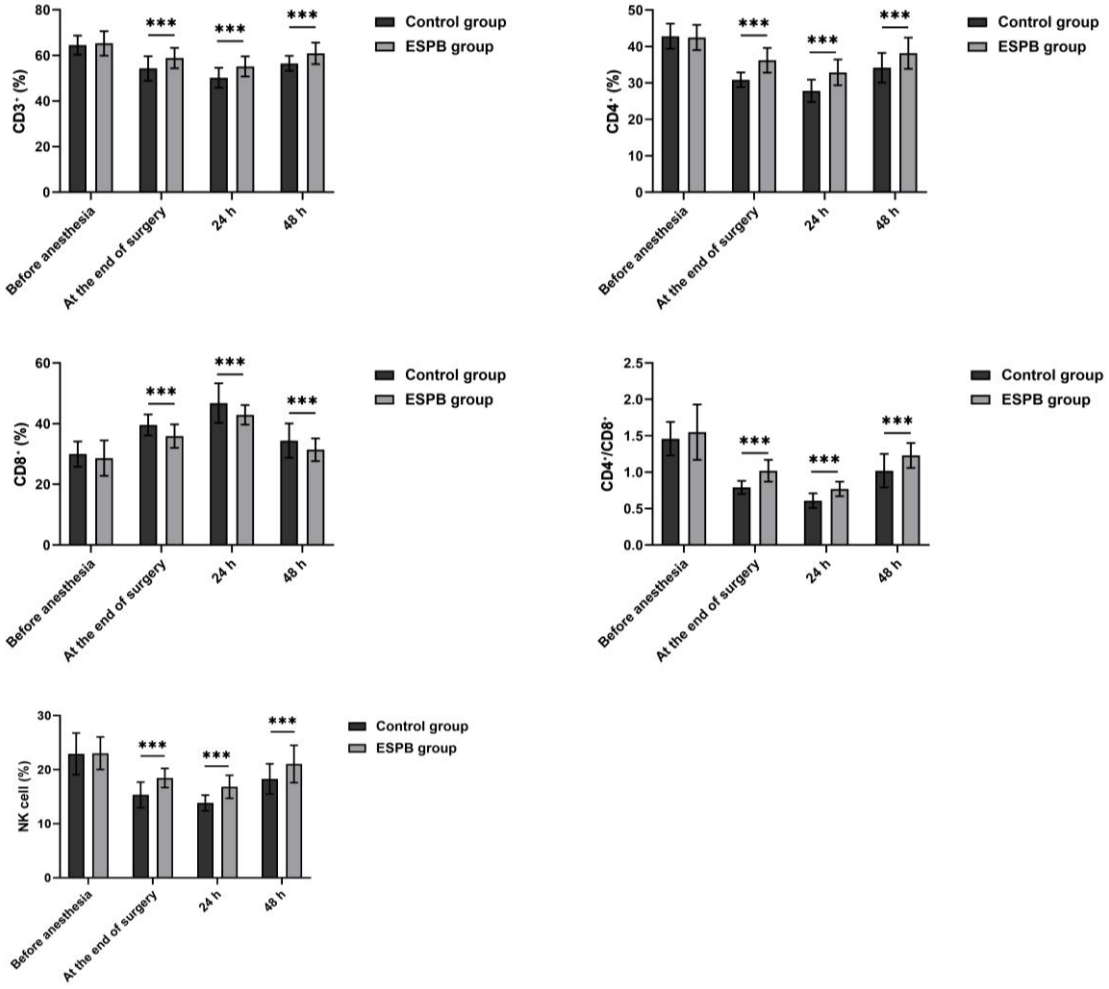

Figure 2. Comparison of T-lymphocyte subsets and NK cells.

Comparison of Inflammatory Cytokine Levels

Compared with pre-anesthesia levels, both groups showed increased levels of IL-6, IL-10, and TNF-α (p<0.05). However, the ESPB group had significantly lower IL-6 and TNF-α, yet higher IL-10, than the control group (p<0.05). Within-group analyses also revealed significant temporal changes for all three cytokines (p<0.05). See Table 8 and Figure 3.

Comparison of Analgesic Rescue Rate, Adverse Reactions, and Postoperative Complications

The ESPB group required significantly fewer analgesic rescues and experienced less postoperative dizziness than the control group (both p<0.05). Incidences of postoperative nausea and vomiting and somnolence were comparable between groups (p>0.05). See Table 9.

Regarding postoperative complications, the ESPB group demonstrated lower rates of pneumonia (5.17% vs 9.23%), prolonged air leak (>5 days; 6.90% vs 12.31%), atelectasis requiring bronchoscopy (3.45% vs 6.15%), and wound infection (1.72% vs 3.08%) compared with the control group, although none of these differences reached statistical significance (all p>0.05). The overall complication rate was numerically lower in the ESPB group (17.24% vs 27.69%, p=0.168). See Table 10.

Table 8. Comparison of inflammatory cytokines.

Variables	Time	Control group (n=65)	ESPB group (n=58)	t	*p*
TNF-α, pg/mL	Before anesthesia	40.56±8.94	41.33±9.54	-0.462	1.000
	At the end of surgery	52.05±5.35	46.75±6.44	4.983	<0.001
	24 hours	61.55±6.01	54.86±7.12	5.649	<0.001
	48 hours	56.26±6.71	51.09±7.87	3.935	<0.001
Group		F=30.719, η^2=0.202			<0.001
Time		F=133.620, η^2=0.525			<0.001
Time × Group		F=6.803, η^2=0.053			<0.001
IL-6, pg/mL	Before anesthesia	19.52±5.46	18.62±5.61	0.911	1.000
	At the end of surgery	24.05±4.36	21.25±5.41	3.183	0.008
	24 hours	32.55±5.21	26.82±4.65	6.439	<0.001
	48 hours	27.86±5.47	23.59±5.46	4.339	<0.001
Group		F=54.209, η^2=0.309			<0.001
Time		F=91.222, η^2=0.430			<0.001
Time × Group		F=4.754, η^2=0.038			0.003
IL-10, pg/mL	Before anesthesia	12.45±3.22	12.73±4.17	-0.428	1.000
	At the end of surgery	18.69±4.51	21.45±5.55	-3.037	0.012
	24 hours	24.55±5.44	28.12±4.43	-3.965	<0.001
	48 hours	21.78±5.07	24.32±5.78	-2.606	0.040
Group		F=28.290, η^2=0.189			<0.001
Time		F=179.972, η^2=0.598			<0.001
Time × Group		F=2.580, η^2=0.021			0.053

ESPB: erector spinae plane block; IL: interleukin; TNF: tumor necrosis factor.

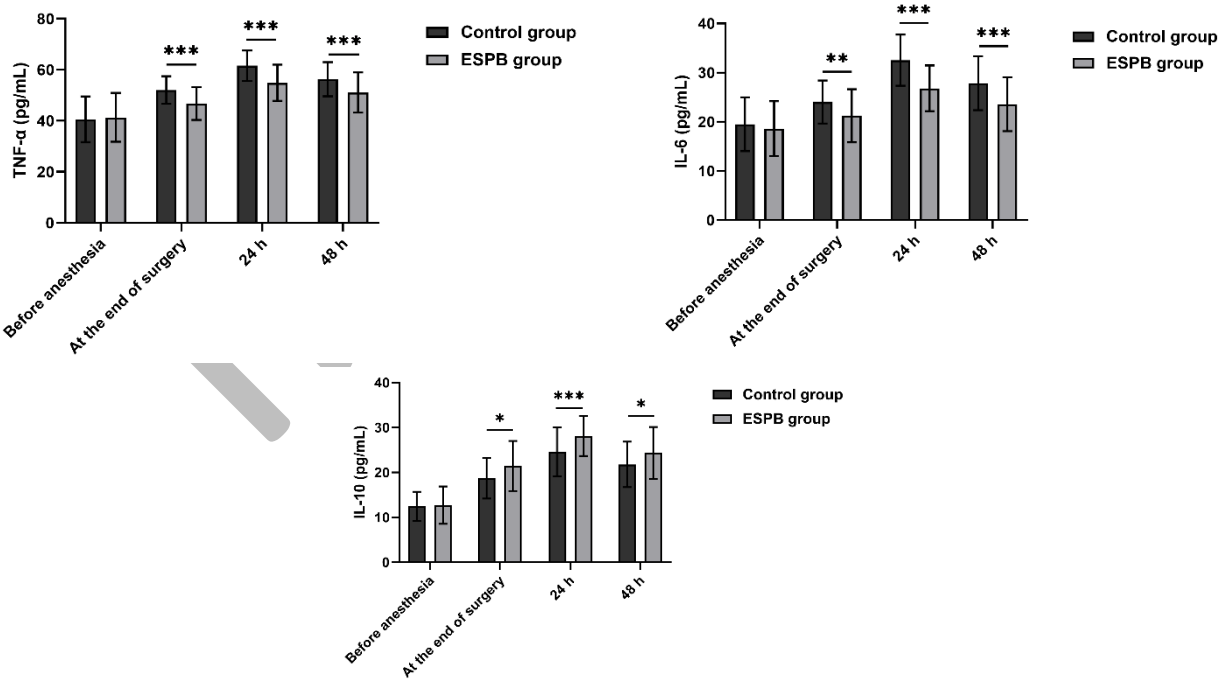

Figure 3. Comparison of inflammatory cytokines.

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Table 9. Comparison of analgesic rescue rate and adverse reactions.

Variables	Control group (n=65)	ESPB group (n=58)	χ^2	*p*
Analgesic rescue rate, No. (%)	32 (49.23)	18 (31.03)	4.206	0.040
Nausea and vomiting, No. (%)	22 (33.85)	15 (25.86)	0.929	0.335
Dizziness, No. (%)	9 (13.85)	2 (3.45)	4.069	0.044
Drowsiness, No. (%)	7 (10.77)	2 (3.45)	1.463	0.226

ESPB: erector spinae plane block.

Table 10. Comparison of postoperative complications.

Variables	Control group (n=65)	ESPB group (n=58)	χ^2	*p*
Pneumonia, No. (%)	6 (9.23)	3 (5.17)	0.266	0.606
Prolonged air leak (>5 days), No. (%)	8 (12.31)	4 (6.90)	0.497	0.481
Atelectasis requiring bronchoscopy, No. (%)	4 (6.15)	2 (3.45)	0.076	0.782
Wound infection, No. (%)	2 (3.08)	1 (1.72)	0.010	0.920
Any complication, No. (%)	18 (27.69)	10 (17.24)	1.904	0.168

ESPB: erector spinae plane block.

DISCUSSION

Although minimally invasive lung surgery for early-stage lung cancer significantly curtails tissue trauma and physiological disturbance compared with traditional thoracotomy, it still provokes a notable stress and inflammatory response. This leads to an imbalance in proinflammatory cytokine release and suppression of cellular immune function, ultimately impacting patient postoperative recovery and long-term prognosis.[23–25] This study used a retrospective cohort analysis to systematically evaluate the impact of ESPB on perioperative cytokine networks and cellular immunity in minimally invasive lung surgery patients. The results demonstrate that ESPB not only effectively stabilizes intraoperative hemodynamics, optimizes postoperative analgesia, and reduces opioid consumption but also, more importantly, exhibits significant regulatory effects. These include suppressing proinflammatory factors, modulating anti-inflammatory factors, and alleviating the functional suppression of T lymphocytes and NK cells. Consequently, ESPB may offer a new clinical strategy for improving perioperative immune balance and promoting postoperative recovery. Our findings are consistent with previous reports demonstrating immunoprotective effects of regional anesthesia. For instance, Reysner et al[15] showed that regional blockade attenuates the systemic stress response, while De Cassai et al[26] highlighted the immunosuppressive effects of opioids. Our results extend these observations by specifically demonstrating that ESPB modulates both cytokine networks and cellular immunity in the context of minimally invasive lung surgery.

The inflammatory response triggered by surgical trauma is a central component of perioperative immune dysregulation. Compared with baseline, postoperative levels of IL-6 and TNF-α were elevated in the control group, reflecting a strong proinflammatory response induced by surgical stress. Research by Liu et al[27] demonstrated that IL-6 and TNF-α are significantly upregulated in non-small cell lung cancer patients and closely associated with cancer-related pain incidence and prognosis. In this study, the ESPB group exhibited markedly lower postoperative levels of both cytokines versus the control, suggesting the block may inhibit their overproduction by blocking nociceptive signals and alleviating surgical stress. This inhibitory effect not only helps mitigate local and systemic inflammatory damage but may also reduce the risk of postoperative complications. Additionally, the ESPB group exhibited significantly elevated postoperative levels of the anti-inflammatory cytokine IL-10 when compared with the control group. IL-10 helps maintain immune homeostasis by inhibiting proinflammatory factor production in monocytes and macrophages and modulating T-cell function.[28] ESPB may indirectly promote an anti-inflammatory environment by reducing pain-related stress and opioid exposure, thereby

balancing proinflammatory and anti-inflammatory responses, which could be one of the key mechanisms underlying its immunoprotective effects.

Surgical trauma and the associated stress response often led to an immunosuppressed state characterized by a decrease in T-lymphocyte numbers and functional suppression. In this study, it was observed that the percentages of $CD3^+$, $CD4^+$, and NK cells in both groups of patients decreased postoperatively compared with preoperative levels, and the $CD4^+/CD8^+$ ratio declined, which is consistent with previous reports on postoperative suppression of cellular immune function.[29] $CD4^+$ T cells are crucial for coordinating adaptive immunity; a decline in their numbers and the $CD4^+/CD8^+$ ratio often signifies immune suppression.[30] As key mediators of innate immunity, NK cells contribute to anti-infection and anti-tumor surveillance. Postoperatively, the ESPB group demonstrated significantly elevated levels of $CD3^+$ and $CD4^+$, a higher $CD4^+/CD8^+$ ratio, and increased NK cells at multiple time points compared with controls, alongside relatively lower $CD8^+$ T cell levels. These findings imply that ESPB may mitigate the surgery-induced reduction in total T-lymphocytes, specifically preserving the $CD4^+$ subset and restoring $CD4^+/CD8^+$ balance. Notably, NK cells play a critical role in tumor immunosurveillance by recognizing and eliminating malignant cells without prior sensitization. The relative preservation of NK cell levels observed in the ESPB group may therefore be clinically relevant, as perioperative NK cell suppression has been associated with increased risk of tumor recurrence following cancer surgery. This suggests that ESPB could potentially contribute to improved long-term oncologic outcomes, although this hypothesis requires prospective validation. Simultaneously, the relative preservation of NK cell levels may help maintain early postoperative immune surveillance, which is of positive significance for preventing infections and potential tumor cell dissemination. This protective effect on cellular immune function may be related to ESPB mitigating the neuroendocrine response induced by surgical stress and pain.[31]

Pain, as a potent physiological and psychological stressor, shares a complex bidirectional regulatory relationship with the immune system. Severe postoperative pain directly activates the hypothalamic-pituitary-adrenal axis and sympathetic nervous system. This promotes glucocorticoid and catecholamine release, leading to suppressed immune cell function, and is frequently associated with increased opioid consumption.[32] Opioids, particularly μ-receptor agonists, besides their analgesic effects, have been confirmed to possess direct immunosuppressive properties, affecting lymphocyte proliferation, cytokine production, and NK cell activity.[26] The ESPB group exhibited significantly lower resting and coughing pain scores (VAS), higher comfort scores (BCS), and reduced opioid consumption and PCA demand both during and after surgery. This indicates that ESPB provides superior analgesic efficacy and effectively blocks pain signal transmission. This not only directly mitigates the negative impact of pain itself as a stressor on the immune system but also significantly reduces the opioid dosage required to achieve equivalent analgesia, thereby potentially lowering opioid-related immunosuppression. Opioids, particularly μ-receptor agonists, have been shown to directly suppress lymphocyte proliferation, impair natural killer (NK) cell activity, and modulate cytokine production, independent of their analgesic effects.[26] Therefore, the marked reduction in perioperative opioid consumption in the ESPB group likely contributes directly to the preservation of cellular immune function and the attenuation of proinflammatory cytokine responses observed in this study. Therefore, the positive regulatory effect of ESPB on perioperative immune function is likely achieved through the synergistic pathway of analgesia and opioid reduction, which highlights the core value of the multimodal analgesia concept in optimizing perioperative management.

The regulation of perioperative physiological homeostasis by ESPB is not limited to the domains of immunity and analgesia. This study also found that patients receiving ESPB showed less hemodynamic fluctuation during intense stimuli (eg, skin incision), earlier first ambulation, a shorter hospital stay, and reduced postoperative dizziness. Hemodynamic stability reflects the buffering effect of ESPB on surgical stress response, which may help maintain tissue perfusion and alleviate organ ischemia-reperfusion injury.[33] Effective pain control and overall improvement in condition promoted early activity. Patients undergoing thoracoscopic lobectomy/segmentectomy require postoperative coughing and expectoration to promote pulmonary function recovery and prevent atelectasis, as well as early ambulation to facilitate rapid recovery. The reduction in hospital stay represents a comprehensive reflection of optimized postoperative recovery progress.

These improvements in clinical outcomes corroborate the observed trend toward cytokine network balance and preserved cellular immune function, collectively indicating that ESPB may promote overall postoperative recovery through multi-target mechanisms. Regarding the clinical significance of the observed immune differences, the magnitudes of change—approximately 4% to 5% higher $CD4^+$ T-cell percentages and 2% to 3% higher NK cell levels in the ESPB group—are consistent with effect sizes reported in prior studies linking regional anesthesia to immune preservation. While these differences were statistically significant, whether they translate into meaningful reductions in postoperative infections or improved cancer-specific survival remains unknown. Nevertheless, even modest preservation of $CD4^+$ and NK cell populations may be clinically relevant in the context of cancer surgery, where perioperative immune suppression is associated with increased susceptibility to minimal residual disease and metastatic progression. From a clinical perspective, the preservation of $CD4^+$ T cells and NK cell activity observed in the ESPB group is mechanistically linked to enhanced anti-infective capacity and anti-tumor immune surveillance, which may translate into reduced risks of postoperative infectious complications and potentially improved long-term oncologic outcomes. Although the current study did not directly measure infection rates or cancer recurrence, the immunological findings provide a plausible mechanistic basis for such clinical benefits and warrant further investigation in larger prospective studies. While the immunological differences observed between groups reached statistical significance, their direct translation to clinical outcomes such as postoperative infection rates or long-term cancer recurrence remains to be established. Nevertheless, the preservation of $CD4^+$ T cells and NK cell activity is mechanistically associated with enhanced anti-tumor surveillance and reduced susceptibility to infections, suggesting potential clinical relevance that warrants investigation in future prospective studies.

As a retrospective analysis, this study has certain limitations. For instance, it cannot completely exclude the influence of unknown confounding factors, the sample size is relatively limited, and only short-term immunological parameter changes up to 48 hours postoperatively were observed. Whether these changes persist beyond the early postoperative period and their potential impact on long-term outcomes such as infection or tumor recurrence remain unknown. In particular, the single-center design limits the generalizability of our findings to other institutions with different patient populations, surgical practices, or perioperative protocols. Multicenter studies are needed to validate the immunomodulatory effects of ESPB across diverse clinical settings. The precise mechanisms by which ESPB affects immune function, particularly whether it directly regulates immune cell function by influencing specific neural pathways or acts through indirect means, require further basic and clinical research for clarification. Potential confounders such as intraoperative steroid administration, blood transfusion, or use of other immunosuppressive medications were not systematically controlled for in this retrospective analysis. Although no significant differences in baseline characteristics or intraoperative management were observed between groups, these factors may influence immune markers and should be addressed in future prospective studies. Additionally, although baseline characteristics were comparable between groups, we did not perform multivariate regression analysis to adjust for potential confounders in assessing the independent effect of ESPB on immune parameters. The relatively modest sample size and retrospective design precluded robust multivariable modeling; however, future prospective studies with larger cohorts should confirm whether ESPB independently predicts immune preservation.

In summary, this retrospective study suggests that ESPB in minimally invasive lung surgery is associated with alleviated suppression of T lymphocytes and NK cells, and may contribute to a more favorable perioperative immune profile. These findings indicate that ESPB may serve not only as an effective regional analgesic technique but also as a potentially valuable component of perioperative immune management strategies in minimally invasive lung surgery, warranting further prospective validation. A prospective randomized controlled trial is warranted to confirm the immunomodulatory effects of ESPB and to evaluate whether these immunological benefits translate into improved long-term outcomes, including reduced infection rates and enhanced tumor-free survival.

STATEMENT OF ETHICS

This study was approved by the Ethics Committee of The First Affiliated Hospital of Chengdu Medical College (Approval No.: 2023CYFYIRB-BA-May02).

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

Not applicable.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

AI ASSISTANCE DISCLOSURE

Not applicable.

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