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Original Article

Effect of sevoflurane combined with intercostal block on postoperative pulmonary function, opioid consumption, and stress response in lung cancer surgery patients

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Abstract: Objective: To investigate the efficacy of sevoflurane combined with intercostal block in lung cancer surgery. Methods: A retrospective analysis was conducted on 252 patients who underwent lung cancer surgery between January 2020 and December 2023. Patients were divided into two groups: the sevoflurane with intercostal block group (Group S, n = 108) and the propofol group (Group P, n = 144). Anesthesia protocols involved sevoflurane and intercostal nerve block or propofol. Postoperative pulmonary function, opioid consumption, stress response, and cognitive effects were compared between the two groups. Results: The VAS scores were significantly lower in Group S at postoperative 2 h (1.96 ± 0.52 vs 2.15 ± 0.56, P = 0.005) and 24 h (3.84 ± 0.95 vs 4.14 ± 0.98, P = 0.015), indicating superior pain management. Group S also showed better preservation of lung function, with higher FEV1 values at postoperative 2 hours (1.49 ± 0.29 L vs 1.36 ± 0.65 L, P = 0.033) and 24 hours (1.59 ± 0.39 L vs 1.45 ± 0.45 L, P = 0.012). Opioid consumption was lower in Group S at both postoperative 24 h (1307.52 ± 259.41 μg vs 1742.26 ± 253.12 μg, P < 0.001) and 48 h. Cognitive function was better preserved immediately post-surgery in Group S (26.03 ± 4.42 vs 24.14 ± 5.28, P = 0.003). However, adverse reactions like nausea were more common in Group S (9.26% vs 2.78%, P = 0.026). Conclusion: Sevoflurane combined with intercostal block outperforms propofol in enhancing postoperative pulmonary function, reducing opioid reliance, and modulating stress responses in lung cancer surgery patients.

Keywords: Lung cancer surgery, sevoflurane, intercostal block, pulmonary function, opioid consumption, stress response

Introduction

Lung cancer remains one of the most prevalent malignancies worldwide, with surgery being a cornerstone in curative treatment, particularly for early-stage disease [1]. Despite advances in surgical techniques and postoperative care, postoperative pain management and pulmonary function preservation remain significant challenges following thoracic procedures [2]. Effective postoperative analgesia is crucial not only for patient comfort but also for facilitating recovery by promoting early mobilization, reducing pulmonary complications, and shortening hospital stays [3]. However, the widespread use of systemic opioids for pain management is often accompanied by side effects, including respiratory depression, nausea, vomiting, and cognitive dysfunction [4, 5]. These issues underscore the pressing need for improved analgesic strategies that minimize opioid consumption while optimizing pulmonary function and stress responses [6].

Sevoflurane, a volatile anesthetic with rapid onset, ease of titration, and minimal respiratory depressant effects, has been suggested as a valuable component of anesthesia regimens in thoracic surgery [7]. Its bronchodilatory properties may potentially aid in better preservation of pulmonary function postoperatively [8]. In parallel, regional anesthesia techniques, such as intercostal nerve blocks, have gained popularity as part of multimodal analgesia protocols in

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thoracic surgeries, primarily due to their effective pain-relieving capabilities at the surgical site with fewer systemic effects [9]. The synergistic use of a volatile anesthetic like sevoflurane in conjunction with an intercostal block may therefore enhance analgesic efficacy, minimize opioid consumption, and improve respiratory outcomes [10]. However, the specific effects of this combination on postoperative outcomes, particularly pulmonary function, opioid consumption, and stress responses, require further elucidation [11].

Clinical interest in the modulating the stress response during the perioperative period has been growing, driven by its implications for surgical recovery and long-term prognosis [12]. Stress-induced hormonal changes can significantly influence metabolic processes, immune function, and, ultimately, patient recovery [13]. Moreover, effective control of the stress response has been associated with improved postoperative outcomes, including reduced risks of infections and enhanced wound healing [14]. If combined anesthetic approaches can attenuate this stress response more effectively, they may offer significant benefits in terms of postoperative recovery and complication rates.

Despite these potential advantages, data specifically addressing the combination of sevoflurane and intercostal block in the context of lung cancer surgery remains limited. Prior studies have often focused on isolated interventions without fully exploring the potential synergistic effects of combining inhalational anesthesia with regional anesthesia techniques [15]. Our study seeks to fill this gap by providing a detailed analysis of how this combination affects key postoperative outcomes in lung cancer surgery patients, including pulmonary function, opioid consumption, cognitive effects, and stress responses. This study also investigated the impact of systemic opioids and certain anesthetics on postoperative cognitive function. By analyzing the immediate effects of anesthetics on cognitive function and their influence on the stress response, a key mediator of cognitive health, this research aims to further understand this relationship.

Future research should explore the long-term benefits of integrating multimodal perioperative strategies, such as the combination of sevoflurane and intercostal block, into enhanced recovery after surgery (ERAS) protocols. Understanding how various anesthetic strategies can preserve cognitive function while providing adequate analgesia and reducing overall stress could have profound implications for anesthetic management in thoracic surgery patients. By addressing these gaps in knowledge, our study aims to provide clinicians with evidence-based recommendations for optimizing perioperative care and improving patient outcomes. This research also lays the groundwork for larger-scale studies to further validate these findings and assess the broader applicability of these approaches in other surgical contexts.

Materials and methods

Study design

A retrospective analysis was conducted on 252 patients treated at Cangzhou People's Hospital between January 2020 and December 2023. Patient data were obtained from the medical record system. The patients were categorized into two groups based on the anesthesia administered during surgery: the sevoflurane combined with intercostal block group (Group S, n = 108), and the propofol group (Group P, n = 144). Despite our institution's capacity to offer a broader range of diagnostic services, this study strictly adheres to a retrospective design, utilizing pre-existing anonymized patient records for analysis. This study was approved by the Institutional Review Board and Ethics Committee of Cangzhou People's Hospital. The flowchart of inclusion and exclusion in this study is shown in **Figure 1**.

Eligibility and grouping criteria

Inclusion criteria: 1) Patients diagnosed with lung cancer via CT or MRI, and classified as American Society of Anesthesiologists (ASA) level I-II, or with measurable or evaluable lung cancer according to the Response Evaluation Criteria in Solid Tumors (RECIST) [16], or through a pathological biopsy; 2) Participants scheduled for radical lung cancer surgery; 3) Patients aged between 21 and 74 years; 4) Patients with a body mass index (BMI) ranging from 22 to 29 kg/m^2.

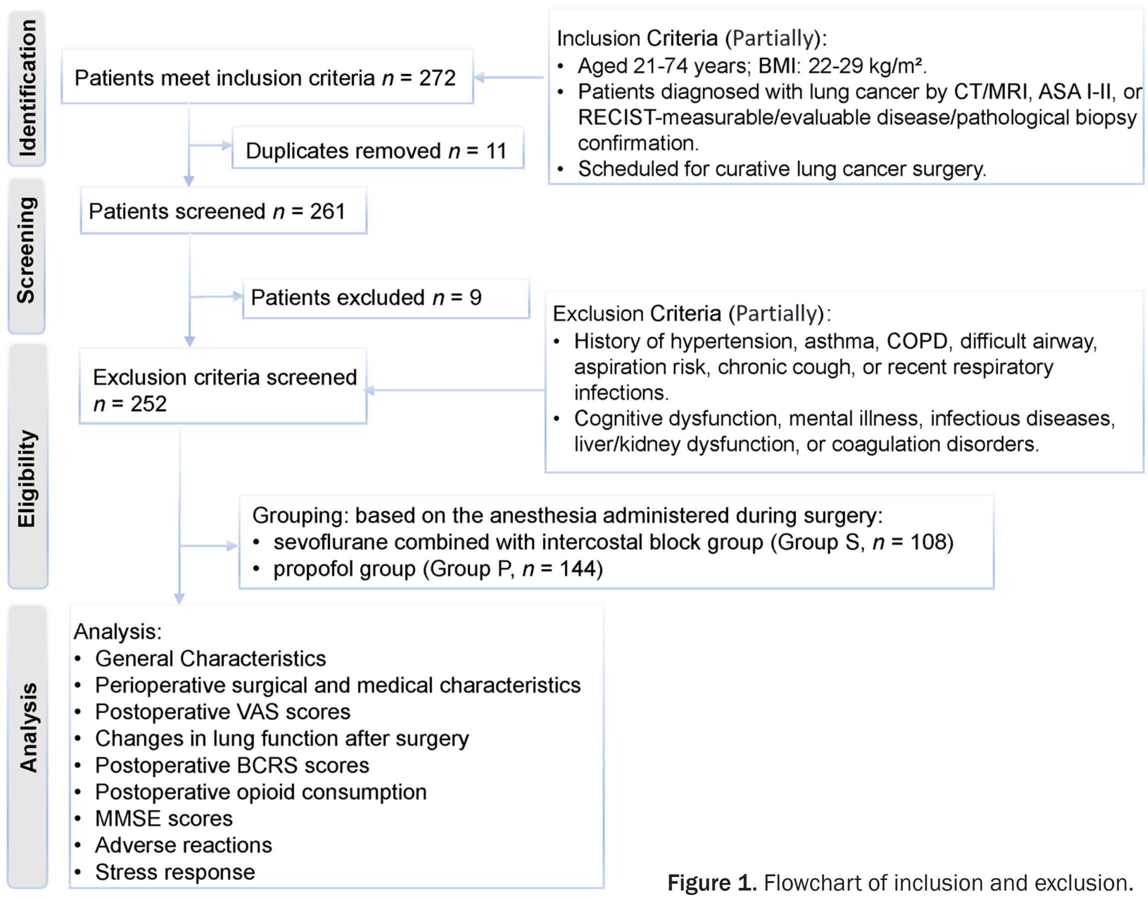


Figure 1. Flowchart of inclusion and exclusion.

Exclusion criteria: 1) Patients with a history of hypertension, asthma, chronic obstructive pulmonary disease, difficult airway, perioperative risk factors for aspiration, chronic cough, or recent respiratory tract infections; 2) Patients with cognitive dysfunction, mental illness, infectious diseases, liver or kidney dysfunction, or coagulation disorders; 3) Patients with brain or bone metastases, allergies to the study drugs, chronic pain history, or opioid abuse history.

Treatment approach

Before anesthesia induction, all patients were equipped with standardized clinical monitoring devices. For extended hemodynamic monitoring, a lithium dilution cardiac output system (LIDCO) was used. A thoracic epidural catheter was inserted at the T6-7 level.

Group P: Anesthesia induction was performed using Propofol (batch number GB739; AstraZeneca, Milan, Italy) at a dose of 1.5-2.0 mg/kg. Group S: Anesthesia induction was guided using a combination of Remifentanil (batch number H20003688; Renfu Pharmaceutical Co., Ltd., Yichang, China) at 0.5 μg/kg and Vecuronium Bromide (batch number S41319; Shanghai Yuan Ye Biotechnology Co., Ltd., China) at 0.1 mg/kg, followed by Sevoflurane (batch number H20040586; Abbott Laboratories, Tokyo, Japan) at 6% for deep breathing. Prior to intubation, all patients received Remifentanil at 0.5 μg/kg and Vecuronium Bromide at 0.1 mg/kg.

For anesthesia maintenance: Group P: Anesthesia was maintained using Propofol (batch number GB739; AstraZeneca, Milan, Italy) at a rate of 4-6 mg/kg/h. Group S: Anesthesia was maintained using Sevoflurane (batch number H20040586; Abbott Laboratories, Tokyo, Japan) at a concentration of 2-2.5%.

In both groups, intravenous Remifentanil (batch number H20003688; Renfu Pharmaceutical Co., Ltd., Yichang, China) was administered intraoperatively for analgesia maintenance at a rate of 0.3-0.5 μg/kg/min.

In Group S, approximately 30 minutes before the end of surgery after tumor resection, patients received a single-shot intrathoracic intercostal nerve block using 20 ml of 0.5% Ropivacaine (batch number H20113463; Hebei Yipin Pharmaceutical Co., Ltd., China). Vital signs, including blood pressure, heart rate, and oxygen saturation, were continuously monitored. The Bispectral Index (BIS) was maintained between 40 and 50 using the Aspect A-2000 BIS monitor (Aspect Medical Systems, Inc., Norwood, MA, USA), while ensuring that blood pressure and heart rate remained within ± 20% of baseline values.

Detection method and scale

The data analyzed in this study were retrospectively obtained from medical records, including routine clinical data and additional tests performed at the discretion of treating physicians and patients.

Detection method: Pulmonary function tests were conducted preoperatively and at 8, 12, and 24 hours post-surgery. Forced vital capacity (FVC, L), forced expiratory volume in 1 second (FEV1, L), and forced vital capacity as a percentage were measured using the KoKo Legend 314000 Spirometer (nSpire Health, USA) by the same physician. Patients performed the forced expiratory maneuver at least three times in a seated position. The results of the pulmonary function tests were expressed as percentages of the predicted values, adjusted for age, height, body weight, and sex. Additionally, postoperative opioid consumption was monitored using patients' original medical records.

On the first postoperative day, a 5 mL venous fasting blood sample was collected from patients before 8 AM. Serum cortisol and insulin levels were measured using a fully automatic chemiluminescence immunoassay analyzer (HISCL-800, SYSMEX, Japan). Blood glucose levels were determined using a BECKMAN Synchron CX20 fully automated biochemistry analyzer (BECKMAN Coulter, Inc., Brea, CA, USA) and the glucose oxidase method (GOD-PAP). Blood samples were centrifuged at 3000 rpm for 5 minutes to separate the supernatant. Levels of epinephrine, norepinephrine, and dopamine were quantified using a high-performance liquid chromatography (HPLC) system (EClassical 3200L, Yilite, Dalian, China).

On the first postoperative day, arterial oxygen pressure (PaO2 in kPa) was measured using a blood gas analyzer (ABL-5 10 analyzer; Radiometer, Copenhagen, Denmark), and the fraction of inspired oxygen (FIO2) was measured with an oxygen analyzer (MOT500-O2, oxygen gas detector, Kolno). The PaO2/FIO2 ratio was calculated using the measured PaO2 and FIO2 values.

Scale: We employed the Visual Analogue Scale (VAS) to evaluate patients' perceived pain and discomfort, with a Cronbach's alpha reliability coefficient of 0.796 [17]. In this assessment, the VAS was a continuum where one end was marked "0", representing "no pain", and the opposite end was marked "10", signifying "unbearable pain". Patients indicated their perceived pain level by marking a point along this scale. The location of the mark provided a quantifiable measure of the patient's pain experience for the purposes of assessment and analysis. VAS assessments were conducted at 2, 4, 8, 12 and 24 hours postoperatively.

We employed the Breast Cancer Resilience Scale (BCRS) to assess the resilience of cancer patients, with a Cronbach's alpha reliability ranging from 0.87 to 0.89 [18]. Each question offers five response options, numbered from 1 to 5, where higher numbers signify a stronger correlation with traits of psychological resilience. The responses were summed to produce a total score, which aids in evaluating the level of psychological resilience in breast cancer patients. Patients were instructed to choose the option that best represented their feelings for each question at 2, 4, 8, 12, and 24 hours postoperatively.

Indicators were monitored and assessed preoperatively, immediately post-surgery, and 24 hours post-surgery. Cognitive function in the two groups was evaluated and compared using a Chinese version of the Mini-Mental State Examination (MMSE). The MMSE scores range from 0 to 30, with scores of 27-30 indicating normal cognitive function, 21-26 suggesting mild cognitive dysfunction, 10-20 reflecting modulate cognitive dysfunction, and 0-9 denoting severe cognitive dysfunction. The reliability of the MMSE, indicated by Cronbach's alpha, was 0.756 [19].

Data cleaning and management

Prior to data analysis, a standardized data cleaning process was implemented to identify and rectify any inconsistencies, errors, or missing values. This process involved thoroughly examining the dataset, removing duplicate entries, correcting data entry errors, and addressing missing values.

Missing values were imputed using the KNN method from the *Impyute* library in Python 3.6.0. This method first creates a basic mean imputation and constructs a KDTree using a complete list. The KDTree was then used to calculate the distances to the nearest points (NN) and identify the K nearest points. The weighted average of these K points was then computed to impute the missing values.

The percentage of missing data was kept within 5% to control for potential selection bias. Sensitivity analyses were performed by calculating the worst-case and best-case scenarios for the outcomes of lost-to-follow-up cases. If the conclusions remained consistent without significant differences, the impact of missing data on the conclusions was considered minimal, and the conclusions were deemed reliable. The final results were reported after imputing the missing values.

Statistical analysis

The sample size for this study was calculated using G*Power software, assuming a moderate effect size (d = 0.5) and a two-tailed significance level ($\alpha = 0.05$). Based on these assumptions, it was estimated that a minimum of 105 patients per group would be required to achieve 95% power to reject the null hypothesis of equality of means using two-sided, two-sample t-tests with equal variance.

All analyses were conducted using SPSS software (version 14.0 for Microsoft Windows; SPSS, Chicago, IL, USA). Statistical significance was determined as a two-tailed Type I error (*P*-value) set at less than 0.05. Categorical data were represented as [n (%)] and analyzed using the chi-square test, with the test statistic denoted as χ^2. For continuous variables, normality was first assessed using the Shapiro-Wilk test. Normally distributed continuous data were expressed as mean ± standard deviation (X ± sd). These data were compared between groups using Student's t-test. Non-normally distributed continuous data were expressed as [median (25% quantile, 75% quantile)], and the Wilcoxon rank-sum test was applied for data comparison. A *P*-value of less than 0.05 was considered statistically significant.

Result

General characteristics

A total of 252 patients were included in the study: 108 patients in the sevoflurane combined with intercostal block (S) group and 144 patients in the propofol (P) group (**Table 1**). The gender distribution was similar between the two groups, with 51.85% females and 48.15% males in the S Group and 50.69% females and 49.31% males in the P Group ($\chi^2 = 0.033$, $P = 0.856$). The mean age was 50.28 ± 5.72 years in the S Group compared to 51.33 ± 6.7 years in the P Group ($t = 1.315$, $P = 0.19$). No significant difference was observed in BMI, with values of 22.26 ± 2.3 kg/m^2 for the S Group and 22.63 ± 2.53 kg/m^2 for the P Group ($t = 1.217$, $P = 0.225$). Ejection fraction (EF) was similar between groups, recorded as 0.6 ± 0.04 for the S Group and 0.59 ± 0.05 for the P Group ($t = 0.777$, $P = 0.438$). Vital capacity demonstrated no significant variance, measuring 2.78 ± 0.66 L in the S Group and 2.91 ± 0.74 L in the P Group ($t = 1.461$, $P = 0.145$). The American Society of Anesthesiologists (ASA) classifications were comparable between groups ($\chi^2 = 1.022$, $P = 0.312$). Additionally, there were no significant differences in the proportion of patients experiencing breathlessness, smoking status, laterality of the resected side, the specific resected lobes, or the number of resected segments (all $P > 0.05$). These baseline similarities affirmed the comparability of the groups for subsequent analysis of postoperative outcomes.

Perioperative surgical and medical characteristics

Total fluid intake over 24 hours was similar between the two groups, with the S group averaging 1505 ± 528 ml and the P group 1525 ±

Table 1. Comparison of the general characteristics between the two groups

Parameters	S Group (n = 108)	P Group (n = 144)	t/χ^2	P
Female/Male	56 (51.85%)/52 (48.15%)	73 (50.69%)/71 (49.31%)	0.033	0.856
Age (years)	50.28 ± 5.72	51.33 ± 6.70	1.315	0.190
Body Mass Index (kg/m^2)	22.26 ± 2.30	22.63 ± 2.53	1.217	0.225
EF	0.60 ± 0.04	0.59 ± 0.05	0.777	0.438
Vital capacity (L)	2.78 ± 0.66	2.91 ± 0.74	1.461	0.145
ASA			1.022	0.312
I	45 (41.67%)	51 (35.41%)		
II	63 (58.33%)	93 (64.59%)		
Breathlessness (None/Mild)	92 (85.19%)/16 (14.81%)	131 (90.97%)/13 (9.03%)	2.030	0.154
Smoker (Yes/No)	31 (28.70%)/77 (71.30%)	37 (25.69%)/107 (74.31%)	0.284	0.594
Resected side (Right/Left)	67 (62.04%)/41 (37.96%)	88 (61.11%)/56 (38.89%)	0.022	0.881
Resected lobe			0.118	0.943
Upper	68 (62.96%)	93 (65.12%)	0.279	0.600
Middle	15 (13.89%)	18 (12.56%)	1.181	0.600
Lower	25 (23.15%)	33 (22.32%)	0.737	0.600
Number of segments	3.64 ± 1.75	3.59 ± 1.05	0.282	0.778

EF, Ejection Fraction; ASA, American Society of Anesthesiologists.

Table 2. Comparison of perioperative surgical and medical parameters between the two groups

Characteristics	S Group (n = 108)	P Group (n = 144)	t/χ^2	P
Total fluid intake (ml/24 hours)	1505 ± 528	1525 ± 675	0.264	0.792
Red blood cell transfusion (% patients)	1 (0.93%)	3 (2.08%)	0.048	0.827
Urine output (ml/24 hours)	772 ± 268	815 ± 356	1.094	0.275
Chest drainage (ml/24 hours)	326 ± 152	351 ± 174	1.191	0.235
PaO2/FIO2 (kPa)	43.2 ± 9.4	45.28 ± 9.9	1.683	0.094
Blood hemoglobin at POD1 (g/l)	122 ± 19	119 ± 11	1.467	0.144
Serum creatinine at POD1 (mg/l)	80 ± 29	85 ± 31	1.304	0.194

PaO2/FIO2, ratio of arterial oxygen pressure to inspiratory fraction of oxygen; POD1, on the first postoperative day.

675 ml (t = 0.264, P = 0.792) (**Table 2**). The incidence of red blood cell transfusion was 0.93% in the S group and 2.08% in the P group (χ^2 = 0.048, P = 0.827). Urine output in 24 hours was also comparable, measured at 772 ± 268 ml for the S group and 815 ± 356 ml for the P group (t = 1.094, P = 0.275). Chest drainage volumes did not differ significantly, recorded as 326 ± 152 ml in the S group and 351 ± 174 ml in the P group (t = 1.191, P = 0.235). The PaO2/FIO2 ratios were 43.2 ± 9.4 kPa for the S Group and 45.28 ± 9.9 kPa for the P group, showing no significant difference (t = 1.683, P = 0.094). Blood hemoglobin levels were similar on the first postoperative day (POD1), with the S group at 122 ± 19 g/l and the P group at 119 ± 11 g/l (t = 1.467, P = 0.144). Similarly, serum creatinine levels at POD1 did not differ significantly, with 80 ± 29 mg/l in the S group and 85 ± 31 mg/l in the P group (t = 1.304, P = 0.194). These findings suggest equivalency in perioperative management between the groups.

Postoperative VAS scores

Preoperative VAS scores were comparable between groups, with the S group averaging 5.52 ± 0.24 and the P group 5.58 ± 0.47 (t = 1.317, P = 0.189) (**Table 3**). However, at 2 hours post-surgery, the S group demonstrated significantly lower VAS scores (1.96 ± 0.52) compared to the P group (2.15 ± 0.56; t = 2.839, P = 0.005). This trend persisted at 4 hours post-surgery, with the S group scoring 2.68 ± 0.69 versus 2.92 ± 1.02 in the P group (t = 2.265, P = 0.024). At 8 hours postoperatively, the S group's score was 3.15 ± 0.86, lower than the P group's 3.48 ± 1.22 (t = 2.477, P = 0.014). At 12 hours, the differences widened, with the S

Table 3. Comparison of postoperative VAS scores between the two groups

Group	S Group (n = 108)	P Group (n = 144)	t	P
Preoperative	5.52 ± 0.24	5.58 ± 0.47	1.317	0.189
2 h after surgery	1.96 ± 0.52	2.15 ± 0.56	2.839	0.005
4 h after surgery	2.68 ± 0.69	2.92 ± 1.02	2.265	0.024
8 h after surgery	3.15 ± 0.86	3.48 ± 1.22	2.477	0.014
12 h after surgery	3.92 ± 0.58	4.19 ± 0.78	3.116	0.002
24 h after surgery	3.84 ± 0.95	4.14 ± 0.98	2.444	0.015

VAS, Visual Analogue Scale.

group at 3.92 ± 0.58 compared to 4.19 ± 0.78 in the P group (t = 3.116, P = 0.002). Finally, at 24 hours post-surgery, the S group's VAS score remained significantly lower at 3.84 ± 0.95 compared to 4.14 ± 0.98 in the P group (t = 2.444, P = 0.015). These results indicate that the combination of sevoflurane and intercostal block effectively reduces postoperative pain in lung cancer surgery patients.

Changes in lung function after surgery

Preoperative FEV1 values were similar between groups, with 1.81 ± 0.52 L in the S group and 1.75 ± 0.68 L in the P group (t = 0.798, P = 0.426) (**Figure 2**). However, significant improvements in FEV1 were noted at 8 hours (1.49 ± 0.29 L S Group vs 1.36 ± 0.65 L P Group; t = 2.146, P = 0.033) and 24 hours postoperatively (1.59 ± 0.39 L S Group vs 1.45 ± 0.45 L P Group; t = 2.516, P = 0.012), although not at 12 hours. FVC exhibited a similar trend: no preoperative differences were observed, but the S group showed significant improvements at 8 hours (1.54 ± 0.66 L vs 1.39 ± 0.25 L; t = 2.249, P = 0.026), 12 hours (1.78 ± 0.27 L vs 1.69 ± 0.29 L; t = 2.633, P = 0.009), and 24 hours (2.25 ± 0.36 L vs 2.09 ± 0.58 L; t = 2.69, P = 0.008) post-surgery. For VC, while preoperative measures were comparable (t = 1.439, P = 0.151), significant differences emerged at 12 hours (2.42 ± 0.52 L vs 2.24 ± 0.32 L; t = 3.198, P = 0.002) and 24 hours (2.81 ± 0.15 L vs 2.65 ± 0.64 L; t = 2.94, P = 0.004) postoperatively. These results suggest that the combined use of sevoflurane and intercostal block was associated with better preservation of lung function following lung cancer surgery.

Postoperative BCRS scores

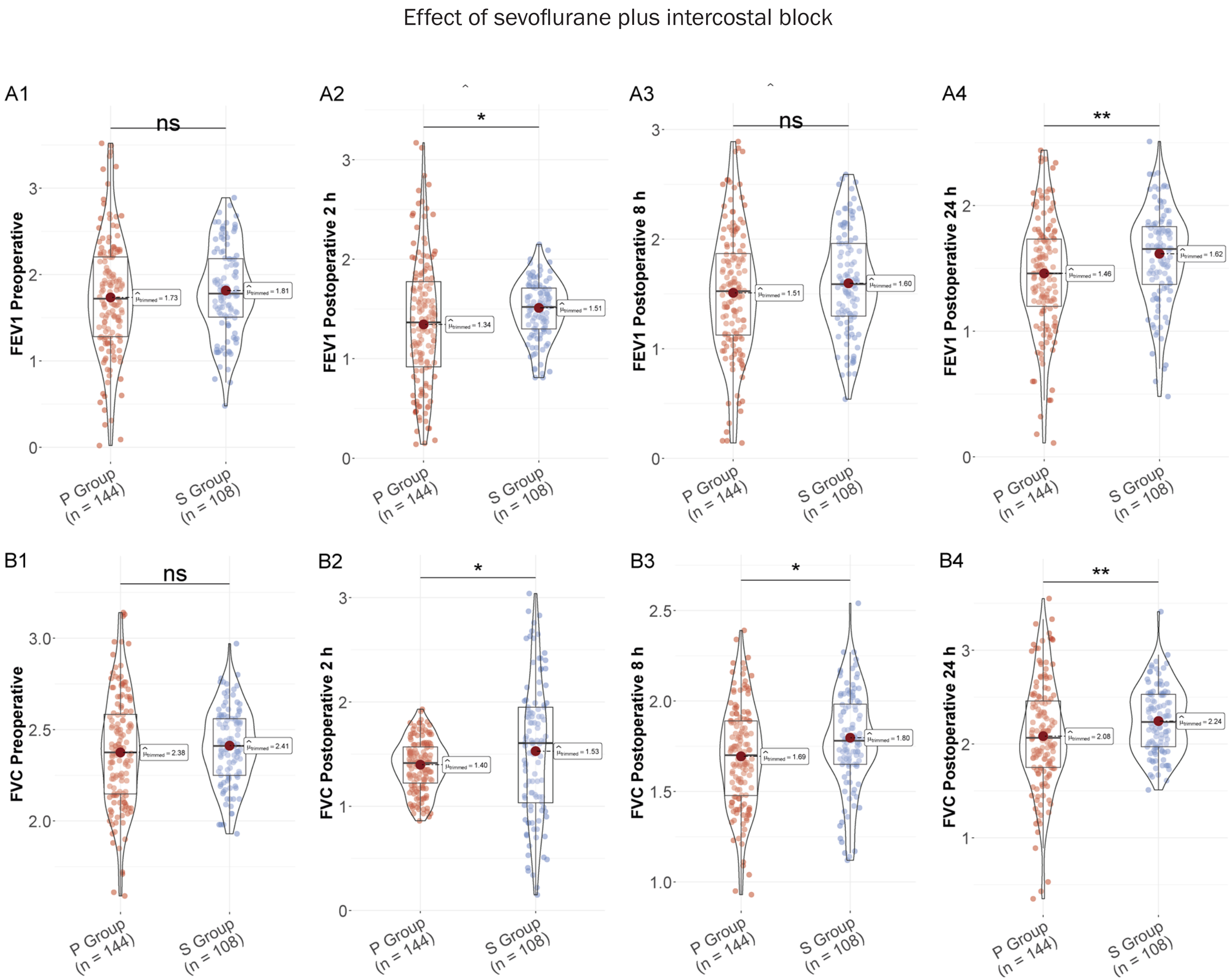
At 2 hours post-surgery, the S group exhibited significantly higher BCRS scores (2.26 ± 0.55) compared to the P group (2.12 ± 0.24; t = 2.375, P = 0.019) (**Table 4**). Similar trends were observed at 8 hours (2.87 ± 0.69 for S group vs 2.64 ± 0.28 for P group; t = 3.332, P = 0.001) and 12 hours post-surgery (3.02 ± 0.57 for S group vs 2.88 ± 0.41 for P group; t = 2.115, P = 0.036), indicating a reduced stress response in the S group at these intervals. However, differences at 4 hours (t = 1.489, P = 0.139) and 24 hours postoperatively (t = 1.7, P = 0.090) were not statistically significant. These results suggest that the combined anesthetic strategy may help in modulating the stress response early in the postoperative period.

Postoperative opioid consumption

Within the first 24 hours post-surgery, cumulative fentanyl consumption was notably lower in the S group (1307.52 ± 259.41 μg) than in the P group (1742.26 ± 253.12 μg; t = 13.35, P < 0.001) (**Table 5**). This reduction continued through the 48-hour mark, with the S group using 2159.58 ± 251 μg compared to 3402.17 ± 352 μg in the P group (t = 32.702, P < 0.001). Despite these differences in opioid consumption, there was no significant difference in the need for rescue analgesics between the groups, with 5.56% in the S group and 6.25% in the P group requiring additional analgesia (χ^2 = 0.053, P = 0.818). Additionally, the S group experienced a shorter hospital stay, with an average of 8.33 ± 1.69 days, compared to 9.25 ± 1.78 days in the P group (t = 4.187, P < 0.001). These findings suggest that the combination of sevoflurane and intercostal block effectively reduces opioid consumption and may contribute to a shorter duration of hospitalization.

MMSE scores

Preoperatively, MMSE scores were similar between the groups, with the S group at 28.71 ±


Effect of sevoflurane plus intercostal block
A1
A2
A3
A4
B1
B2
B3
B4
ns
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FEV1 Preoperative
FEV1 Postoperative 2 h
FEV1 Postoperative 8 h
FEV1 Postoperative 24 h
FVC Preoperative
FVC Postoperative 2 h
FVC Postoperative 8 h
FVC Postoperative 24 h
P Group (n = 144)
S Group (n = 108)

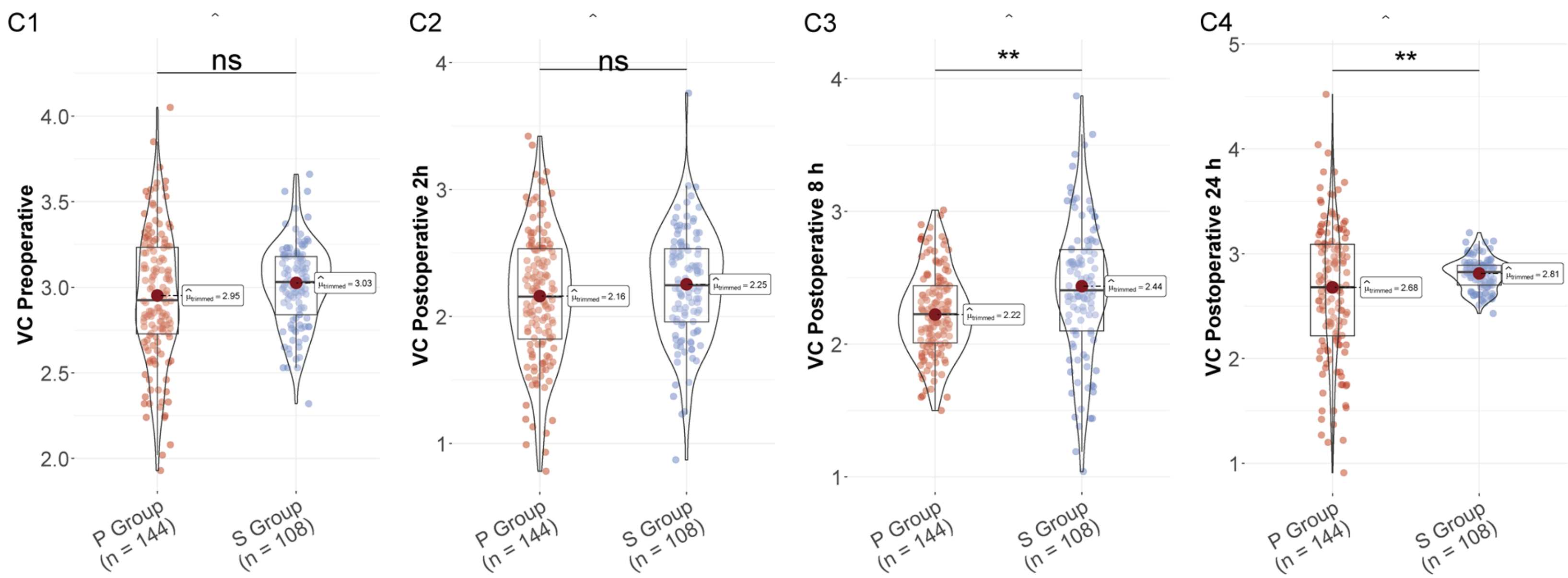

Figure 2. Changes in lung function at 24 hours after surgery in the two groups. A1. FEV1 (L) - Preoperative; A2. FEV1 (L) - Postoperative 8 h; A3. FEV1 (L) - Postoperative 12 h; A4. FEV1 (L) - Postoperative 24 h; B1. FVC (L) - Preoperative; B2. FVC (L) - Postoperative 8 h; B3. FVC (L) - Postoperative 12 h; B4. FVC (L) - Postoperative 24 h; C1. VC (L) - Preoperative; C2. VC (L) - Postoperative 8 h; C3. VC (L) - Postoperative 12 h; C4. VC (L) - Postoperative 24 h. Note: FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; VC, Vital Capacity; ns, non-significance; *, $P < 0.05$; **, $P < 0.01$.

Table 4. Comparison of postoperative BCRS scores between the two groups

Group	S Group (n = 108)	P Group (n = 144)	t	P
2 h after surgery	2.26 ± 0.55	2.12 ± 0.24	2.375	0.019
4 h after surgery	2.35 ± 0.89	2.22 ± 0.32	1.489	0.139
8 h after surgery	2.87 ± 0.69	2.64 ± 0.28	3.332	0.001
12 h after surgery	3.02 ± 0.57	2.88 ± 0.41	2.115	0.036
24 h after surgery	3.32 ± 1.61	2.98 ± 1.55	1.700	0.090

Table 5. Comparison of postoperative fentanyl consumption between the two groups

Cumulative Comparison (μg)	S Group (n = 108)	P Group (n = 144)	t/χ^2	P
0-24 h after surgery	1307.52 ± 259.41	1742.26 ± 253.12	13.35	< 0.001
0-48 h after surgery	2159.58 ± 251	3402.17 ± 352	32.702	< 0.001
Need for rescue analgesics (n)	6 (5.56%)	9 (6.25%)	0.053	0.818
Hospital stay (days)	8.33 ± 1.69	9.25 ± 1.78	4.187	< 0.001

Table 6. Comparison of MMSE scores between the two groups

Groups	S Group (n = 108)	P Group (n = 144)	t	P
Before surgery	28.71 ± 0.98	28.65 ± 0.95	0.446	0.656
At the end of the surgery	26.03 ± 4.42	24.14 ± 5.28	3.013	0.003
At 24 h after surgery	28.55 ± 5.49	27.48 ± 4.37	1.668	0.097

0.98 and the P group at 28.65 ± 0.95 (t = 0.446, P = 0.656) (**Table 6**). However, immediately after surgery, the S group maintained higher MMSE scores (26.03 ± 4.42) compared to the P group (24.14 ± 5.28; t = 3.013, P = 0.003), indicating a potentially favorable effect on immediate postoperative cognitive function. By 24 hours after surgery, MMSE scores in both groups approached baseline levels, with no significant difference observed (S group: 28.55 ± 5.49 vs P group: 27.48 ± 4.37; t = 1.668, P = 0.097). These results suggest that while the combination of sevoflurane and intercostal block may offer some advantage in preserving cognitive function immediately post-surgery, this effect appears to diminish and converge with the control group by 24 hours.

Adverse reactions

The incidence of low blood pressure was higher in the S group at 7.41% compared to 2.78% in the P group, but this difference did not reach statistical significance (χ^2 = 2.917, P = 0.088). Similarly, bradycardia occurred in 0.93% of the S group and 3.47% of the P group (χ^2 = 0.8, P = 0.371), showing no significant difference. In contrast, nausea was significantly more prevalent in the S group, affecting 9.26% of patients compared to 2.78% in the P group (χ^2 = 4.941, P = 0.026). Vomiting also occurred more frequently in the S group at 8.33% versus 2.08% in the P group (χ^2 = 5.316, P = 0.021). The details can be seen in **Figure 3**. These findings suggest that while the combination of sevoflurane and intercostal block was effective, it may be associated with an increased risk of nausea and vomiting postoperatively.

Stress response

As shown in **Table 7**, cortisol levels were notably higher in the S group, with an average of 501.45 ± 57.15 ng/mL compared to 482.14 ± 47.12 ng/mL in the P group (t = 2.857, P = 0.005), indicating increased stress levels in the S group. Additionally, blood glucose levels were also higher in the S group (8.25 ± 1.27 mmol/L) compared to the P group (7.91 ± 1.14 mmol/L; t = 2.264, P = 0.024). Conversely, insulin levels were lower in the S group at 6.37 ± 1.18 IU/mL compared to 6.97 ± 1.87 IU/mL in the P group (t = 3.095, P = 0.002), suggesting a difference in the metabolic stress response. Adrenaline and norepinephrine concentrations were both significantly reduced in the S group (239.32 ± 54.19 pg/mL and 251.47 ± 68.71 pg/mL, respectively) compared to the P group (252.05

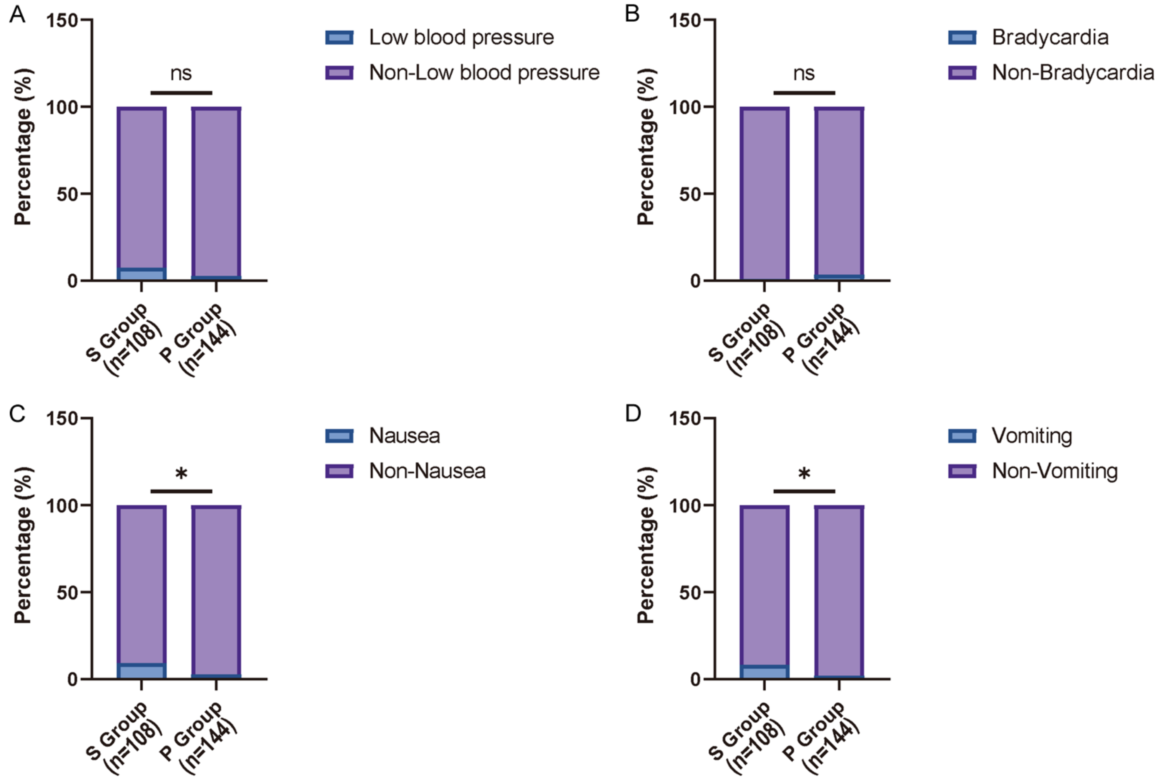

Figure 3. Comparison of postoperative adverse reactions between the two groups (n, %). A. Low blood pressure; B. Bradycardia; C. Nausea; D. Vomiting. Note: ns, non-significance; *, $P < 0.05$.

Table 7. Comparison of postoperative stress response between the two groups (n, %)

Stress response	S Group (n = 108)	P Group (n = 144)	t	P
Cortisol (ng/mL)	501.45 ± 57.15	482.14 ± 47.12	2.857	0.005
Blood glucose (mmol/L)	8.25 ± 1.27	7.91 ± 1.14	2.264	0.024
Insulin (IU/mL)	6.37 ± 1.18	6.97 ± 1.87	3.095	0.002
Adrenaline (pg/mL)	239.32 ± 54.19	252.05 ± 41.75	2.030	0.044
Norepinephrine (pg/mL)	251.47 ± 68.71	269.41 ± 54.79	2.233	0.027
Dopamine (pg/mL)	56.87 ± 11.33	52.47 ± 14.64	2.690	0.008

± 41.75 pg/mL and 269.41 ± 54.79 pg/mL, respectively) (t = 2.03, P = 0.044; t = 2.233, P = 0.027). Similarly, dopamine levels were higher in the S group (56.87 ± 11.33 pg/mL) compared to the P group (52.47 ± 14.64 pg/mL; t = 2.69, P = 0.008). These findings indicate that the combination of sevoflurane and intercostal block effectively modulated the stress response following lung cancer surgery, with notable differences in hormonal and catecholamine levels.

Discussion

The study investigates the efficacy of a sevoflurane-based anesthesia regimen combined with an intercostal block on postoperative outcomes for patients undergoing lung cancer surgery.

First and foremost, the superior preservation of pulmonary function observed with sevoflurane combined with intercostal block could be attributed to the anesthetic properties of sevoflurane [20]. Sevoflurane is known for its minimal impact on respiratory function due to its bronchodilatory effects, which may be particularly beneficial in thoracic surgeries involving the lungs [21]. Unlike propofol, sevoflurane better maintains blood oxygenation, a crucial factor for postoperative recovery in patients undergoing lung resection [22]. The addition of intercostal nerve block provides targeted analgesia, reducing the need for systemic opioids and thereby lessening their respiratory depressive effects [23]. This combination likely contributes to better maintenance of forced expiratory volume (FEV1) and forced vital capacity (FVC), as observed in our results, suggesting enhanced postoperative respiratory mechanics.

The significant reduction in opioid consumption in the S group is another key finding. This can be particularly attributed to the effective pain control achieved by the intercostal block. By providing substantial analgesia directly at the site of surgical trauma, the nerve block minimizes the reliance on systemic opioid, which are often associated with adverse effects like respiratory depression and postoperative nausea and vomiting [24]. Moreover, less opioid use could contribute to shorter hospital stays, as observed in our study, potentially reducing healthcare costs and improving patient throughput. The multimodal analgesia approach used in this study aligns with the objectives of enhanced recovery after surgery (ERAS) protocols, which aim to expedite recovery and improve outcomes by mitigating opioid-related side effects.

The modulation of the stress response, as indicated by biochemical markers, further highlights the beneficial effect of the anesthetic combination, a noteworthy aspect when considering the physiological stress associated with major thoracic surgeries [25]. The reduced levels of catecholamines, including adrenaline and norepinephrine, in the S group may indicate a suppressed sympathetic nervous system response. This effect can be explained by the enhanced analgesic effect achieved by the intercostal block, as pain is a significant trigger for the sympathetic stress response [26]. Furthermore, the hyperpolarizing action of sevoflurane on neuronal membranes may contribute to decreased stress hormone release. The observed reductions in insulin levels, coupled with moderate increases in cortisol, point to the possibility of lower metabolic stress, potentially improving perioperative glycemic control, an important factor for better surgical outcomes. Postoperative hyperglycemia is a known risk factor for surgical site infections and poorer overall recovery, so improved stress and glycemic control could positively influence long-term recovery and complication rates.

The cognitive function assessment also yielded valuable insights. While immediate postoperative cognitive function appeared somewhat preserved in the sevoflurane group, this advantage did not extend to 24 hours post-surgery. This transient cognitive benefit may be due to the reduced requirement for opioids, which are known to adversely affect cognitive function. The localized effect of the intercostal block, combined with the anesthetic properties of sevoflurane (which is less likely to accumulate systemically compared to continuous propofol infusion), likely helped mitigate the central nervous system depressant effects of opioids immediately after surgery, providing some cognitive protection [27, 28]. Nonetheless, the lack of sustained cognitive benefit suggests that other factors, beyond just the choice of anesthetic agent and technique, may contribute to longer-term cognitive outcomes. Underlying neuro-inflammation or other perioperative factors may play a role and warrant further investigation.

Importantly, we must recognize the downside of the observed adverse reactions, particularly the increased incidence of nausea and vomiting in the S group. These symptoms align with well-documented side effects of volatile anesthetics, which are thought to act on the chemoreceptor trigger zone and vestibular system [29], indicating a need for preemptive antiemetic strategies to improve patient comfort and satisfaction in this regimen. Although the benefits of combining sevoflurane with intercostal nerve block remain significant, including improved lung function, reduced opioid consumption, and better regulation of the stress response, effective management of postoperative nausea and vomiting (PONV) remains crucial. Multiple strategies can be implemented to mitigate these adverse effects, focusing on improving patient comfort and satisfaction. For example, the administration of antinausea drugs before anesthesia induction has been shown to reduce the incidence of PONV. In addition, multimodal analgesia techniques that minimize the need for systemic opioids can further reduce the likelihood of PONV. Tailoring preventive measures to individual patient risk factors is also key for effective management of these adverse effects.

While our study presents encouraging results regarding the use of sevoflurane combined with intercostal block in lung cancer surgeries, several limitations must be acknowledged. First, the sample size may have been insufficient to detect all potential differences or rare adverse effects, suggesting the need for larger-scale studies to validate our findings. Additionally, the study's scope was limited to the immediate postoperative period, leaving long-term outcomes unexplored. Variability in surgical techniques and patient comorbidities were not fully controlled for, which may have influenced postoperative recovery profiles. Lastly, while biochemical markers were used to assess stress responses, the lack of comprehensive clinical correlates may not fully capture the complexity of the physiological changes post-surgery, indicating a need for more nuanced investigation in future research.

Our findings underscore the clinical significance of using sevoflurane combined with an intercostal nerve block in thoracic surgery. This approach offers clear advantages in preserving pulmonary function, reducing opioid consumption, and modulating the physiological stress response. Clinicians should consider adopting this strategy within multimodal perioperative care protocols to enhance patient recovery and outcomes. However, it is essential to address potential adverse effects such as postoperative nausea and vomiting through preemptive antiemetic measures. Future research should focus on long-term outcomes and explore ways to optimize cognitive recovery and overall patient satisfaction.

In conclusion, the use of sevoflurane in combination with intercostal block provides a robust anesthesia strategy for patients undergoing lung cancer surgery. This approach demonstrates significant benefits in preserving postoperative pulmonary function, reducing reliance on opioids, and modulating the physiological stress response. However, this method also leads to a high incidence of postoperative nausea and vomiting. Preventive anti-nausea measures and personalized management are recommended to improve patient comfort and satisfaction.

Disclosure of conflict of interest

None.

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