

**RESEARCH ARTICLE** 

## Retrospective Comparison of the Effects of Intrathecal Morphine and Erector Spinae Plane Block on Postoperative Analgesia in Patients Undergoing VATS

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#### ABSTRACT

**Objectives:** This study evaluates the analgesic effects of intrathecal morphine (ITM) and ultrasound-guided erector spinae plane block (ESPB) in managing postoperative pain following video-assisted thoracoscopic surgery (VATS).

**Methods:** This retrospective observational study examined hospital records and anesthesia documents of 40 patients who underwent VATS at a university hospital between January 2021 and January 2022. The patients were divided into two groups: ITM and ESPB. The comparative analysis included cumulative morphine consumption within the initial 12/24 h after VATS, Numeric Rating Scale (NRS) resting/activity scores, rescue analgesic requirements, and the side effect profile.

**Results:** During the first 12 h postoperatively, the ITM group exhibited lower median morphine consumption than the ESPB group (ITM: 1.9 mg [0.85–3] vs. ESPB: 3.65 mg [3–4.23], p=0.003). Further, within the initial 24 h postoperatively, the ITM group also exhibited lower median morphine consumption compared to ESPB (ITM: 4 mg [1.54–5.38] vs. ESPB: 10 mg [10–10], p<0.001). The NRS resting/activity scores were consistently lower in the ITM group than in the ESPB group at all measurement times (p<0.001). The number of patients receiving rescue analgesic medication was lower in the ITM group than in the ESPB group (ITM, n=6 [30%] vs. ESPB, n=20 [100%]; p<0.001). The side effect profiles of both groups were comparable. **Conclusion:** ITM reduced morphine consumption, pain scores, and the requirement for rescue analgesia compared with ESPB, with a comparable side effect profile after VATS.

Keywords: Acute postoperative pain, erector spinae plane block, intrathecal injections, morphine, video-assisted thoracoscopic surgery

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## Introduction

Video-assisted thoracoscopic surgery (VATS) is widely used in the treatment of lung cancer, the most common cancer type worldwide.<sup>[1]</sup> Despite being a minimally invasive technique, approximately two-thirds of the patients present with moderate-to-severe acute pain during the postoperative period due to surgical incision, retraction, costovertebral joint and intercostal nerve damage, rib fracture/dislocation, and pleural irritation due to chest tubes.<sup>[2]</sup> Regional analgesic techniques, such as thoracic epidural analgesia (TEA), paravertebral block (PVB), and intercostal nerve blocks, are employed as multimodal analgesia for postoperative pain management following VATS.<sup>[3,4]</sup> However, employing these techniques is challenging because of technical difficulties, block failure, relative contraindications in patients using anticoagulants, and disadvantages such as hematoma, hypotension, patient immobilization, bladder dysfunction, local anesthetic systemic toxicity, and inadequate analgesia. These challenges are particularly well-documented for TEA and PVB, leading to a noted reluctance among anesthesiologists to use this technique.<sup>[5,6]</sup>

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In recent years, with advancements in ultrasound (USG) technology and its integration into anesthesia practice, an increasing interest has been observed in trunk blocks in VATS.<sup>[7]</sup> One such block is the erector spinae plane block (ESPB), which was first used in 2016 to treat thoracic neuropathic pain.<sup>[8]</sup> In this block, a local anesthetic (LA) is injected into the potential space between the erector spinae muscle and transverse processes of the vertebrae. Possibly, the injected LA spreads craniocaudally at multiple levels and blocks the ventral/dorsal rami of the spinal nerves and sympathetic ganglia. Therefore, postoperative analgesia should be provided during thoracoabdominal surgeries, depending on the injection level.<sup>[9,10]</sup>

In contrast, intrathecal morphine (ITM) administration is a classical technique, recognized for its simplicity, reliability, relative affordability, ease of learning, and low failure rate.<sup>[11]</sup> Despite providing analgesia without motor or sensory blockade in a single shot, this technique has been successfully used for postoperative analgesia in various surgeries, including thoracic surgery, owing to its long duration of action (18–24 h). Nevertheless, this technique faces significant concerns, including late-onset respiratory depression (especially at high doses), side effects such as nausea, vomiting, itching, and urinary retention, and delayed onset of action (6 h).<sup>[12,13]</sup>

To the best of our knowledge, no study has compared the postoperative analgesic efficacy of the ITM and ESPB following VATS. Therefore, this observational study aimed to compare the analgesic efficacy of ITM and ESPB. Notably, differences may occur in morphine consumption between ESPB and ITM, owing to uncertainties regarding the mechanism of action of ESPB and significant inconsistencies in the spread of injectates in cadaver/imaging studies.<sup>[14]</sup> Accordingly, we hypothesize that a significant difference would occur in cumulative morphine consumption within the first 24 h postoperatively between ESPB, applied in the preoperative period, and ITM.

## Methods

## **Study Design**

This retrospective observational study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Ethical approval was obtained from the local ethics committee (Decision No. 462 dated February 1, 2023). The study data of patients who underwent elective VATS between January 2021 and January 2022 was obtained from the Hospital Medical Information System and anesthesia record forms. The research adhered to the principles outlined in the 'Declaration of Helsinki (64<sup>th</sup> WMA General Assembly, Fortaleza, Brazil, October 2013)'.

## Participants

Data from patients aged 18-75 years, ASA I-III, who underwent unilateral elective VATS (metastasectomy, segmentectomy, and lobectomy) and received preoperative ESPB or ITM for postoperative analgesia were used in our study. The exclusion criteria comprised patients with conditions that precluded standard analgesia procedures (such as drug allergy), those with missing Numeric Rating Scale (NRS) scores (due to cognitive dysfunction or neuropsychiatric disorders), those undergoing chronic pain treatment, those using preoperative opioids/alcohol/ drugs, those with a BMI>40 kg/m<sup>2</sup>, and those with cardiac/ hepatic/renal insufficiency. Patients with a history of cardiothoracic surgery and those who developed severe intra-/postoperative bleeding, hemodynamic instability (systolic blood pressure<90 mmHq, OAB<60 mmHq), or who required postoperative mechanical ventilation were also excluded from the study.

A total of 80 patients met the inclusion criteria. Subsequently, their patient files were classified into the ITM and ESPB groups and sorted in descending order according to protocol numbers. Finally, the first 20 patients from each group were included in the study.

## **Block Procedures**

Patients undergoing ESPB received preoperative regional anesthesia in a regional anesthesia room. In contrast, patients receiving ITM underwent the procedure in the operating room. Both groups received standard monitoring, including electrocardiogram (ECG), non-invasive arterial blood pressure, and peripheral oxygen saturation (SpO<sub>2</sub>). Additionally, 2 L/min of nasal oxygen was administered. A 20–22 G IV cannula was inserted into the dorsum of the hand, and normal saline or Ringer's lactate solution was administered at a rate of 5–7 mL/kg. Sedation with 0.02 mg/kg IV midazolam was provided to both groups, achieving a Ramsey Sedation Scale (RSS) score of 2 (awake, calm, followed commands).

## **USG-guided ESPB**

Owing to its greater perceived efficacy, ESPB is performed preoperatively in our clinic.<sup>[15]</sup> After taking aseptic precautions, the patients are seated, and a linear USG probe (8–13 MHz GE LOGIQ V1 Ultrasound System<sup>®</sup>, China) is placed parasagittally lateral to the spinous process of the T5 vertebra (the correct level is determined by counting downward from the first rib to T5). Thereafter, the USG probe is moved laterally 3–4 cm from the spinal process to successively visualize the trapezius, rhomboid major, and erector spinae muscle group, and the transverse process of the T5 vertebra underneath. The plane between the transverse process and the erector spinae muscles is reached using an in-



**Figure 1.** The sonoanatomy for the ESPB. US-guided ESPB, the relevant technique, is depicted in an ultrasound image.

The white line indicates needle trajectory, the blue highlighted area is the desired spread of local anesthetic, and the dashed line denotes the pleura. ESPB: Erector spinae plane block; TP: Transverse process; PVS: Paravertebral space; LA: Local anesthetic.

plane technique with a block needle (80-mm long, 21G short bevel; Stimuplex<sup>®</sup> Ultra 360<sup>®</sup> by B. Braun, Germany). <sup>[8]</sup> Following hydrodissection with 1–2 mL of normal saline and negative aspiration at every 5 mL, a total of 30 mL of a mixture of 0.25% bupivacaine (Marcaine<sup>®</sup>, AstraZeneca, Türkiye) and 1:400000 adrenaline is injected. Craniocaudal spread of the local anesthetic mixture is simultaneously observed (Fig. 1). Sensory block is assessed using an ice pack along the T2–T8 dermatomes at the midclavicular line. The contralateral side is evaluated for sensory changes. Subsequently, after 30 min, successful ESPB is defined based on a sensory block; 1=touch sensation present, no pain; 2=no touch sensation and no pain).

#### **ITM Administration Technique**

For the ITM, the patient is seated before the anesthesia induction, and the procedure area is disinfected and sterilized. Intervention is performed at the L3–L4 or L4–L5 interspace using a spinal needle (Pencil Point, 88 mm, 25 G), and a mixture of 5 mcg/kg (IBW) morphine (Morphine HCI, Galen, Türkiye) and normal saline (total volume 3 mL) is administered within 15–20 s. The dose of intrathecal morphine was determined based on previous studies indicating effective analgesia with minimal side effects. Subsequently, the patient is placed in the supine position, and general anesthesia induction is initiated after radial artery catheterization.

#### **Anesthesia Management**

The standard protocol detailed below is applied to all patients undergoing VATS at our clinic for anesthesia management. In the operating room, patients are monitored based on ECG, SpO<sub>2</sub>, invasive arterial blood pressure, central venous catheter (CVP), and train-offour neuromuscular monitoring. Anesthesia induction is performed with IV propofol 2-3 mg/kg, remifentanil infusion at 0.1–0.25 mcg/kg/min, and rocuronium 0.6–1.2 mg/kg (train-of-four ratio of zero) IV for endotracheal intubation with a left double-lumen tube. Anesthesia is achieved using O<sub>2</sub>/air (fraction of inspired oxygen: 0.60), IV infusion of propofol (6-12 mg/kg/h), and remifentanil (0.1–0.25 mcg/kg/min). The infusion rates of remiferitanil and propofol are adjusted intraoperatively based on the mean arterial pressure and heart rate (within ±20% of the preoperative values). The CVP is maintained within ±2 of the baseline value. Intraoperative ventilation is maintained at a tidal volume of 6–8 mL/kg, I ratio of 1:2, and a respiratory rate (ETCO<sub>2</sub>) at 30–35 mmHg. In addition, all patients undergo urinary catheterization after induction. At the end of surgery, patients are extubated with IV atropine 0.02 mg/kg and IV neostigmine 0.04 mg/kg.

Routine prophylaxis for postoperative nausea and vomiting (PONV) is performed using IV dexamethasone (4 mg) before induction and IV ondansetron 0.15 mg/kg administered 20 min before the end of surgery. PONV is assessed at 0, 3, 6,

12, 18, and 24 h using a verbal descriptive scale (0=none; 1=mild nausea; 2=moderate nausea; 3=vomiting once; 4=vomiting more than once). If the score is  $\geq$ 3, patients are administered IV ondansetron 0.15 mg/kg.

#### **Analgesia Management**

The patients are informed about patient-controlled analgesia (PCA) and NRS scores during the preoperative visit. Patients are told that they will be asked to assess their pain severity according to the NRS score using a 10-cmlong chart with options ranging from "no pain" to "the worst pain imaginable."

Intraoperatively, after induction, patients received IV tenoxicam (20 mg), IV paracetamol (1 g) before the end of surgery, and IV paracetamol (1 g) postoperatively, which is repeated every 8 h. The PCA device (Body Guard 575 Pain Manager, UK) is set without baseline infusion, with a requested dose of 20 mcg/kg morphine, a lockout interval of 6-10 min, and a 4-h limit set at 80% of the total calculated dose. Patients begin using PCA once they are able to communicate in the recovery unit. In cases where rescue analgesia is needed (if the NRS score is>4 at rest despite PCA demand), 100 mg of tramadol is administered as a 30-min IV infusion (maximum 300 mg/day). If the score remains>4, additional IV morphine at a dose of 1-3 mg is administered. Pain intensity, NRSrest (at rest), and NRSactivity (with coughing or deep breathing) are evaluated at 0 (when the patient could communicate), 3, 6, 12, 18, and 24 h postoperatively.

# Postoperative Sedation Level, Respiratory Depression, and Pruritus

The sedation level is assessed using the RSS score at 0, 3, 6, 12, 18, and 24 h (1=anxiety, agitation present; 2=cooperative, awake; 3=calm, responsive to commands; 4-easily awakened by auditory or tactile stimulus, drowsy; 5=drowsy, deep response to auditory or tactile stimulus; 6=no response to auditory or tactile stimulus, asleep). If RSS score is  $\geq$  5, the patient is considered oversedated, and the PCA lockout interval is extended to 40 min. For respiratory depression, all patients are administered oxygen via a nasal cannula at 2 L/min and monitored using pulse oximetry for 24 h postoperatively. Respiratory depression is defined and recorded as oxygen saturation<90% or respiratory rate<8 breaths/min during this period. In cases of respiratory depression, the patient's airway is secured, oxygen therapy is continued, naloxone 0.4–2 mg IV is administered if high-dose opioids were induced, and respiratory support with a bagvalve mask is provided if necessary. Postoperative pruritus is evaluated using a pruritus score (1=none; 2=mild; 3=severe) at 0, 3, 6, 12, 18, and 24 h postoperatively. When the score is>2, patients are administered IV diphenhydramine 25-50 mg, and if it persists, IV prednisolone 0.5 mg/kg is administered.

#### **Surgical Procedure**

Patients are placed in the lateral decubitus position with the side to be operated on facing upward, and surgery is performed through a 3 cm incision made at the 5<sup>th</sup> intercostal space, where an Alexis port was inserted under single-lung ventilation. In addition, depending on the surgeon's preference, a second port is placed in the 7<sup>th</sup> and 8<sup>th</sup> intercostal spaces in some patients.

#### Outcomes

The primary outcome of the study was the cumulative morphine consumption within the first 24 hours postoperatively. Secondary outcomes encompassed the cumulative morphine consumption within the first 12 hours postoperatively, NRS scores at rest and during activity, the number of patients requiring rescue analgesia, intraoperative consumption of remifentanil and propofol, RSS scores, PONV scores, pruritus scores, hemodynamic parameters, complications associated with regional anesthesia techniques (such as postspinal headache, hematoma, infection, and local anesthetic systemic toxicity), and opioid-related side effects (including respiratory depression, excessive sedation, urinary retention, nausea, vomiting, pruritus, constipation, hypotension, and bradycardia).

#### Sample Size Calculation and Statistical Analysis

Using the cumulative morphine consumption data from 10 patients in each group (ITM, [mean±standard deviation] 22±15 mg; ESPB, 36±15 mg), calculations were performed using Minitab Statistical Software (version 16.0, Minitab Inc.), assuming a Type I error of 5% and study power of 80%, with an effect size of 0.93. Although the minimum number of individuals required was determined to be 18 per group, considering the potential data loss, 20 patients were included in each group.

Statistical analysis was performed using the SPSS software package (version 28.0, SPSS Inc.). The normality of the distribution of variables was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean±standard deviation (95% confidence interval) and median (Q1-Q3), whereas categorical variables were expressed as frequency (n) and percentage (%). Categorical variables were compared using the chisquare or Fisher's exact test, as appropriate. Student's T-test and Mann-Whitney U test were used to compare normally and non-normally distributed data, respectively. The Bonferroni-corrected Mann-Whitney U test was used for post-hoc comparisons when necessary. P<0.05 was considered statistically significant (p<0.017 was considered statistically significant for the Bonferronicorrected Mann-Whitney U test).



#### Results

Data from 130 patients were evaluated for eligibility. Fifty patients were excluded from the study because of morbid obesity (17 patients), drug allergy (13 patients), previous VATS/thoracotomy (8 patients), and hemodynamic instability (12 patients). Consequently, data from the remaining 40 patients were analyzed (Fig. 2). No differences in demographic, clinical, or surgical data were found between the groups (except for the surgical side) (Tables 1, 2).

Significant differences in cumulative morphine consumption in the first 12/24 h postoperatively (for 12 h postoperatively, ITM=1.9 mg [0.85–3] vs. ESPB=3.65 mg [3–4.23], p=0.003; for 24 h postoperatively, ITM=4 mg [1.54–5.38] vs. ESPB=10 mg [10–10], p<0.001) were found between the groups (Fig. 3). The postoperative NRSrest and NRSactivity scores were lower in the ITM group than in the ESPB group at all time points (p<0.001) (Fig. 4). The number of patients requiring rescue analgesia differed between the groups (ITM=6 patients [30%] vs. ESPB=20 patients [100%], p<0.001) (Table 2).

Both groups exhibited similar intraoperative remifentanil/ propofol consumption, sedation scores, pruritus scores, and PONV scores (Tables 2, Appendix 1-3). Although no difference in heart rate based on hemodynamic data was observed between the groups, the mean arterial pressure was lower in the ITM group than in the ESPB group at the four measurement times (15, 30, 45, and 60 min) (p<0.05) (Appendix 4, 5). Finally, no block-related complications were encountered in our study, and none of the patients met the definition of respiratory depression among the opioid-related side effects. PONV occurred in four patients with ESPB and five patients with ITM, two of whom vomited once and responded to treatment. Pruritus was observed in three patients in each group and resolved spontaneously without medication. No patient was oversedated in either group (maximum RSS=3). Additionally, urinary catheters were removed smoothly in all patients on the second day postoperatively, and none developed urinary retention.

#### Discussion

In our study, ITM and ESPB were applied as part of multimodal analgesia in patients undergoing VATS.

Table 1. Patient demographic data								
	Group ITM (n=20)		Grou (r	up ESPB 1=20)	р			
Age (years)	60.5 (	(47–68.8)	61.5	(49.5–68)	0.914 m			
BMI (kg/m²)	23.7 (22.8–27.3)		23.8 (22.3–27.2)		0.561 m			
Sex (n, %)								
Female	6	30%	7	35%	0.736 X <sup>2</sup>			
Male	14	70%	13	65%				
ASA score (n, %)								
ASA I	3	15%	2	10%	0.633 X <sup>2</sup>			
ASA II	16	80%	14	70%				
ASA III	1	5%	4	20%				
Comorbidities (n, %)								
No		15%	2	10%	0.633 X <sup>2</sup>			
Yes	17	85%	18	90%				
Respiratory system*	2	11.7%	3	16.6%				
Cardiovascular system <sup>+</sup>	3	17.6%	2	11.1%				
Endocrine system <sup>‡</sup>	4	23.5%	2	11.1%				
>1 systemic disease	6	35.2%	6	33.3%				
Other	2	11.7%	5	27.7%				

X<sup>2</sup> Chi-Square test; m: Mann-Whitney U test. Data are presented as median (Q1-Q3), number of patients (n), and percentage (%). p<0.05 is considered to be statistically significant. Respiratory system \*: Asthma; Cardiovascular †: Hypertension, Coronary arterial disease; Endocrine \*: Type 2 diabetes, hypothyroidism. ITM: Intrathecal morphine; ESPB: Erector spinae plane block; BMI: Body mass index; ASA: American Society of Anesthesiologists.

#### Table 2. Patient intraoperative outcomes and surgical characteristics

Grou (n=	p ITM 20)	Grou (n:	p ESPB =20)	р
2000 (10	50–2845)	2000 (10	)50–3000)	0.655 m
1700 (72	25–2425)	1510 (6	25–3150)	0.52 m
425 (20	00–775)	550 (2	200–975)	0.683 m
100 (5	0–188)	125 (1	00–200)	0.165 m
180 (125–263)		165 (1	20–300)	0.967 m
4 (3–4)		3 (	3–4)	0.443 m
6	30%	15 <sup>§</sup>	75%	0.004 X <sup>2</sup>
14 <sup>  </sup>	70%	5	25%	
11	55%	14	70%	1.000 X <sup>2</sup>
9	45%	6	30%	
6	30%	20¶	100%	
15	75%	13	65%	0.490 X <sup>2</sup>
5	25%	7	35%	
9	45%	15	75%	0.053 X <sup>2</sup>
11	55%	5	25%	
	Grou (n= 2000 (10 1700 (72 425 (20 100 (5 180 (12 4 (3 6 14 <sup>  </sup> 11 9 6 15 5 9 11	$\begin{array}{                                    $	$\begin{array}{ c c c c }\hline Group ITM & Group (n=20) & (n=20$	Group ITM (n=20)Group ESPB (n=20)2000 (1050-2845)2000 (1050-3000)1700 (725-2425)1510 (625-3150)425 (200-775)550 (200-975)100 (50-188)125 (100-200)180 (125-263)165 (120-300)4 (3-4)3 (3-4)630%15 <sup>\$</sup> 75%1470%5945%1575%100%15945%1575%1155%945%1575%1575%1630%20*100%

X<sup>2</sup> Chi-Square test; m: Mann-Whitney U test. Data are presented as median (Q1-Q3), number of patients (n), and percentage (%). A statistically significant difference is in bold, p<0.05. <sup>5</sup>: The data of Group ESPB was significantly higher than that of Group ITM (p=0.004); <sup>1</sup>: The data of Group ITM was significantly higher than that of Group ESPB (p=0.004); <sup>1</sup>: The data of Group ESPB were significantly higher than that of Group ITM (p<0.001). ITM: Intrathecal morphine; ESPB: Erector spinae plane block; VATS: Video-assisted thoracoscopic surgery.

Notably, ITM reduced cumulative morphine consumption, pain scores, and the number of patients requiring rescue analgesia in the first 24 h postoperatively.

Previous meta-analyses have suggested that ESPB is effective for postoperative analgesia after VATS compared to the control group.<sup>[16-19]</sup> Although statistically significant



**Figure 3.** Comparison of postoperative 12 and 24-hour morphine consumption by study groups. Data are presented as median. \*: Group ESPB data were significantly higher than Group ITM (p=0.003 and p<0.001, respectively). ITM: Intrathecal morphine; ESPB: Erector spinae plane block.



Figure 4. Postoperative NRS pain scores at rest and activity in the groups at different time points. Data are presented as median. Group ESPB data were significantly higher than Group ITM at all measuring times. NRS: Numerical rating scale; ITM: Intrathecal morphine; ESPB: Erector spinae plane block.

differences in cumulative morphine consumption in the first 24 h (mean difference, -8.7 to -2.32 mg) and pain scores (mean difference, -1.3 to -0.77) were found between the block group and the control group in these meta-analyses, the difference was not clinically significant. However, the clinical significance of any difference remains debatable. Generally, a difference of 10 mg or more in total IV morphine (or equivalent doses of opioids) consumption within 24 h is considered a minimal clinically significant difference in facial plane blocks.<sup>[20]</sup> Further, a 1.3-unit reduction on an 11unit numeric pain scale over 24 h is considered clinically significant.<sup>[21]</sup> Notably, a meta-analysis by Scorsese et al.<sup>[18]</sup> reported a much higher (-20 mg) mean difference than in other meta-analyses. Although this value is clinically significant, the high heterogeneity and bias in the studies reduce the level of evidence for the results.

ITM adequately provides analgesia in patients undergoing VATS at different doses (200–600 mcg) compared to the control group.<sup>[22,23]</sup> This effect is dose-dependent, and increasing doses are associated with complications. Notably, at a low dose (200 mcg), differences in pain scores are only observed in the early postoperative period,

whereas with increasing doses (600 mcg), the analgesic efficacy also increases. At a low ITM dose of 600 mcg, a decrease in morphine consumption (4.14±5.62 mg vs. 3.65±2.14 mg, p=0.624) similar to our study, along with reduced complications (nine vs. five patients) with the decreasing morphine dose, was observed. Despite the lower dose of intrathecal morphine (0.5 mg/kg) used in our study, effective analgesia was achieved as demonstrated by the reduced morphine consumption and lower pain scores in the ITM group compared to the ESPB group. However, it is important to note that some patients experienced high pain scores (NRS: 4-8) until the sixth postoperative hour, even at rest. This can be attributed to the inherent nature of VATS, which involves significant postoperative pain due to factors such as surgical incision, costovertebral joint disruption, intercostal nerve damage, rib fractures, and pleural irritation. Additionally, the delayed onset of ITM's analgesic effect, typically around six hours post-administration, may have contributed to these higher pain scores.<sup>[2,12]</sup> These findings underscore the need for adjunctive analgesic strategies in the early postoperative period to ensure optimal pain control.<sup>[24]</sup>

Based on our findings, ITM is superior to ESPB, whose clinical efficacy is debatable. Although it is theoretically expected that ESPB would provide superior analgesia compared to ITM in the immediate postoperative period, our findings did not support this assumption. The variability in ESPB's analgesic efficacy among patients may be due to differences in technique and the distribution of the local anesthetic. Studies have shown that the effectiveness of ESPB can vary based on the injection level, volume of local anesthetic used, and its spread. Additionally, the delayed onset of ITM's analgesic effect (typically 4–6 hours) could necessitate supplementary analgesia in the early postoperative period. The potentially lower efficacy of ESPB in our study might explain why ITM, even at lower doses, demonstrated superior pain control.<sup>[9,12,14]</sup> However, using ITM at appropriate doses and thoroughly analyzing its possible complications is crucial. Respiratory depression is a concerning side effect of ITM, and information on its safe doses is inconsistent in the literature owing to variations in the definition of respiratory depression and type of surgery.<sup>[25]</sup> Nevertheless, based on meta-analyses, respiratory depression occurs at high ITM doses (>500 mcg or >7 mcg/kg) used in cardiothoracic and major abdominal surgeries,<sup>[26-28]</sup> which is also consistent with our study findings, as no respiratory depression was observed with ITM at 5 mcg/kg IBW. Notably, the monitoring room type (intensive care units or surgical wards), monitoring duration, and monitoring techniques are also crucial in this regard. Further, although controversial, the use of sedation scores for monitoring respiratory depression is also recommended. <sup>[26]</sup> For the doses of ITM used in our study, monitoring for at least 12 h in the surgical ward was sufficient.<sup>[26]</sup> In addition, these doses were acceptable in terms of other opioid-related side effects (itching, PONV, sedation, and urinary retention). Therefore, ITM, as a part of multimodal analgesia, is a safe and viable option for patients undergoing VATS.

#### Limitations

Our study has some limitations. First, owing to its retrospective observational design, potential data loss is common, which may influence the outcomes. Second, the modest sample size of the groups may have increased the likelihood of chance findings regarding the efficacy of analgesic techniques, hindering the detection of clinically significant side effects. <sup>[29,30]</sup> Finally, the absence of a control group may impede a more comprehensive assessment of the efficacy of ESPB. Future studies should involve prospective randomized trials evaluating the ESPB, ITM, and control groups, including the assessment of the effects on patient satisfaction, early/late-stage recovery, and the development of chronic pain.

## Conclusion

In patients undergoing VATS, ITM reduces morphine consumption, pain scores, and the need for rescue analgesia compared with ESPB, with a similar side-effect profile.

#### Disclosures

**Ethics Committee Approval:** The study was approved by The Ondokuz Mayıs University Clinical Research Ethics Committee (no: 462, date: 01/02/2023).

Authorship Contributions: Concept – C.K., B.K.; Design – C.K., B.K., E.T., H.C.; Supervision – E.B.Ş., İ.S.K.; Fundings – E.T., C.K., B.K.; Materials – C.K., B.K.; Data collection &/or processing – C.K., B.K.; Analysis and/or interpretation – C.K.; Literature search – E.B.Ş., İ.S.K.; Writing – C.K., B.K.

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	Group ITM (n=20)		Group ESPB (n=20)		р
	n	%	n	%	
0 h					
Agitated or restless	7	35	8	40	0.744 X <sup>2</sup>
Cooperative, oriented	12	60	12	60	
Awake but responds to commands only	1	5	0	0	
3 <sup>rd</sup> h					
Agitated or restless	1	5	0	0	1.000 X <sup>2</sup>
Cooperative, oriented	19	95	20	100	
6 <sup>th</sup> h					
Cooperative, oriented	20	100	20	100	1.000 X <sup>2</sup>
12 <sup>th</sup> h					
Cooperative, oriented	20	100	20	100	1.000 X <sup>2</sup>
18 <sup>th</sup> h					
Cooperative, oriented	20	100	20	100	1.000 X <sup>2</sup>
24 <sup>th</sup> h					
Cooperative, oriented	20	100	20	100	1.000 X <sup>2</sup>

**Appendix 1.** Comparison of postoperative sedation scores by study groups

X<sup>2</sup> Chi-square test (Fischer test). Number of patients (n) is presented as percentage (%). ITM: Intrathecal morphine; ESPB: Erector spinae plane block.

Appendix 2. Comparison of postoperative pruritis scores by study groups						
	Group ITM (n=20)		Group ESPB (n=20)		р	
	n	%	n	%		
0 h						
None	20	100	17	85	0.231 X <sup>2</sup>	
Mild	0	0	3	15		
3 <sup>rd</sup> h						
None	19	95	17	85	0.292 X <sup>2</sup>	
Mild	1	5	3	15		
6 <sup>th</sup> h						
None	17	85	17	85	1.000 X <sup>2</sup>	
Mild	3	15	3	15		
12 <sup>th</sup> h						
None	17	85	19	95	0.292 X <sup>2</sup>	
Mild	3	15	1	5		
18 <sup>th</sup> h						
None	18	90	20	100	0.487 X <sup>2</sup>	
Mild	2	10	0	0		
24 <sup>th</sup> h						
None	18	90	20	100		
Mild	2	10	0	0	0.487 X <sup>2</sup>	

Appendix 2. Comparison of postoperative pruritis scores by study groups

X<sup>2</sup> Chi-square test (Fischer test). Number of patients (n) is presented as percentage (%). ITM: Intrathecal morphine; ESPB: Erector spinae plane block.

	Grouj (n=	Group ITM (n=20)		ESPB 20)	р
	n	%	n	%	
0 h					
None	17	85	17	85	1.000 X <sup>2</sup>
Mild nausea	2	10	2	10	
Moderate nausea	1	5	1	5	
3 <sup>rd</sup> h					
None	16	80	19	95	0.151 X <sup>2</sup>
Mild nausea	3	15	1	5	
Moderate nausea	1	5	0	0	
6 <sup>th</sup> h					
None	15	75	19	95	0.328 X <sup>2</sup>
Mild nausea	3	15	1	5	
Vomiting once	2	10	0	(0	
12 <sup>th</sup> h					
None	18	90	19	95	1.000 X <sup>2</sup>
Mild nausea	2	10	1	5	
18 <sup>th</sup> h					
None	19	95	20	100	1.000 X <sup>2</sup>
Mild nausea	1	5	0	0	
24 <sup>th</sup> h					
None	20	100	20	100	1.000 X <sup>2</sup>

Appendix 3. Comparison of postoperative nausea vomiting scores by study groups

X<sup>2</sup> Chi-square test (Fischer test). Number of patients (n) is presented as percentage (%). ITM: Intrathecal morphine; ESPB: Erector spinae plane block.



**Appendix 4.** Comparison of intraoperative heart rate values by study groups. Data are presented as median. ITM: Intrathecal morphine; ESPB: Erector spinae plane block.



Appendix 5. Comparison of intraoperative mean arterial pressure values by study groups.

Data are presented as median. \*The data of group ESPB is significantly higher than that of Group ITM (p<0,05)). ITM: Intrathecal morphine; ESPB: Erector spinae plane block.