RESEARCH PROTOCOL

Official Title of the Study:
Comparison of the Effect of Preoperative and Postoperative Erector Spina Plan Block and Paravertebral Block on Postoperative Pain in Video Assisted Thoracic Surgery (VATS)

NCT Number: NCT06488014
Date: 05.06.2024

Summary of Findings from Non-Clinical Studies, Potentially Clinically Relevant Findings, and Findings from Clinical Studies Related to the Research

Pain after thoracic surgery is common and often severe due to surgical incisions, damage to lung tissue and ribs, and irritation of the pleura and intercostal nerves by the chest tube (1). Thoracotomy is one of the most painful surgical procedures, and the incidence of chronic pain has been reported to be approximately 65% in most studies.

Video-assisted thoracic surgery (VATS) has become increasingly common in recent years. Compared with open thoracotomy, VATS reduces postoperative pain, morbidity, and length of hospital stay due to less tissue trauma. However, VATS still causes moderate to severe acute postoperative pain and chronic pain with a reported incidence of 25–35% (2,3).

Enhanced recovery after thoracic surgery is important. Postoperative outcomes are influenced by the patient's ability to mobilize and participate in physical respiratory therapy exercises (4).

Inadequate analgesia is directly associated with impaired postoperative pulmonary function. Pain may lead to ineffective coughing and inadequate sputum clearance, resulting in atelectasis, hypoxemia, and pneumonia (1).

Effective pain management after VATS is crucial for reducing postoperative complications. Multimodal analgesia approaches combining systemic intravenous (IV) analgesics—such as lidocaine, nonsteroidal anti-inflammatory drugs, steroids, alpha-2 adrenergic agonists, or N-methyl-D-aspartate (NMDA) antagonists—with regional analgesia techniques such as thoracic epidural analgesia, paravertebral block, erector spinae plane (ESP) block, and serratus anterior plane block have been proven effective in recent studies and guidelines (4).

Regional analgesia has the potential to reduce acute postoperative pain, decrease the development of chronic pain, and enhance early postoperative recovery.

Thoracic epidural anesthesia (TEA) is considered the gold standard for postoperative pain management in thoracic surgery. However, possible side effects such as dural puncture, nerve injury, epidural hematoma, hypotension, and urinary retention suggest that less invasive analgesic techniques may be preferable for VATS (3).

Thoracic paravertebral block (TPVB) provides unilateral thoracic analgesia comparable to TEA. Additionally, it is less invasive than TEA, maintains hemodynamic stability, and carries a lower risk of complications. According to the Enhanced Recovery After Surgery (ERAS) guidelines (5) and the PROSPECT group (4), TPVB is recommended as the primary regional analgesic technique for thoracic surgery.

Paravertebral local anesthetic may spread to the epidural and intercostal spaces across multiple levels, blocking spinal nerves and sympathetic fibers, resulting in segmental block and ipsilateral sympathectomy. Major risks or complications of PVB include pneumothorax, hypotension (especially in bilateral blocks), dural puncture, epidural abscess, and epidural hematoma.

In recent years, there has been increasing interest in fascial plane blocks, which involve the spread of large volumes of local anesthetic within fascial planes containing or communicating with target nerves. The erector spinae plane block is one of the most studied fascial plane blocks for thoracic surgery. It is technically easier to perform and theoretically carries a lower risk of serious adverse events such as epidural hematoma, abscess, or pneumothorax compared with TEA and PVB. It is also less likely to cause sympathectomy or hypotension.

ESPB targets the fascial plane between the erector spinae muscles and the posterior aspect of the transverse processes, blocking the dorsal rami of spinal nerves and potentially spreading anteriorly to the paravertebral and epidural spaces to block ventral rami and the sympathetic chain (6).

In VATS patients, ESPB has been shown to result in lower PACU pain scores during the first six hours, reduced opioid consumption, and shorter PACU stay compared to placebo (7). However, mixed evidence exists regarding its efficacy compared to PVB. While two non-inferiority studies found no clinically meaningful difference in postoperative pain scores between PVB and ESPB in VATS (8,9), two other clinical studies demonstrated superior analgesia with PVB (10,11).

Preemptive analgesia is a type of antinociceptive treatment based on the clinical observations of Crile (12) and experimental studies of Woolf (13). These studies showed that antinociceptive interventions applied before injury are more effective in reducing central nervous system sensitization compared to those applied after injury.

Proposed mechanisms of chronic postoperative pain include peripheral sensory neuron sensitization, neuroplasticity in the central nervous system, and neuropathic signaling along the neuro-immune axis (14). The aim of preemptive analgesia is to prevent central sensitization caused by surgical incision and the associated inflammatory process by initiating analgesic interventions before incision.

In our clinic, within the framework of multimodal analgesia, we routinely perform both paravertebral block and erector spinae plane block before incision and/or after surgery. Different anesthesiologists may prefer different block techniques. In this study, we aim to investigate the effects of preoperative and postoperative paravertebral block and erector spinae plane block on postoperative pain scores and prevention of chronic pain in VATS patients.

Summary of Known and Potential Risks and Benefits for Volunteers

Both regional anesthetic techniques used in this study—erector spinae plane block and paravertebral block—are routinely used in clinical practice and have demonstrated analgesic efficacy. The purpose of this study is to compare the effectiveness of these two routinely used methods.

Although no additional risk is expected for patients participating in the study, both techniques have potential complications.

Expected Benefits

- Identification of the more effective analgesic method
- Reduction in acute pain severity
- Decreased opioid requirement
- Shorter ICU stay and hospital discharge time
- Reduced incidence and/or severity of chronic pain

Possible Complications

- Infection at the needle insertion site
- Local anesthetic toxicity/allergy
- Vascular puncture (due to anatomical proximity)
- Pleural puncture, pneumothorax (due to anatomical proximity)
- Block failure

These complications have been reported rarely in previous studies.

Route of Administration, Dosage, Dose Regimen, Duration of Treatment and Justification

Erector Spinae Plane Block

Under ultrasound guidance, local anesthetic will be injected into the fascial plane between the erector spinae muscle and the transverse process.

Paravertebral Block

Under ultrasound guidance, local anesthetic will be injected adjacent to the vertebral body near the exit of the spinal nerves from the intervertebral foramina.

In both groups, the relevant block technique will be applied after induction of anesthesia, before surgical incision (preemptive), and again at the end of surgery before the patient awakens, at the level corresponding to the surgical incision.

The local anesthetic dose will be the same in both groups.

Drug Composition to Be Administered*

Total volume: 25 mL

- 13.5 mL of 0.5% bupivacaine
- 5 mL of 2% lidocaine
- 1.5 mL morphine (diluted with 0.9% NaCl to 1 mg/mL concentration)
- 5 mL of 0.9% NaCl

(This dosing regimen reflects routine clinical practice in our department for such surgeries.)

Reference for local anesthetic dosing in regional anesthesia: Lirk, P. H., & Berde, C. B. (2020). Local anesthetics. In Miller's Anesthesia, 9th ed. Philadelphia: Elsevier Inc., pp. 878–879.

The study will be conducted in accordance with the research protocol, Good Clinical Practice (GCP) guidelines, and applicable regulations.

Study Population

Patients scheduled for Video-Assisted Thoracic Surgery (VATS).

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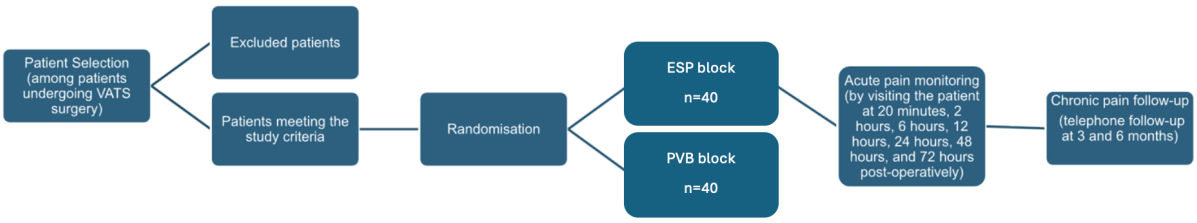
Research Objective:

To compare the effects of dual (pre-emptive and postoperative) application of paravertebral block and erector spinae plane block on acute pain, additional analgesic requirements, and chronic pain incidence after video-assisted thoracoscopic surgery (VATS).

Study Design

- **Primary Endpoint:** Similar or lower pain scores (with NRS) with erector spina plan block in acute post-thoracoscopy pain control
- **Secondary Endpoint:** Similar or less CPSP incidanse with erector spina plan block
- **Study Type:** Prospective, randomized trial.
- **Study Flow Diagram:**



Method:

Patients scheduled for Video-Assisted Thoracic Surgery (VATS) who provide informed consent during the preoperative evaluation and meet the inclusion criteria will be enrolled in the study.

Patients will be grouped according to the analgesic method applied.

Demographic data of patients meeting the inclusion criteria will be recorded.

Standard ASA Monitoring

- ECG
- Peripheral oxygen saturation (SpO_2)
- Non-invasive blood pressure
- Neuromuscular junction monitoring (TOF)
- Depth of anesthesia monitoring (BIS)

Anesthesia Induction

- Fentanyl 1 mcg/kg
- Lidocaine 1 mg/kg
- Propofol 2–2.5 mg/kg
- Rocuronium 1 mg/kg

Intubation

Performed when BIS is between 40–60 and TOF ratio is 0%.

Patients will be positioned in the right or left lateral decubitus position according to the side of surgery.

Before surgical incision and at the end of surgery, at the T5 level on the operative side, the applied block (ESPB or Paravertebral Block) will be performed under routine ultrasound (USG) guidance and recorded.

Local Anesthetic Mixture*

Total volume: 25 mL

- 13.5 mL of 0.5% bupivacaine
- 5 mL of 2% lidocaine
- 1.5 mL morphine (diluted with 0.9% NaCl to a concentration of 1 mg/mL)
- 5 mL of 0.9% NaCl

(This dosage reflects routine clinical practice in our department.)

Maintenance of Anesthesia

- Desflurane titrated to maintain BIS between 40–60 (MAC titration)

Within the Multimodal Analgesia Protocol

- Lidocaine infusion 1 mg/kg/h
- Dexketoprofen 50 mg IV
- Magnesium infusion 40 mg/kg (in 100 mL 0.9% NaCl over 15 minutes)
- Paracetamol 1 g IV infusion (at the end of surgery)

Anesthetic agents will be discontinued at the end of surgery.

Neuromuscular blockade reversal will be achieved with sugammadex 4 mg/kg.

Extubation will be performed when BIS >90% and TOF ratio >90%.

Postoperatively, intravenous PCA (patient-controlled analgesia) will be prepared.

PCA Settings

- Continuous infusion: none
- Bolus: fentanyl 0.25 mcg/kg
- Lockout time: 15 minutes

Postoperative Pain Assessment

Acute and chronic pain will be evaluated using the Numeric Rating Scale (NRS) (Appendix 1).

Acute Pain Follow-up

Pain assessments will be performed at:

- PACU (20th minute)
- Postoperative 2nd, 6th, 12th, 24th, 48th, and 72nd hours

Pain scores at rest, during coughing, and with movement (NRS), additional analgesic requirements, PCA bolus attempts and deliveries, and postoperative oxygen requirements will be recorded.

Postoperative Analgesia

- IV Fentanyl PCA (Bolus 0.25 mcg/kg; lockout 15 minutes)
- If NRS >4 and PCA is insufficient: Paracetamol 1 g IV or Dexketoprofen 50 mg IV infusion

Chronic Pain Assessment

Patients will be contacted by telephone at postoperative 3 and 6 months.

Recorded parameters:

- Presence/absence of pain
- NRS score (if present)
- Chronic analgesic requirement
- Need for additional interventions
- Type of intervention performed (if applicable)

For the assessment of chronic pain, patients were contacted by telephone at 3 and 6 months postoperatively to inquire about their pain status. The structured telephone interview protocol was developed by the authors based on ICD-11 diagnostic criteria for chronic postsurgical pain. The interview protocol (consisted of a structured questionnaire comprising the following two sections):

Section 1: Confirmation of CPSP Presence (According to ICD-11 Diagnostic Criteria)

1. "At 3/6 months after VATS surgery, did you feel any pain in or around your surgical incision?" (To assess the relationship of pain with the surgical field)
2. "Did you have pain in this area before the surgery? If yes, is your current pain the same as your preoperative pain?" (To exclude pre-existing pain and changes in pain characteristics)
3. "Is there any other cause for your pain, such as infection or tumor recurrence?" (To exclude alternative causes)

Section 2: Assessment of CPSP Severity and Management
After confirming the presence of CPSP, pain severity and patients' coping strategies were evaluated:

1. Pain Severity: Patients were asked to rate the most severe pain they had experienced in the last week on a scale from 0 to 10 (NRS: 0 = no pain, 10 = the worst pain imaginable).
2. Pain Management: Patients were asked whether they had taken any measures to relieve pain (e.g. self-medication, seeking medical help).

Randomization

Randomization will be performed based on the chronological order of surgical scheduling, predetermined randomly during protocol development.

After study initiation, patients will be allocated according to surgical order as follows:

E ARM (ESP Group):
1, 3, 4, 6, 8, 10, 14, 15, 17, 18, 22, 23, 24, 27, 28, 29, 32, 33, 36, 38, 44, 45, 46, 47, 53, 54, 55, 56, 57, 58, 61, 64, 65, 68, 70, 72, 73, 76, 77, 80

P ARM (Paravertebral Group):
2, 5, 7, 9, 11, 12, 13, 16, 19, 20, 21, 25, 26, 30, 31, 34, 35, 37, 39, 40, 41, 42, 43, 48, 49, 50, 51, 52, 59, 60, 62, 63, 66, 67, 69, 71, 74, 75, 78, 79

Study Duration

- Estimated total study duration: 1 year
- The study will be completed after the 6-month pain assessment of the last patient (78th patient).

Source Data Recorded Directly in Case Report Forms

- Patient name/surname, protocol number
- Demographics: sex, age, weight, height
- Medical history: smoking status, allergy history, comorbidities, medications, previous surgeries
- Operative data: surgical plan, duration, intraoperative muscle relaxant/opioid amounts, fluids administered, urine output, blood loss
- Postoperative follow-up: acute and chronic pain (NRS)

Inclusion Criteria

- Scheduled for VATS
- Age >18 years
- ASA I–II
- Provided informed consent

Exclusion Criteria

- Age <18 years, weight <40 kg, BMI >35
- Allergy to study medications
- History of chronic analgesic use
- Refusal to participate

Withdrawal / Discontinuation Criteria

- Conversion to open surgery
- Development of allergic reaction to routine medications
- Requirement for repeat thoracic surgery within 6 months
- Death before completion of follow-up

- Patient request to withdraw at any stage

Data from withdrawn patients before study completion will not be used and will be destroyed.

After study completion, withdrawal requests will not result in data deletion; data will remain confidential.

Replacement patients meeting inclusion criteria and providing consent will be enrolled.

Study Groups and Follow-up

E ARM: Ultrasound-guided erector spinae plane block
P ARM: Ultrasound-guided paravertebral block

Both groups will receive the block pre-incision (preemptive) and at the end of surgery.

Both groups will be followed for:

- Acute pain: first 72 hours (PACU (at 20 minute) and postoperative 2, 6, 12, 24, 48, 72 hours)
- Chronic pain: postoperative 3rd and 6th months via telephone

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Permitted and Rescue Medications

If NRS> 4:

- IV Fentanyl PCA (bolus 0.25 mcg/kg, 15-minute lockout)

If insufficient:

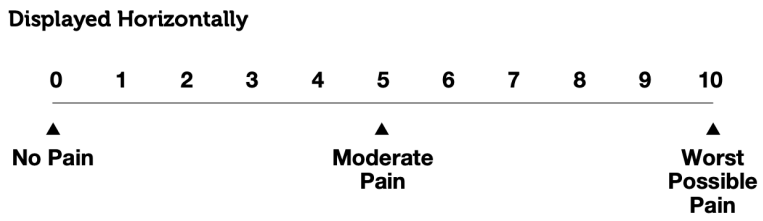
- Paracetamol 1 g IV or Dexketoprofen 50 mg IV infusion

Adverse Event Reporting

All adverse events will be recorded in the case report form. Minor events were defined as nausea, vomiting, and pruritus, while major events were defined as pneumothorax requiring intervention, hematoma formation at the injection site, local anesthetic systemic toxicity (LAST), and surgical site infection.

Patients experiencing adverse events will be monitored for at least 48 hours until vital signs stabilize and no life-threatening risk remains.

Appendix 1: Numeric Rating Scale (NRS)*



* The Australian Pain Society Pain in Residential Aged Care Facilities: Management Strategies, 2nd Edition 2018 Chapter 2 page 30

Statistical analysis

Sample size: The sample size of the study was calculated *in G*Power 3.1.9.2 programme. In the sample article, the mean PCA demand dose was 36.64±26.9 in the ESPB group and 18.82±13.67 in the TPVB group. When these data were taken into consideration, the effect size was calculated as 0.83, α=0.05 and 95% power and the sample size required for each group was calculated as 39 (total 78).

A post-hoc power analysis using the observed effect size for the primary outcome (NRS during movement at 48 hours, d = 0.63) demonstrated an achieved power of 80.2%, confirming that the final sample size was adequate. No interim analyses were conducted.

Statistical analyses were performed using IBM SPSS Statistics (version 23). Descriptive statistics are presented as mean ± standard deviation (SD) for normally distributed continuous variables, median (25-75% percentil) for non-normally distributed continuous variables, and number of cases with percentages for categorical variables. The normality of continuous data was assessed using appropriate tests (e.g., Shapiro–Wilk test). Between-group differences were analysed using the independent samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed continuous variables. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as appropriate. A two-sided p-value <0.05 was considered statistically significant.

All analyses were performed on a per-protocol basis, including all eligible volunteers who completed the study. No interim analyses were planned, and no imputation was performed for missing data.