Video-assisted Thoracoscopic Surgery - Exparel Study Protocol

NCT04864210

10/07/2025

Video-assisted Thoracoscopic Surgery - Exparel Study

ClinicalTrials.gov Identifier: NCT04864210

Recruitment Status: Completed

Sponsor:

Nada Sadek

Collaborators:

American Society of Regional Anesthesia

Information provided by (Responsible Party):

Nada Sadek, University of Iowa

Study Description

Purpose of Study

Video-assisted thoracoscopic surgery (VATS) greatly decreased the number and types of surgery that required open thoracotomy. Initially it was thought that VATS would lead to a reduction of respiratory problems and less acute pain in patients when compared to patients receiving open thoracic surgery. However, VATS can cause moderate to severe postoperative pain in a significant number of patients. Moreover, for reasons that are not fully understood, approximately 25%-47% of VATS patients suffer from persistent chronic pain like that seen after open thoracic surgeries. Physicians are still faced with the challenge of providing care that will manage both the respiratory issues as well as managing acute pain. Of additional concern is the finding that post-surgical pain has been shown to be a strong predictor for development of chronic pain. Inadequate control of acute pain not only causes serious discomfort and significant respiratory problems but may place these patients at greater risk for chronic pain and prescription-opioid dependence. The letter is now recognized as a significant public health problem. It is therefore of utmost importance that we achieve effective postoperative pain management to reduce both immediate- and long-term morbidity in these patients.

Current protocols to manage and/or reduce VATS associated pain include combining the use of regional anesthesia techniques with opioid and non-opioid analgesics. Recent

studies have investigated the efficacy of intercostal blocks using liposomal bupivacaine after thoracic surgery. However, these studies lacked an active comparator population of patients. Our long-term goal is to identify the most suitable regimen to effectively manage VATS-related pain. The objective here in this study, which is our next step in pursuit of that goal, is to determine the best possible regional analgesia technique that can be used in patients coming for VATS surgeries. In this study, we compare the efficacy of regional analgesia with an intercostal nerve block with liposomal bupivacaine (ILiB) to paravertebral block with plain bupivacaine (PB).

The study is designed as a prospective randomized study evaluating intercostal blocks using liposomal bupivacaine. The control population of patients will be treated with a paravertebral block using plain bupivacaine.

Study Design

Study Type:	Interventional
Actual Enrollment:	176 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Single (Outcomes Assessor)
Primary Purpose:	Treatment
Official Title:	Analgesia for Video-assisted Thoracoscopic Surgeries: A Comparison Between Intercostal Blocks With Liposomal Bupivacaine and Paravertebral Blocks With Plain Bupivacaine
Actual Study Start Date:	February 2, 2021
Actual Primary Completion Date:	August 1, 2024
Actual Study Completion Date:	January 30, 2025

Study Population

Patients undergoing VATS procedures (with wedge resection, biopsy, lobectomy, segmentectomy, decortication, diaphragm plication, thymectomy, mediastinal mass/cyst resection and pericardial window) in Main Operating room.

Patients will be identified from the pre-op clinic visit. We will look at the surgical plan to determine if they are eligible as well as the need to undergo (VATS) Video Assisted Thoracoscopic Surgery. All patients for VATS are offered a nerve block (in the absence of contraindications) for post-op pain control as part of their standard care. >95% of patients consent to this block in the pre-op period. Paravertebral block is the current standard of care at our institute (Control group). Intercostal block with liposomal bupivacaine will be the study group.

Eligibility Criteria

Ages Eligible for Study:	18 Years to 80 Years
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Age over 18 years and less than 80 years
- Undergoing video-assisted thoracoscopic surgery (VATS) procedure
- BMI less than 40

Exclusion Criteria:

- Unable to provide informed consent
- Non-English speaking
- Pregnant
- BMI greater than 40

- Video-assisted thoracoscopic surgery pleurodesis subjects
- Patients with pre-existing chronic pain
- Opioid tolerance
- Pain syndromes including fibromyalgia, regional pain syndrome or post therapeutic neuralgia in a thoracic distribution
- Allergy to the study medication
- Patients with infectious disease
- Patients with impaired coagulation
- Severe hepatic disease
- Incarcerated

Arms and Interventions

Patients will be randomized to receive either paravertebral block with plain bupivacaine or intercostal block with liposomal bupivacaine.

Paravertebral blocks under ultrasound guidance: Paravertebral blocks will be performed in the designated block area within 1 hour of starting the surgical procedure by the regional anesthesia team. All paravertebral blocks will be performed under ultrasound guidance. The local anesthetic drug, 0.5% bupivacaine with epinephrine 10 mL, will then be injected into 3- to 5-mL increments until the total volume is injected. The block will be repeated at another level in a similar fashion skipping one intervertebral space. The blocks will be done at a level between T3 and T7.

Intercostal blocks under thoracoscopic guidance: Intercostal blocks will be done in the operating room by the surgical team. After induction of general anesthesia and positioning in the lateral decubitus position, patients will be prepped and draped according to standard institutional practice. The block will be performed before surgical incision at various points using liposomal bupivacaine 266 mg/20 mL with 40 mL of 0.25% bupivacaine HCL.

Arm	Intervention/treatment
Experimental: Liposomal bupivacaine The patient will receive an intercostal nerve block by the surgeon in the operating room after anesthetic has been administered. The surgeon will use thoracoscopic guidance to administer the intercostal nerve block. The medication used in this block will liposomal bupivacaine (Exparel).	Drug: Liposomal bupivacaine Surgeons will perform an intercostal nerve block in the operating room under thoracoscopic guidance while the patient is asleep under anesthesia. This intervention (block) is one of the standards of care but the medication (liposomal bupivacaine) currently is not FDA approved for this type of block.
Active Comparator: Bupivacaine The patient will receive a paravertebral block by the anesthesiologist staffing the pain service area within the hospital prior to surgery. This regional anesthesia will be done using ultrasound guidance. The medication used in this block will be plain bupivacaine with epinephrine.	Drug: Bupivacaine An anesthesiologist trained in regional anesthesia will perform a paravertebral block in the hospital's pain service unit. This intervention is standard of care and will use plain bupivacaine with epinephrine as the medication

Data collection

Preoperative pain and psychosocial assessments: Preoperative opioid use will be determined from review of the patient's medical records. All pain medications will be reviewed with the patient to ensure accuracy, including the average daily dose. Baseline pain: Patients will be asked to rate their pain at rest using the numerical rating scale (NRS, 0–10). In addition, we will ask patients to rate their average expected postoperative pain severity for each of their first 3 postoperative days and after 6 months. Overall body pain will be assessed with Brief Pain Inventory (BPI –short form), which is a self-reported scale that assesses both the severity of pain and impact of pain on daily functioning. BPI will be used to detect pain in other body locations during the preoperative assessment and at the

3 and 6 months postoperative assessments. Pain catastrophizing will be assessed using the Pain Catastrophizing Scale preoperatively and at 2 weeks postoperatively. Quality of Recovery-15 (QoR-15) scores are patient-reported outcome measures evaluating recovery after surgery and anesthesia: scores will be recorded preoperatively, postoperatively daily (up to 3 days) and at 2 weeks. Baseline incentive spirometry value (average of 3 attempts) will also be recorded at this time. In addition, patients will be educated about study-related follow-up assessments during this visit. Their preference to receive telephone calls, e-mail messages to answer the follow-up questions electronically or to use a paper form (receive stamped return envelope) to answer these questions will be documented.

First 3 postoperative days: A research team member blinded to study group allocation will call upon patients during the first 3 days after surgery. The data will be collected each day may include by is not limited to: A) Pain Scores: Average pain scores for the last 24-hour period B) Incentive spirometry values: Average of 3 different attempts; C) Opioid consumption at 24, 48, and 72 h; D) Recovery of bowel function: First passage of flatus and first bowel movement will be queried at each visit until they occur; E) QoR-15: Scores will be recorded on daily visits. Patients being discharged 72 hours before they will be educated on a pain diary and will be asked to document the severity of average pain and the amount of opioid consumption during the previous 24 hours each day for remainder of the first 3 postoperative days. Depending on their preference, they will either accept a telephone call, answer e-mail messages or return a paper questionnaire in a stamped return envelope. Length-of-stay at the hospital will be recorded as well.

Follow-up Assessments: A) Postoperative clinic visit (around 2 weeks): Pain scores - average in the last 3-day period, total opioid consumption, pain catastrophizing scores and QoR-15 scores will be recorded. B) 3- and 6-month assessments: average pain scores in the last 7-day period, average opioid consumption in the last 7-day period and BPI-short form scores will be recorded. Again, per their preference, patients will either receive a telephone call, e-mail message or return a paper questionnaire.

Risks

A. Procedure related: Less Likely / Less Common (<10%) Mild: Bleeding, Infection, Fever, Failure to have adequate block (numbness of surgical area). Rare (<0.5%): Local Anesthetic toxicity which may include - Seizure, Cardiac arrest (Code Blue), Respiratory failure, Patient death.

B. B. Drug related:
   Bupivacaine Liposome (study drug) Common: Cardiovascular: Tachycardia (1.7% to 3.9%), Dermatologic: Pruritus (3.1% to 5.2%), Gastrointestinal: Constipation (2.1% to 21.9%), Nausea (up to 40.2%), Vomiting (10.1% to 27.8%), Neurologic: Dizziness (6.2%), Headache (3.3% to 8.3%), Somnolence (up to 5.2%), Other: Fever (2.1% to 23.3%). Serious (rare): Cardiovascular: Cardiac arrest, Hematologic: Methemoglobinemia, Neurologic: Seizure
   Bupivacaine HCl (Routinely used drug) Serious: Cardiovascular: Cardiac arrest, Hypotension, Negative inotropic effect on myocardium, Ventricular arrhythmia, Hematologic: Methemoglobinemia, Immunologic: Allergic reaction (Rare), Musculoskeletal: Chondrolysis of articular cartilage, Neurologic: Bacterial meningitis, Septic, Central nervous system depression, Central nervous system stimulation, Cranial nerve disorder, Paraplegia, Seizure (0.1%), Total spinal nerve blockade following local anesthetic injection, Respiratory: Respiratory arrest.

C. Confidentiality breaches: Risks of breaches of confidentiality are small but nonetheless possible. However, all possible efforts taken to ensure the security of study data and minimize the risks of accidental disclosure of identifiable data elements.

Outcome Measures

Primary Outcome Measure:

1. Measure post-operative opioid usage [Time Frame: Up to 48 hours post procedure]

Review the subject medical record to determine opioid use by the subject in the first 48 hours after surgery.

Secondary Outcome Measures:

1. Measure lung function [Time Frame: Up to 24 hours post procedure]

Using an incentive spirometer device, the amount of air volume is inhaled and exhaled by the lungs post VATS procedure. The subject will be asked to do 3 attempts in succession and the number recorded will be the average of the 3 attempts. The air volume inhaled is

measured on a scale from near 0 to 2500 milliliters with the low number indicating little air movement whereas 2500 milliliters indicates good air flow. These results will be compared to the volume determined at baseline prior to surgery.

2. Measure post-operative opioid use following discharge from the hospital [Time Frame: Up to 6 months post procedure.]

Patients will be asked to keep a pain medication diary to record their use of opioid and non-opioid medications for pain control.

3. Measure post-operative pain scores after discharge from the hospital [Time Frame: Up to 6 months post procedure.]

Using a numerical rating scale, patients will be asked to report their pain level. The scale is from 0 to 10 with 0 being no pain and 10 representing the most intense pain. The goal for measuring after acute hospitalization is to determine if the patient is experiencing the onset of chronic pain.

4. Measure post-operative acute pain scores [Time Frame: Up to 24 hours post procedure]

Using a numerical rating scale (0-10), patients will be asked to report their pain level. The scale is from 0 to 10 with 0 being no pain and 10 representing the most intense pain.

Contacts and Locations

Locations

United States, Iowa

University of Iowa

Iowa City, Iowa, United States, 52242

Investigators

Principal Investigator: Nada Sadek, MD University of Iowa

More Information

Other Resources:

Links provided by Nada Sadek, University of Iowa

"FDA Advisors Skeptical of Liposomal Bupivacaine for Regional Pain Control"

Publications:

Bayman EO, Parekh KR, Keech J, Larson N, Vander Weg M, Brennan TJ. Preoperative Patient Expectations of Postoperative Pain Are Associated with Moderate to Severe Acute Pain After VATS. Pain Med. 2019 Mar 1;20(3):543-554. doi: 10.1093/pm/pny096.

Bayman EO, Parekh KR, Keech J, Selte A, Brennan TJ. A Prospective Study of Chronic Pain after Thoracic Surgery. Anesthesiology. 2017 May;126(5):938-951. doi: 10.1097/ALN.0000000000001576.

Furrer M, Rechsteiner R, Eigenmann V, Signer C, Althaus U, Ris HB. Thoracotomy and thoracoscopy: postoperative pulmonary function, pain and chest wall complaints. Eur J Cardiothorac Surg. 1997 Jul;12(1):82-7. doi: 10.1016/s1010-7940(97)00105-x.

Steegers MA, Snik DM, Verhagen AF, van der Drift MA, Wilder-Smith OH. Only half of the chronic pain after thoracic surgery shows a neuropathic component. J Pain. 2008 Oct;9(10):955-61. doi: 10.1016/j.jpain.2008.05.009. Epub 2008 Jul 16.

Steinthorsdottir KJ, Wildgaard L, Hansen HJ, Petersen RH, Wildgaard K. Regional analgesia for video-assisted thoracic surgery: a systematic review. Eur J Cardiothorac Surg. 2014 Jun;45(6):959-66. doi: 10.1093/ejcts/ezt525. Epub 2013 Nov 27.

Adhikary SD, Pruett A, Forero M, Thiruvenkatarajan V. Erector spinae plane block as an alternative to epidural analgesia for post-operative analgesia following video-assisted thoracoscopic surgery: A case study and a literature review on the spread of local anaesthetic in the erector spinae plane. Indian J Anaesth. 2018 Jan;62(1):75-78. doi: 10.4103/ija.IJA_693_17.

Shariat A, Bhatt H. Successful Use of Serratus Plane Block as Primary Anesthetic for Video-Assisted Thoracoscopic Surgery (VATS)-Assisted Pleural Effusion Drainage. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):e31-e32. doi: 10.1053/j.jvca.2017.10.038. Epub 2017 Oct 31. No abstract available.

Khalil KG, Boutrous ML, Irani AD, Miller CC 3rd, Pawelek TR, Estrera AL, Safi HJ. Operative Intercostal Nerve Blocks With Long-Acting Bupivacaine Liposome for Pain Control After Thoracotomy. Ann Thorac Surg. 2015 Dec;100(6):2013-8. doi: 10.1016/j.athoracsur.2015.08.017. Epub 2015 Oct 24.

Parascandola SA, Ibanez J, Keir G, Anderson J, Plankey M, Flynn D, Cody C, De Marchi L, Margolis M, Blair Marshall M. Liposomal bupivacaine versus bupivacaine/epinephrine after video-assisted thoracoscopic wedge resectiondagger. Interact Cardiovasc Thorac Surg. 2017 Jun 1;24(6):925-930. doi: 10.1093/icvts/ivx044.

Rice DC, Cata JP, Mena GE, Rodriguez-Restrepo A, Correa AM, Mehran RJ. Posterior Intercostal Nerve Block With Liposomal Bupivacaine: An Alternative to Thoracic Epidural Analgesia. Ann Thorac Surg. 2015 Jun;99(6):1953-60. doi: 10.1016/j.athoracsur.2015.02.074. Epub 2015 Apr 23.