

**ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES,
SCHOOL OF MEDICINE DEPARTMENT OF SURGERY**



PREVALENCE AND RISK FACTORS OF POST THORACOTOMY PAIN SYNDROME IN ADDIS ABEBA PUBLIC HOSPITALS, ETHIOPIA, A PROSPECTIVE COHORT STUDY FROM JUNE-OCTOBER 2024 GC.

PROPOSAL SUBMITTED TO ADDISABABA UNIVERSITY COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE DEPARTMENT OF SURGERY FOR THE PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE GENERAL SURGERY RESIDENCY

BY: DR. ABEL GETACHEW

JUNE, 2024

ADDIS ABABA, ETHIOPIA

**ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES,
SCHOOL OF MEDICINE DEPARTMENT OF SURGERY**

PREVALENCE AND RISK FACTORS OF POST THORACOTOMY PAIN SYNDROME

Investigator: Dr. Abel Getachew (MD)

Contact details: email- abelhareg2222@gmail.com

Advisor:

Dr. Abebe Bezabih (Consultant General and Cardiothoracic surgeon)

Co-advisor

Dr. Seyoum Kassa (Consultant General and Cardiothoracic surgeon)

Declaration

I, the undersigned, declare that this proposal is my original work in partial fulfillment of the requirements for the General surgery Residency. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced.

Name: Abel Getachew

Signature

Submission to: Post graduate program, department of Surgery, Addis Ababa University

Date of submission

This proposal work has been submitted for examination with my approval as advisor and tutors on

Approval of the advisor:

Name

Signature

Date

1.

2.

Approval

The undersigned certify that they have read and hereby recommend to Addis Ababa University to accept the Proposal submitted by Abel Getachew entitled, incidence and risk factors of post thoracotomy pain syndrome in Addis Ababa public hospitals in partial fulfillment of the requirements for General surgery residency.

Department head's Name

Signature

Date

Advisor's Name

Signature

Date

Co-advisor's Name

Signature

Date

Internal examiner's Name

Signature

Date

Acknowledgment

I would like to express my heartfelt gratitude to my advisor Dr. Abebe Bezabih (Consultant General and cardiothoracic surgeon) for his invaluable assistance and guidance during the thesis project. I would also like to extend my Gratitude to Dr. Seyoum Kassa (Consultant General and cardiothoracic surgeon) for his guidance additional advice.

I also want to express my gratefulness to my sponsoring organization Addis Ababa University for the financial support I obtained. Finally, I would like to say thanks to my data collectors and study participants.

Table of Contents

DECLARATION.....	I
APPROVAL	II
ACKNOWLEDGMENT	III
TABLE OF CONTENTS	IV
ACRONYMS AND ABBREVIATIONS.....	VII
ABSTRACT	VIII
CHAPTER ONE: INTRODUCTION	1
1.1 BACKGROUND	1
1.2 STATEMENT OF THE PROBLEM	2
1.3 SIGNIFICANCE OF THE STUDY	3
CHAPTER TWO: LITERATURE REVIEW	4
2.1 PATHOPHYSIOLOGY OF PTPS	4
2.2 PREDICTIVE FACTORS	5
2.2.1 <i>Surgical factors</i>	5
2.2.2 <i>Preoperative factors</i>	6
2.2.3 <i>Postoperative Factors</i>	7
2.3 MANAGEMENT OF PTPS	7
CHAPTER THREE: OBJECTIVE OF THE STUDY	11
3.1 GENERAL OBJECTIVE	11
3.2 SPECIFIC OBJECTIVE.....	11
CHAPTER FOUR: METHODOLOGY	12
4.1 STUDY AREA.....	12
4.2 STUDY DESIGN AND PERIOD.....	12
4.3 POPULATION	12
4.3.1 <i>Source population</i>	12
4.3.2 <i>Study population</i>	12
4.4 ELIGIBILITY CRITERIA	13
4.4.1 <i>Inclusion criteria</i>	13
4.4.2 <i>Exclusion criteria</i>	13
4.5 STUDY VARIABLES	13
4.5.1 <i>Dependent variable</i>	13
4.5.2 <i>Independent variable</i>	13
4.6 OPERATIONAL DEFINITIONS.....	13
4.7 SAMPLE SIZE AND SAMPLING TECHNIQUE	14
4.7.1 <i>Sample size</i>	14
6.5. SAMPLE SIZE AND SAMPLING TECHNIQUE	ERROR! BOOKMARK NOT DEFINED.
4.7.3 <i>Data collection procedure and patients handling technique</i>	14
4.7.4 <i>Data quality control and assurance</i>	14
4.7.5 <i>Data analysis and interpretation</i>	15

4.7.6	<i>Ethical consideration</i>	15
4.7.7	<i>Dissemination plan</i>	15
CHAPTER FIVE: RESULTS AND DISCUSSION		16
5.1	PATIENT CHARACTERISTICS	16
	<i>Fig. 2 Pie chart illustrating male and female composition of the study</i>	16
	<i>Fig. 3 Histogram showing the age distribution of the study</i>	17
	<i>Table 1 Age composition of the study</i>	18
5.2	EPIDURAL ANESTHESIA STATUS	18
	<i>Fig. 4 Percentage of patients who were and were not given an epidural anesthesia</i>	18
5.3	INTRAOPERATIVE ANESTHESIA	18
	<i>Fig. 5 Bar chart showing the type of analgesic agent given intra-op</i>	19
5.4	PREOPERATIVE PAIN STATUS	19
	<i>Table 2 Pre-operative pain status</i>	19
	<i>Fig. 6 Pre-operative pain status</i>	20
5.5	ACUTE POST THORACOTOMY PAIN SYNDROME	20
	<i>Table 3 Acute Post Thoracotomy pain status at 1 week</i>	21
	<i>Fig. 7 Acute Post Thoracotomy pain status at 1 week</i>	21
5.6	CHRONIC POST THORACOTOMY PAIN	21
	<i>Table 4 Acute Post Thoracotomy pain status after 2 months</i>	22
	<i>Fig. 8 Acute Post Thoracotomy pain status after 2 months</i>	22
5.7	ASSOCIATION OF RISK FACTORS WITH PTPS	22
5.7.1	<i>Association of Age with PTPS</i>	22
	<i>Table 7 Age * numerical pain rating scale post op 1 week Correlations</i>	23
	<i>Table 8 Age * numerical pain rating scale post op 2 month Correlations</i>	23
5.7.2	<i>Association of Gender with PTPS</i>	23
	<i>Table 9 Sex * numerical pain rating scale post op 1 week</i>	24
	<i>Table 9 Sex * numerical pain rating scale post op 2 months</i>	24
5.7.3	<i>Association of Epidural aneesthesia with PTPS</i>	24
	<i>Table 11 Epidural anesthesia * numerical pain rating scale post op 1 week</i>	25
	<i>Tabel 12 Epidural_ anesthesia * numerical pain rating scale post op 2 month</i>	25
5.7.4	<i>Association of Pre-operative pain with PTPS</i>	26
	<i>Table 13 Preoperative pain status * numerical pain rating scale post op 1 week Parameter Estimates for AOR</i>	26
	<i>Tabel 14 Preoperative pain status * numerical pain rating scale post op 2 month Parameter Estimates for COR</i>	27
5.7.4	<i>Association of Pre-operative pain with PTPS</i>	28
	<i>Table 15 Post operative pain status * NRS post op 2 month Parameter Estimates for COR</i>	28
	<i>Table 16 Post-operative pain status * numerical pain rating scale post op 2 month Parameter Estimates for AOR</i>	29
CHAPTER SIX: CONCLUSION		30
REFERENCE		1
ANNEX ONE: INFORMATION SHEET TO GET PERMISSION FOR THE RESEARCH		3
ANNEX TWO: CONSENT FORM		4
ANNEX THREE: PATIENT DATA		5
SECTION II: DATA DURING THE PREOPERATIVE PERIOD		5
ANNEX FOUR: THE NUMERIC RATING SCALE (NRS) FOR PREOPERATIVE PAIN ASSESSMENT		6

ENGLISH VERSION: THE NUMERIC RATING SCALE (NRS).....	6
ANNEX FOUR: THE NUMERIC RATING SCALE (NRS) FOR POSTOPERATIVE PAIN ASSESSMENT AT 1 WEEK.....	7
ENGLISH VERSION: THE NUMERIC RATING SCALE (NRS).....	7
ANNEX FOUR: THE NUMERIC RATING SCALE (NRS) FOR POSTOPERATIVE PAIN ASSESSMENT AT 2 MONTH.....	8
ENGLISH VERSION: THE NUMERIC RATING SCALE (NRS).....	8
ANNEX SIX: DATA ACCURACY CHECK SHEET.....	9

Acronyms and Abbreviations

AAU- Addis Ababa University

ASA - American Society of Anesthesiologists

PTPS- Post Thoracotomy Pain Syndrome

IASP- International Association for the Study of Pain

PLT- Posterolateral Thoracotomy

VATS- Vedio Assisted thoracoscopic surgery

DBP- Diastolic Blood Pressure

DLT- Double lumen tube

ETT- Endotracheal tube

ICNB- Intercostal nerve block

IM- Intramuscular

ICU- Intensive care unit

IV- Intravenous

MAP- Mean arterial pressure

ml – Milliliter

Mg- Milligram

NMDA- N-Methyl-D-Aspartate

NRS- Numerical Rating Scale

NSAIDs- Nonsteroidal anti-inflammatory drugs

OR- Operation room

PACU- Post anesthesia care unit

PO-Per os

Abstract

Background: Thoracotomy is one of the most painful operative procedures. Ineffective postoperative pain management practice in this procedure will result in physiological and psychosocial deterioration which increases the risk of morbidity and mortality. This can be reduced by ensuring adequate analgesia using multimodal technique with regional blocks. So far epidural block is the gold standard, intercostal, and paravertebral blocks are the alternatives which results in somatic and sympathetic blockade of multiple dermatomes and reduce pain.

Objective: The Prevalence and Risk factors of post thoracotomy pain syndrome in TAH, Addis Ababa, Ethiopia, was assessed during the study period from July to November 2024 GC.

Method: A prospective Crossectional study was done

Results: Overall Prevalence of Acute Post thoracotomy Pain Syndrome was 100%. Of this 29.3% of patients had a pain intensity Numeric Rating Scale >7(severe), 56.1% of patients had a pain intensity Numeric Rating Scale is between 4 and 6(moderate) and 14.6% had mild pain (=3). The Prevalence of Chronic Post Thoracotomy pain syndrome was 87.8% with 51.2% having moderate pain, 36.6% mild pain and 12.2% of patients did not have any pain. Ordinal regression analysis showed the association of Preoperative pain with Acute PTPS is strong with crude odds ratio of 18.7 with P value of 0.001 and CI of 95% and Adjusted Odds ratio of 21.7. The association of Preoperative pain with Chronic PTPS is also strong with crude odds ratio of 6.8. The association of APTPS with CPTPS was also computed in this study using both the Crude odds Ratio and Adjusted Odds Ratio. Patients who had APTPS had COR of 17.7 with P value of 0.001 and CI of 95%. The AOR is 9.6 with P of 0.012 and CI of 95%.

Conclusions: The prevalence of both APTPS and CPTPS is high in our setup. In both types of PTPS most of the patients report a moderate intensity of pain on the NRS scale. The Use of epidural anesthesia has statistically insignificant but weak association with APTPS but interestingly its effect though still statistically insignificant it is stronger with CPTPS. The association of Preoperative pain with CPTPS is strong with patients who had pre-operative pain are 21.7 times more likely to have APTPS. The association of APTPS with CPTPS is also strong with patients having APTPS are 9.6 times more likely to have CPTPS. Pre-operative pain status and presence of APTPS are both strong predictors of CPTPS hence close follow up adequate analgesic management and use of epidural anesthesia in this type of patients would reduce the prevalence as well as intensity of pain.

Keywords: post-thoracotomy pain and analgesia,

Chapter one: Introduction

1.1 Background

Thoracic surgery is a type of surgical procedure that is performed on the chest wall to access intra-thoracic organs. This procedure can be done either thoracoscopically or through open thoracotomy. Thoracoscopy is a minimally invasive surgical procedure done by making a small incision and thoracoscopy ports for thoracoscopic camera and surgical instruments to manage Intra-thoracic pathology. While open thoracotomy is an invasive open chest surgery with a large incision made to gain access to the thoracic organs.[1][3]

Numerous approaches of thoracotomy exist to access the Pleural cavity depending on the underlying pathology to be dealt with but posterolateral incision which is associated with intense pain is mostly used for intrathoracic surgical procedures because it has better access to the thoracic cavity. PLT is also widely practiced in our country.

Overall, thoracotomy is a painful procedure because of chest wall trauma, manipulation, and potential injury of peripheral nerves by rib retractors compression as well as incisional pain from the skin, muscle, pleural, costovertebral joint disruption, and central nervous system hyperexcitability.

Acute postoperative pain affects patient's recovery through both decreased quality of life and due to decreased respiratory effort and decreased mobility they are prone to develop atelectasis, cardiac rhythm abnormalities, post-surgery infections and deep vein thrombosis. This also predisposes them for Chronic Post Thoracotomy Pain Syndrome (CPTPS), for which the management would be prolonged affecting the quality of life of the patient in the long term and also adding to the financial burden.[2] Therefore, adequate perioperative pain control and maintenance of pulmonary function are the major goals during the postoperative period of thoracotomy. Adequate perioperative analgesia gets achieved by using preemptive analgesia, multimodal intraoperative, and postoperative analgesia which should continue even after discharge. Pulmonary complications can be reduced by ensuring adequate analgesia and facilitation of deep breathing, coughing, and clearing secretion.

Various analgesic techniques are used to manage and prevent both acute and chronic post-thoracotomy pain. Some of them are patient-controlled analgesia, multimodal systemic analgesia combined with local anesthetics wound site infiltration, intercostal nerve block, thoracic paravertebral block, and thoracic epidural block.[6]

Thoracic epidural block is thought to manage Acute post thoracotomy pain and also prevent CPTPS in long run. Thoracic paravertebral block is a technique of depositing local anesthetics at the paravertebral space adjacent to the thoracic vertebra and block spinal nerves as they emerge from the thoracic intervertebral foramen. Application of local anesthetics within the unilateral paravertebral space produces sensory and motor block of multiple

thoracic dermatomes at the same side of the block above and below the injection site which results in reduction in pain intensity and used as an option of analgesia for thoracotomy. Intercostal nerve block is a technique of blocking intercostal nerves which arise from thoracic spinal nerves and lie adjacent to the caudal border of each rib. It can be blocked subcutaneously by landmark technique and it can also be blocked by direct visualization of the nerves while the chest is open by inserting the needle directly distal to the angle of the ribs and directing it dorsally along caudal border of the rib into internal intercostal muscle then inject local anesthetics into each intercostal bundles around the paravertebral line in subpleural plane. This direct infiltration of intercostal nerves done by the surgeon before the closure of fascia is an easy technique used for thoracotomy. Overall, ICNB results in a unilateral somatic and sympathetic block which further reduces postoperative pain severity and dependence on opioids.[6][12][24]

1.2 Statement of the problem

The international association for the study of pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Post thoracotomy pain is probably the most severe pain experienced by the patient as incision penetrates several layers of muscle tissue, neurovascular bundles, and other structures of the thoracic region. Pain following thoracic procedures can occur in >70% of patients and is considered to be one of the most severe types of postoperative pain than surgeries in another body system. Immediate severe postoperative pain stays 72-96hr but can also persist for many months and even years, substantially worsening quality of life.

Post thoracotomy pain is associated with much postoperative morbidity including respiratory failure, deep vein thrombosis, cardiac instability, infection due to immunosuppression, depression, and limitation in daily living activity due to the development of chronic post-thoracotomy pain syndrome with the incidence of 30-80% which persists for two or more month. The overall incidence of post-thoracotomy pulmonary complication (19- 59%) is much higher than following upper (16-17%) or lower abdominal surgery (0-5%).[8]

Generally, inadequately treated post-thoracotomy pain has significant morbidity and mortality effect associated with low quality of life due to chronic body pain, depression, decreased physical function, and economic impact due to limitations in working activity as well as unintended expenses on pain associated complications. Postoperative pain management of thoracic surgical patients is mandatory not only for ethical reasons but also because it can modulate stress response, preserve cardiorespiratory function and it is important for patient recovery.

Despite years of advance in pain management, the mostly used postoperative pain management technique in many settings is still full dose opioids however their use is limited by side effects. Specifically in thoracic surgery opioids exacerbate postoperative pulmonary complications; therefore, the best approach of pain management requires multimodal analgesia with local anesthetics to block nociceptive inputs from the periphery. An epidural block is widely used as an adjuvant to multimodal analgesia in thoracotomy because it provides optimal anesthesia and analgesia, but other techniques such as paravertebral and intercostal blocks are also utilized. When an epidural block cannot be done then some studies conclude paravertebral block has a similar degree of analgesic effect with less complication, and some say intercostal block has comparable analgesia effectiveness with less complication than an epidural.

Thus, this study will be conducted to evaluate the incidence of PTPS in patients undergoing open thoracotomy and compare the incidence between those receiving Pre-emptive analgesia and thoracic epidural block with those that did not receive either of them.

1.3 Significance of the study

Postoperative intense pain resulting from thoracotomy requires adequate analgesia to prevent cardiorespiratory morbidities. In our setup either NSAID or opioid is mostly used for postoperative pain management.

Since open thoracotomy which has intense pain is performed in our setup and epidural catheter is not available widely and is costly for the patient it is both informative and crucial to know the magnitude of the problem in our setup and to compare the difference among those who received Pre-emptive multimodal analgesia with epidural block and those who did not so as to improve the postoperative outcomes and increase patients' satisfaction by improving comfort and cost-effectiveness.

Doing this study will also reduce the chance of high dose repetitive opioid administration and reduce the risk of associated side effects which further reduce postoperative morbidities and improve patient satisfaction. On the other hand, it will contribute to improvement of education quality and use as a baseline for further researches.

Chapter two: Literature review

Thoracotomy is the first step in thoracic surgical procedures done to gain access to the pleural space, to the lungs, to the heart, to the esophagus, to the thoracic aorta or anterior mediastinum to perform pneumonectomy, lobectomy, lung segment resection, biopsies, and decortication or to get access for thoracic exploration in major trauma.[3]

Chronic Post thoracotomy pain syndrome according to international association for the study of pain (IASP) is defined as “pain that recurs or persists along a thoracotomy incision at least two months following the surgical procedure”. The same association, international association for the study of pain (IASP) also defines Pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”[9]

The prevalence of post thoracotomy pain syndrome is variable in different literatures but it is generally agreed to be as high as 50-85%. In a study done in Egypt on post thoracotomy pain the incidence of post-thoracotomy pain was reported to be 80% at 3 months, 75% at 6 months, and 61% at one year post-thoracotomy; the incidence of severe pain was 3–5%, and pain that interferes with normal life was seen in 50% of the patients.[3] In our country it is difficult to know the prevalence as there are no studies done on this specific topic hence; difficult to know the magnitude of the problem and manage it.

2.1 Pathophysiology of PTPS

The pathophysiology of Post thoracotomy pain syndrome is still not fully understood, but most studies would agree it arises from nociceptive and neuropathic mechanisms which may originate from somatic and visceral afferents or it can also be a referred one. The pain inflicted during skin incision, rib retraction, muscle splitting, incision on the parietal pleura, and chest drain insertion during thoracotomy is through the nociceptive somatic afferents to the ipsilateral dorsal horn of the spinal cord (T4–T10). These afferents are then transmitted to the limbic system and somatosensory cortices via the contralateral anterolateral system of the spinal cord. The Visceral pain arising from injury to the bronchi, visceral pleura, and pericardium are conveyed by nociceptive visceral afferents through phrenic and vagus nerves.[8][1]

Inflammatory mediators that activate nociceptors, enhance their activity, and reduce the pain threshold, such as prostaglandins, histamine, bradykinin, and potassium, are released in response to tissue injury and if not managed well their sustained production and release will cause an amplified response to pain which is called primary sensitization and leads to intensified pain on breathing or coughing after surgery.

Continued nociception during the perioperative period leads to hyperexcitability of the dorsal horn neurons and higher pain centers through activation of N-methyl-D-aspartate (NMDA) receptors in response to substance P, calcitonin gene-related peptide, and glutamate, which causes central sensitization. This, along with the development of neuropathic pain, can herald the onset of chronic pain which is defined as pain that persists or recurs along the site of the thoracotomy incision at least 2 months after the procedure.[1]

2.2 Predictive factors

2.2.1 Surgical factors

Most of the surgical factors affecting post thoracotomy pain are attributed to Extensive dissection and tissue manipulation during the procedure hence dependent on type of surgical access. The posterolateral approach to thoracotomy provides the best surgical access for most thoracic procedures. However, it involves dividing the latissimus dorsi, and at times the serratus anterior and trapezius muscles, resulting in one of the most painful surgical incisions. Many surgeons now use alternative muscle-sparing approaches where incision of the muscles is replaced with dissection and reflection onto the ribs. The reduced field of view, however, may lead to excessive rib retraction, fracture, dislocation, costovertebral disruption, and damage to the intercostal nerves.[18]

Two studies ($n = 335$ and $n = 20$) with a primary goal to present data on the difference between muscle-sparing posterolateral thoracotomy versus traditional posterolateral thoracotomy and none of them found any difference between the two methods. Also, data from the prospective study primarily designed to measure the pre-emptive effect of thoracic epidural analgesia (TEA), showed no difference in chronic pain incidence based on the type of incision.[2][14]

When considering the classical posterolateral access versus an anterior access, two retrospective investigations by the same authors found the anterior access to result in reduced PTPS. Methodologically, different rating scales for acute and chronic pain were used and both investigations consisted of retrospectively matched groups. Summarizing, the lack of prospective studies with details on relevant pre-, intra- and postoperative factors does not allow any firm conclusions as to the consequences of type of open surgery technique in relation to the development of PTPS, although nerve damage seems to be a risk factor.[5]

Minimally invasive technic like VATS reduces tissue and nerve damage during surgery. Investigations comparing the prevalence of PTPS after Open thoracotomy vs VATS are rare. According to one study done comparing the prevalence of PTPS after open thoracotomy Vs VATS it concludes that open thoracotomy leads more frequently to chronic post-thoracotomy pain than VATS, but once PTPS occurred, there was no difference in pain intensity with regard to the surgical technique used. According to their data, age is a relevant predictive factor for

developing PTPS with young patients (<65 years of age) being at a higher risk for chronic pain. This is in line with other investigations. Although the reason is unclear, limited inflammatory processes and higher pain tolerance in older patients may be possible explanations.[2][31]

2.2.2 Preoperative factors

2.2.2.1 Patient factors

Genetics: Sensitivity to physiological nociceptive and clinical pain differs considerably between individuals. Consequently, it has been recognized that genetic factors may be important in pain perception and several pain gene candidates have been identified including genetic polymorphisms of catechol-*O*-methyltransferase (COMT), genetic variants to determine voltage-gated sodium channels, and GTP cyclohydrolase and tetrahydrobiopterin-related genes among others. Because of the complexity of persistent postsurgical pain, the exact roles of genetic disposition have not yet been verified, and especially not when combining different pain gene candidates' characteristics.[5]

Psychosocial factors: It is well established that several psychosocial conditions can affect perception and consequences of chronic pain conditions, including, anxiety, depression, malignant disease, social network and social status. Two studies assessed preoperative anxiety/depression in relation to the development of PTPS, both showing no relationship. Consequently, more detailed studies are required on the role of psychosocial factors combined with other risk factors of PTPS.[23]

Preoperative pain: little information in relation to PTPS is available in contrast to the well documented relationship from hernia, hysterectomy and amputation surgery. Unfortunately, no study on PTPS has included specific information on preoperative pain complaints in other sites of the body, which is important, since such complaints have been related to development of chronic pain at the surgical site after hysterectomy and hernia surgery.[33]

Although studies from the general surgical population suggest that patients who are young, of female gender, with a history of depression and anxiety and who are poorly informed about their management plan are more likely to experience acute post-surgical pain, these risks have not been demonstrated in thoracotomy patients.[15]

Preemptive Analgesia: This method is the control of pain through the prevention of central sensitization that occurs secondary to nociceptive stimuli associated with surgical trauma, before the beginning of the stimulus. For this purpose, local anesthetics, opioids, non-steroid anti-inflammatory drugs (NSAID) can be used preoperatively. This method has been shown to prevent PTPS development in addition to providing pain control in the acute phase.[4] Performing regional anesthesia has shown beneficial effects regarding the development of chronic pain.

According to the study done comparing the prevalence of PTPS after open thoracotomy Vs VATS Compared with intravenous PCA, patients with thoracic epidural analgesia developed PTPS less frequently. Paravertebral block seems to be effective as well. It is unclear, if the protective effect is based on effective postoperative pain management or on the regional anesthesia technique itself. But the epidural anesthesia was only used on patients with open thoracotomy and not operated with VATS.[30][31]

2.2.3 Postoperative Factors

Severe acute postoperative pain and inadequate early control of pain are among the most important risk factors for the development of PTPS. Therefore, it is necessary to control the pain immediately in the postoperative period.

2.3 Management of PTPS

Knowledge on the analgesic management and its efficacy in case of PTPS is limited. Current investigations reported that between 33.0% and 53.0% of patients use analgesic medications. According to the study done comparing the prevalence of PTPS after open thoracotomy Vs VATS 46.2% of the patients regularly used analgesics.[3] Although there are many treatment options for postoperative pain control, it has been reported that the use of high-dose analgesics in the first week of surgery, especially the use of oral morphine equivalents, may be a risk factor for the development of PTPS.[4]

Most literatures recommend the following medical management options for treatment of PTPS

1. Tricyclic Antidepressants: Tricyclic antidepressants are among the first-line treatments in neuropathic pain treatment guidelines. They are thought to produce analgesic effects by providing central blockade of monoamine reuptake. Amitriptyline and nortriptyline are used. Their efficacy in neuropathic pain has been demonstrated in many randomized controlled trials. Analgesic effects are independent of antidepressant effects. Advantages include being single dose daily, low cost, and relief of depression in neuropathic pain. The most important disadvantage is anticholinergic side effects. They can cause sedation, dry mouth, constipation, urinary retention, and orthostatic hypotension. They should be used with great caution due to cardiotoxic side effects especially in patients with ischemic heart disease and ventricular dysfunction.[21]

2. Anticonvulsants: Pregabalin therapy has been reported to be an effective and reliable method for reducing chronic post thoracotomy pain. These classes of drugs bind to the alpha 2-delta subunit of voltage-dependent calcium channels, and reduce the release of neurotransmitters such as glutamate, noradrenaline, and substance P. The effects, side effects and patient tolerance profiles of pregabalin and gabapentin have similar properties. Dizziness, somnolence, peripheral edema, and dry mouth may develop after the use of this group of drugs. Because pregabalin has linear pharmacokinetics, dose adjustment is easier, analgesic effects occur faster than

gabapentin, and there are also positive effects on common anxiety disorder and sleeping. It has been reported that the use of gabapentin in the treatment of PTPS is effective and reliable in reducing neuropathic pain and can be used because of the low side effects and high patient compliance.[21]

3. Selective Serotonin Noradrenaline Reuptake Inhibitors: Duloxetine and venlafaxine were found effective in the treatment of peripheral neuropathic pain. They are also effective in the treatment of depression and generalized anxiety disorder. The most common side effect of duloxetine is nausea. Apart from this, there are also gastrointestinal side effects, such as dry mouth and constipation. Tolerance to these side effects can be improved by appropriate dose titration in patients with nausea. Venlafaxine should be used with caution in patients with cardiac problems as it may cause hypertension and impaired cardiac conduction. It should be kept in mind that withdrawal symptoms may occur when venlafaxine is discontinued. These drugs are among the first-line treatments in neuropathic pain treatment guidelines.[22][23]

4. Topical lidocaine: 5% lidocaine patch was found to be effective in localized peripheral neuropathic pain cases where allodynia was predominant.

5. Opioids: Opioids bind to opioid receptors (μ , κ , δ), which are common in the brain, spinal cord and peripheral tissues. In meta-analyses they have been shown to be the most potent pain relievers in neuropathic pain. Opioids have adverse effects on postoperative recovery due to side effects such as sedation, nausea, and constipation. The induction of opioid-induced respiratory failure may further deepen pulmonary complications, and opioids may also increase existing pain due to opioid-induced hyperalgesia side effects. Although the use of opioids in acute pain, postoperative pain, and cancer-related pain are common, the use of this group of drugs in the long-term treatment of pain is controversial due to the tolerance to analgesic effects, addiction, drug abuse, and side effects such as high dose-mortality. Due to these side effects and disadvantages, opioids are among the second- or third-line medical treatments in the final guidelines.

6. Tramadol: It is a weak μ -opioid agonist and also provides analgesia by inhibiting serotonin and noradrenaline reuptake. Tramadol is used more commonly because of less constipation, sedation, dizziness, and lower risk of addiction than other opioids. It is among the second-line treatments in neuropathic pain treatment guidelines. However, it can be used as a first-line treatment in acute exacerbations of pain.

7. NSAIDs: Since there is no evidence that these drugs have an effect on neuropathic pain, they are not commonly used in PTPS treatment. However, when used to provide preemptive analgesia, they reduce peripheral sensitization by reducing the release of inflammatory mediators. It has been reported that combined thoracic

epidural analgesia with preemptive intravenous dexketoprofen administration reduces and prevents chronic post-thoracotomy pain formation.[1]

In addition to the above medical management options currently Interventional methods for both management as well prevention of PTPS have been developed and those mostly used are discussed below:

1. Intercostal Nerve Blockage: The intercostal nerve block prevents the neural impulses from the motor and sensory fibers of the intercostal nerve from transmitting to the spinal cord and higher centers as an impediment to ipsilateral transmission. With this method, spinal nerves between T1 and T11 can be effectively blocked and the pain can be controlled. Especially neurolytic blockade can be used to control chronic post-thoracotomy pain effectively. Complications include local anesthetic toxicity, pneumothorax, bleeding, infections, and hypotension.
2. Thoracic Paravertebral Block: The local anesthetic is injected near the intervertebral foramen of the spinal nerves near the thoracic vertebrae. Ipsilateral sympathetic and somatic nerve blockage is achieved in dermatomes below and above the thoracic level after injection. It is used in acute and chronic chest pain of unilateral origin. Contraindications include allergies to local anesthetics, infections at the injection site, and edema. Complications of the thoracic paravertebral block can be listed as vascular and pleural injury, pneumothorax, and hypotension.[6]
3. Spinal Cord Stimulation: Large diameter afferent fibers in the spinal cord are stimulated to inhibit chronic pain. It is based on the principle of electrical stimulation of the posterior column and dorsal roots with electrodes placed in the posterior epidural space. It is an effective and reliable method of neuromodulation that can be used for the symptoms of drug-resistant neuropathic pain.
4. Dorsal Root Ganglion Pulse Radiofrequency Application: Dorsal root ganglion pulse radiofrequency application inhibits excitatory C fiber response by providing a repetitive, burst-like stimulus to A-delta fibers in neuropathic pain treatment, resulting in decreased evoked synaptic activity. There is less risk of damaging the tissues than other radiofrequency methods; therefore, it is the more preferred method.
5. Intercostal Block: Local anesthetics are injected into the parietal and visceral pleura and attempt to block ipsilateral somatic nerve blockage at multiple thoracic dermatomal levels. After the bilateral spread of local anesthetic material, sympathetic chain and splanchnic nerve blockage develop, resulting in decreased pain. Although it is reported to be effective in unilateral surgery and non-surgical acute and chronic chest pain, it is not widely used due to the difficulty of application and the risk of lung parenchyma damage. Contraindications include infection in the treatment area, allergy to local anesthetics; and complications of this type of block include local anesthetic toxicity, phrenic nerve palsy, pneumothorax and infections.

Thoracic Sympathetic Block: This method is used in the diagnosis and treatment of chronic thoracic pain syndromes such as neuropathic pain, chest wall pain, and thoracic visceral pain.

7. Thoracic Epidural Anesthesia: This method used in the early postoperative pain control and have been reported in numerous studies to reduce the risk of development PTPS.

Chapter three: Objective of the study

3.1 General objective

PREVALENCE AND RISK FACTORS OF POST THORACOTOMY PAIN SYNDROME IN ADDIS ABEBA PUBLIC HOSPITALS, ETHIOPIA, FROM TO GC.

3.2 Specific objective

- To determine the prevalence of acute PTPS
- To determine the prevalence of Chronic PTPS
- To List out some of the risk factors for PTPS
- To determine the association of risk factors with APTPS
- To determine the association of risk factors with CPTPS

Chapter four: Methodology

4.1 Study area

Addis Ababa is the capital city of Ethiopia which has an area of 527 square kilometers and 10 sub-cities. There are around 13 public hospitals at different sub-cities from them Tikur Anbesa Specialized Hospital, Minilik II Referral Hospital, and St. Petros Referral Hospitals serve the community with different departments; Cardiothoracic surgery department is one of them therefore they are selected to be our study area by convenient sampling technique.

Tikur Anbesa Specialized Hospital also called Black Lion Specialized Hospital established in 1972 EC, at Lideta sub-city. This specialized hospital gives surgical health service with a capacity of 9 OR tables, 1 adult, 1 CICU and 1 neonatal ICU. It has 2 cardiothoracic OR tables and 1 chest ward with 16 beds.

Minilik II Referral Hospital established in 1910 EC at Yeka sub-city. This hospital gives health services with a surgical bed capacity of 135. The surgery department is one of the major departments having 6 major OR tables, 1 ICU.

St. Petros Specialized Hospital established in 1965 EC at Gulele sub-city. Gives health services including surgery with a capacity of 54 surgical beds, 5 major OR tables, and 1 ICU.

Both Minilik II and St. Petros Hospitals schedule thoracic surgeries on two days whereas Black Lion Specialized hospital schedule thoracic surgery on five days a week.

4.2 Study design and period

Multicenter based prospective cohort study will be conducted from July to November 2024

4.3 Population

4.3.1 Source population

All elective patients admitted for thoracic surgery at Black lion specialized hospital, St. Petros specialized hospital, and Minilik II referral hospital.

4.3.2 Study population

All elective patients admitted for thoracic surgery at Black lion specialized hospital, St. Petros specialized hospital, and Minilik II referral hospital.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

Patients aged from 18 to 75 years who underwent thoracotomy under general anesthesia with ETT in the selected study period, and were alive at least for 2 months post op.

4.4.2 Exclusion criteria

Those who don't fulfill inclusion criteria, lack of consent for the study, inability to comprehend or visualize pain scale (psychiatric, dementia, intubated, sedated, delayed recovery, both visual and auditory impairment).

4.5 Study variables

4.5.1 Dependent variable

The dependent variable of this study is pain severity which was assessed by NRS of patients at rest and with movement.

4.5.2 Independent variable

Independent variables of this study are sociodemographic factors (age, sex), type of incision (posterolateral, anterolateral, axillary), types of performed procedure, preemptive analgesia, intraoperative analgesia, and Post op analgesics administration.

4.6 Operational definitions

Acute post thoracotomy pain: when a patient has pain at thoracotomy site with score other than 0 persisting to 1 month post op

Chronic post thoracotomy pain: when a patient has pain at thoracotomy site with pain score other than 0 persisting for 2 months post op

Preemptive analgesia: analgesia initiated 20min to 2h before the start of surgery incision with the timing for IV opioids and acetaminophen 20-30min before surgery whereas 1-2hr before surgery for IM opioids and NSAIDs.

Numerical pain rating scale (NRS): presented by 11 points scale and can be reported graphically or verbally. In this pain assessment tool pain severity is represented as 0=no pain, 1- 3= mild pain, 4-6= moderate pain, 7-10=sever pain over 24hr.

Evidence supports NRS to be used to measure acute pain in clinical studies because it has good sensitivity and the responded data can be statistically analyzed. Besides high test-retest reliability has been observed in both literate and illiterate patients

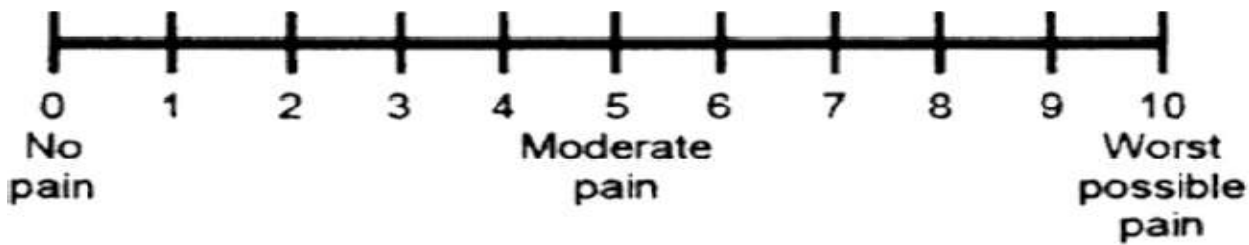


Figure 1: Adopted from the National Initiative on Pain Control (NIPC)

4.7 Sample size and sampling technique

4.7.1 Sample size

All patients operated from July to September 2024, who fulfill the inclusion criteria in all 3 hospitals, were included in the study.

4.7.2 Sampling technique

All patients operated from July to September 2024, who fulfill the inclusion criteria in all 3 hospitals, were included in the study.

4.7.3 Data collection procedure and patients handling technique

Well-structured open and close-ended questioner was used to collect data by three data collectors at each hospital. All patients scheduled for elective thoracotomy who fulfill the inclusion criteria based on information found by chart review and patient interview during the preoperative period were requested for their volunteer to involve in our study after explaining to them about the objective of the study, their chance of being excluded from the study in the postoperative period based on some seated exclusion criteria, the risk and benefits they get from being involved in the study and then verbal consent was taken.

4.7.4 Data quality control and assurance

Data collection was done by trained personnel under regular supervision and follow up by the principal investigator. The collected data was checked by the principal investigator for completeness, accuracy, and clarity every day. Data quality assurance by cleanup and cross- checking of entered data on SPSS V 22 was also done before analysis.

4.7.5 Data analysis and interpretation

The collected study data was entered into SPSS V 22 for analysis.

4.7.6 Ethical consideration

Before the start of the study, an ethical clearance was obtained from the department's research and ethical review committee of AAU. An official support letter was requested and acquired for responsible authority to get permission for data collection.

4.7.7 Dissemination plan

This study on the completion will be presented for the department General surgery. It will serve as a reference to experts. The paper will also be submitted to the school of medicine and department of Surgery. Besides, a copy of this material will be given to Black lion, St. Petros, Minilik II hospital, and Addis Ababa University student research office. The result will also be submitted to journals, disseminated through publication in peer-reviewed local and international journal.

Chapter Five: Results and Discussion

PTPS remains a significant long-term complication of thoracic surgery despite the use of minimally invasive thoracic surgical approaches and optimal acute pain management in the perioperative period. The pathogenesis of PTPS is believed to be neuropathic in most cases but there may also be non-neuropathic elements, such as myofascial pain.[4][26]

In this study a total of 41 patients were followed for 5 months. Using standardized questioner patient s demographic data (age, sex), Diagnosis, performed procedure, type of skin incision used, pre-emptive analgesia administration status, Epidural anesthesia administration status, the type of intraoperative IV analgesic that was given and preoperative pain status using NRS was assessed Preoperatively, then after 1 week for evaluation of APTPS and after 2 months for CPTPS.

5.1 Patient Characteristics

From the total of 41 patients in our study 25 were Male and 16 were Females.

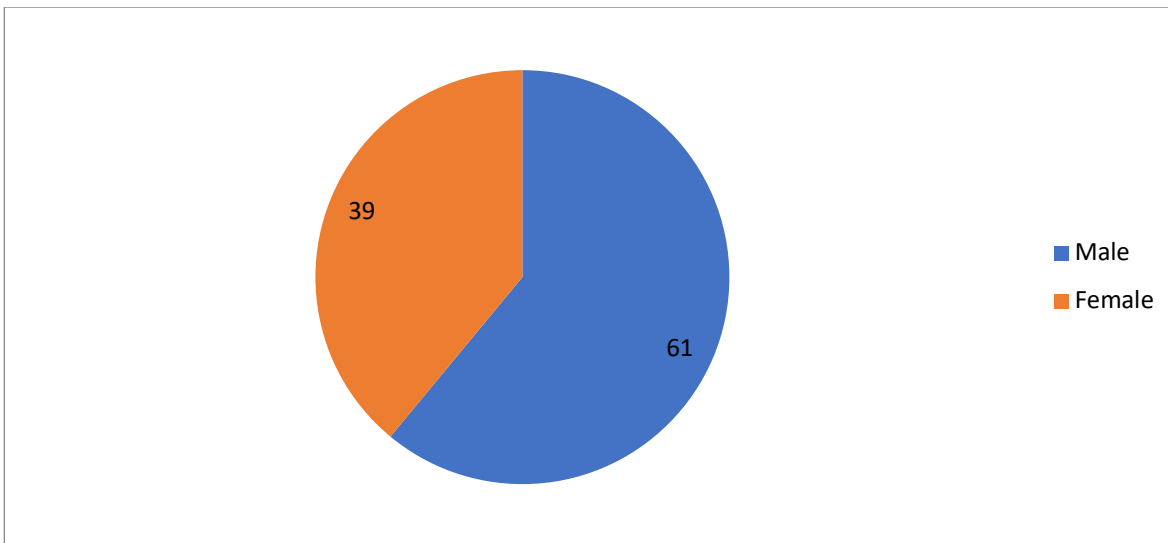


Fig. 2 Pie chart illustrating male and female composition of the study

The mean age of the patients in this study is 39.5 with 18 and 75 being the maximum and minimum ages of the patients enrolled in this study.

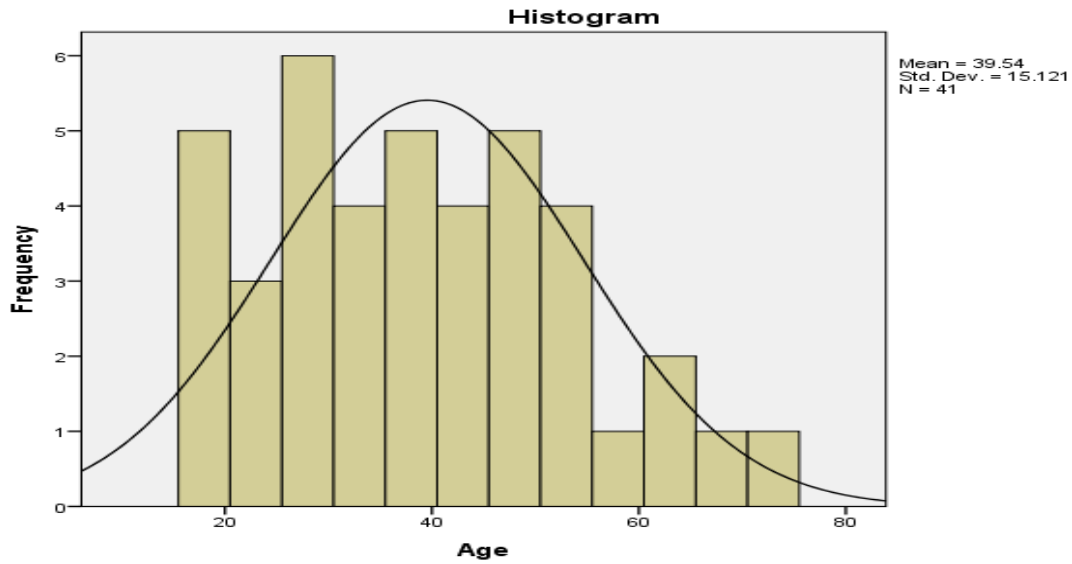


Fig. 3 Histogram showing the age distribution of the study

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid 18	5	12.2	12.2	12.2
23	1	2.4	2.4	14.6
24	1	2.4	2.4	17.1
25	1	2.4	2.4	19.5
28	4	9.8	9.8	29.3
30	2	4.9	4.9	34.1
32	2	4.9	4.9	39.0
33	1	2.4	2.4	41.5
34	1	2.4	2.4	43.9
36	1	2.4	2.4	46.3
37	1	2.4	2.4	48.8
38	1	2.4	2.4	51.2
40	2	4.9	4.9	56.1
42	2	4.9	4.9	61.0
44	1	2.4	2.4	63.4
45	1	2.4	2.4	65.9
46	1	2.4	2.4	68.3
48	2	4.9	4.9	73.2
50	2	4.9	4.9	78.0
53	2	4.9	4.9	82.9

54	1	2.4	2.4	85.4
55	1	2.4	2.4	87.8
60	1	2.4	2.4	90.2
65	2	4.9	4.9	95.1
70	1	2.4	2.4	97.6
75	1	2.4	2.4	100.0
Total	41	100.0	100.0	

Table 1 Age composition of the study

5.2 Epidural Anesthesia status

With regards to administration of Epidural anesthesia in our study 12(29.3%) of the patients did not receive an Epidural anesthesia and the majority of them 29(70.7%) had an Epidural anesthesia.

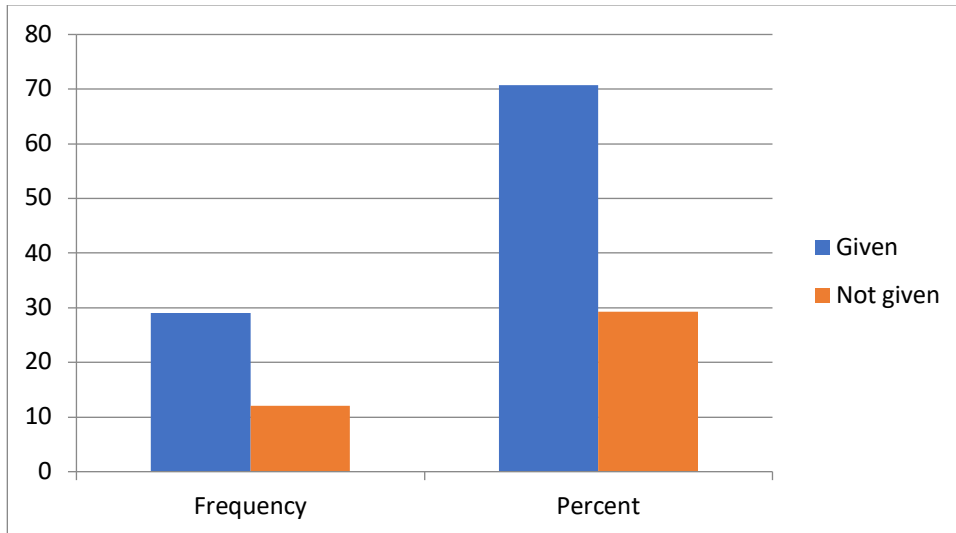


Fig. 4 Percentage of patients who were and were not given an epidural anesthesia

5.3 Intraoperative Anesthesia

All of the patients received some type of anesthesia intraoperatively. In this study we have also evaluated the type of anesthesia they received and 23(56.1%) of them were given intra venous Multiple analgesic types, 17(41.5%) were given IV Fentanyl and 1 had an IV PCM only.

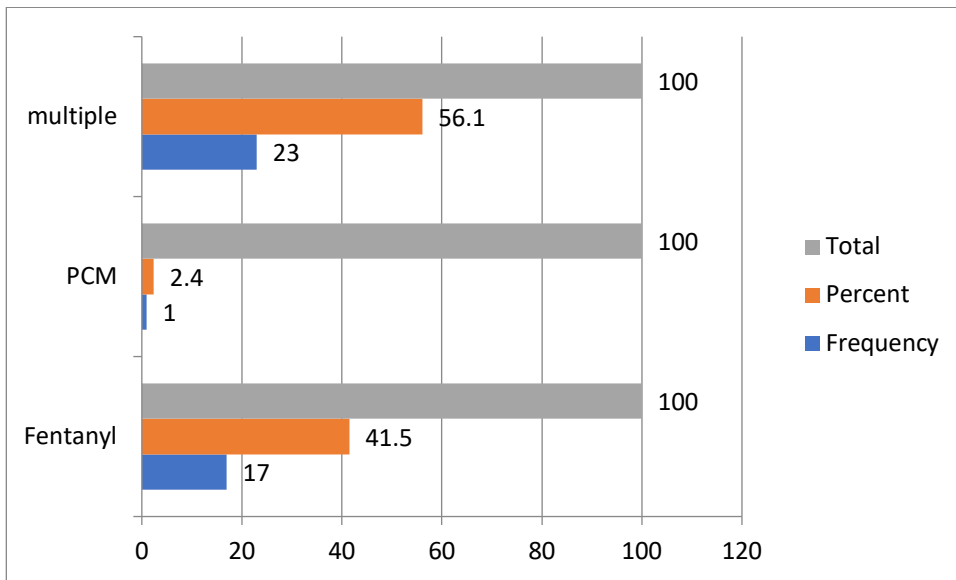


Fig. 5 Bar chart showing the type of analgesic agent given intra-op

The type of skin incision used was also assessed and majority of the patients 34(82.9%) had PLT, 6(14.6%) had MS and only one had ALT.

5.4 Preoperative Pain Status

A total of 41 patients were followed for the entire duration of the study and 5 their pain status was assessed at 3 points in time using the NRS pain scale. The first pain score was taken preoperatively; the patients were inquired if they have pain related to their chest pathology and the severity was assessed using the preoperative NRS scale on the questioner, this result was then used to assess the association of preoperative pain status with post-operative pain level.

Of all the 41 patients followed most of them 17(41.5%) had no pain, 15(36%) had mild pain, 9(22%) had moderate pain and there were no patients with severe pain.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid No Pain	17	41.5	41.5	41.5
Mild Pain	15	36.6	36.6	78.0
Moderate Paine	9	22.0	22.0	100.0
Total	41	100.0	100.0	

Table 2 Pre-operative pain status

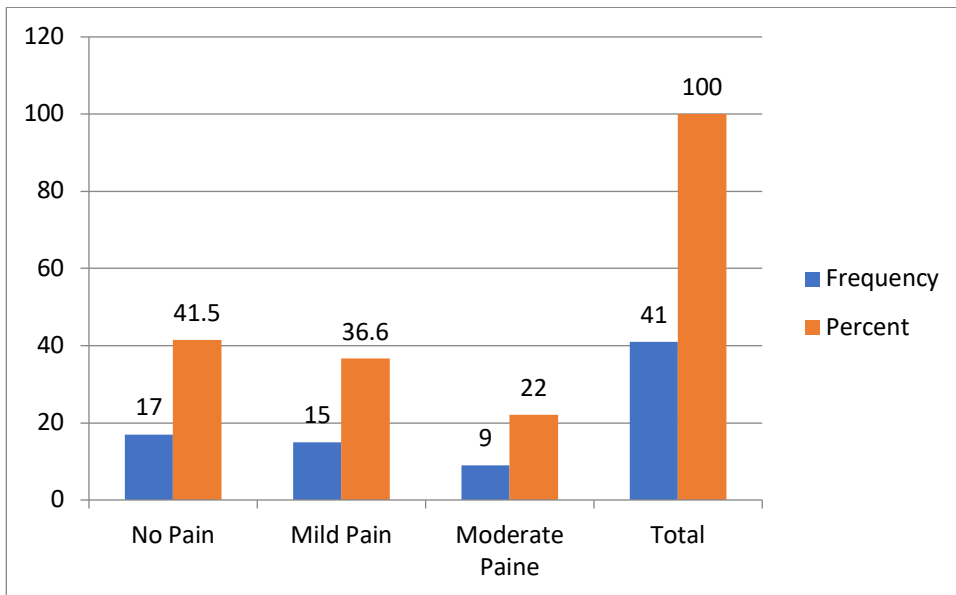


Fig. 6 Pre-operative pain status

5.5 Acute Post Thoracotomy Pain Syndrome

APTPS was assessed after 1 week of the procedure using the NRS scale for Acute post thoracotomy pain syndrome; only the pain related to their thoracotomy site was inquired and the severity was assessed using the 1 week post procedure NRS scale on the questioner, the result was used to assess the prevalence of Acute post thoracotomy pain syndrome and the association of acute post thoracotomy pain syndrome with Chronic post thoracotomy pain syndrome.

All 41 patients were followed for 1 week post op and most of them 23(56.1%) had moderate pain, 12(29.3%) had severe pain, 6(14.6%) had mild pain. All of the patients had some level of pain and there was no patient with NRS score of 0. This makes the prevalence of Acute Post Thoracotomy Pain Syndrome in this study to be 100%. The prevalence of post thoracotomy pain syndrome is variable in different literatures but it is generally agreed to be as high as 50-85%. In a study done in Egypt on post thoracotomy pain the incidence of post-thoracotomy pain was reported to be 80% at 3 months, 75% at 6 months, and 61% at one year post-thoracotomy; the incidence of severe pain was 3–5%, and pain that interferes with normal life was seen in 50% of the patients.[3][10]

	Frequenc y	Percent	Valid Percent	Cumulative Percent
Valid Mild Pain	6	14.6	14.6	14.6
Moderate Paine	23	56.1	56.1	70.7

Severe Pain	12	29.3	29.3	100.0
Total	41	100.0	100.0	

Table 3 Acute Post Thoracotomy pain status at 1 week

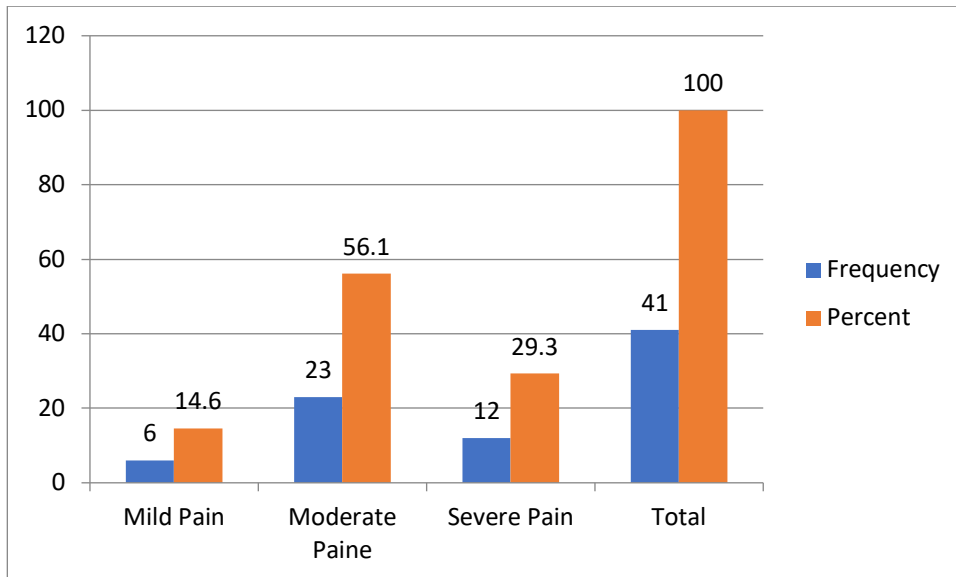


Fig. 7 Acute Post Thoracotomy pain status at 1 week

5.6 Chronic Post Thoracotomy Pain

In our study on the second month post procedure all of the patients were followed and those who were still alive were assessed again using the NRS scale for chronic post thoracotomy pain syndrome. Only the pain related to their thoracotomy site was inquired and the severity was assessed using the 2 month post procedure NRS scale on the questioner, this result was then used to calculate the prevalence of chronic post thoracotomy pain syndrome.

All (41patients) of the patients which were assessed with APTPS were assessed at 2 months and most of them 21 (51.2%) had moderate pain, 15(36.6%) had mild pain, and 5(12.2%) had no pain. None of the patients reported to have severe pain which is more than 7 on the NRS scale.

Chronic Post-thoracotomy pain syndrome (CPTPS) is reported with a prevalence ranging between 33% and 91% in literature.[2][13][22] In our study the prevalence of Chronic Post Thoracotomy pain syndrome after 2 months in this study to be 87.8%, which seems to be higher than most of the reports in other literatures.

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid No Pain	5	12.2	12.2	12.2
Mild Pain	15	36.6	36.6	48.8
Moderate Paine	21	51.2	51.2	100.0
Total	41	100.0	100.0	

Table 4 Acute Post Thoracotomy pain status after 2 months

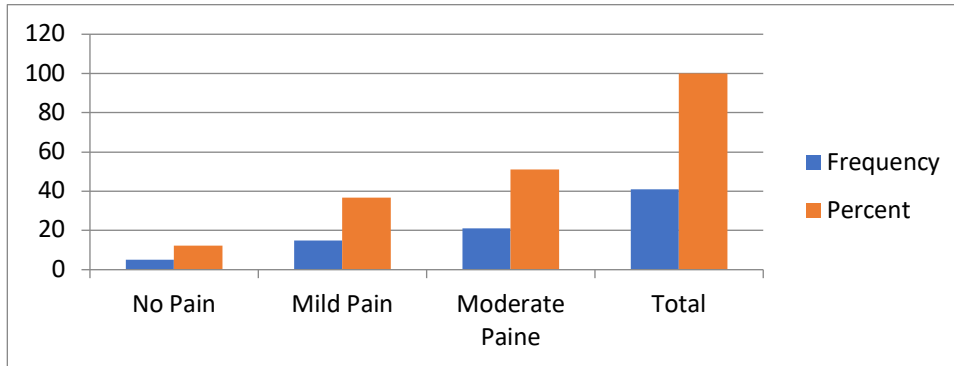


Fig.8 Acute Post Thoracotomy pain status after 2 months

Although studies from the general surgical population suggest that patients who are young, of female gender, with a history of depression and anxiety and who are poorly informed about their management plan are more likely to experience acute post-surgical pain, these risks have not been well demonstrated in thoracotomy patients.[7][18]

The association of some factors listed as risk factors in the literature for PTPS including patient demographics and the preoperative pain status with Acute and Chronic post thoracotomy pain syndrome was assessed and the parameters with association are listed below.

5.7 Association of Risk factors with PTPS

5.7.1 Association of Age with PTPS

In the articles Post thoracotomy pain syndrome is associated with an increasing age.[2][24] In our study even though on the Pearson correlation index the correlation of age with both the acute and chronic PTPS is weak and statistically insignificant; but taking into account the smaller sample size we can clearly see the association of Age with Acute PTPS is positive meaning with an increasing age the incidence of APTPS increases. Approximately 84% of the patients reporting severe pain on the first post op week were older than 40 years of age.

		numerical pain rating scale post op 1 week	Age
numerical pain rating scale post op 1 week	Pearson Correlation	1	.204
	Sig. (2-tailed)		.200
	N	41	41
Age	Pearson Correlation	.204	1
	Sig. (2-tailed)	.200	
	N	41	41

Table 7 Age * numerical pain rating scale post op 1 week Correlations

For chronic PTPS a strong association is not seen with older age and moderate pain but interestingly Younger age (patients less than 40 years) has strong association with mild pain as 60% of the mild pain responses were seen in this patient age group.

		Age	numerical pain rating scale post op 2 month
Age	Pearson Correlation	1	.017
	Sig. (2-tailed)		.914
	N	41	41
numerical pain rating scale post op 2 month	Pearson Correlation	.017	1
	Sig. (2-tailed)	.914	
	N	41	41

Table 8 Age * numerical pain rating scale post op 2 month Correlations

5.7.2 Association of Gender with PTPS

In most literatures about sex-related differences states that pain is generally more frequent and intense in women, but data regarding association of sex with PTPS is scarce and One Study Done on 344 patients out of which 130 were female; concluded that there are no general sex-related differences in pain intensity and analgesic requirement after thoracotomy.[7]

In this study the correlation of sex with both the acute and chronic PTPS on the pearson correlation scale is weak and statistically insignificant; But taking the sample size into account we can clearly establish the positive association of Female sex with both Acute and Chronic PTPS.

		numerical pain rating scale post op 1 week			Total
		Mild Pain	Moderate Paine	Severe Pain	
Sex	Male	3	14	8	25
	Female	3	9	4	16
Total		6	23	12	41

Table 9 Sex * numerical pain rating scale post op 1 week

		numerical pain rating scale post op 2 month			Total
		No Pain	Mild Pain	Moderate Paine	
Sex	Male	2	11	12	25
	Female	3	4	9	16
Total		5	15	21	41

Table 9 Sex * numerical pain rating scale post op 2 months

5.7.3 Association of Epidural anaesthesia with PTPS

Most of the articles done on Post thoracotomy pain syndrome strongly associate Epidural anesthesia with reduction of Acute and Chronic PTPS. Thoracic epidural block is thought to manage Acute post thoracotomy pain and also prevent CPTPS in long run. Thoracic paravertebral block is a technique of depositing local anesthetics at the paravertebral space adjacent to the thoracic vertebra and block spinal nerves as they emerge from the thoracic intervertebral foramen. Application of local anesthetics within the unilateral paravertebral space produces sensory and motor block of multiple thoracic dermatomes at the same side of the block above and below the injection site which results in reduction in pain intensity and used as an option of analgesia for thoracotomy. A Prospective cohort study design done to evaluate the incidence of APTPS and CPTPS and the association of Different types of analgesic agents with the incidence of PTPS on 56 pediatric patients concluded there was no statistically significant difference between the type of anesthesia and the incidence and severity of acute post-operative pain.[5][32]

In our study out of 41 patients 79% of them received an Epidural anesthesia and 21% did not get the Epidural anesthesia. In this study on the Pearson correlation index the correlation of Epidural anesthesia with both the acute and chronic PTPS is statistically insignificant. The association of Epidural anesthesia with Acute PTPS is weakly associated with negative correlation meaning epidural anesthesia was associated with decreased APTPS.

Interestingly the correlation of Epidural anesthesia with CPTPS though statically insignificant is moderately strong and stronger than its association with APTPS. This implies Epidural anesthesia is not only associated with APTPS reduction but also and even more to a greater extent with reduction in CPTPS.

		numerical pain rating scale post op 1 week			Total
		Mild Pain	Moderate Paine	Severe Pain	
Epidural_anesthesia	Given	4	19	6	29
	Not given	2	4	6	12
Total		6	23	12	41

Table 11 Epidural anesthesia * numerical pain rating scale post op 1 week

Out of the 29 patients who had epidural anesthesia only 6(20.6%) had severe pain on 1 week post procedure day in contrast out of 12 patients who did not receive epidural anesthesia 6(50%) of them developed severe pain. After 2 months post op from the group of patients who had epidural anesthesia 13.7% of them were free of pain in contrast out of those who did not receive epidural only 8.3% reported to have no pain and 58.3% had moderate pain.

		numerical pain rating scale post op 2 month			Total
		No Pain	Mild Pain	Moderate Paine	
Epidural_anesthesia	Given	4	11	14	29
	Not given	1	4	7	12
Total		5	15	21	41

Tabel 12 Epidural_anesthesia * numerical pain rating scale post op 2 month

5.7.4 Association of Pre-operative pain with PTPS

The association of Preoperative pain with PTPS is one of the areas which have not been studied well and much of the positive association of Preoperative pain status with PTPS comes from extrapolation of data from studies done on surgeries other than thoracotomy.[6] In this study we have tried to see the association of preoperative pain status with both APTPS and CPTPS using the Pearson correlation index to enumerate the correlation and crude odds ratio and using Ordinal regression analysis to calculate the adjusted odds ratio. Pre-operative pain status is strongly associated with APTPS with crude odds ratio of 18.3% with P value of 0.001 and CI of 95%. The Adjusted Odds ratio is 21.7%, Specially this is true for moderate and severe APTPS.

	Estimate		Std. Error	Wald	df	Sig.	95% Confidence Interval	
							Lower Bound	Upper Bound
Threshold [NRS_1_week = 2]	2.245		1.010	4.940	1	.026	.265	4.224
[NRS_1_week = 3]	6.888		1.758	15.355	1	.000	3.443	10.332
Location NRS_preoperatively	2.906	18.290	.783	13.778	1	.000	1.372	4.441

Table 13 Preoperative pain status * numerical pain rating scale post op 1 week Parameter Estimates for AOR

Parameter Estimates									
		Estimate		Std. Error	Wald	df	Sig.	Interval	
								Lower Bound	Upper Bound
Threshold	[NRS_1_week = 2]	7.939		4.351	3.330	1	.068	-.588	16.467
	[NRS_1_week = 3]	12.821		4.866	6.943	1	.008	3.284	22.358
Location	NRS_preoperatively	3.080	21.765	.821	14.075	1	.000	1.471	4.690
	intraop_analgesic_type	-.046	0.955	.129	.125	1	.724	-.299	.208
	Age	.036	1.036	.031	1.326	1	.250	-.025	.096
	Skin_incision	1.764	5.835	1.290	1.869	1	.172	-.765	4.293
	[Sex=1]	-.004	0.996	.762	.000	1	.996	-1.497	1.489
	[Sex=2]	0 ^a	#VALUE!			0			
	[Epidural_anesthesia=1]	.696	2.005	1.066	.426	1	.514	-1.395	2.786
	[Epidural_anesthesia=2]	0 ^a	#VALUE!			0			
	[Preemptive_analgesia_within_1_to_3hr_before_surgery=1]	1.046	2.846	.982	1.135	1	.287	-.879	2.971
[Preemptive_analgesia_within_1_to_3hr_before_surgery=2]	0 ^a	#VALUE!			0				

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Pre-operative pain status is also strongly associated with CPTPS with crude odds ratio of 6.1 with P value of 0.01 and CI of 95%. The Adjusted Odds ratio is 3.45. This shows the association of preoperative pain status with CPTPS is strong but much less stronger than the association seen with APTPS.

				Std. Error	Wald	df	Sig.	95% Confidence Interval	
								Lower Bound	Upper Bound
Threshold	[NRS_2_month = 1]	.725		.880	.679	1	.410	-1.000	2.449
	[NRS_2_month = 2]	3.192		1.013	9.930	1	.002	1.207	5.177
Location	NRS_preoperatively	1.809	6.103	.554	10.678	1	.001	.724	2.894

Tabel 14 Preoperative pain status * numerical pain rating scale post op 2 month Parameter Estimates for COR

Preoperative pain status * numerical pain rating scale post op 2 month Parameter Estimates for AOR									
		Estimate		Std. Error	Wald	df	Sig.	95% Confidence Interval	
								Lower Bound	Upper Bound
Threshold	[NRS_2_month = 1]	5.258		2.355	4.984	1	.026	.642	9.874
	[NRS_2_month = 2]	8.389		2.647	10.042	1	.002	3.200	13.577
Location	NRS_preoperatively	1.240	3.457	.750	2.735	1	.098	-.230	2.710
	Age	-.022	0.978	.026	.700	1	.403	-.074	.030
	NRS_1_week	2.269	9.669	.899	6.369	1	.012	.507	4.031
	[Sex=1]	-.456	0.634	.749	.371	1	.543	-1.924	1.012
	[Sex=2]	0 ^a	#V AL			0			

			UE!						
	[Epidural_anesthesia=1]	.035	1.036	.882	.002	1	.968	-1.694	1.764
	[Epidural_anesthesia=2]	0 ^a	#V AL UE!			0			
	[Preemptive_analgesia_within_1_to_3hr_before_surgery=1]	1.025	2.787	.970	1.116	1	.291	-.877	2.927
	[Preemptive_analgesia_within_1_to_3hr_before_surgery=2]	0 ^a	#V AL UE!			0			

5.7.4 Association of Pre-operative pain with PTPS

A cross-sectional study done in South Korea evaluated CPTPS in 100 patients who underwent thoracotomy after trauma and they stated the prevalence of CPTPS to be 80% and Multivariable logistic regression analysis showed weak evidence of association between acute, severe postoperative pain and chronic postsurgical pain (adjusted odds ratio 2.4, 95% confidence intervals 0.9 to 6.4).[5][23][24]

The association of APTPS with CPTPS was also computed in this study using both the Crude odds Ratio and Adjusted Odds Ratio. Patients who had APTPS had COR of 17.7 with P value of 0.001 and CI of 95%. The AOR is 9.6 with P of 0.012 and CI of 95%. This indicates the association of APTPS with CPTPS is strong with patients having APTPS 17.7 times more likely to have CPTPS.

		Estimate		Std. Error	Wald	df	Sig.	95% Confidence Interval	
								Lower Bound	Upper Bound
Threshold	[NRS_2_month = 1]	6.152		2.056	8.951	1	.003	2.122	10.182
	[NRS_2_month = 2]	9.009		2.355	14.636	1	.000	4.393	13.624
Location	NRS_1_week	2.876	17.737	.761	14.282	1	.000	1.384	4.367

Table 15 Post operative pain status * NRS post op 2 month Parameter Estimates for COR

		Estimate		Std. Error	Wald	df	Sig.	95% Confidence Interval	
								Lower Bound	Upper Bound
Threshold	[NRS_2_month = 1]	5.258		2.355	4.984	1	.026	.642	9.874
	[NRS_2_month = 2]	8.389		2.647	10.042	1	.002	3.200	13.577
Location	NRS_1_week	2.269	9.669	.899	6.369	1	.012	.507	4.031
	NRS_preoperatively	1.240	3.457	.750	2.735	1	.098	-.230	2.710
	Age	-.022	0.978	.026	.700	1	.403	-.074	.030
	[Sex=1]	-.456	0.634	.749	.371	1	.543	-1.924	1.012
	[Sex=2]	0 ^a	#VALUE!			0			
	[Preemptive_analgesia_within_1_to_3hr_before_surgery=1]	1.025	2.787	.970	1.116	1	.291	-.877	2.927
	[Preemptive_analgesia_within_1_to_3hr_before_surgery=2]	0 ^a	#VALUE!			0			
	[Epidural_anesthesia=1]	.035	1.036	.882	.002	1	.968	-1.694	1.764
	[Epidural_anesthesia=2]	0 ^a	#VALUE!			0			

Table 16 Post-operative pain status * numerical pain rating scale post op 2 month Parameter Estimates for AOR

Chapter six: Conclusion

Most of the Thoracic and Cardiac procedures done in this country are in an open thoracotomy incision, but it seems the attention given towards diagnosis and management of Post Thoracotomy pain syndrome is very small. In our study the prevalence of APTPS is 100% and CPTPS is 87.8%; which is a very high number indicating the need for accurate diagnosis and the need for change in attitude of physicians towards management of this syndrome. The Intensity of pain as measured on the NRS scale shows for higher percentage of patients reporting higher number on the scale depicting most patients suffer a moderate to severe intensity pain leading to increased post-op analgesic need, poor quality of life and dissatisfaction. Pre-emptive analgesia and Epidural anesthesia have been reported to have a protective effect on especially on the incidence of APTPS in the literatures and in our study also there is an association of epidural anesthesia with decreased APTPS even though it is statistically insignificant. More over The association of epidural anesthesia with CPTPS in our study is also strong and even stronger than its association with APTPS so use of epidural anesthesia for prevention of PTPS should be encouraged not only for prevention of APTPS but also for its effect in reducing both the prevalence but also the intensity of CPTPS. Another area this study shades light is also on the association of Preoperative pain with PTPS which is strong and statistically significant particularly with APTPS and the Association even though less strong is also positive for CPTPS. Patients who had pre-operative pain are 18.3 times more likely to have APTPS. The association of APTPS with CPTPS is also strong with patients having APTPS are 17.7 times more likely to have CPTPS. Pre-operative pain status and presence of APTPS are both strong predictors of CPTPS hence close follow up, adequate analgesic management and use of epidural anesthesia in this type of patients would reduce the prevalence as well as intensity of pain.

Reference

1. A Mesbah MB BCh FCAI FRCA1, J Yeung MB ChB FRCA PhD FFICM2,3,* and F Gao MB BS PhD MPhil FRCA MD FFICM Pain after thoracotomy BJA Education, 16 (1): 1–7 (2016)
2. Sven Arends,^{a,*} Andreas B. Böhmer,^b Marcel Poels,^b Marc Schieren,^b Aris Koryllos,^c Frank Wappler,^b and Robin Joppich^b Post-thoracotomy pain syndrome: seldom severe, often neuropathic, treated unspecific, and insufficient Pain Rep. 2020 Mar-Apr; 5(2): e81
3. Fawzy Abbas Badawy, Abd El-Rahman Hasan Abd El-Rahman, Salah Ahmed Mohamed, Asmaa Saad-Eldeen Farghaly Gad-Allah*, Khaled Abdelfattah Mohamed Abdelfattah, Post-Thoracotomy Pain, The Egyptian Journal of Hospital Medicine (October 2021) Vol. 85 (2), Page 3519-3523 3519
4. Yaşı E, Yakşı O. Current treatment options for post-thoracotomy pain syndrome: a review. *Curr Thorac Surg* 2017;2(3): 103-110.
5. Kim Wildgaard, Jesper Ravn, Henrik Kehlet, Chronic post-thoracotomy pain: a critical review of pathogenic mechanisms and strategies for prevention, *European Journal of Cardio-Thoracic Surgery*, Volume 36, Issue 1, July 2009, Pages 170–180
6. Comparing analgesia effect of post-operative thoracic paravertebral block and intercostal nerve block for unilateral thoracotomy at addis abeba public hospitals, ethiopia, december 25, 2019 to april 30,2020 gc a prospective cohort study.
7. ***Is There an Impact of Sex on Acute Postthoracotomy Pain? A Retrospective Analysis*** Auinger, Daniel et al. *The Annals of Thoracic Surgery*, Volume 109, Issue 4, 1104 - 1111
8. Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. *Br J Anaesth* 2005;95:69–76. - PubMed
9. Classification of Chronic Pain, Second Edition, IASP Task Force on Taxonomy, edited by H. Merskey and N. Bogduk, IASP Press, Seattle, ©1994.
10. Benedetti F, Vighetti S, Ricco C, Amanzio M, Bergamasco L, Casadio C, Cianci R, Giobbe R, Oliaro A, Bergamasco B, Maggi G. Neurophysiologic assessment of nerve impairment in posterolateral and muscle-sparing thoracotomy. *J Thorac Cardiovasc Surg* 1998;115:841–7. - PubMed
11. Bonica JJ. The management of pain. Philadelphia: Lea & Febiger; 1953.
12. Diener HC, Putzki N. Therapie neuropathischer Schmerzen. Leitlinien für Diagnose und Therapie in der Neurologie. S. Georg Thieme Verlag KG; 2008.
13. Dworkin RH, O'Connor AB, Audette J, Baron R, Gourlay GK, Haanpaa ML, Kent JL, Krane EJ, Lebel AA, Levy RM, Mackey SC, Mayer J, Miaskowski C, Raja SN, Rice AS, Schmader KE, Stacey B, Stanos S, Treede RD, Turk DC, Walco GA, Wells CD. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc* 2010;85(3 Suppl):S3–14. - PMC - PubMed
14. 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;12:82–7. - PubMed
15. Gotoda Y, Kambara N, Sakai T, Kishi Y, Kodama K, Koyama T. The morbidity, time course and predictive factors for persistent post-thoracotomy pain. *Eur J Pain* 2001;5:89–96. - PubMed
16. Guastella V, Mick G, Soriano C, Vallet L, Escande G, Dubray C, Eschalier A. A prospective study of neuropathic pain induced by thoracotomy: incidence, clinical description, and diagnosis. *PAIN* 2011;152:74–81. - PubMed

17. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. *Clin J Pain* 1996;12:50–5. - PubMed
18. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet* 2006;367:1618–25. - PubMed
19. Kinney MA, Hooten WM, Cassivi SD, Allen MS, Passe MA, Hanson AC, Schroeder DR, Mantilla CB. Chronic postthoracotomy pain and health-related quality of life. *Ann Thorac Surg* 2012;93:1242–7. - PMC - PubMed
20. Kirby TJ, Mack MJ, Landreneau RJ, Rice TW. Lobectomy—video-assisted thoracic surgery versus muscle-sparing thoracotomy. A randomized trial. *J Thorac Cardiovasc Surg* 1995;109:997–1001; discussion 1–2. - PubMed
21. Komatsu T, Sowa T, Takahashi K, Fujinaga T. Paravertebral block as a promising analgesic modality for managing post-thoracotomy pain. *Ann Thorac Cardiovasc Surg* 2014;20:113–6. - PubMed
22. Koryllos A, Althaus A, Poels M, Joppich R, Lefering R, Wappler F, Windisch W, Ludwig C, Stoelben E. Impact of intercostal paravertebral neurectomy on post thoracotomy pain syndrome after thoracotomy in lung cancer patients: a randomized controlled trial. *J Thorac Dis* 2016;8:2427–33.
23. Landreneau RJ, Mack MJ, Hazelrigg SR, Naunheim K, Dowling RD, Ritter P, Magee MJ, Nunchuck S, Keenan RJ, Ferson PF. Prevalence of chronic pain after pulmonary resection by thoracotomy or video-assisted thoracic surgery. *J Thorac Cardiovasc Surg* 1994;107:1079–85; discussion 85–6.
24. Macrae WA. Chronic post-surgical pain: 10 years on. *Br J Anaesth* 2008;101:77–86.
25. Peng Z, et al. A retrospective study of chronic post-surgical pain following thoracic surgery: Prevalence, risk factors, incidence of neuropathic component, and impact on quality of life. *PLoS ONE*. 2014;9:e90014. doi: 10.1371/journal.pone.0090014.
26. Wildgaard K, Ravn J, Kehlet H. Chronic post-thoracotomy pain: A critical review of pathogenic mechanisms and strategies for prevention. *Eur. J. Cardiothorac. Surg.* 2009;36:170–180. doi: 10.1016/j.ejcts.2009.02.005.
27. Arends S, et al. Post-thoracotomy pain syndrome: Seldom severe, often neuropathic, treated unspecific, and insufficient. *PAIN Rep.* 2020;5:e810. doi: 10.1097/PR9.0000000000000810.

Annex one: Information sheet to get permission for the research

Introduction

This information sheet is prepared to explain the research project that you are asked to join by research investigators.

The research team includes a General surgery resident, one senior advisor from AAU

Name of Principal investigator: - Abel Getachew, MD, General surgery resident

Advisor's name: - Dr. Abebe Bezabih MD, Consultant General and Cardiothoracic surgeon

Name of sponsor: - AAU

Name of organization: - AAU, College of Health Sciences, department of Surgery

This information sheet is prepared by the above investigators.

Risk: There is no risk or harm that you will face by participating in this research. Any personal information recorded will not be copied and transferred to other bodies. No need for writing participant name but by a code. Every piece of information will be kept confidential.

Benefits: There is no incentive or payment to be gained by taking part in this project but your pain status and presence of adverse events will be followed and get treated early. The information collected from this research project will be kept confidential and only accessed by the researcher and research assistants. This research project was reviewed and approved by the ethical committee of the department. If you want to know more information, you can contact the committee through the address below.

Abel Getachew- principal investigator

Department of surgery, Addis Ababa University

Email: abelhareg2222@gmail.com

Dr. Abebe Bezabih MD, Consultant General and Cardiothoracic surgeon– advisor

Department of Surgery, Addis Ababa University

Annex Two: Consent form

Dear participant:

My name is Abel Getachew, I have been attending a postgraduate program in the field of General surgery at Addis Ababa University. I am doing research to determine the prevalence and Risk factors of post thoracotomy pain syndrome. Data collection will be done at 1- and 2-month post op. To conduct our study, I would like to ask you some questions which may take about 5 minutes at 3 different times until 2nd post op month which are prior to the surgery, at 1 month post op and 2nd month post op. As your participation is very important to the outcome of the study and for you in helping you to get treatment by recognizing your complications and pain intensity early, we kindly request you to give us your sincere and truthful answer. All the information that you and other patients going to provide us will remain confidential and you don't need to mention your name.

Are you willing to participate in the study, please? YES/NO (please encircle your response) If your answer is no, you don't have to continue to the following questions. Thank you!

If your answer is yes, please continue your response to the following questions. Thank you for taking part in the study!

Signature of the interviewer certifying that consent has been obtained verbally. Signature Date

For further question ask investigator Abel Getachew Tel: - +251987064521

E-mail: abelhareg2222@gmail.com

Annex three: patient data

Section I: Sociodemographic data (chart review)

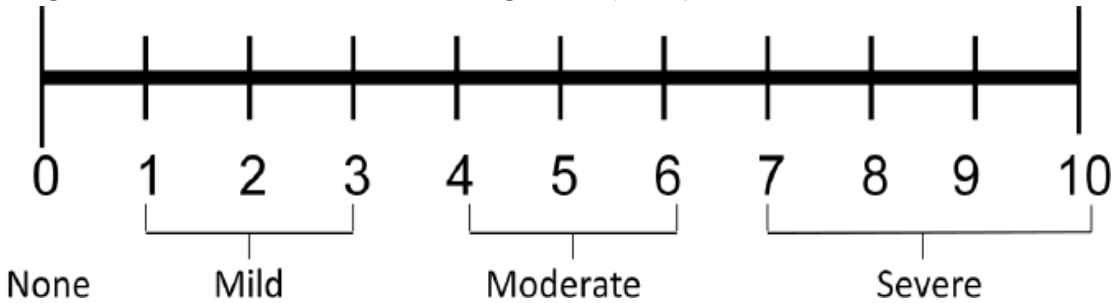
S.no	Question	Response	
1.1	Hospital card number		
1.2	Age		
1.3	Sex	A. Male B. Female	

Section II: Data during the preoperative period

S.no	Question	Response	
2.1	Diagnosis		
2.2	Does the patient take preemptive analgesia medications orally or intramuscularly within 1 –3hr before surgery?	1. Yes 2, No	If no skip No 2.3
2.3	If yes, specify the drug, and duration of time from administration to skin incision?	_____, ____ hr _____, __ _hr	

Annex four: The numeric rating scale (NRS) For Preoperative Pain assessment

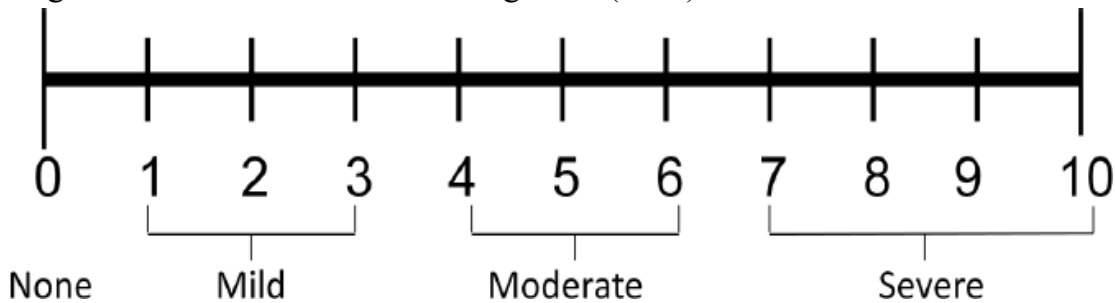
English version: The numeric Rating scale (NRS)



- A. The scale will be taken 3 times within 2 months. Patients will be asked to rate their pain.
- B. The patient will be asked one of the following questions:
 - 1. What number on a 0 to 10 scale would you give your pain right now?
 - 2. When the explanation suggested above is not sufficient for the patient, further explanation or conceptualization of the scale will be done:
 - 0 = No Pain
 - 1-3 = Mild Pain (nagging, annoying, interfering little with activity)
 - 4-6 = Moderate Pain (interferes significantly with activity)
 - 7-10 = Severe Pain (disabling; unable to perform activity)

Annex four: The numeric rating scale (NRS) For Postoperative Pain assessment at 1 week

English version: The numeric Rating scale (NRS)



- A. The scale will be taken 3 times within 2 months. Patients will be asked to rate their pain.
- B. The patient will be asked one of the following questions:
 - 1. What number on a 0 to 10 scale would you give your pain right now?
 - 2. When the explanation suggested above is not sufficient for the patient, further explanation or conceptualization of the scale will be done:

0 = No Pain

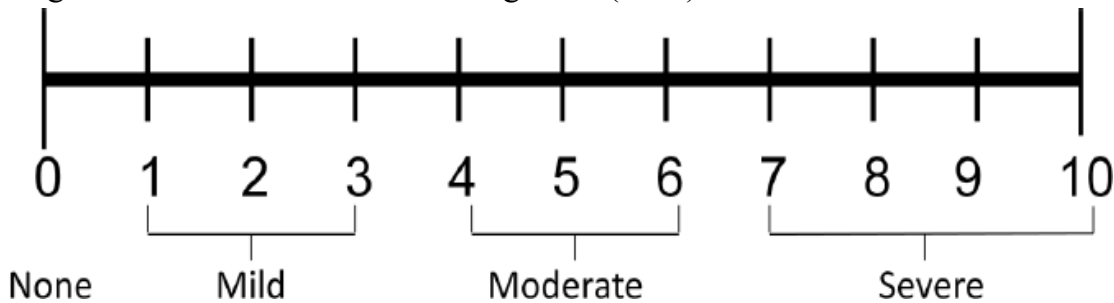
1-3 = Mild Pain (nagging, annoying, interfering little with activity)

4-6 = Moderate Pain (interferes significantly with activity)

7-10 = Severe Pain (disabling; unable to perform activity)

Annex four: The numeric rating scale (NRS) For Postoperative Pain assessment at 2 month

English version: The numeric Rating scale (NRS)



- A. The scale will be taken 3 times within 2 months. Patients will be asked to rate their pain.
- B. The patient will be asked one of the following questions:
 - 1. What number on a 0 to 10 scale would you give your pain right now?
 - 2. When the explanation suggested above is not sufficient for the patient, further explanation or conceptualization of the scale will be done:

0 = No Pain

1-3 = Mild Pain (nagging, annoying, interfering little with activity)

4-6 = Moderate Pain (interferes significantly with activity)

7-10 = Severe Pain (disabling; unable to perform activity)

Annex six: Data accuracy check sheet

S.No	Tools	Yes	No
1	Are the Inclusion criteria /exclusion criteria done appropriately?		
2	Are all questions on Socio-demographic data filed appropriately?		
3	Are all questions on preoperative period data filled appropriately?		
4	Are all questions on intraoperative period data filled appropriately?		
5	Are all questions on postoperative period data filled appropriately?		
6	Did the postoperative analgesic drugs filled based on request time, type and dose?		
7	Did the pain assessment follow standard operating procedure strictly on time?		
8	Was the presence of complications assessed?		

