Effects of Thoracic Epidural Analgesia in Thoracic and Upper Abdominal Surgery on Perioperative Stress and Morbidity

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DECLARATION

This dissertation is my own original work and has not been presented for a degree in any other University. All resources obtained therein have been duly acknowledged.

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ABSTRACT

Background:

Thoracotomies and laparotomies are surgical procedures prescribed for the management of multiple ailments resulting from trauma, malignancy, congenital, acquired defects and source control in sepsis. Despite multiple gains from safe anaesthesia administration, sympathetic arousal that is associated with surgery results in multiple physiological changes that may be harmful to patients. Thoracotomies are widely known as one of the surgical interventions with excruciating pain. There are attempts to minimize these unwanted effects of surgery by safe anesthesia administration and multimodal pain management. Studies have demonstrated epidural analgesia to be a superior form of pain management compared to conventional modes of analgesia. However, we had no local data and information on the effects of these modes of analgesia on patient outcomes following major abdominal and thoracic surgery.

Methodology:

An observational cohort study was performed at The Kenyatta National Hospital and The Coptic Hospital Nairobi. Eligible patients undergoing thoracic and upper abdominal surgeries under general anaesthesia were recruited into the study by consecutive sampling. Preoperative fasting blood sugar and vitals were determined. Thoracic epidural catheter was inserted, and general anaesthesia administered as per physician's protocol. Intraoperative physiologic vital parameters were recorded as per protocol. Postoperative fasting blood sugar, haematological profile, pain scores and need for rescue analgesia were recorded and compared among participants undergoing epidural and conventional anaesthesia.

Results:

The study involved 127 eligible and consented patients. 32 patients had thoracic epidural analgesia while 95 patients received conventional modes of analgesia. The patients were well matched in terms of age, gender and clinical comorbidities. The patients across all groups had the same hemodynamic profile with no alterations observed based on mode of analgesia. The patients under thoracic epidural analgesia showed better postoperative pain control compared to those who received multimodal conventional analgesics. Alterations in postoperative white blood cell count

and fasting blood sugars were seen across all groups with significant changes observed in patients who received thoracic epidural analgesia.

Conclusion:

Thoracic epidural analgesia confers better perioperative pain control in patients under thoracic and abdominal surgery. Multimodal conventional analgesics and thoracic epidural analgesia confer same and adequate intraoperative hemodynamic profiles.

1 INTRODUCTION

In the recent past, the global prevalence of significant perioperative pain has been reported to vary between 20-80%. Efforts have been made to try and reduce the incidences of untreated perioperative pain; however, a significant proportion of patients still suffer from suboptimal postoperative pain management. Surgery predisposes to perioperative stress and morbidity in an almost predictable manner and is the most prevalent cause of postoperative pain. It has also been suggested that the surgeries associated with a high pain intensity include thoracic surgeries, and open abdominal surgeries. Complications of sub-optimally treated perioperative pain are numerous, devastating and can be life-threatening to the patient. These complications include delayed wound healing, increased risk of deep vein thrombosis, pulmonary embolism, myocardial infarctions, and development of chronic pain syndrome.

Significant progress has been made in perioperative pain management but there is scarcity of local data in perioperative stress and morbidity research. Appreciable research has been done elsewhere on the different modalities available for perioperative pain control. The shortcoming of this is that the African population was not adequately represented in many of the studies done. This could dampen the application of the results outside the populations studied. These gaps offer an excellent opportunity for research into perioperative stress and morbidity in Kenya. The outcome from this study will highlight the need for a possible more regular application of epidural analgesia in the perioperative setting.

2 LITERATURE REVIEW

2.1 Background

Epidural catheterization is widely used for anaesthesia administration, employed in pain control and as an adjunct to general anaesthesia. Its indication cuts across a wide spectrum of surgical disciplines including diagnostic procedures, chronic pain management and end of life settings. Its application, safety and success are dependent on the medical practitioner's experience and knowledge of its use. Winter et al. did a randomized controlled trial in 2010[1] on thoracic epidural analgesia or patient controlled opioid analgesia (PCA) on perioperative quality of life following thoraco-abdominal surgeries. They demonstrated that the pain outcomes were markedly better in the group of patients under epidural therapy at most periods. They further showed that patients exhibited mental and physical outcomes in the epidural group that were much better than for the patients in the PCA group. They concluded that epidural analgesia with local anaesthetic and opioids enhances quality of life (QOL) and offers better pain control compared with PCA in patients scheduled for major thoracic and abdominal surgery.

Surgery and anaesthesia are associated with a significant stress feedback exemplified by a sympathetic response, hypermetabolism, alterations in catabolic and anabolic hormones balance, alterations in carbohydrate metabolism and immune function. These are natural responses geared towards maintenance of homeostasis after trauma and illness. In 2019 Y. Li, Dong, Tan, Qian, & Jin, Long did an RCT on *the effects of thoracic epidural anesthesia/analgesia on the stress response, pain relief, hospital stay, and treatment costs of patients with esophageal carcinoma undergoing thoracic surgery* and concluded that thoracic epidural analgesia reduces the stress responses, improves postoperative recovery, reduces costs and hospital stay for with Esophageal carcinoma[2].

There is a marked rise in the plasma quantities of norepinephrine in the initial first day post-surgery. A rise in catecholamine and glucocorticoid amounts pose a risk not only to patients with coronary artery disease but may also lead to the development of stress-induced heart disease[3]. In 2005 Nygård et al., demonstrated that thoracic epidural analgesia reduces the number and duration of episodes of cardiac ischemia, levels of troponin T and I in these patients[4]. Caputo et al., in a 2011 study, thoracic epidural analgesia markedly lowered the incidence of postoperative

cardiac arrhythmias, enhanced analgesia and quality of recovery, permitting quicker extubation and hospital discharge in patients scheduled for off pump coronary artery bypass surgery[5].

A meta-analysis done by Rodgers et al in 2000 on the effect of neuraxial anaesthesia on postoperative mortality and morbidity noted risk of venous thromboembolism, hemorrhagic complications, myocardial infarction, pneumonia, respiratory depression and renal complications were significantly lowered. It also reduced postoperative mortality[6]. In a study by Lattermann et al. in 2007 epidural analgesia was shown to inhibit the increase in whole-body protein breakdown[7]. Li et al. in 2017 demonstrated that epidural analgesia reduced intraoperative and postoperative alterations of glucose metabolism with a better intraoperative glycemic control compared to conventional modes of anaesthesia and analgesia in diabetic patients[8]. Volk et al. in 2004, demonstrated that thoracic epidural analgesia (TEA) preserves lymphocyte function thus offering postoperative resistance to infectious complications[9].

Ballantyne et al. performed a meta-analysis in 1998 of randomized control trials to evaluate the effects of seven analgesic therapies on postoperative respiratory function after a variety of procedures. They concluded that the use of epidural opioid with local anaesthetic optimized analgesia and quicker mobilization thus reducing the risk of respiratory complications[10]. In 2017 Zoumprouli et al. performed an RCT on the effects of thoracic epidural analgesia on gastrointestinal (GI) motility following thoracic surgery and concluded that epidural analgesia plus or minus morphine improved GI motility compared to intravenous morphine thus offering a better postoperative quality of life[11].

2.2 Anaesthesia and Immunomodulation

Surgical stress is characterized by profound endocrine changes that have been demonstrated to influence the host defense system by affecting the immune system or activating hypothalamic – pituitary-adrenal axis and sympathetic nervous system. Studies have shown that a variety of stress, including surgery and pain induce alterations in immune function. Immune dysfunction predisposes postoperative and intensive care patients to prolonged infections and sepsis[12].

The autonomic nervous system and the hypothalamic – pituitary – adrenal axis provide an interface between stress and organ systems. Anaesthetics may influence immune function by reducing the catecholamine release induced and cortisol mediated stress responses. Lymphoid organs are

extensively innervated by noradrenergic sympathetic nerve fibers that are modulated by anaesthetics.

Epidural and spinal anaesthesia offer an afferent neural block that profoundly inhibits hormonal and metabolic stress responses. A study by Kelbel and Weiss in 2001, showed that surgery related increase in serum cortisol and the depression of cytokine production are attenuated by extradural analgesia[12]. In contrast to the pronounced inhibition of the stress response by neural blockade, opioids administered systemically or epidurally have little or no stress reducing effect.

2.3 History of Epidural Anaesthesia

The vertebral epidural access as a route and as a method of injecting anaesthetic solution was initially proposed by a neurologist, J. Leonard Corning, in the 1880s. Later in the early 20th century Jean Sicard and Fernand Cathelin, pioneering French physicians, were the first to intentionally inject cocaine into the epidural space for neurologic and genitourinary procedures[13]. Fidel Pages Mirave, a Spanish surgeon later described how to locate the epidural space by use of different tactile differences in the ligaments[14]. An Italian surgeon, Achille Dogliotti later developed and popularized loss of resistance technique to locate the epidural space[15].

Initially epidural analgesia was used as a single shot technique and later in 1947 a Cuban anaesthesiologist, Manuel Martinez Curbello initiated the use of continuous drug administration for the epidural space[16]. The epidural catheter in initial use was a rubber ureteral tube and has evolved to the current nylon materials that produce quite thin, and bend resistant catheters[13].

2.4 Indications

Epidural anaesthesia can be employed as the primary anaesthetic or as an adjunct to general anaesthesia or other regional techniques of anaesthesia administration in areas of sensory-motor distribution of the thoracic and lumbar spine (cord and nerve roots)[17].

Specialty	Surgical procedure
Obstetrics	Caesarean section, pain management in labor
Gynecology	Hysterectomies
Orthopedics	Hip and knee fractures, major pelvic surgeries
Cardiothoracic	Thoracotomies, esophagectomies, coronary artery bypass grafting, thymectomies, vascular surgery and amputation of lower limbs
General surgery	Hepatic, colonic, gastric, breast surgeries, bowel resection, pancreatectomies.
Urology	Prostatectomies, nephrectomies, cystectomies
Pediatric surgery	Hernioplasty, pediatric urology and orthopedic surgeries

Table 1.Surgical Indications for Epidural Anaesthesia

Thoracic epidural anaesthesia and Analgesia benefits include:

1. Better perioperative pain management compared with other modalities; reduces over-reliance on opioids for postoperative pain control[10], [18].
2. Reduction in postoperative respiratory complications[10], [19].
3. Incidence of postoperative ileus are minimal[1], [20].
4. Reduced period of postoperative mechanical ventilation
5. Incidence of mortality after rib fractures is significantly reduced[18].

2.5 Contraindications

Absolute contraindications of epidural access include patient refusal and severe coagulopathies such as disseminated intravascular coagulopathy. Relative contraindications include sepsis, elevated intracranial pressure, anticoagulants (which must be discontinued as appropriate preoperatively)[21], thrombocytopenia with a cut-off platelet count of 70,000/mm^3, bleeding diathesis, pre-existing conditions of the nervous system, infection, pre-load dependent cardiac conditions (e.g., aortic stenosis), prior spinal surgery, preexisting nervous system injury, back pain, and more importantly the presence of back dyed tattoo.

2.6 Anatomy

2.6.1 Vertebral Column

It comprises seven cervical, twelve thoracic, five each lumbar and fused sacral and 3-5 fused coccygeal vertebrae. The vertebral column is straight when viewed dorsally; posteriorly lumbar and cervical form a concave shape (lordosis) while the thoracic and sacral form a concave shape known as a kyphosis anteriorly.

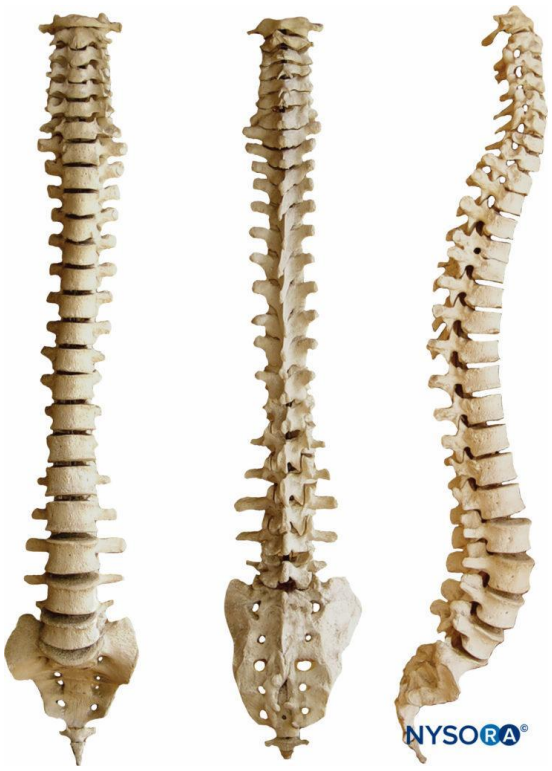

Figure 1. Ventral, Dorsal and lateral views of the vertebral column. Credit: NYSORA

2.6.2 Thoracic Vertebra

These are 12 in number. They exhibit a vertebral body that is wider posteriorly than anteriorly that's characteristic of the thoracic curvature. The spinous processes of the thoracic vertebra are slender and longer posteriorly and points caudally (an acute angle at T4-T9 vertebra) making the midline epidural insertion more difficult in these regions. Paramedian approach is preferred.

2.6.3 Anatomic landmarks

Anatomic landmark	Spinal Level
Vertebral prominence	C7
Root of spine of scapula	T3
Inferior angle of scapula	T7
Rib margin	L1
Superior aspect of iliac crest	L3-L4
Posterior aspect of iliac crest	S2

Table 2.Descriptive Image of anatomical surface landmarks for spinal level identification

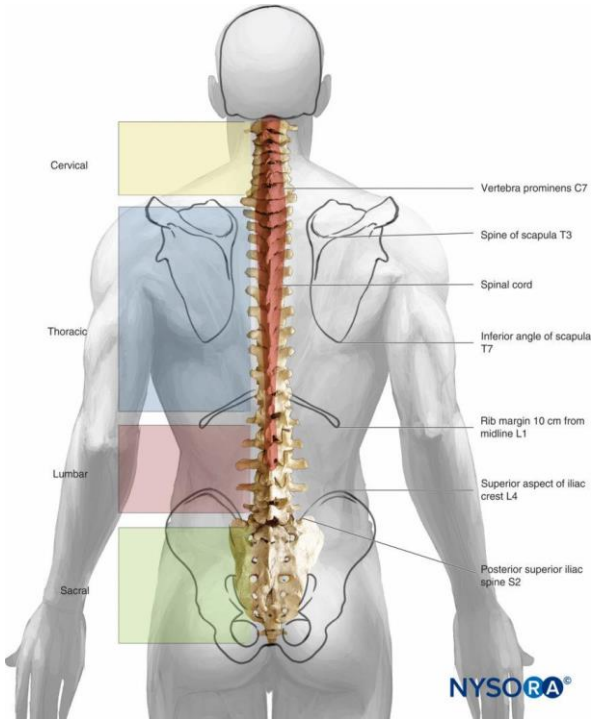

Figure 2. Descriptive Image of anatomical surface landmarks for spinal level identification. Credit: NYSORA

2.6.4 Spinal cord

The spinal cord is the caudal extension of the central nervous system with 31 pairs of spinal nerves. There are 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal nerve pairs. The adult cord measures 45cm and has two regions of enlargement corresponding to origins of nerve supply to upper and lower limbs. The spinal cord terminates at L3 lumbar vertebral level at birth and at L1 from infancy to adulthood although with some individual variations. Below L1 vertebral level the spinal nerve roots form the cauda equina.

2.6.5 Blood Supply

The spinal cord gets its blood supply from vertebral and segmental arteries. The anterior spinal artery gives blood to the anterior two-thirds of the spinal cord and the two posterior spinal arteries supply the rest. The spinal arteries emerge from the vertebral artery. Corresponding anterior and posterior spinal veins channel into the hemiazygos, azygos and internal iliac venous systems.

2.6.6 Epidural Space

This overlies the dura mater circumferentially extending from the foramen magnum all the way to the sacrococcygeal ligament. The boundaries to the epidural space are posterior longitudinal ligament anteriorly, ligamentum flavum posteriorly, and pedicles and the intervertebral foramina laterally. The space posteriorly is the one with clinical relevance. It comprises adipose tissue, connective tissue, blood vessels and nerve roots. Venous channels in the epidural space are valveless and communicate with iliac vessels, azygos venous system, and thoracic venous system. Therefore, any increase in pressure within these venous systems creates back flow into the epidural vessels.

2.7 Anaesthetic Epidural blockade.

2.7.1 Differential blockade

The effects of anaesthetic application on the nerves are not always uniform. Variation in blockade is seen when sensory, motor, and sympathetic nerves are blocked at different rates and to varying degrees. Sympathetic nerves are the first to be blocked and at a higher dermatome level than the rest. Sensory blockade follows and on a higher dermatome level than motor. During sensory blockade, temperature is the first to be blocked, then pin prick, last is touch.

Differential blockade is as a resultant of a distinction in the anatomy of nerves, that is, the diameter, the presence of myelin sheath, the extents the of obtunded nerve (a certain minimal length of blocked nerve is needed for an effective block), nerve lipid membrane differences and composition of the ion channel, and local anesthetic (LA) type and concentration.

2.7.2 Central Nervous System Effects

Multiple studies have indicated that spinal and epidural anaesthesia can lower anaesthetic needs and induce sedation. A review by Höhener, Blumenthal, & Borgeat, showed a relationship between the depth of sedation and the density and extent of the block[22]. Decreased anesthetic requirements is a result of a reduction in afferent input of the neuraxial blockade and not the systemic effects of LA.

2.7.3 Cardiovascular Effects

Freise & Van Aken[3] in a 2011 analysis of the effects of thoracic epidural analgesia showed that blockade involving the sympathetic nervous system is characterized by venous and arterial vasodilation, reduction in the systemic vascular resistance, variations in inotropy and changes in chronotropy with adjustments in blood pressure and cardiac output. Lumbar and low thoracic blockade are associated with less marked hemodynamic alterations.

2.7.4 Pulmonary Effects

There are minimal or no changes in the tidal volume with high thoracic blockade while there may be alterations in the vital capacity due to a decrease in expiratory reserve volume because of blockade of accessory muscles of respiration. There could be an impairment to cough and ability to clear secretions in patients with preexisting compromised pulmonary function. Post operatively thoracic epidural analgesia has a positive effect on lung function because enhanced pain relief prevents splinting[1].

2.7.5 Gastrointestinal (GI) system effects

Sympathectomy associated with epidural blockade presents clinically as an increase in peristalsis, sphincter relaxation, increased gastrointestinal secretions and a quicker restoration of GI motility in the post-operative phase[1].

2.7.6 Renal / Genitourinary Effects

Epidural anaesthesia has minimal effect on the renal system due to renal blood flow autoregulation. Lumbar neuraxial blockade can impair bladder function due to S2-S4 roots blockade leading to acute urinary retention. Normal urinary function is restored after the block wears off [23].

2.7.7 Thermoregulation

Hypothermia as a result of peripheral vasodilation results in redistribution of heat from the core organ systems to the peripheries. Thermoregulation is also impaired. Hypothermia can result in an increase in cardiac motility, coagulopathy, increase in blood loss, and a risk of infection[22].

2.7.8 Coagulation

Surgery is a hypercoagulable state resulting from the sympathetic vasoconstriction and impaired endothelial function. Williams, Sullivan, & Ramakrishna, 1999 elucidated that thoracic epidural blockade minimizes the inflammatory response associated with clot formation[24]. Hypercoagulability is a known postoperative phenomenon. Neuraxial block is linked with a reduction in risk of deep venous thrombosis and pulmonary thromboembolism. There's also a reduction in risk of thrombosis in the arterial and venous system.

2.8 Pharmacology of Epidural Blockade

Epidural blockade is achieved through local anaesthetics with or without the use of adjuvants. Local anaesthetics act by blocking neuron cell membrane Na^+ channels thus blocking the generation of action potentials.

Nerve fibers comprise type A, B and C fibers that are all blocked during epidural anaesthesia. They differ in dimensions and existence of myelin sheath. A-delta fibers and C-fibers transmit pain and temperature respectively. Large A-alpha fibers are for motor transmission. B -fibers are responsible for autonomic function, are slighter in dimension than A- delta fibers, but bigger than C-fibers. The B-fibers are more responsive to local anaesthetics than the sensory and motor fibers thus explaining the more extensive sympathetic block achieved compared to sensory and motor blocks during neuraxial anaesthesia. Motor fibers need a larger dose of local anaesthetic and more duration for a block because of their thick myelin sheaths.

Epidural analgesia is most potent when the catheter placement is at a level that corresponds to the dermatome covered by surgical incision. The onset is the quickest and most dense block at the site of injection[18]. Correct placement at the right dermatome site ensures lower drug dose minimizing side effects.

2.9 Choice of Local Anaesthetic

2.9.1 Bupivacaine

Bupivacaine is a long-acting amide local anaesthetic that comes in 0.5% preparations locally. It is currently the mainstay of epidural infusions in labor and postoperative analgesia. The onset of action is intermediate; 15-20 minutes with a duration of action of 160 – 220 minutes. It is highly protein bound and is metabolized in the liver by dealkylation to pipecolic acid and pipecolylxylidine. It has a potential for severe cardiotoxicity and neurotoxicity with systemic administration.

A 2003 study by Bharti, Madan, Mohanty, & Kaul showed that the addition of other drugs to the local anaesthetics improves the quality of blockade[25]. Examples include opioids (fentanyl, morphine, and alfentanil), alpha adrenergic agonists (clonidine, dexmedetomidine), ketamine, and midazolam.

The necessary dose or degree of block is based on the concentration of the solution and volume for injection. Duggan, et al, study noted that concentration affects density of blockade, the higher the concentration the higher the extent of motor and sensory block[26].

2.9.2 Guideline for dosing of Local Anaesthetics

The drug volume administered is 1-2 ml per segment planned for blockade, adjusted for short and tall patients. Time to repeat dosing is a factor of duration of action of the drug. A top up dose should be given before regression of the block to a point the patient feels pain known as "*time-to two-segment regression*', estimated at 180 – 260 minutes for bupivacaine administered at 0.1% concentration.

2.9.3 Intermittent blockade versus Continuous blockade

The decision on either intermittent or continuous epidural blockade is based on the nature of surgery, staffing and availability of equipment. The benefits of intermittent dosing are that it is

easy to administer and does not require extra equipment e.g., infusion pumps. Fettes et al., in 2006, showed that regular intermittent epidural injection was associated with a reduction in need for epidural rescue analgesia, and reduced epidural drug use[27]. Continuous epidural infusion confers better hemodynamic stability, less trained personnel required, reduced incidence of tachyphylaxis, reduction in frequency and severity of complications associated with bolus injections, a reduction in the risk of contamination, and offers a better steady state of anaesthesia.

2.10 Epidural Technique

2.10.1 Patient evaluation

The hazards and benefits of epidural catheter placement should be discussed with the patient and informed consent obtained. The patient's treatment history and ongoing medication should be evaluated prior to epidural placement. Clinical states that could predispose the patient to neuraxial infection e.g., Diabetes Mellitus, immunosuppression and drug use should be evaluated further. Physical examination must include spine evaluation for scoliosis, prior back surgery, local infection, presence of tattoos and severely reduced range of motion that could hinder placement of epidural catheter.

2.10.2 Preparation

As any other form of anesthetic administration, standard monitoring i.e. cardiac monitoring, Blood Pressure and pulse oximetry must be in place prior to epidural placement.

Large bore cannula for fluid administration and pre-loading or co-loading must be done unless contraindicated. Communication with the surgical team to discuss procedure, surgical approach, duration of surgery, anaesthetic and analgesic goals is important. Emergency medications for resuscitation must be availed. Equipment to ensure sterility should be in place comprising– standard anaesthetic tray with sterile gauze and antiseptic solution, povidone iodine or chlorhexidine. Commercial Epidural set with a Tuohy needle and catheter should be availed

2.10.3 Positioning

Optimal positioning of the patient is a necessity for a successful epidural catheter placement. The lateral decubitus or sitting, and prone positioning may be uneventfully used depending on patient's medical and physical status, and anaesthesia provider's experience,

Sitting – much better position for identifying the midline. It offers the quickest way to the epidural space with a shorter distance from skin to the epidural space. It confers better superior spread of the sensory block.

Lateral decubitus position – maybe suitable for patients uncomfortable in the sitting position, sedation can be liberally used, haemodynamic changes are better tolerated, less need for an assistant to help with positioning and preferable for unilateral blocks with hyperbaric local anaesthetics.

The common approaches are midline and paramedian (better for thoracic epidural catheter placement).

2.10.4 Initiation and Maintenance of Epidural block

Intravascular, subarachnoid and subdural placement must be ruled out before a local anaesthetic is administered. A classical test dose uses 3mls of 2% lignocaine and 15 micrograms of epinephrine. Subarachnoid injection of 60mg lignocaine should be able to elicit a significant motor blockade for subarachnoid space placement, a difference in pulse of 20% or higher (or an alternative rise in pulse rate of 15-25 beats in a minute) within a minute would suggest an intravascular catheter place or migration into a vessel. If these changes do not occur within 5 minutes, placement should be in right space. Though there are exceptions in patients under anaesthesia and patients receiving beta blockers. Guay, did a review on use of 45mg of lidocaine and 15mcg epinephrine in obstetric patients and found the doses to be efficacious in ruling out intravascular and intrathecal catheter placement[28].

2.10.5 Dosing Regimen

Initial loading dose is determined as 0.7ml of Local Anaesthetic per vertebral level for thoracic epidural. A loading dosage should be dispensed into the epidural catheter in 3-5ml boluses at 3–5-minute intervals. Loading dose for adequate postoperative analgesia is suggested at 10ml of 0.2-0.25 % bupivacaine plus or minus an adjuvant. Manual boluses are given at a quarter to a third of the loading dose at intervals based on the drug's duration of action. Continuous infusions have a wide infusion range of 4-15ml per hour depending on weight, age, extent of sensory or motor blockade required, and the dose of local anaesthetic used. Multiple dosing regimens should be

considered to lower incidences of hemodynamic instability and respiratory complications in awake patients in thoracic epidural analgesia.

2.11 Complications of Epidural Anaesthesia

2.11.1 Local Anaesthetic Systemic Toxicity

Excess plasma levels of LA as a result of accidental injection into the intravascular space or absorption at the site of injection may lead to local anaesthetic systemic toxicity. Flexible epidural catheters use may lower the risk of intravascular catheter migration. Dosing the catheter with 3-5ml volumes of local anaesthetic with regular negative aspirations for blood and CSF flow to rule out catheter misplacement is advised. Nervous system effects of Local Anaesthetic toxicity include dizziness and lightheadedness, slurred speech, perioral numbness, restlessness, blurred vision and confusion. Muscle twitching, tremors, shivering, and generalized convulsions are witnessed with larger plasma concentrations, with subsequent extensive CNS depression, characterized by drowsiness, loss of consciousness, and respiratory arrest. Cardiac manifestations include bradycardia, hypotension, arrhythmias, and cardiac arrest.

Management involves airway support, treatment of seizures, and cardiopulmonary resuscitation. Intralipid (20%) therapy is initiated with a bolus dose of 1.5 ml/kg, which is followed by an infusion at 0.25 ml/kg/min for a duration of 10 minutes after cardiovascular stability has been achieved. Neal, Mulroy, & Weinberg, American Society of Regional Anaesthesia and Pain Management did a checklist on the management of Local Anaesthetic Systemic Toxicity[29].

2.11.2 Arachnoiditis

This is a complication characterized by post inflammation changes in the arachnoid mater. Rice, Wee, & Thomson described the pathophysiology involved in development of fibrosis and adhesions around the neve roots and membrane that engulfs the brain and the spinal cord[30]. Pathophysiology involves development of fibrosis and adhesions around the neve roots and membrane that engulf the brain, the spinal cord and cauda equina. Collagen deposition on the nerve roots lead into nerve root atrophy from interruption to the blood supply. This is seen in chronic cases. Clinical symptoms include pain on the back radiating to the lower limbs, reduced range of motion in the trunk, sensory and motor dysfunction, and urinary system dysfunction.

2.11.3 Backache

Backache is the most common post – operative complaint after neuraxial blockade, with an incidence 3-31% after obstetric surgery. Backache following epidural analgesia is more common, and more severe than backaches following subarachnoid blocks. Postulated causes are trauma, ligamentum inflammation, intervertebral disk needle puncture and muscle spasms.

2.11.4 Post-dural Puncture Headache

Results mainly from accidental dural puncture with subsequent CSF discharge through the dural hole. PDPH as defined by the *International Headache Society is a headache that emerges inside 5 days of a lumbar puncture and is mostly associated with neck stiffness and hearing symptoms that resolve in 2 weeks or after management with epidural blood patch.*

Predisposing for PDPH comprises the younger age group, a low BMI, pregnancy, female gender, spinal needles in use (cutting versus atraumatic needles) and use of larger-gauge epidural needles.

Treatment is by agents or drugs having vasoconstricting properties, for example, theophylline caffeine and sumatriptan. Analgesics play a major role. Evidence has shown epidural blood patch with saline, dextran 40, and gelatin could be beneficial in the treatment of post-dural puncture headache.

2.11.5 Subdural Injection

Subdural Injection may result in profound haemodynamic and sympatholytic effects. It's a rare complication. The incidence is estimated at 0.1%-0.8% after epidural injections. It's characterized by a higher sensory block with weak distal spread and associated higher segmental motor block. Mainstay of treatment is cardiovascular support with intravenous fluid administration and vasopressors.

2.11.6 Total Spinal Anaesthesia

This is seen in approximately 1 in 400 attempted epidural catheter placements. Symptoms result from unrecognized dural puncture with subsequent administration of epidural dose of LA or non - detected misplacement of the tip of the epidural catheter into the subarachnoid space. Total spinal anesthesia effects are seen within a short duration of injection. Symptoms may also occur after alterations in the patient's position with catheter migration into the intrathecal space. Total spinal

anaesthesia gives a spread that blocks the entire spinal cord and at times brainstem resulting in bradycardia, hypotension, dysphonia, and difficulty in swallowing. This is aggressively managed by airway support and cardiovascular resuscitation; epinephrine infusion is advised early until the effects of the local anaesthetic wear off.

2.11.7 Spinal Epidural Abscess

This is a common complication in the geriatrics and immunosuppressed patients, in patients with prolonged ICU admissions, intravenous drug users, patients with bacterial septicemia, diabetes mellitus, Alcohol dependency, malignancy, HIV and chronic renal disease. Prevalence is 5% of epidural procedures. Thoracic and lumbar epidurals are associated with more episodes than cervical placements. Prolonged epidural infusions and systemic infections at time of placement and non-adherence to sterility are risk factors to development of spinal epidural abscesses. Patients may have features of urinary bladder dysfunction, meningitis, septicemia, motor weakness, mental status changes, catheter site inflammation, headache and neck stiffness.

Treatment is by broad spectrum antibiotics tailored to tissue or blood culture; surgical intervention may be necessary in the presence of neurological symptoms. Morbidity remains high at 33 – 47% most likely from misdiagnosis, delay in diagnosis and intervention. Mortality rate is estimated at 5%.

2.11.8 Meningitis

Meningitis is rare following epidural anaesthesia. Most incidences seem to be a consequence of contaminating the epidural injection site by organisms of the oropharynx or nasopharynx of the clinician that migrate into the epidural space. Meningitis presents with fever, headache, alterations in mental status, nausea and vomiting, photophobia, nuchal rigidity and a positive Kernig's Sign. Initial symptoms develop within 6-36 hours of anaesthetic procedure. Fever, mental status changes and severe headache are clinical features that differentiates meningitis from PDPH. Treatment is by broad spectrum antibiotics.

2.11.9 Spinal Cord and Nerve Root Trauma

This is a complication that may result from direct local injury to the cord and spinal nerves from ischemia, accidental administration of neurotoxic medications and chemicals, haematoma and abscesses. With an incidence of 0.03-0.1%, cases of spinal cord injury are rare. Horlocker et al

evaluated records of over 4,000 patients with lumbar epidurals with no evidence of neurological complications[31]. Spinal cord or nerve root injury may present as a peripheral neuropathy.

2.11.10 Cauda Equina Syndrome

It's a rare syndrome that results from compression of the lumbosacral root. It presents with bowel and bladder dysfunctions, perineal sensory impairment, low back pain, sciatica, and lower extremities motor weaknesses. Cauda Equina Syndrome could result from direct nerve root trauma, infections, lithotomy and compression from a sacral haematoma, abscess and neurotoxicity from high concentrations or large volumes of Local Anaesthetics in the sacral CSF.

2.11.11 Epidural Hematoma

Epidural hematoma as a complication of epidural catheter placement is an occasional phenomenon with an incidence of 1:150,000 epidural cases. The pressure from the haematoma may lead to compression and ischemia of the spinal cord, and myelopathy. This may be more common in patients with less compliant epidural space and those predisposed to coagulopathies that are secondary to underlying bleeding disorders. It presents with acute severe backache, sensory and motor symptoms and is by surgical decompression.

2.11.12 Cardiac Arrest

Cardiac Arrest is an adverse event that may result from total spinal anaesthesia, local anaesthetic systemic toxicity (LAST), myocardial ischemia or respiratory compromise. It's a rare complication post epidural analgesia that can lead to death or ischemic encephalopathy.

Predisposing patient characteristics for a cardiac arrest after neuraxial blockade are the male gender, low baseline pulse rate, a higher sensory block, prior use of beta-adrenergic blockers and prolonged PR interval on ECG.

Pollard et al advised administration of adequate preload, use of vasopressor and vagolytic agents early to minimize haemodynamic compromise[32].

2.12 The Visual Analogue Scale in Pain Assessment.

This is a tool that tries to evaluate a characteristic or attitude that ranges across values and cannot be measured directly easily[20]. Its use in clinical research is to quantify the frequency or intensity of various symptoms. It can be used to measure the intensity of pain a patient perceives; that can

range across a continuum from nil to an extreme excruciating pain[33]. For the patient assessed, pain appears to be a continuous process and cannot be categorized as mild, moderate, and severe.

Visual analogue scales are filled by patients themselves though they can also be used to derive opinions from healthcare providers. The patient is to fingermark on the line the spot that they feel captures their perception of their present condition. The VAS score is established by measuring in millimeters from the left end of the line to the spot that the patient marks[33].

A ruler is used to measure the interval in millimeters on the 10-cm line between the “no pain” point and the patient’s mark, giving a range of scores from 0–100. A high score would point towards higher pain intensity. Scores on the VAS have the following scores recommended for stratifying pain intensity: no pain (0–4 mm), mild pain (5-44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm) (11). The VAS scale being a visual one must be shown to the patient. Normative values are not available.

3 STUDY JUSTIFICATION

Patients with a successful epidural placement encounter superb and often absolute pain relief after surgery with a continuous epidural infusion. They often report lower pain intensity at rest and on movement which is favorable for early mobilization. Studies have shown a greater level of fulfilment and quality of recovery post epidural analgesia[1] [1]. Catecholamine surges result in an increased workload of the heart and subsequent myocardial oxygen requirements. A mismatch in the oxygen supply versus demand in patients with underlying coronary disease may result in myocardial ischemia and infarction, cardiac arrhythmias and cardiac failure[4], [34]. Catabolic response leads to hyperglycemia and result in impaired wound healing postoperatively[8]. There have been no local studies done on this subject to date, and a positive outcome of this study would be the basis for a change in our practice guidelines.

4 RESEARCH QUESTION

Does thoracic epidural analgesia as adjunct to general anaesthesia confer better pain control and better perioperative quality of life than conventional multimodal pain management?

5 HYPOTHESIS

5.1 Null Hypothesis

Thoracic Epidural Analgesia doesn't confer better intraoperative hemodynamic stability and postoperative quality of life over conventional modes of analgesia.

6 OBJECTIVES

6.1 Broad Objective:

Determination of physiological and biomedical effects of thoracic epidural analgesia in thoracic and upper abdominal surgery on perioperative stress and morbidity

6.2 Specific Objectives:

i. To determine the intraoperative haemodynamic effects of thoracic epidural analgesia
ii. To determine the effect of thoracic epidural analgesia on the control of postoperative pain and need for rescue analgesia.
iii. To determine effect of thoracic epidural analgesia on perioperative blood sugar levels.
iv. To determine the postoperative neutrophil count after thoracic epidural analgesia

7 MATERIALS AND METHODS

7.1 Study population

The study involved all eligible patients undergoing elective thoracotomies and upper abdominal surgery under general anaesthesia at the Kenyatta National Hospital and Coptic Hospital Nairobi theatres.

7.2 Study design

This was an observational cohort study.

7.3 Inclusion and Exclusion Criteria

7.3.1 Inclusion Criteria

i) Consenting patients aged over 18 years
ii) Patients with no history of immunomodulation or immunosuppressant therapies.
iii) ASA I - III patients slated for thoracotomies or upper abdominal surgeries.

7.3.2 Exclusion Criteria

i) Immunocompromised patients
ii) Patients with metabolic disorders e.g., diabetes mellitus or adrenal gland disorders
iii) Patients on postoperative mechanical ventilation and sedation
iv) Patients who decline to be enrolled in the study
v) Patients with severe cardiovascular disease
vi) Patients with contraindication to thoracic epidural e.g., coagulopathies, local infection, or local anaesthetic allergy

7.4 Sample size

To detect a difference of 50% in physiological and biochemical parameters between two groups, and assuming an alpha error of 5% and a beta error of 20% we required 128 patients in the study. Sample size and power calculations were done using G*power software v3.1.6 (Universität Kiel, Germany)[35] with the following parameters:

t tests *- Means: Difference between two independent means (two groups)*

Analysis:	*A priori: Compute required sample size*	
Input:	*Tail(s)*	*= Two*
	Effect size d	*= 0.50*
	α err prob	*= 0.05*
	Power (1-β err prob)	*= 0.80*
	Allocation ratio N2/N1	*= 1*
Output:	*Non-centrality parameter δ*	*= 2.8284271*
	Critical t	*= 1.9789706*
	Df	*= 126*
	Sample size group 1	*= 64*
	Sample size group 2	*= 64*
	Total sample size	*= **128***

The software uses the following standard formula[36] to calculate sample size:

$$n = \left(\frac{r+1}{r}\right)\frac{\sigma^2(Z_\beta + Z_{\alpha/2})^2}{(\mu_1 - \mu_2)^2}$$

Where:

n = Sample size

r = allocation ratio

σ2 = the population variance of measures of interest i.e., neutrophil counts, blood sugar and visual analogue pain scores

$Z\alpha_{/2}$ = the critical value of the Normal distribution at α/2 (for a confidence level of 95%, α is 0.05 and the critical value is 1.96)

Z_β = the critical value of the Normal distribution at β (for a power of 80%, β is 0.2 and the critical value is 0.84)

μ_1- μ_2 = difference in means to be detected (effect size) which is 0.50

7.5 Sampling procedure

Total enumerative sampling was used to recruit patients who met our inclusion criteria until the required sample size of 128 participants was attained. Sampling was non-randomized and was conducted by the principal investigator and a research assistant in three broad steps. First, the theatre list of the main KNH theatre and Coptic Hospital was reviewed every day and the demographics and site of admission of the patients noted. Then, patients who met our inclusion criteria were approached in wards and objectives of the study explained. The type of data to be

collected, the expectations from the participants, and the potential risks and benefits were explained, and consent sought. If a patient was sedated or not in a position to read and understand the informed consent form, which was in English and Kiswahili, an immediate family member was approached and asked to consent on behalf of the patient. Patients who offered written informed consent or were consented for by family members were recruited until the required sample size was attained.

7.6 Ethical consideration

7.6.1 Study approval

The study protocol and all data collection tools were submitted to the KNH-UoN ethics review committee (ERC) for clearance. As the custodian of patient's data, approval was sought from the KNH administration before recruitment of patients and the collection of primary data. Epidural anaesthesia and analgesia are a standard clinical procedure already in use in KNH. The study's aim was to further the knowledge and enhance its use in the facility.

7.6.2 Informed consent

The autonomy of participants is one of the cornerstones of the Belmont principles of research ethics, which we upheld by administering informed consent. The theatre lists of the KNH Main Theatre Coptic Hospital were reviewed every day and patients scheduled for surgery approached by a trained research assistant. After a preliminary evaluation, consent was administered to patients who met our inclusion criteria. Consent forms were in English and Kiswahili and covered all particulars of the study such as the procedures and potential risk and benefits of the study. The research assistant also answered questions satisfactorily before signing of consent forms, which was in two ways. Literate participants appended their signatures, while illiterate patients append their thumb print or delegated consenting to a next of kin or a family member.

7.6.3 Confidentiality

The Principal Investigator, research assistant, and other parties involved in the study upheld the confidentiality of patients. During data collection, no personal identification such as the name and national identification numbers of patients were recorded. For identification, unique study numbers were generated for all participants and used throughout the study. Consent forms were filed and stored under lock and key and information shared with guidance from the ERC.

7.7 Data collection

The data collection tool in *Appendix 11.1* was used. The tool was researcher-administered and designed to record a plethora of variables that answered our objectives. The age and gender of patients were some of the demographic data recorded. We also recorded any preoperative comorbidities in the patients, preoperative white blood cell picture and the fasting blood sugar. Intraoperative hemodynamics were recorded. Postoperatively we sought data on fasting blood sugar, need for rescue analgesia and pain scores using visual analogue scale. The tool was in sections for easier administration.

7.8 Data Management and Analysis

Information collected using the Data Collection Tool was entered into an MS Excel database and curated for statistical analysis. Quantitative data was tested for Gaussian distribution by the D'agostino and Pearson's omnibus normality test and Shapiro–Wilk normality test. The Mann – Whitney U- test was used to compare variables that are not normally distributed between the two groups while the Student's t test was used for variables that were normally distributed. One-way analysis of variance (ANOVA) with post-tests was used for comparison of continuous variables at different time points. Chi-square and Fisher's Exact tests were used to assess the significance of the categorical demographic variables between groups. Statistical analyses were performed using GraphPad Prism 8 (version 8.0; GraphPad Software) and significance was accepted if $p \leq 0.05$

7.9 Quality assurance

To ensure the collection, analysis, and presentation of quality data, the regulatory procedures were implemented during the data collection process, analysis, and dissemination. Only patients who met our inclusion criteria were recruited. The PI conducted a preliminary evaluation of patients scheduled for a surgery and suitable ones recruited. The principal investigator checked all data collection tools for completeness before filing or de-identification and data analysis. Clarifications were sought when needed. Only qualified medical personnel were engaged during the data collection process. The PI and a trained research assistant handled the entire process of data collection. Patients not able to read were adequately assisted by the trained research assistants during consent signing and data collection. Data analysis was done by an experienced statistician to ensure integrity of results.

8 RESULTS

8.1 Sociodemographics

An observational cohort study was conducted between April and July 2021. The purpose of this study was to compare whether thoracic epidural analgesia used in combination with general anesthesia confer better pain control and better perioperative quality of life than conventional multimodal pain management. 127 patients participated in the study. The study was conducted at Kenyatta National Hospital and Coptic Hospital, Nairobi, majority of participants being from Coptic Hospital. 25 patients underwent thoracotomies while 102 patients underwent laparotomies. 47 patients were male(p=0.291) while 80 were female with no significant difference in outcomes between the two gender distributions. Among patients who underwent thoracotomies, 11 received epidural analgesia while 14 received conventional analgesia. 21 patients in the laparotomy group received epidural analgesia whereas 81 received conventional analgesia. The patients were well matched in age, gender distribution and other clinical comorbidities as no significant statistical differences were observed. Hypertension was the most predominant comorbid found in 24 of the participants. Table 1 summarizes the demographic and clinical characteristics of the participants.

	Thoracotomies (n=25)			**Laparotomies (n=102)**		
	Epidural n=11	Conventional n=14	*p-value*	Epidural n=21	Conventional n=81	*p-value*
Age: [**Mean (SD)**]	51 (14.4)	52.3 (16.5)	0.842	54.2 (16.8)	53.8 (15.1)	0.918
Sex: Male	7 (63.6%)	8 (57.1%)	>0.999	9 (42.9%)	23 (28.4%)	0.291
Female	4 (36.7%)	6 (42.9%)		12 (57.1%)	58 (71.6%)	
Hypertension	2 (18.2%)	2 (14.3%)	>0.999	8 (38.1%)	16 (19.7%)	0.089
Cardiac disease	0 (0%)	0 (0%)	>0.999	2 (9.5%)	2 (2.5%)	0.186
Kidney disease	0 (0%)	0 (0%)	>0.999	1 (4.76%)	0 (0%)	0.205
Smoking	1 (9.1%)	1 (7.14%)	>0.999	0 (0%)	2 (2.5%)	>0.999
Alcohol use	0 (0%)	1 (6.67%)	>0.999	0 (0%)	8 (9.8%)	0.201
Anticoagulant use	0 (0%)	0 (0%)	>0.999	1 (4.76%)	4 (4.94%)	>0.999
Coagulation disorders	0 (0%)	0 (0%)	>0.999	0 (0%)	0 (0%)	>0.999
Spontaneous bleeding	0 (0%)	0 (0%)	>0.999	0 (0%)	0 (0%)	>0.999

Table 3. Sociodemographic and clinical characteristics of the participants

8.2 Heart Rate

First, intraoperative variations in heart rate were evaluated within each group of patients. No significant changes in heart rate were observed during surgery in patients undergoing thoracic and abdominal procedures whether on epidural or conventional analgesia (Figure 1). Further, when comparing epidural relative to conventional analgesia, no statistically significant differences were observed at each time point for both thoracotomies and laparotomies (Table 2), suggesting there's no difference in the effect of epidural and conventional analgesia on the heart rate.

	Baseline	**30 minutes**	**60 minutes**	**90 minutes**	**120 minutes**	**150 minutes**	**180 minutes**
Thoracotomies							
Epidural	88 (12.9)	95.18 (20.5)	93.27 (17.7)	88.91 (14.4)	97.27 (28.5)	101.4 (16.0)	101 (18.9)
Conventional	91 (12.8)	98.57 (18.2)	100.1 (18.2)	95.15 (13.7)	93 (18.5)	84.25 (9.9)	-
p-value	*0.569*	*0.666*	*0.358*	*0.289*	*0.731*	*0.076*	-
Laparotomies							
Epidural	91.2 (27.5)	93.14 (11.7)	91.6 (13.0)	93.72 (19.5)	89.63 (18.5)	91.25 (22.9)	112.5 (10.6)
Conventional	88.9 (17.2)	91.9 (13.9)	90.4 (15.8)	92.1 (18.5)	89.97 (17.9)	89.06 (29.1)	81.5 (22.8)
p-value	*0.635*	*0.711*	*0.736*	*0.722*	*0.949*	*0.855*	*0.125*

Table 4. Baseline and intraoperative mean heart rates across all groups

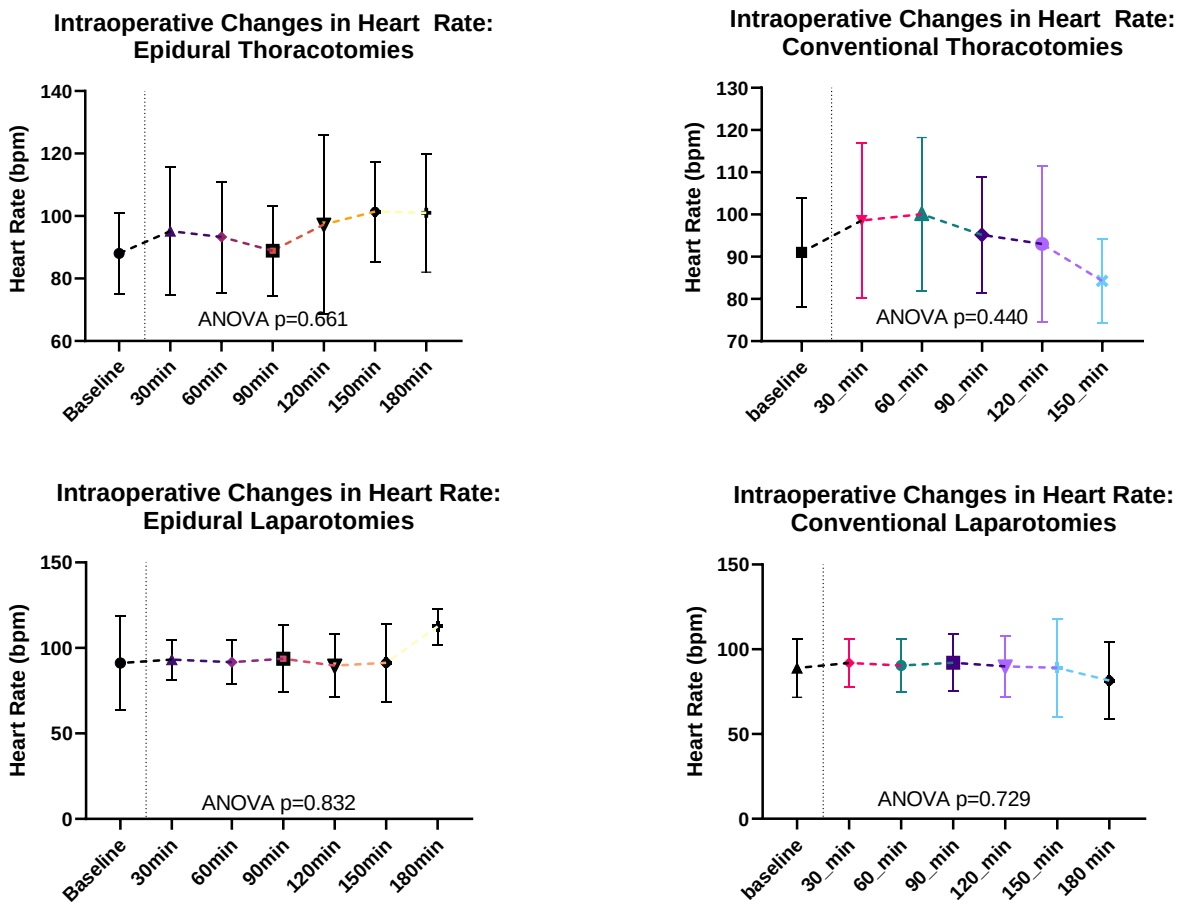

Figure 3. Trends in Changes in heart rates between groups

8.3 Intraoperative Blood Pressure

Variations in intraoperative blood pressure (systolic and diastolic) were then assessed. A significant drop in systolic blood pressure was observed after 150 minutes compared to the baseline in Epidural and Conventional analgesia Thoracotomies (Figure 2). However, in laparotomies, epidural analgesia had no effect on intraoperative systolic BP while a significant drop was observed with conventional analgesia at 30min, 60min, 90 min and 120 min during the surgery (Figure 2). A similar observation was made for diastolic blood pressure which were relatively lower than the baseline in conventional laparotomies (Figure 3). Side by side comparison

of epidural and conventional analgesia revealed no significant differences on their effect on mean systolic and diastolic blood pressure (Table 3).

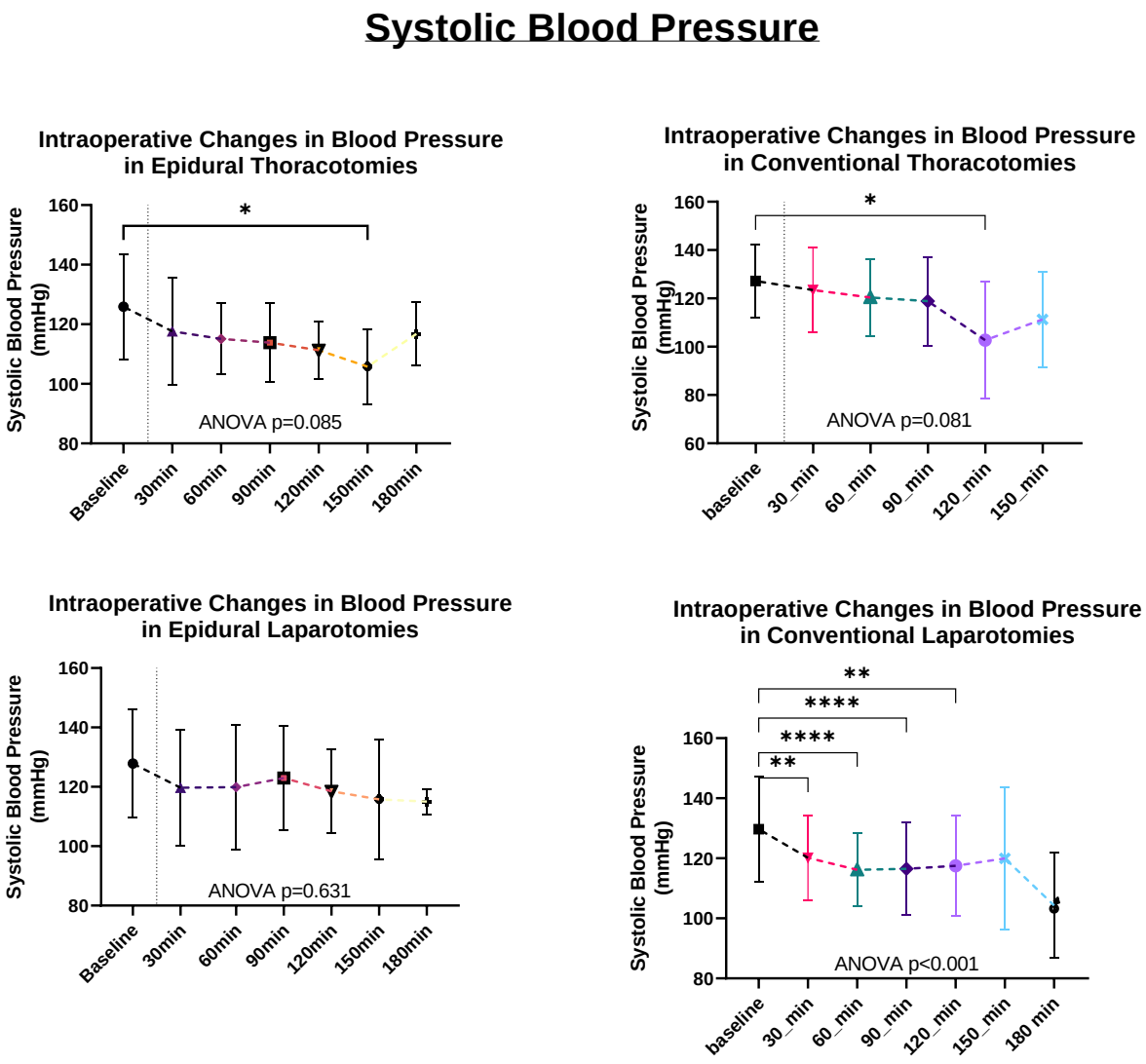

Figure 4. Trends in Systolic Blood Pressure between Epidural analgesia and Conventional Analgesia during Surgery

Diastolic Blood Pressure

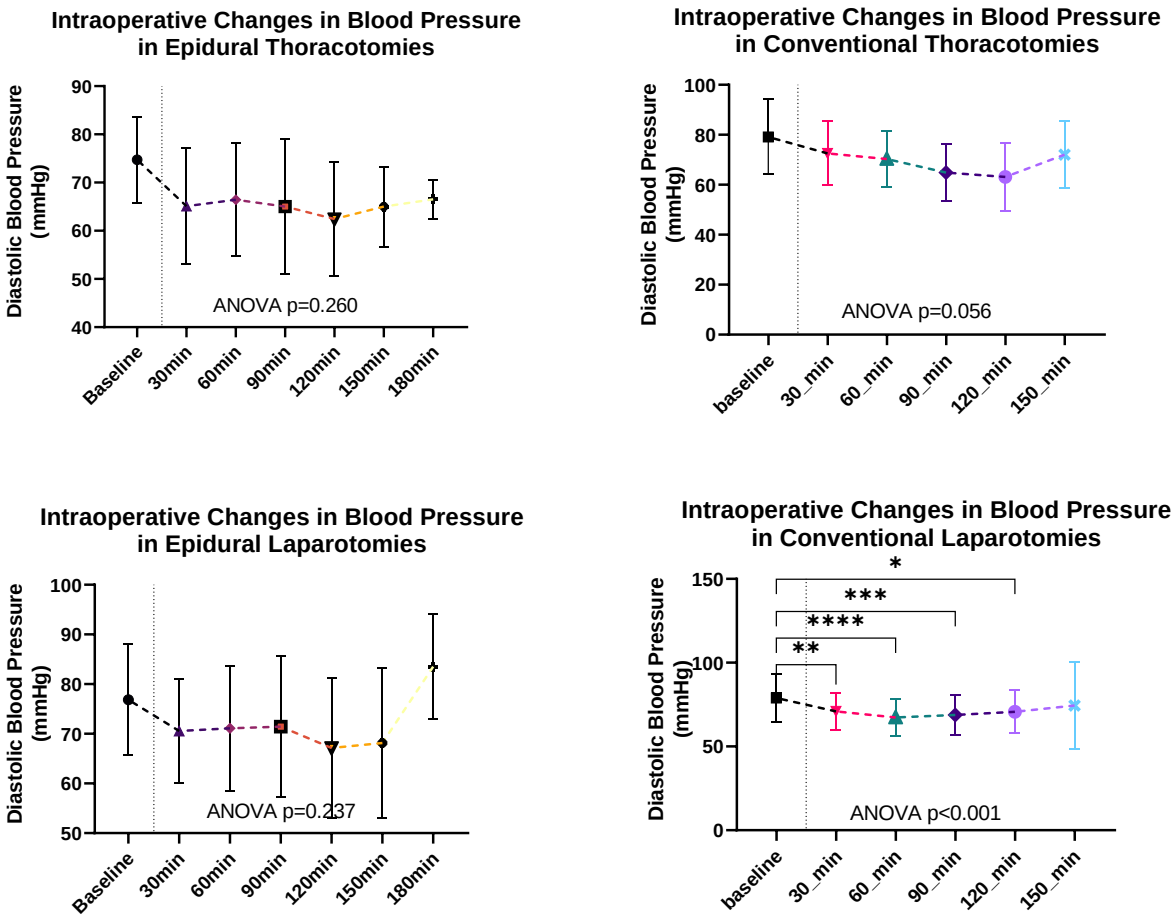

Figure 5. Trends in Diastolic Blood Pressure between Epidural Analgesia and Conventional Analgesia during Surgery

		Baseline	30 minutes	60 minutes	90 minutes	120 minutes	150 minutes	180 minutes
Systolic	**Thoracotomies**							
	Epidural	125.9 (17.6)	117.6 (17.9)	115.1 (11.9)	113.8 (13.3)	111.3 (9.5)	105.8 (12.6)	116.8 (10.5)
	Conventional	127.2 (15.2)	123.4 (17.5)	120.4 (16.0)	118.8 (18.3)	102.7 (24.3)	111.3 (19.9)	-
	p-value	*0.845*	*0.426*	*0.374*	*0.457*	*0.304*	*0.555*	-
	Laparotomies							
	Epidural	127.8 (18.1)	119.7 (19.6)	119.9 (20.9)	122.9 (17.6)	118.5 (14.0)	115.8 (20.3)	115 (4.2)
	Conventional	129.7 (17.6)	120.1 (14.2)	116.2 (12.2)	116.5 (15.3)	117.5 (16.7)	119.9 (23.6)	104.3 (17.6)
	p-value	*0.667*	*0.902*	*0.292*	*0.136*	*0.834*	*0.673*	*0.449*
Diastolic	**Thoracotomies**							
	Epidural	74.7 (8.9)	65.1 (12.1)	66.5 (11.8)	65.0 (14.0)	62.5 (11.8)	65.0 (8.3)	66.5 (4.1)
	Conventional	79.1 (15.0)	72.5 (12.8)	70.3 (11.4)	64.8 (11.3)	63.1 (13.5)	72.0 (13.3)	-
	p-value	*0.398*	*0.152*	*0.418*	*0.976*	*0.911*	*0.265*	-
	Laparotomies							
	Epidural	76.8 (11.1)	70.5 (10.5)	71.1 (12.6)	71.4 (14.2)	67.1 (14.1)	68.1 (15.2)	83.5 (10.6)
	Conventional	78.9 (14.4)	70.8 (10.9)	67.3 (10.8)	68.7 (12.0)	70.6 (12.7)	74.4 (26.0)	68.0 (21.1)
	p-value	*0.534*	*0.909*	*0.166*	*0.429*	*0.378*	*0.534*	*0.374*

Table 5. Comparison of baseline and intraoperative mean blood pressure across groups

8.4 Need for rescue analgesia

Patients who underwent thoracotomies under conventional analgesia reported significantly higher pain scores with a mean pain score of 50.6 at 12 hours post-surgery compared to their epidural counterparts, mean pain score of 33.6. However, at 24 hours post-surgery, the pain scores were similar between the two groups. In laparotomies, the mean pain sore was significantly higher in patients who underwent conventional analgesia at both 12 hours (mean of 40) and 24 hours (mean of 31.9) (Figure 4).

The need for rescue analgesia was also assessed. Consistent with the observation in pain scores, a greater proportion of patients who underwent conventional thoracotomies needed rescue analgesia compared to epidurals (0% versus 9.1%), (Table 4). For the patients who underwent thoracotomies with epidural analgesia 1 out of 11 needed rescue analgesia, against 7 out of 14 patients who underwent thoracotomies minus epidural analgesia who needed rescue analgesia. There was no statistical significance in need for rescue analgesia for patients undergoing laparotomy between the two modes of analgesia.

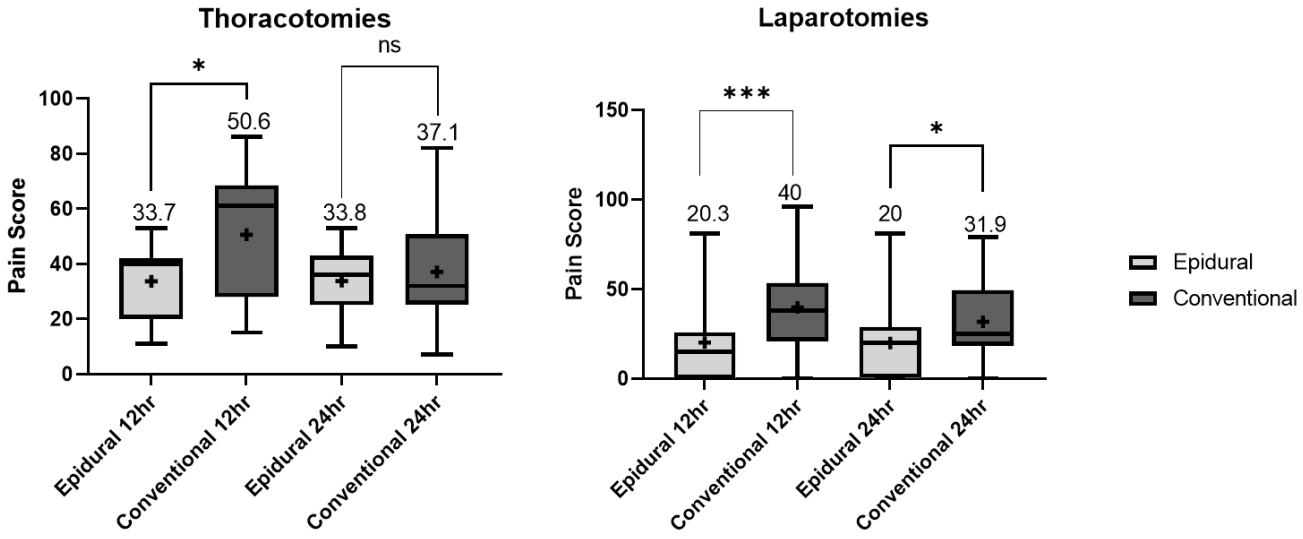

Figure 6. Mean Pain Scores reported in the two major groups

	Thoracotomies			Laparotomies		
Needed Analgesia (12hours)	**Epidural**	**Conventional**	***p***	**Epidural**	**Conventional**	***p***
Yes	1 (9.1%)	7 (50%)	***0.042***	3 (14.3%)	17 (21%)	*0.758*
No	10 (90.9%)	7 (50%)		18 (85.7%)	64 (79%)	
Needed Analgesia (24hours)						
Yes	0 (0%)	3 (21.4%)	*0.23*	2 (9.5%)	8 (10.3%)	*>0.999*
No	11 (100%)	11 (78.6%)		19 (90.5%)	70 (89.7%)	

Table 6. Need for Post-Operative Rescue Analgesia

8.5 Pre- and Post-operative Blood Sugar

No significant differences were observed in pre-operative blood sugar. Thoracic epidural analgesia resulted in significantly higher postoperative blood sugar with a mean of 9.6 compared to conventional analgesia with a mean of 6.1 in those who underwent thoracotomies (Figure 5 and 6). No significant difference in postoperative blood sugars in patients undergoing laparotomies under epidural or conventional mode of analgesia, means of 7.2 and 6.5 respectively.

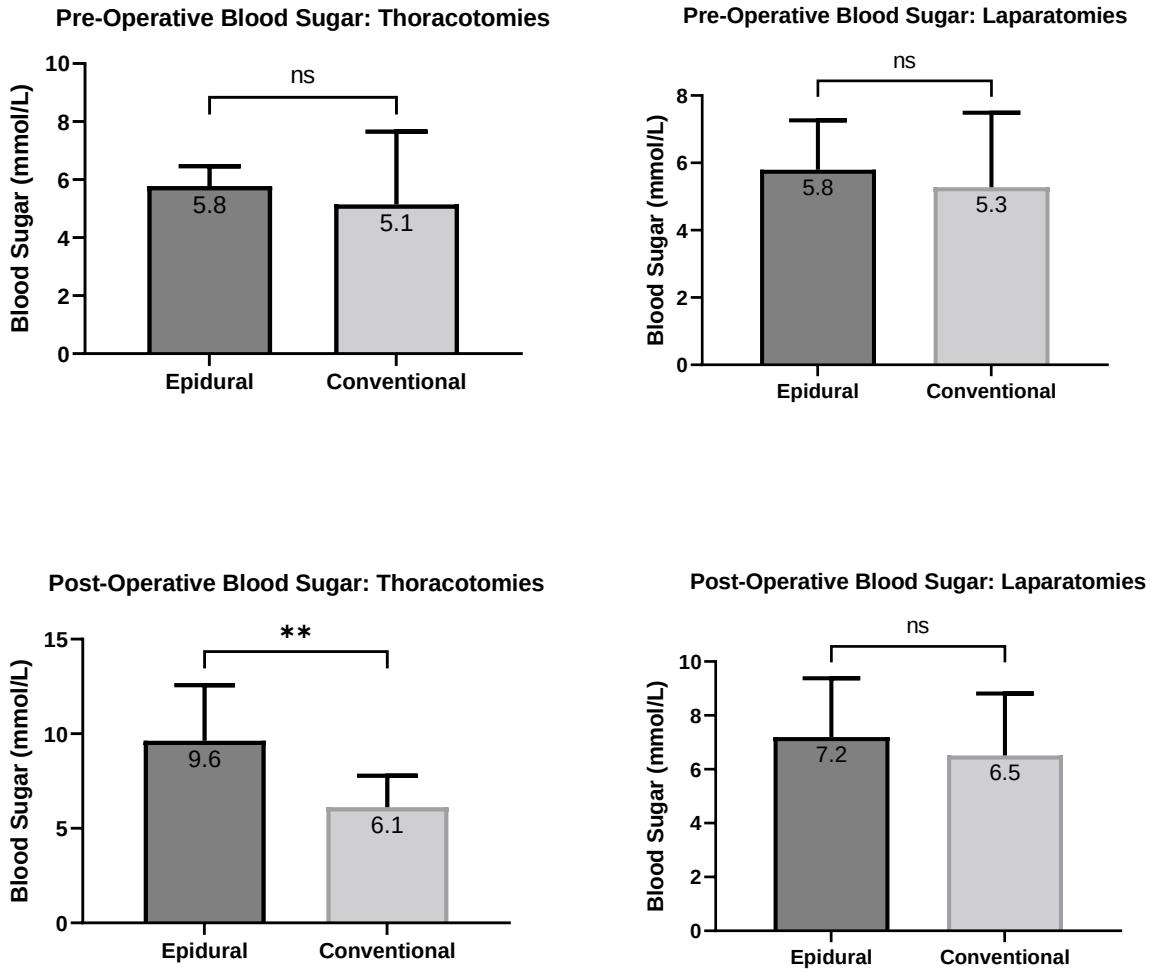

Figure 5. Mean Preoperative and postoperative fasting blood sugar levels between the two main groups.

8.6 Immunological Parameters

Significant increases in total white blood cell and neutrophil count were observed post-operatively in both thoracic and abdominal surgery with epidural or conventional analgesia. Lymphocyte counts were significantly lower post-operatively in epidural augmented thoracotomies and laparotomies. Eosinophil counts were also significantly lower post-surgery in thoracotomy procedures where epidural analgesia was applied.

When comparing epidural versus conventional analgesia in each of the study groups, the post-operative total white blood cell and neutrophil count were significantly higher in thoracotomy patients who had epidural analgesia. However, the lymphocyte and eosinophil count were significantly lower in this group. Similarly, on the laparotomy arm, patients who received epidural analgesia had lower lymphocyte count postoperatively compared to those who received conventional analgesia. These data are summarized in Table 5.

	Pre-Operative	Post-Operative	*p-value*		Pre-Operative	Post-Operative	*p-value*
Total White Blood Cell Count							
Epidural	6.53 (2.44)	16.1 (9.5)	***0.002***	**Epidural**	7.26 (3.77)	10.6 (3.9)	***0.003***
Conventional	6.42 (2.11)	9.98 (3.4)	***0.003***	**Conventional**	7.44 (2.9)	9.63 (2.9)	***<0.001***
p-value	*0.902*	***0.041***		*p-value*	*0.814*	*0.225*	
Neutrophil Count							
Epidural	3.95 (2.06)	14.1 (8.8)	***0.001***	**Epidural**	4.37 (3.2)	8.8 (3.7)	***<0.001***
Conventional	4.35 (2.2)	7.73 (3.8)	***0.006***	**Conventional**	5.84 (10)	8.2 (9.7)	***<0.001***
p-value	*0.649*	***0.028***		*p-value*	*0.507*	*0.775*	
Lymphocyte Count							
Epidural	1.56 (0.8)	0.95 (0.37)	***0.05***	**Epidural**	1.62 (0.65)	1.03 (0.43)	***<0.001***
Conventional	1.53 (0.59)	1.59 (0.65)	*0.621*	**Conventional**	4.5 (22.4)	1.53 (0.64)	*0.238*
p-value	*0.924*	***0.012***		*p-value*	*0.559*	***0.001***	
Monocyte Count							
Epidural	0.69 (0.5)	0.95 (0.8)	*0.089*	**Epidural**	0.60 (0.37)	0.55 (0.24)	*0.635*
Conventional	0.62 (0.34)	0.58 (0.3)	*0.679*	**Conventional**	0.58 (0.26)	0.55 (0.27)	*0.182*
p-value	*0.647*	*0.152*		*p-value*	*0.859*	*0.985*	
Eosinophil Count							
Epidural	0.13 (0.07)	0.02 (0.01)	***<0.001***	**Epidural**	0.18 (0.24)	0.20 (0.29)	*0.265*
Conventional	0.24 (0.55)	0.10 (0.10)	*0.425*	**Conventional**	0.32 (0.67)	0.44 (1.24)	*0.945*
p-value	*0.488*	***0.013***		*p-value*	*0.365*	*0.407*	

Table 7. Comparison of pre-operative and post-operative immune cell counts across study groups

9 DISCUSSION

This study set to establish the effectiveness of the application of epidural analgesia as adjuvant to standard general anaesthetic techniques for thoracotomy and abdominal surgery. In the two hospitals where the study was carried out, the gender, age and differential distribution of disease profile were matched, and no statistical variance was found. Similarly, baseline vital signs were matched for all the groups in which studies and observations were taken. Intraoperative hemodynamics however showed different changes in relationship to procedures and intervention.

No significant changes in heart rate were observed during surgery in patients undergoing thoracotomies and laparotomies whether on epidural or conventional analgesia. This suggests that epidural and conventional multimodal analgesia have no significant difference on the effect of intraoperative heart rate**.** Caputo et al., in a 2011 study demonstrated that thoracic epidural analgesia markedly lowered the incidence of postoperative cardiac arrhythmias and enhanced analgesia[5].

There was a significant drop in blood pressure seen at 150minutes compared to the baseline blood pressure in patients undergoing thoracotomies under both epidurals and conventional multimodal analgesia. This could be explained by significant blood loss witnessed and associated with this type of surgery.

Patients undergoing laparotomies under epidural analgesia had no significant change in systolic blood pressure from the baseline during the entire surgical period. There was significant drop observed with conventional analgesia at 30min, 60min, 90 min and 120 min during laparotomies with a p-value =<0.001(figure 2). Comparison of epidural and conventional analgesia revealed no significant differences on their effect on mean systolic and diastolic blood pressure suggesting that epidural analgesia confer no better intraoperative hemodynamic profile for laparotomy over conventional multimodal forms of analgesia.

Patients undergoing thoracotomies under conventional form of analgesia had a higher mean pain score of 6 at 12-hour postoperative compared to epidural analgesia who had a mean pain score of 4 at 12 hours postoperatively. The mean pain scores were similar (3) at 24 hours post-operative. In participants undergoing laparotomies, the mean pain score (4) was significantly higher in

patients under conventional analgesia at both 12 hours and 24 hours. The need for rescue analgesia was consistent with the observation in pain scores, a greater proportion of patients who underwent thoracotomies under conventional analgesia needed rescue analgesia compared to epidurals. This is consistent with a study by Winter et al. 2010 that postulated that epidural analgesia confers better postoperative pain management on patients under epidural at most times[1].

Post-operative fasting blood sugars were measured on the morning after surgery and compared to preoperative fasting blood sugars, thoracic epidural analgesia resulted in significantly higher postoperative blood sugar compared to conventional multimodal analgesia which is in contrary to a study by Li et al. in 2017 that demonstrated that thoracic epidural analgesia reduced intraoperative and postoperative alterations of glucose metabolisms with a better intraoperative glycemic control compared to conventional modes analgesia[8].

However, this study had no control over the intended therapeutic interventions and hence the choice of fluids and other medications administered to the patients. Sugar levels therefore cannot be used conclusively as surrogates to biochemical profiles influenced primarily by anesthesia and analgesic choices. The different perioperative fluid regimens could have been confounders to the postoperative fasting blood sugar findings.

Previous randomized control trials have demonstrated that thoracic epidural analgesia reduces the stress response and improves postoperative recovery in patients undergoing thoracotomy for esophageal carcinoma[2].

All participants had a blood sample taken for post-operative complete blood count analysis, significant increases in total white blood cell and neutrophil count were observed post-operatively in both thoracotomies and laparotomies whether on epidural or conventional analgesia. These mirror observations seen in abdominal operations under the different modes of analgesia. Although these findings suggest that thoracic epidural analgesia confers no better postoperative immunological outcomes compared to conventional multimodal analgesia, the stress markers used in this study are fairly basic to make an objective conclusion on this factor. Previous more defined and specific studies have showed that extradural analgesia attenuates depression of cytokine production during surgical related stress[12].

10 CONCLUSION

1) Epidural analgesia and conventional multimodal analgesia confer the same intraoperative hemodynamic profile for patients undergoing thoracotomies and laparotomies.
2) Patients undergoing surgery under thoracic epidural analgesia have a significantly better postoperative pain control than those under conventional multimodal analgesics.
3) Epidural analgesia confers no better postoperative attenuation of the immune system and glycemic response in comparison to conventional multimodal form of analgesia.

11 RECOMMENDATIONS

The practice of epidural catheterization for postoperative pain management should be widely adopted in our practice as indicated. A randomized controlled trial, standardizing all intraoperative and postoperative analgesics administered during the surgeries may give a more precise outcome between these two forms of analgesia.

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13 APPENDICES

13.1 Data collection Tool

Physiological and Biochemical Effects of Thoracic Epidural Analgesia in Thoracic and Upper Abdominal Surgery on Perioperative Stress and Morbidity

Serial No: …….

SECTION I: PREOPERATIVE ASSESSMENT

1. Sex …… **2. Age: ……..**

3. Weight ……. (kg) **4. Height (cm)…….**

Comorbidities	**YES**	**NO**
Hypertension		
If yes, on treatment		
Medications……		
Cardiac Disease		
Excluded if severe		
If yes, medications……		
Chronic Kidney Disease		
Smoking		
Alcohol use		
History of Anticoagulation		
If yes, medications……		
Coagulation Disorders		
If Yes, which type……		

History of Spontaneous Bleeding

Active Bacterial Infection……

Complete Blood Count Parameters

White Blood Cell Count……10^9/L

Neutrophil Count ……10^9/L

Lymphocyte Count……10^9/L

Monocyte Count……10^9/L

Eosinophil Count……10^9/L

SECTION II: INTRAOPERATIVE

Preoperative Fasting Blood Sugar …… mmol/L

Baseline Vitals: BP ……mmHg Heart Rate……. b/min

$SP0_2$ ……%

Epidural Placement:

Position Sitting……..…… Lateral Decubitus ……

Local Anaesthetic Infiltration

Type……... Dosage……

Level of Placement……

Difficulty Encountered in Placement?

Explain ……..

Test Dose Administered (60mg 2% Lidocaine + 15mcg epinephrine)

Local Anaesthetic Administered (10mls 0.25% Bupivacaine + 20mcg Fentanyl)

YES NO

Sensory Block

Motor Block

Top Up Dose …….

Time of Top Up ……

Intraoperative Incidences

……

……

……

……

……

Intraoperative Vitals: Intraoperative Anaesthetic Chart

Time

SECTION III: POST OPERATIVE

Post-Operative Fasting Blood Sugar (12 hours post operative)

Fasting Blood Sugar…….mmol/L

Post-Operative Complete Blood Count Parameters

White Blood Cell Count……10^9/L

Neutrophil Count ……10^9/L

Lymphocyte Count……10^9/L

Monocyte Count……10^9/L

Eosinophil Count……10^9/L

Epidural infusion postoperative 4 – 6ml/hour (Bupivacaine 0.1% plus Fentanyl 2mcg/ml)

Post-Operative Duration	**Volume of Infusion Running**
12 Hours Post-Operative	**…….. (ml)**
24 Hours Post-Operative	**…….. (ml)**

VISUAL ANALOGUE SCALE

12 hours Post – Operative

Need for Rescue Analgesia YES NO

Drug Administered ……

24 hours Post Op

Need for Rescue Analgesia YES NO

Drug Administered ……

Post – operative Incidences

……

……

……

……

……

13.2 Study Explanation and Consent Form: English

Physiological and Biochemical Effects of Thoracic Epidural Analgesia in Thoracic and Upper Abdominal Surgery on Perioperative Stress and Morbidity

Principal Investigator:
Dr. Eddy O Mboya

Supervisors:
Dr. Patrick Olang'
Dr. Thomas Chokwe

Background

My name is Eddy Omondi Mboya, a postgraduate student studying Anaesthesia at the University of Nairobi. I am conducting a study on physiological and biochemical effects of thoracic epidural analgesia in thoracic and upper abdominal surgery on perioperative stress and morbidity at the Kenyatta National Hospital.

Purpose

The purpose of this study is to determine changes in heart functions during surgery, quality pain control after surgery, white blood cell changes and glucose levels response to thoracic epidural analgesia post chest surgeries and upper abdominal surgeries.

Study Procedure

This study will be done in three parts and participation will end 24 hours following surgery. Following your consent, you will be asked to fill a questionnaire prior to surgery which is the first part. The second part of the study, if in the epidural arm of the study, will involve placement of a thoracic epidural catheter then surgery shall be done, and intraoperative heart rate and blood pressure shall be monitored as is the standard practice. If in the conventional analgesia arm, you will undergo surgery as indicated and all prescribed medications will be administered as standard practice. The third part will be done while in the ward within 24 hours postoperatively will involve fasting blood glucose monitoring, blood sampling for a full haemogram and you'll be asked questions on your pain intensity.

Role of the Participant

Your role in the study is to fill the questionnaire and to rate pain on a validated pain scale. Other information pertinent to the study will be taken from your anaesthesia record chart by a trained research assistant during the second part of the study in the recovery room.

Participation

You will be welcomed to participate in the study after the information regarding the study has been explained to you. After this, you will be asked to sign the consent form. Epidural catheterization for anaesthesia administration is a standard practice at our facility and your involvement in the study will facilitate us in determining its effects on the body and possible superiority over other forms of pain control. Participation is entirely voluntary, and you have the right to withdraw from the study at any time without consequence in your treatment plan. You will not incur any extra cost due to participation in this study other than the usual cost of care at the Kenyatta National Hospital. There will be no financial gain or benefits from participation. Any extra cost incurred in the study will be met by the principal investigator.

Risks of participation

Minimal risk and discomfort, outside of the nature of your treatment, will be experienced by participating in the study. Your planned treatment will not be affected. There's a risk of transient post - operative right upper limb weakness because of the epidural. This wears off spontaneously with no major disabilities.

Confidentiality

We will keep your identity as a research subject confidential. Your responses to questions will be kept private. We will not publish or discuss in public anything that could identify you, any patient identifiers will be omitted from the study. All the information obtained will be handled with respect and confidentiality.

Sharing of results

The results obtained from this study will be shared during the departmental presentation of results and other relevant platforms. Any publication of this study will not use your name or identify you personally.

Questions and Concerns

For any other questions, enquires or concerns, you may contact me or my supervisors on the following: -

Mobile: 0721332639/073555603

Email: emboya@students.uonbi.ac.ke or eddymboya@gmail.com

Or:

Dr Patrick Olang'

Telephone No: +254722523116

Email: patrick.olang@uonbi.ac.ke or olangpatrick@gmail.com

Or:

Dr Thomas Chokwe

Telephone No: +254722528237

Email: chokwe@uonbi.ac.ke or tmchokwe@gmail.com

Or:

Kenyatta National Hospital- University of Nairobi Ethics Review Committee

Telephone number: 2726300 ext. 44102

Email: uonknh_erc@uonbi.ac.ke

CONSENT FORM

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with the principal researcher/ research assistant. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me.

I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree to participate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential.

By signing this consent form, I have not given up any of the legal rights that I have as a participant in a research study.

Participant's printed Name: _____

Participant Signature / Thumb stamp _____

Date _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name: _____

Date: _____

Signature _____

Role in the study: _____

13.3 Study Explanation and Consent Form: Swahili

Utafiti Wa Athari Za Kimwili Na Za Kibayologia Katika Matumizi Ya Kifaa Cha Epidural Kwa Kudhibiti Maumivu Wakati Wa Upasuaji Wa Kifua Na Sehemu Ya Juu Ya Tumbo

Mchunguzi Mkuu:
Dk Eddy Omondi Mboya

Wasimamizi:
Dk Patrick Olang'
Dk Thomas Chokwe
Usuli

Jina langu ni Eddy Omondi Mboya, mwanafunzi wa uzamili anayesoma Anesthesia katika Chuo Kikuu cha Nairobi. Ninafanya utafiti juu ya athari za kibayologia na kemikali katika matumizi ya kifaa cha epidural kwa upasuaji wa kifua na sehemu ya juu ya tumbo na athari ya kwa mafadhaiko ya muda mrefu na ugonjwa katika Hospitali ya Kitaifa ya Kenyatta.

Kusudi

Madhumuni ya utafiti huu ni kuchunguza majibu ya moyo wakati wa upasuaji, ubora wa kudhibiti maumivu baada ya upasuaji, majibu ya kipengee ya damu na sukari baada ya matumizi ya kifaa cha epidural kwa kudhibiti uchungu wakati wa upasuaji wa kifua na upasuaji wa juu wa tumbo.

Utaratibu wa Utafiti

Utafiti huu utafanyika katika sehemu tatu na ushiriki utamalizika masaa 24 kufuatia upasuaji. Kufuatia idhini yako, utaulizwa kujaza dodoso kabla ya upasuaji ambayo ni sehemu ya kwanza. Sehemu ya pili ya utafiti itahusisha kuwekwa kwa kifaa cha epidural kwa kifua kisha upasuaji utafanyika. Shinikizo na kiwango cha moyo wakati wa upasuaji kitafuatiliwa kawaida. Sehemu ya tatu itafanywa ukiwa wadini ndani ya masaa 24 baada ya upasuaji itajumuisha ufuatiliaji wa sukari ya damu, sampuli ya damu wa kuchunguza kipengee ya damu kamili na utaulizwa maswali juu ya maumivu yako.

Wajibu wa Mshiriki

Jukumu lako katika utafiti ni kujibu dodoso na kupima maumivu kwa kiwango cha maumivu kilichothibitishwa. Habari zingine zinazohusiana na utafiti zitachukuliwa kutoka kwa chati yako

ya kumbukumbu ya anesthesia na msaidizi wa utafiti aliyefundishwa wakati wa sehemu ya pili ya utafiti kwenye chumba cha kupona.

Ushiriki

Utakaribishwa kushiriki katika utafiti baada ya kuelezewa habari kuhusu utafiti huo. Baada ya haya, utaulizwa kusaini fomu ya idhini. Kushiriki ni kwa hiari kabisa na una haki ya kujiondoa kwenye utafiti wakati wowote bila matokeo katika mpango wako wa matibabu. Hautapata gharama yoyote ya ziada kwa sababu ya kushiriki katika utafiti huu isipokuwa gharama ya kawaida ya utunzaji katika Hospitali ya Kitaifa ya Kenyatta. Hakutakuwa na faida ya kifedha au faida kutoka kwa ushiriki.

Hatari za kushiriki

Hatari ndogo na usumbufu, nje ya asili ya matibabu yako, utapata uzoefu kwa kushiriki kwenye utafiti. Matibabu yako uliyopanga hayataathiriwa.

Usiri

Tutatunza utambulisho wako kama mmoja ya watu utafiti. Majibu yako kwa maswali yatawekwa faragha. Hatutachapisha au kujadili hadharani chochote kinachoweza kukutambulisha, vitambulisho vyovyote vya mgonjwa vitaondolewa kwenye utafiti. Habari zote zilizopatikana zitashughulikiwa kwa heshima na usiri.

Kushiriki matokeo

Matokeo yaliyopatikana kutoka kwa utafiti huu yatashirikiwa wakati wa uwasilishaji wa matokeo wa idara na majukwaa mengine muhimu. Uchapishaji wowote wa utafiti huu hautatumia jina lako au kukutambulisha kibinafsi.

Maswali na wasiwasi

Kwa maswali mengine yoyote, kuuliza au wasiwasi, unaweza kuwasiliana nami kwa yafuatayo: -

Simu ya Rununu : 0721332639/073555603

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FOMU YA IDHINI

Nimesoma fomu hii ya idhini/nimesomewa habari kwenye hii fomu ya idhini. Nimekuwa na fursa ya kujadili kuhusu utafiti huu na mtafiti mkuu/ mtafiti masidizi. Maswali yangu yamejibiwa kwa lugha ambayo ninaelewa. Nimeelezewa athari na manufaa ya kushiriki. Ninaelewa kuwa kushiriki kwangu katika utafiti huu ni kwa hiari yangu na ninaweza amua kujiondoa wakati wowote. Ninakubali bila kulazimishwa kushiriki kwenye utafiti huu. Ninaelewa kwamba juhudi zote zitafanywa ili kuweka siri habari zinazonihusu. Kwa kutia sahihi kwenye hii fomu ya idhini, sijajiondolea haki zangu za kisheria ambazo ninazo kama mshiriki katika huu utafiti.

Jina la mshiriki lililochapishwa_____

Sahihi ya mshiriki / kidole gumba _____ Tarehe_____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher 's Name: _____

Date: _____

Signature _____

Role in the study: _____