Serratus Anterior Plane Blocks: Effectiveness in the management of pain associated with multiple traumatic rib fractures.

Dr Laura Beard
MBChB, FRCA, PGCME, EDRA

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Institute of Inflammation and Ageing
College of Medical and Dental Sciences,
The University of Birmingham

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ABSTRACT OF RESEARCH

Background

Patients with multiple rib fractures are at significant risk of respiratory complications such as pneumonia if their pain is not controlled. Regional analgesia with thoracic epidural is seen as the optimal method, but its use is limited to between 3% and 18.4% of patients. Opioids despite causing respiratory depression and sedation still dominate [1-5].

Serratus anterior plane blocks (SAP) with their ease of insertion, haemodynamic stability and perceived safety, are increasing in popularity; however, conclusive evidence for their use in rib fractures is lacking[6]. This research aims to understand better the role of SAP analgesia in patients with traumatic rib fractures.

Objectives

(i) Improve understanding of the mechanisms by which SAP blocks produce analgesia in patients with rib fractures.

(ii) Assess the clinical effectiveness and safety of SAP analgesia.

(iii) Evaluate the impact of SAP analgesia on patient outcomes.

Methods

To answer these questions, the thesis is split into:-

a) A systematic review of existing literature,

b) A cadaveric study

c) Propensity matched retrospective studies comparing SAP analgesia to thoracic epidural, paravertebral catheters, and opioid medication.

Results

A review of the literature and the findings of the studies presented in this thesis support the opinion that SAP analgesia is a safe technique that improves analgesia and respiratory mechanics in patients with multiple rib fractures.

Words: 215

DEDICATIONS

This thesis is dedicated to my family. Without their support I would not have been able to complete this body of work. I am extremely grateful to my sister, Emma for her time and unparalleled knowledge of medical statistics. Thank you to my husband, Luke and parents Edward and Maryann for giving me the time and space to concentrate on this thesis. Finally, thank you to my daughter Clara who was born half-way though my research time and provided the motivation and inspiration to continue.

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LIST OF PUBLICATIONS

1. Beard L, Hillermann C, Gao Smith F et al. Response to letter: 'Serratus anterior plane block for posterior rib fractures: why and when it may work?'. Regional Anesthesia and Pain Medicine. 2021;46:836.

2. Beard L, Hillermann C, Beard E*, et al* Multicenter longitudinal cross-sectional study comparing effectiveness of serratus anterior plane, paravertebral and thoracic epidural for the analgesia of multiple rib fractures *Regional Anesthesia & Pain Medicine* 2020;**45:**351-356.

3. Beard L, Holt B, Snelson C, Parcha C, Smith FG, Veenith T. Analgesia of Patients with Multiple Rib Fractures in Critical Care: A Survey of Healthcare Professionals in the UK. Indian J Crit Care Med 2020; 24 (3):184-189.

4. Manning N, Beard L, Snelson C, *et al.* 0331 Impact of Advanced Critical Care Practitioner led analgesia service in Critical Care Unit patients after multiple rib fractures. Journal of the Intensive Care Society 2020, Vol. 21(2) Supplement 1–225.

5. Beard L, Hillermann C, Beard E*, et al* ESRA19-0333 A multicentre observational study comparing the effectiveness of serratus anterior plane catheters against paravertebral and epidural analgesia in patients with multiple RIB fractures *Regional Anesthesia & Pain Medicine* 2019;**44:**A105-A106.

6. Beard L, Edwards C, ESRA19-0329 Use of pythagorean theorem to optimise needle length selection for in-plane ultrasound guided approaches to regional anaesthesia *Regional Anesthesia & Pain Medicine* 2019;**44:**A201-A202.

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STATEMENT OF CONTRIBUTIONS

CHAPTER 3:

How does the insertion of two serratus anterior plane catheters, one directed more posteriomedially affect injectate spread across the hemithorax: a cadaveric study

I was first author on this article currently in the process of journal submission. My role extended from methodology, undertaking SAP catheter insertion in the cadavers, interpretation and measurement of the CT images, data analysis and main author for all sections. R Sachdeva a Consultant Anaesthetist assisted with the insertion of SAP catheters and appraised the article prior to submission. S Ramalingham, a Consultant Radiologist offered his opinion and advice on how to best interpret the CT images using a standardised approach. He appraised the article prior to submission and offered comments on the methodology and results. Professor Tunstall, academic lead for clinical anatomy & imaging supported the performance and ethical approval for the cadaveric insertion of SAP catheters. He appraised the article prior to submission and offered comments on the introduction, methodology and discussion. Dr Whitehouse a consultant intensivist appraised the article prior to submission and offered comments on the introduction and discussion sections. Professor Fang Gao Smith appraised the article prior to submission and offered comments on the introduction and discussion sections. Professor T Veenith advised on the methodology before undertaking the project. He also appraised the article prior to submission and offered comments on all sections.

CHAPTER 4:

Effectiveness of serratus anterior plane catheters compared with opioid only analgesia in patients with multiple traumatic rib fractures admitted to critical care.

I devised the methodology, undertook data collection, ran the statistical syntax in R Studio, analysed the results and authored the article. Dr E Beard, a statistician offered advice on the best statistical tests and assisted in the statistical analysis, providing syntax for the propensity matching and adjustments. Data collection was supported by a small team of medical students and junior doctors using a standardised collection form. (Henry Gibbons, Amy Newnham, Priya Ramesh, Sophie Winter, Catherine Railton, Alice Oatham, Kate McMurrugh, Oliver Williams).

CHAPTER 5:

A multi-centre longitudinal cross-sectional study comparing serratus anterior plane, paravertebral and thoracic epidural for the analgesia of multiple rib fractures.

I devised the methodology, collected data for one site, analysed the results, undertook statistical analysis not involving regression/adjustment and was first author for all sections. Dr Hillermann and S Millerchip provided the data for site 2 and reviewed the article prior to submission offering comments on the introduction, results, and discussion. Dr E Beard advised on the statistical tests and undertook the regression statical tests, she reviewed the article prior to submission and offered comments on the methodology and results. Dr R Sachdeva, Professor Fang Gao Smith and Professor T Veenith reviewed the article prior to submission offering comments on all sections.

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LIST OF ABBREVIATIONS

ACCP	Advanced Critical Care Practitioner
ADL	Activities of Daily Living
AIS	Abbreviated injury score
ARDS	Acute respiratory distress syndrome
ASA	American Society of Anaesthetists
BCTU	Birmingham Clinical Trial Unit
CARMS	Clinical Audit and Risk Management Service
CCI	Charlson Comorbidity Index
CI	Confidence Interval
CPAP	Continuous positive airway pressure
CPIS	Clinical Pulmonary Infection Score
CQC	Care Quality Commission
CT	Computerised tomography
CTPA	Computerised tomography pulmonary angiogram
EAST	Eastern Association for the Surgery of Trauma
EPOC	European Perioperative Clinical Outcome
ERASER	Early Rib Fracture Analgesia with Serratus Block
ESP	Erector spinae plane
FIO_2	Fraction of inspired oxygen
GABA	g-aminobutyric acid
HDU	High dependency unit
INR	International normalised ratio
IQR	Interquartile range
IRR	Incidence rate ratio
ISS	Injury severity score
ITU	Intensive care unit
IV	Intravenous
IVI	Intravenous infusion
LAST	Local anaesthetic systemic toxicity
LOS	Length of stay
LOSCC	Length of stay in Critical Care
MDT	Multidisciplinary Team
MECIR	Methodological Expectations of Cochrane Intervention Reviews
MESH	Medical Subject Headings
MPR	Multi-planar reconstruction
MRC	Medical Research Council
MRF	Multiple rib fracture
MTC	Major Trauma Center
MTL	Mid-thoracic line
MTS	Major trauma service
NIAA	The National Institute of Academic Anaesthesia

NIHR	National Institute for Health and Care Research
NMDA	N-methyl-D-aspartate
NRS	Numerical rating scale
NSAID	Non-steroidal anti-inflammatory drugs
OME	Oral morphine equivalent
PA	Paravertebral Analgesia
PAL	Posterior Axillary Line
PCA	Patient controlled analgesia
PEC	Pectoral
PONV	Post operative nausea and vomiting
PPI	Patient and public involvement
PROMS	Patient reported outcome measures
PA	Paravertebral analgesia
PVB	Paravertebral block
PVS	Paravertebral Space
QOL	Quality of life
RCOA	Royal College of Anaesthetists
RCT	Randomised controlled trial
RFS	Rib fracture score
RR	Respiratory rate
RTC	Road traffic collision
SAP	Serratus anterior plane
SMD	Standardised absolute mean difference
TARN	Trauma Audit and Research Network
TEA	Thoracic epidural analgesia
TPVB	Thoracic paravertebral block
VAS	Visual analogue scale
VATS	Video Assisted Thoracoscopic Surgery
VRS	Verbal Response Score

CHAPTER ONE:

INTRODUCTION

Rib fractures resulting from trauma are a major cause of morbidity and mortality worldwide. They cause significant pain along with altered breathing mechanics and damage to the underlying lung. These predispose the patient to develop respiratory failure and pneumonia which may result in the need for intensive care treatment with invasive ventilation and even death. Optimum pain management is essential in the treating of patients with rib fractures to help them breathe deeply, cough and mobilise. However, analgesia can be challenging to obtain, due to a multitude of issues such as limitations of the current analgesic techniques, patient factors and practitioner skill level. This thesis will investigate a novel type of pain relief, the serratus anterior plane block and evaluate its safety, mechanism of action and effectiveness in patients who have experienced rib fractures following trauma.

BLUNT THORACIC TRAUMA

The most common cause of rib fractures is blunt force trauma, where the rapid transfer of energy through acceleration and deceleration forces produces injury. This energy transfer's magnitude and orientation and patient factors such as osteopenia determine the injury pattern and severity [7]. Most blunt trauma is a result of road traffic collisions or falls from height. Rib fractures are present in 10% of all patients presenting to the hospital following blunt trauma, and 90% of these patients will have associated injuries[1]. Trauma is the leading cause of death in patients under the age of 40 years[8].

Other causes of rib fractures include penetrating trauma, commonly a result of stabbing or shooting injuries, stress fractures from repetitive use and pathological rib fractures which occur in the presence of minimal trauma but where the patient's bone strength is severely weakened.[9] Penetrating trauma, stress fractures and pathological rib fractures will not be examined in this thesis due to their rarer occurrence and differing impact on underlying lung trauma and patient outcome.

There are many different types of rib fracture pattern that occur as a result of blunt force thoracic trauma:-

Single versus multiple

Fractures can occur in either a single rib or in multiple ribs. The more ribs that are broken the greater the impact this will have on a patient's pain and respiratory mechanics.

Unilateral versus bilateral

Broken ribs can occur on just one side of the chest (unilateral) or on both sides (bilateral). Bilateral fractures are often a marker of greater energy transfer.

Displaced versus non-displaced

Displacement describes where one part of the broken rib is pushed inwards or outwards. In severely displaced fractures there is loss of contact between the distal and proximal segments which can impact breathing mechanics [1].

Flail segments

This is where three or more consecutive ribs are broken in at least two places.[1] The unsecured segments of the ribs move with respiration, further accentuating underlying lung injury.

Anterior, lateral and posterior

The location of the rib fracture in the thorax can be described radiologically or via anatomical landmarks. Radiologically, the posterior segment is from the head of the rib to the costal angle, lateral segment from the costal angle to the serratus anterior insertion tubercle and anterior segment from the serratus anterior insertion tubercle to the distal rib [1]. Anatomically the anterior section is from the costal cartilage to anterior axillary line, lateral section from the anterior axillary line to angle of the rib and posterior section from the angle of the rib to the head of the rib[10]. See Figure 1.

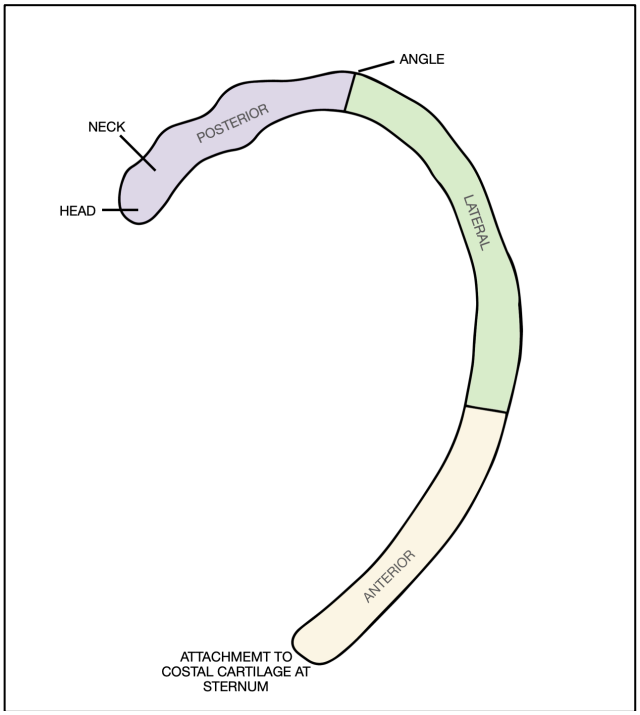


Figure 1 Anterior (yellow), lateral (green) and posterior (purple) anatomical sections of the rib

The different descriptions for rib fractures illustrate the broad spectrum of injury patterns that arise, ranging from the mildest, an isolated single rib fracture to its most severe, a bilateral flail chest. The presence of rib fractures following trauma can, therefore, be viewed as a marker of injury severity[1]

Many different scoring systems exist to try and categorise the severity of the rib fracture pattern and the impact that this might have on patient outcomes. The most commonly used scoring system used in the UK is the rib fracture score (RFS)[9]. It is composed of the number of breaks in the bone, if the fractures are unilateral or bilateral and the patients age (Figure 2).

Rib Fracture Score (RFS) = (Breaks x Sides) + Age Factor

Breaks:	Number of fractures
Sides:	Unilateral = 1 Bilateral = 2
Age Factor:	
	0 = ≤50 years 1 = 51-60 years 2 = 61-70 years 3 = 71-80 years 4 = ≥ 81 years

Figure 2 Rib Fracture Score (RFS)

COMPLICATIONS ASSOCIATED WITH RIB FRACTURES

Respiratory complications (see Table 1) occur due to the initial primary injury or a consequence of secondary insults. The primary injury results in lung trauma e.g. contusions, lacerations and lung collapse (atelectasis) due to pneumo and haemothoraces. Altered breathing mechanics are seen in the presence of multiple displaced rib fractures and flail segments. Secondary insults are typically present 48-72 hours after the primary injury and result from inadequate

respiration, sputum clearance and immobilisation. It is impossible to reverse the primary insult, but pre-emptive and effective analgesia can help reduce secondary lung injury[9].

RESPIRATORY COMPLICATION	DEFINITION
Respiratory infection	Antibiotics required, new or changed sputum, new or changed lung opacities, fever, raised white blood cell count (EPCO definition)
Respiratory failure	Pa_{O2} <8Kpa on room air Pa_{O2}:Fi_{O2} ratio <40kpa Arterial saturation <90% (EPOC definition)
Pleural effusion	Chest radiograph with blunting of the costophrenic angle in upright position. (EPOC definition)
Atelectasis	Lung opacification with mediastinal shift, hilum or hemidiaphragm shift towards the affected area with compensatory hyperinflation on chest radiograph. (EPOC definition)
Pneumothorax	Air in the pleural space on chest radiograph. (EPOC definition)
Pneumonia	Multiple definitions exist in the literature many state the presence of radiological changes on the chest radiograph and requirement for antibiotic therapy.
ARDS	Bilateral chest infiltrates on chest radiograph Pa_{O2}:Fi_{O2} < 300
Pulmonary embolism	Identified on computed tomography pulmonary angiogram (CTPA)
Death	

Table 1 Respiratory complications and their common definition in the literature. EPOC = European Perioperative Clinical Outcome.[14][11]

When the rib fracture moves during respiration, on coughing or movement the pain this produces causes the patient to limit their tidal volumes, resulting in hypoventilation and subsequent lung atelectasis. Avoidance of deep breathing, coughing and immobilisation encourages the retention of secretions predisposing the patient to pneumonia. Atelectasis and pneumonia reduce the compliance of the lungs and result in intrapulmonary shunting causing

hypoxia. A consequence of hypoventilation and hypoxia is respiratory failure that initially requires supplemental oxygen. However, in some cases the respiratory failure is severe enough to require non-invasive ventilation, known as continuous positive airway pressure (CPAP). When this is inadequate invasive ventilation requiring intubation and sedation is necessary [9, 12-14].

33% of patients will develop respiratory complications and 50% will require intensive care treatment with ventilatory support during their hospital admission [1]. Mortality ranges from 10-22% in hospitalised patients. Mortality and length of hospital stay are higher amongst the elderly despite lower median Injury Severity Scores (ISS) compared to their younger counterparts.[15] Other factors associated with increased morbidity and mortality include an increasing number of rib fractures, flail segments, bilateral rib fractures, pulmonary contusions, pneumonia, polytrauma and pre-existing comorbidities[1, 16]. Up to 31% of patients with multiple rib fractures will develop pneumonia, which is associated with nearly four times the odds of mortality than those who do not [17]. Aggressive analgesia and physiotherapy treatments are therefore vital in this high-risk cohort to reduce the risk of respiratory deterioration, complications, and death.

PAIN MANAGEMENT

Management of pain for rib fractures is challenging. Traditional pain relief strategies that include patient controlled intravenous analgesia (PCA) with morphine, thoracic epidural (TEA) and paravertebral analgesia (PVB) may not be suitable for all patients due to injury factors, side effects, contraindications, and staff skill mix. The limitations of these traditional methods have

led to the rapid uptake of novel fascial plane blocks such as the serratus anterior plane block (SAP) which is thought to be associated with fewer contraindications and side effects.

PHARMACOLOGICAL	INTERVENTIONAL	SURGICAL
Paracetamol and Non-Steroidal analgesia (NSAIDs)	Thoracic Epidural	Rib Fixation
Codeine, Tramadol, Oramorph (Oral Opioids)	Paravertebral Catheters	
Morphine boluses, continuous infusions and patient-controlled regimes (PCA)	Inter Pleural Analgesia	
Pregabalin and Gabapentin (Neuropathic Agents)	Intercostal Nerve Blocks	
Ketamine infusions		
Local anaesthetic patches and infusions		

Table 2 Traditional pain relief strategies for rib fractures

Traditional pain relief strategies utilise pharmacological, interventional, and surgical treatments (Table 2) to break the triad of pain, altered breathing mechanics and secondary lung injury associated with multiple rib fractures (See Figure 3).

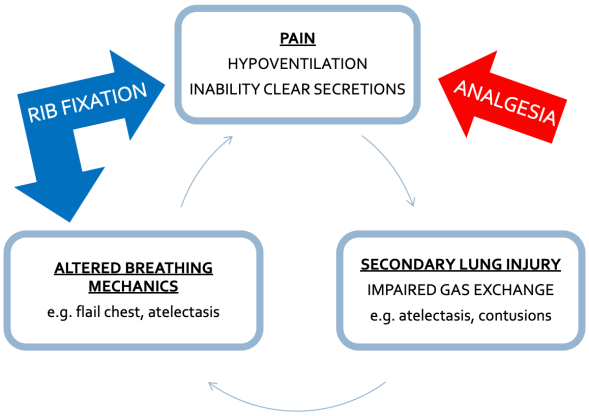


Figure 3 Triad of pain, secondary lung injury and altered breathing mechanics associated with multiple rib fractures and the impact of analgesia and surgical rib fixation.

Pharmacological analgesic options are escalated in a stepwise approach. With simple analgesics such as paracetamol and non-steroidals in selected patients started first. Some form of oral

opioid is often required either regular codeine and/or oramorph, a form of liquid morphine. For patients whose pain is still not optimally controlled intravenous opiates in the form of a PCA is required where the patient has control of their analgesia with a hand pump that administers the drug [9]. Neuropathic agents and local anaesthetic patches can also be used but the evidence for their use is limited[18, 19]. Intravenous infusions of morphine, ketamine and lidocaine represent the highest point of escalation of pharmacological methods and need to be administered in the High Dependency (HDU) or intensive Care setting (ITU).

Pharmacological methods should be administered promptly and are the mainstay of analgesic treatment due to their ease of administration. However, they are associated with side effects. Non-steroidal medications (NSAIDS) reversibly inhibit the cyclo-oxygenase enzymes (COX1 and COX 2) which is also responsible for the side effects of renal impairment, thrombotic events and platelet dysfunction meaning they are not appropriate for all patients, especially the elderly [20].

Opioid based medications activate opioid receptors that are coupled with inhibitory G-proteins located throughout the central nervous system. There are four types of opioid receptor; Mu, Kappa, Delta and Nociceptin. Their activation reduces the transmission of pain impulses. Commonly used opioids include codeine, tramadol and morphine. Their side effects include sedation, hallucinations, bradycardia, respiratory depression, cough suppression, nausea and vomiting and constipation[9, 21]. These side effects are at odds to the goal of optimising respiratory function in patients with rib fractures.

Ketamine is a dissociative anaesthetic agent that exerts its effect by non-competitive N-methyl-D-asparate (NMDA) antagonism reducing the presynaptic release of the excitatory neurotransmitter glutamate[22]. Ketamine exhibits analgesic properties when used as a low dose infusion. It needs to be administered in a high care setting due to the risk of respiratory depression. Side effects include nausea and vomiting, hypertension and delirium [23].

Lidocaine patches are applied topically at the site of the fracture. Lidocaine is absorbed transdermal and blocks neuronal cell membrane voltage gated sodium channels, preventing signal conduction in proximity nerves. Intravenous lidocaine has both analgesic and anti-inflammatory actions. It is considered a 'high risk' analgesic option due to central nervous system toxicity occurring at plasma levels marginally higher than therapeutic levels. It is for this reason that patient's receiving lidocaine infusions need to be carefully selected and be closely monitored in a high dependency or intensive care setting for features of local anaesthetic systemic toxicity (LAST).[24]

Gabapentin and Pregabalin are the most used neuropathic agents. Gabapentin was first used as an anticonvulsant, it is a structural analogue of γ-aminobutyric acid (GABA), a neurotransmitter. Gabapentin's analgesic effect is from its inhibition of voltage gated calcium channels reducing neurotransmitter release, neuronal excitability and pain transmission[25]. Recent studies in patients with rib fractures show no significant reduction in pain score, opioid consumption, oxygen requirement or respiratory rate with gabapentin use.[18, 19]

Used in isolation, paracetamol, non-steroidal (NSAIDs) and neuropathic agents are often insufficient. A multimodal approach with a combination of oral and intravenous agents including opiates is therefore required. Interventional and surgical techniques are important to limit the side effects seen with escalating doses of oral and intravenous analgesics.

Multidisciplinary analgesic pathways coordinating input from clinicians, surgeons, physiotherapist's and acute pain teams can assist with the choice of analgesic agent and ensure rapid escalation from pharmacological to interventional and surgical methods for those with the most severe injuries[9].

Protocolised clinical pathways that target pain-control services to high-risk trauma patients and reduce inter-clinician variability have been shown to decrease rib fracture–associated morbidity and mortality[26]. Our survey of healthcare professionals with an interest in acute pain management of thoracic trauma showed that pain control is reported to be better handled when pain protocols are present (Appendix 2)[27].

REGIONAL ANAESTHETIC TECHNIQUES

Regional anaesthesia describes the technique whereby local anaesthetic agents are deposited directly around nerves or in fascial planes where the nerves are in proximity, with the aim of stopping nociceptive signal transmission. Regional anaesthesia can be in the form of single shot block where long last local anaesthetic agents such as bupivacaine can provide analgesia for between 8-16hours[28] or with the insertion of a catheter where local anaesthesia is infused for several days.

Traditional regional anaesthetic techniques for patients with rib fractures include (Figure 4):-

1. Thoracic Epidural Analgesia (TEA)
2. Thoracic Paravertebral Block (PVB)
3. Intercostal nerve blocks
4. Pleural Blocks

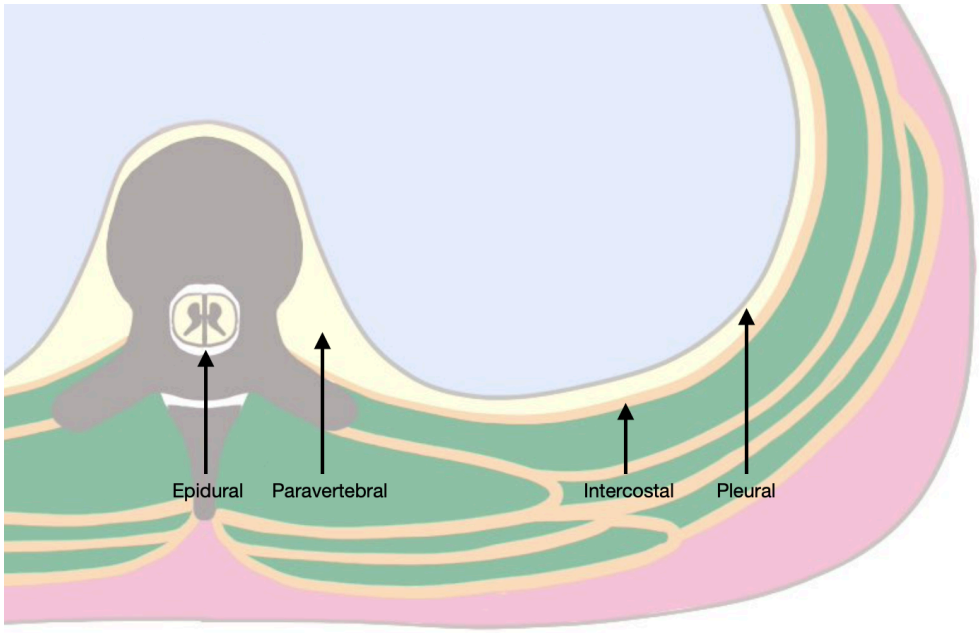


Figure 4 Transverse section of the thorax with the anatomical locations marked for the different regional anaesthetic techniques of epidural, paravertebral, intercostal and pleural blocks.

1. THOACIC EPIDURAL ANALGESIA

In this method of analgesia, a catheter is inserted into the epidural space using a curved blunt needle called a Tuohy needle. The operator feels a loss of resistance when the tough ligamentum flavum is pierced and the needle enters the epidural space (figure 5). The epidural space lies outside of the dura which encapsulates the spinal cord and cerebral spinal fluid. When local anaesthetic is injected into the epidural space the spinal nerve roots and sympathetic preganglionic fibres (T1-L2) that transverse this space are blocked and nerve

transmission halted. Epidural analgesia produces a bilateral block, the number of dermatomes covered depends on the level of insertion and volume of local anaesthetic administered[29].

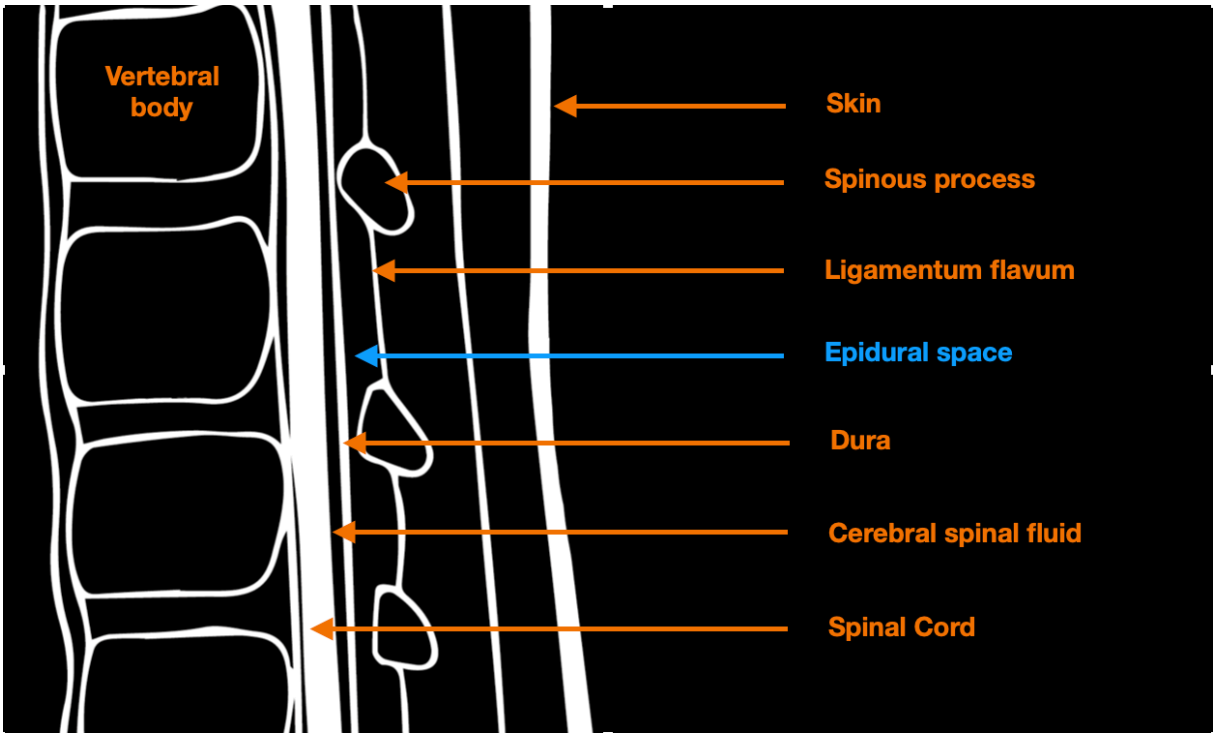


Figure 5 Sagittal cross section showing the different anatomical structures related to epidural insertion.

Thoracic epidural insertion is considered an advanced skill and only inserted by experienced anaesthetists. This is because of the complications that can occur during and after insertion which includes dural puncture, neurological damage, epidural haematoma, epidural abscess and haemodynamic instability[30]. Haemodynamic instability is a result of sympathetic block which causes vasodilatation of blood vessels resulting in a drop in blood pressure which is more pronounced in those that are hypovolaemic. Bradycardia occurs if the cardioaccelerator fibres (T1-T4) are blocked. It is for this reason that a thoracic epidural block height should not exceed the T4 dermatomal level, making epidural analgesia less suitable for patients with high level rib fractures.

Due to the insertion of the epidural close to the spinal cord there are several important contraindications to insertion which includes: patient refusal, spinal cord injury, coagulopathy (platelets <50-80x10^9 $litre^{-1}$, INR >1.4), local infection or sepsis, severe traumatic brain injury, unstable spinal fractures, hypotension, and hypovolaemia. To insert an epidural, the patient must be sitting or in the lateral position, this may not be possible in patients with multiple traumatic injuries[9].

Other limitations to epidural insertion include post procedure monitoring. This needs to be performed on wards or high dependency settings where observations and block height can be checked regularly, and any complications identified and acted on early.

A survey of clinicians working in UK trauma units with an interest in MRF management identified that although thoracic epidurals are favoured by physicians they can be of limited use in this cohort because of contraindications, time pressures, and staff skill mix. This published survey was undertaken in support of this thesis see, Appendix 2 [31].

2. THORACIC PARAVERTEBRAL ANALGESIA

Paravertebral analgesia is also considered an advanced skill performed only by experienced anaesthetists. This is again due to the proximity of neuraxial structures which means the same contraindications, positioning requirements and post procedural monitoring apply as for an epidural insertion. In addition, the lung pleura is in close proximity which if pierced can cause a

pneumothorax. Development of a pneumothorax can result in cardiorespiratory instability which requires decompression and chest drain insertion.

The paravertebral space is a wedge-shaped cavity that extends from the 1st to 12th thoracic vertebrae and is bound by the vertebral bodies, parietal pleura and the costotransverse ligament. Paravertebral analgesia is performed either by landmark methods where a loss of resistance is felt as the Tuohy needle pierces the costotransverse ligament and the paravertebral space is entered or under direct ultrasound guidance. (See Figure 6)

The insertion of a multi-holed catheter for both epidural and paravertebral analgesia allows the continuous infusion of local anaesthesia, usually for a maximum of 3-5 days[32, 33].

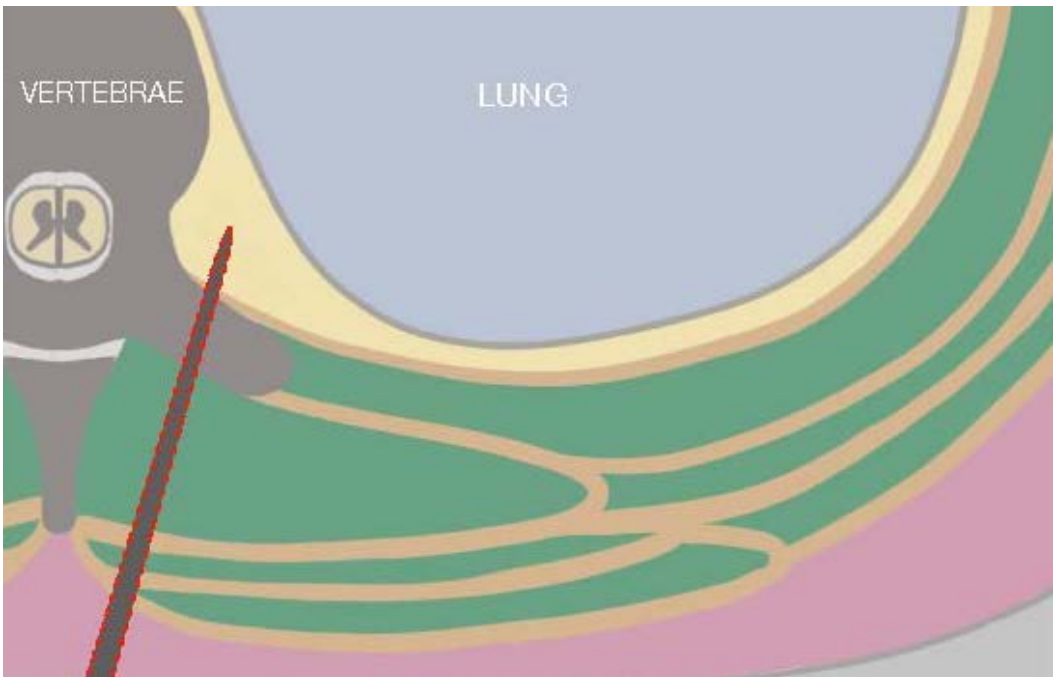


Figure 6 Longitudinal approach to paravertebral catheter insertion

Paravertebral analgesia produces a unilateral block of the thorax meaning that haemodynamic consequences of hypotension and bradycardia are reduced compared to epidural

analgesia[34]. Due to their infrequent use in everyday clinical practice fewer anaesthetists are competent to perform paravertebral catheter insertion compared to epidural catheter insertion.

3. INTERCOSTAL NERVE BLOCK

With this technique local anaesthetic is placed around the intercostal nerve with either landmark or ultrasound guided needle positioning. Palpation to determine injection site can cause pain due to underlying fractured ribs and multiple, repeated injections are required.

These blocks carry a risk of pneumothorax due to the proximity of the pleural and local anaesthetic toxicity can occur due to rapid absorption of local anaesthetic in this highly vascular area.

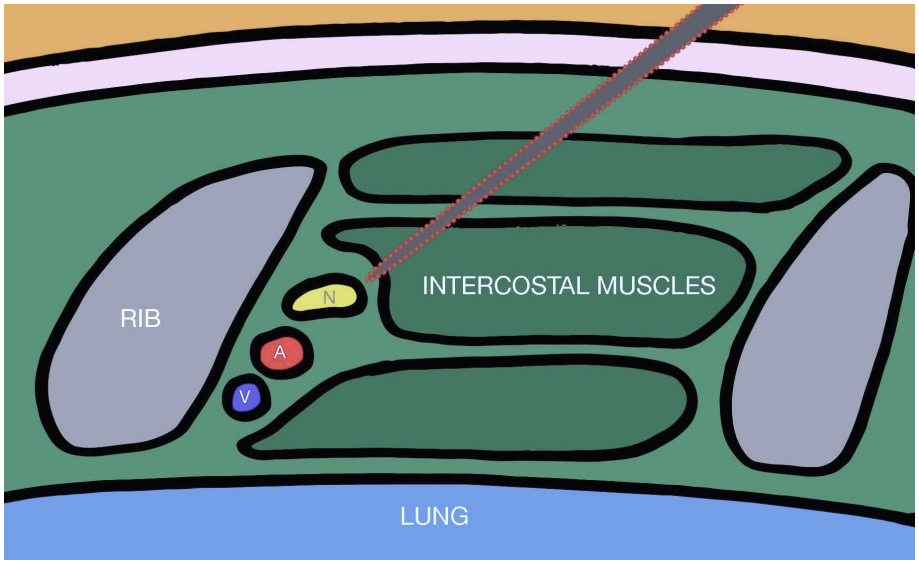


Figure 7 Intercostal nerve block showing needle trajectory (dotted red line) with ultrasound guidance. A = intercostal artery, V = intercostal vein N = intercostal nerve.

4. PLEURAL BLOCK

Local anaesthetic is injected down a chest drain into the pleural space. Large volumes of local anaesthetic are required and local anaesthetic toxicity due to rapid vascular absorption is a risk. Patient positioning and pre-existing pleural fluid/blood can all reduce the effectiveness of the block. It is a rarely performed technique.

SURGICAL RIB FIXATION

Surgical rib fixation aims to correct the thoracic instability seen with flail chest, a result of multiple consecutive rib fractures[35]. Limited studies suggest a potential benefit in pain management with surgical fixation (RR 0.18, CI 95% -0.46 to 0.83)[36]. Improvements in length of mechanical ventilation, pneumonia, and length of stay have been reported but no difference in mortality between operative and non-operative management for flail chest has been reported[36]. Further randomised controlled trials investigating the timing of surgery are needed.

CURRENT PRACTICE AND CHALLENGES

The challenges of achieving adequate analgesia are reflected in the lack of a recognised gold standard for this cohort. In 2016 the Eastern Association for the Surgery of Trauma (EAST) and the Trauma Anesthesiology Society (TAS) downgraded their previous endorsement of TEA and instead only conditionally recommended the use of TEA over non-regional modalities of pain control for the treatment of pain in patients with blunt chest trauma. [37]. This revision was due to the exclusion of papers that included post-operative surgical patients along with further studies and systematic reviews that failed to demonstrate an improvement in patient outcomes with TEA use in this cohort [37]. Other specialist societies have also recognised that especially

in those with unilateral injuries, the days of TEA use in clinical practice are numbered[38]. These limitations are reflected in the literature where studies have reported TEA and PVB use to be between 3% and 18.4%[1, 2, 5]. A retrospective review of the Trauma Audit and Research Network (TARN) database of all patients admitted to UHB in 2017-2018 with multiple rib fractures (≥3) identified that 17% (47/282) of patients received TEA and 1% (3/282) PVB.

Our published survey of health care professionals with an interest in the management of patients with multiple rib fractures signalled similar issues (Appendix 2)[27]. The survey revealed that there was considerable variation amongst physicians in their use of analgesic modalities. Morphine PCA was most used, followed by thoracic epidural, continuous infusion of opiates and paravertebral block (PCA 38.6%, TEA 30%, infusion opiates 18.6%, PVB 7.1%). When questioned on their preferred analgesic modality TEA, SAP and PVB led (TEA 37.1%, SAP 21.4%, PVB 17.1%). Opiate based methods dominate clinical practice despite a physician preference for regional techniques. The survey showed that it was contraindications, lack of skilled staff, service and time pressures, patient positioning and ward related factors that most commonly impacted the analgesic choice selected by physicians[27].

SERRATUS ANTERIOR PLANE BLOCKS

Limitations of the traditional analgesic techniques has led to the rapid uptake of fascial plane blocks. Fascia is a connective tissue that envelopes and separates organs and muscles. In a fascial plane block the potential space between two fascial layers is targeted. Local anaesthetic opens and then spreads throughout the plane via a combination of bulk flow and diffusion. Muscle contraction, respiration, gravity, and movement all encourage local anaesthetic spread.

Fascial plane blocks exert their effect by anaesthetising nerves that run in the fascial plane. Other suggested mechanisms of action include direct analgesic effects on pain receptors located in the fascia, spread of anaesthetic to nerves and pain receptors outside of the fascial plane due to traumatic disruption and systemic absorption of local anaesthetic[39-41]. One of the most popular fascial plane blocks in contemporary clinical practice is the fascia iliaca block used to provide analgesia for patients with hip fractures.

The Serratus Anterior Plane Block (SAP) was first described by Blanco in 2013[6]. Injection of local anaesthesia under ultrasound guidance is performed into the fascial plane between the serratus anterior and latissimus dorsi muscles (superficial SAP) or between the rib and serratus anterior (deep SAP) in the midaxillary line at the level of the 4th rib (Figure 8).

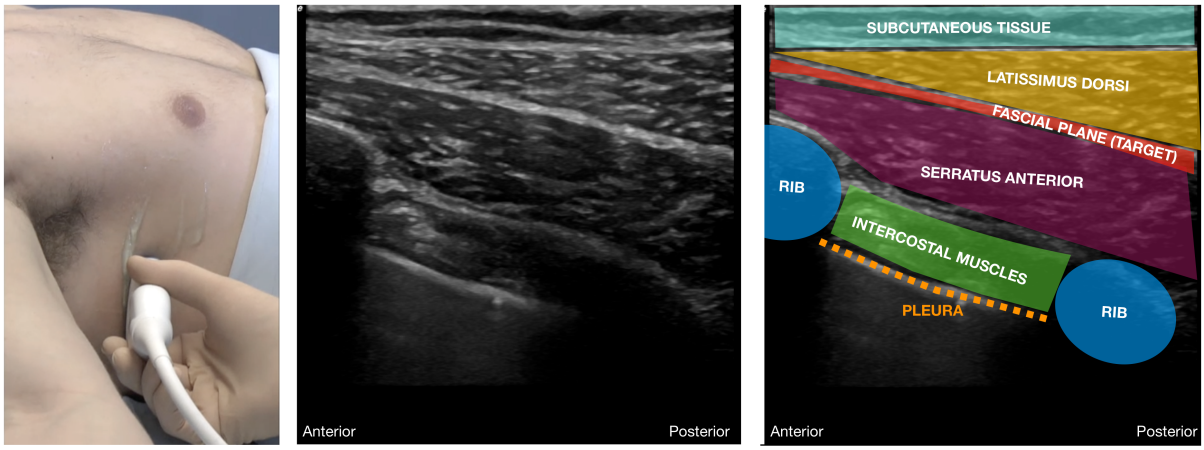


Figure 8 Ultrasound anatomy of superficial SAP Block

SAP anaesthetises the lateral cutaneous branches of the intercostal nerves that supply the anterior–lateral chest wall between the T2-T9 dermatomes. Cadaveric studies have shown occasional spread of injectate to the intercostal, long thoracic and thoracodorsal nerves.[42,

43] [44, 45]. The deep SAP block is considered a more advanced technique due to the proximity of the pleura and intercostal vessels. Studies have shown that superficial and deep injections both provide long lasting analgesia and it is the volume of injectate that effects spread rather than if the injection is superficial or deep to the serratus anterior muscle[6, 46].

SAP analgesia was originally devised for the management of post-operative pain following breast and thoracic surgical procedures, it has also been used more recently for certain types of cardiac surgery. SAP blocks can be inserted in the supine position, negating the need for patient repositioning. Up to 90% of patients with rib fractures will have associated injuries that can make repositioning for procedures painful and potentially risky. For example, patients with severe spinal or pelvic injuries cannot be sat up and log rolling into the lateral position requires multiple members of trained staff and can be painful.[1]. The risk of haematoma formation is less severe in the fascial plane than epidural space and therefore, SAP blocks can be inserted in patients with abnormal coagulation. Due to their superficial nature and use of ultrasound, SAP blocks are perceived as more accessible and safer to insert, potentially allowing non-anaesthetists to undertake the procedure. Finally, because peripheral nerves are being anaesthetised, they produce no sympathetic block or haemodynamic instability. SAP blocks reduced side effect profile, fewer contraindications, ease of insertion with ultrasound guidance and relative safety in comparison to TEA and PVB is what has driven their expanded use in the trauma cohort. However, there is little data at present on their efficacy in comparison to standard practice.

SERVICE SET UP

WHAT WAS THE NEED FOR A NEW THORACIC ANALGESIA SERVICE:

Although there is no current gold standard, the recommendations from specialist societies and clinician opinion is that any applicable form of regional anaesthesia should be promoted over opioid based methods alone and protocolised multidisciplinary pain pathways should be used to assist in the safe and effective delivery of analgesia [26, 27, 37].

In 2017 University Hospitals Birmingham had no dedicated pain guidelines for thoracic trauma. A retrospective review of analgesic practice showed that 17% of patients with 3 or more rib fractures received TEA and 1% PVB analgesia. The low rates of regional anaesthesia were influenced by patient injury factors. UHB is a major trauma centre (MTC) where many of the patients had associated head and spinal injuries that precluded TEA and PVB use. An aging population, patient polypharmacy, presence of multiple comorbidities, staffing pressures and staff skill mix also contributed[27]. A 2017 review of length of stay in hospital of patients over the aged of 75years with severe chest trauma (ISS>15) at University Hospitals Birmingham (UHB) showed that poor pain control, development of respiratory complications and delirium were important causes of delayed hospital discharge (Appendix 1).

University Hospitals Coventry and Warwickshire (UHCW), a nearby MTC already had a successful protocolised pain pathway for thoracic trauma[9]. With guidance from the acute pain team at UHCW and support from a multidisciplinary team (MDT) at UHB including acute pain, anaesthetics, critical care, major trauma service and ward-based nursing staff, I led the introduction of new multidisciplinary pain guidelines incorporating SAP blocks at UHB for

patients with multiple rib fractures (Appendix 3,4). A collaborative approach with input from the MDT was essential as trauma patients utilise many different hospital services due to their injuries and comorbidities.

SERVICE OBJECTIVES:

The objectives for the new analgesia service for thoracic trauma at UHB were to:

1. Improve patient comfort, satisfaction and outcomes.
2. Increase patients access to regional anaesthesia with the use of SAP
3. Provide guidance and reduce inter-clinician variability with the use of a protocolised multidisciplinary pain pathway.

IMPLEMENTATION

It was essential that any new analgesic services embodied the five quality assessments of the Care Quality Commission (CQC); that a service be safe, effective, well led, caring and responsive[47]. To achieve this, the introduction of the new analgesic service can be divided into two stages; stage 1 education and training (Table 3), stage 2 service administration.

EDUCATION AND TRAINING

Multidisciplinary education and training was required to ensure that all staff were safe and competent in the use of the new protocolised pain guideline (Appendix 3 and Figure 9) and SAP block selection, insertion and management (appendix 4). The education and training programme was targeted to different learning needs of those inserting the SAP blocks and the clinicians and nurses managing SAP catheters post procedure (see Table 3). An infographic was

used to raise awareness of the issue and help promote the work of the new service (Appendix 5).

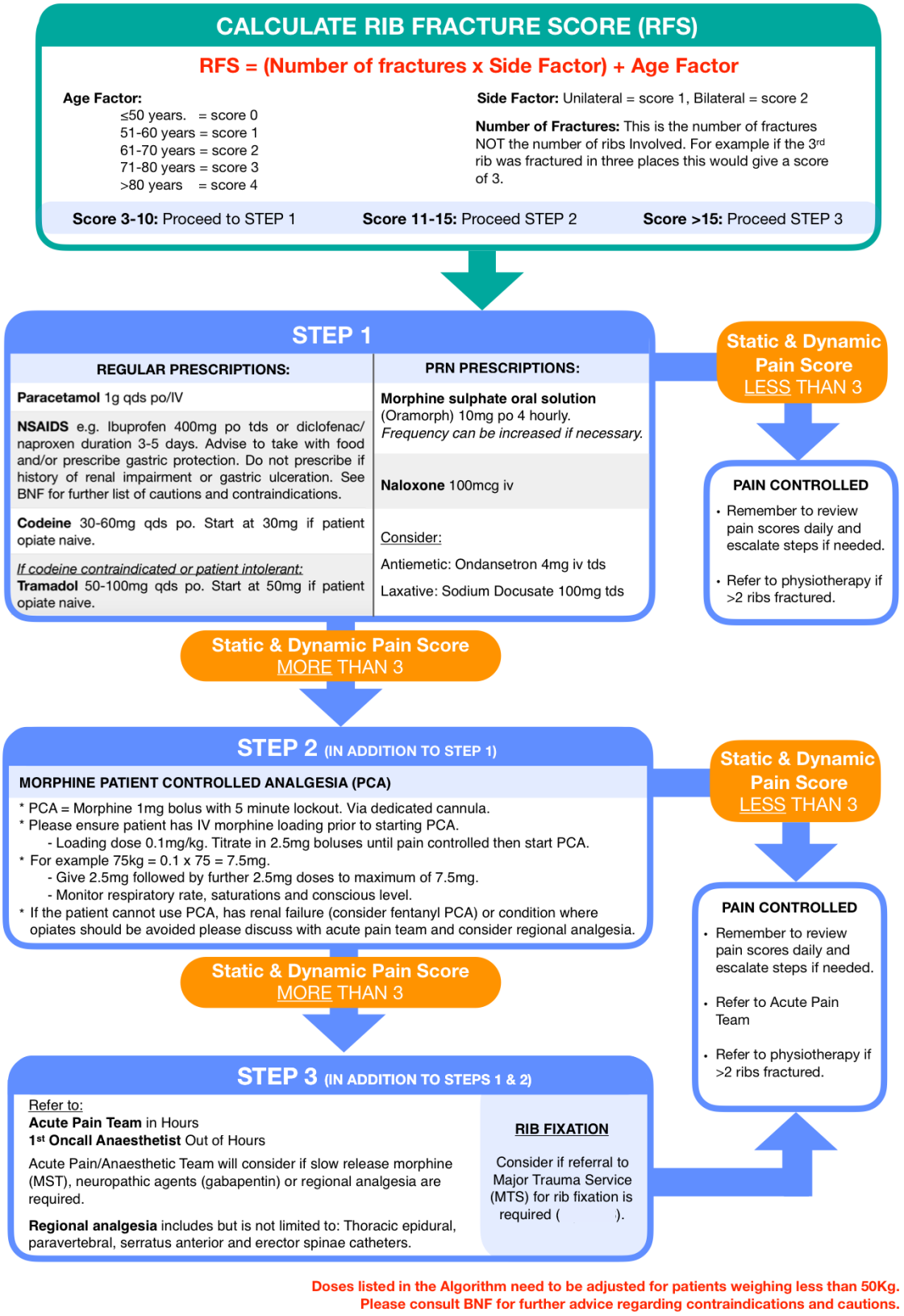
For those undertaking SAP block insertion E-learning materials with background information, insertion technique, galleries of images and videos, complications and contraindications was produced[48]. This information was supported by the 'Management of Thoracic Wall Blocks' UHB guideline that received input from the cross-site acute pain teams and offered further guidance on regional anaesthesia selection, patient consent, local anaesthetic prescription, catheter and complication management (Appendix 4). To gain clinical skills and competency in block insertion different teaching methods were utilised (Table 3). Small group teaching using ultrasound phantoms to practice in-plane needling technique and ultrasound 'ward rounds' of consenting inpatients improved ultrasound anatomy interpretation. Hands on experience of single shot SAP blocks on select breast surgery lists and 1:1 supervision of SAP catheter insertion on consenting patients with rib fractures was undertaken and feedback given. Competency sign off for trainee doctors and consultants was in the form of logbook, work based placed assessments and continuing professional development activities (CPD). For the Advanced critical care practitioners (ACCPs) a separate sign off document was produced (Appendix 6).

For all those involved in the pain management of thoracic trauma patients targeted e-learning relevant to the specific learning needs of different MDT members was developed (see Table 3). A quick reference guide on SAP blocks was also produced for nursing staff (Appendix 7). This was again supported by the acute pain protocol (Appendix 3) and management of thoracic wall

blocks guideline (Appendix 4). Departmental teaching and governance/audit meetings for nursing and medical staff were utilised to promote the new service.

STAFF GROUP	EDUCATION AND TRAINING STRATEGY
ALL GROUPS	Acute pain protocol (Appendix 3) Management of thoracic wall blocks (Appendix 4) Infographic: The problem with rib fractures (Appendix 5)
ANAESTHETIC DOCTORS / ICU DOCTORS / ACCPS	E learning[48] Small group teaching - In plane needling: ultrasound phantom - Ultrasound ward rounds 1:1 supervision - Single shot blocks on breast surgery lists - SAP catheter insertion
MTS DOCTORS	Teaching on the use of the pain protocol and thoracic wall block guideline at staff induction Small group sessions on SAP block top ups.
NURSING STAFF	Quick reference guide on SAP (Appendix 7) E-Learning
ACUTE PAIN TEAM	E-Learning Small group sessions on SAP block top ups.

Table 3 Summary of the multidisciplinary education and training strategy.



*Modified from the University Hospitals Coventry and Warwickshire (UHCW) protocol published in the BJA 2016 covering 'Rib fracture management'.[1]

Figure 9 Thoracic trauma pain protocol, full protocol document available in appendix 3

SERVICE ADMINISTRATION

When planning the administration and implementation of this service the five quality assessments of the CQC, that a service be safe, effective, well led, caring and responsive were prioritised [47].

QUALITY 1: SAFETY

Safety influenced our decision to preferentially use and teach the superficial SAP block. The deep SAP block is where local anaesthetic is deposited between the rib and serratus muscle and is in proximity to the pleura and intercostal vessels making this a more advanced technique with theoretically higher risk of complication. The superficial SAP block where local anaesthetic is deposited between serratus anterior and latissimus dorsi muscles is a greater distance away from these structures providing a larger safety margin.

The competent recognition and management of complications by all those performing and managing patients with SAP blocks was essential. The E-Learning package and the management of thoracic wall blocks guideline (Appendix 4) covered possible complications, their recognition and management[48]. A regional block trolley was introduced with funding from the Queen Elizabeth Hospital Charities (Appendix 8). The trolley contained all the equipment needed to perform a SAP block along with a safety notice on 'stop before you block', the acute pain and thoracic wall block guidelines and access to training resources.[49]

All medical staff performing SAP blocks were required to keep a logbook and work based placed assessment of their competency as per the Royal College of Anaesthetists Guidance for their

level of training [50]. The Advanced Critical Care Practitioners had their own sign-off documentation developed in collaboration with their lead and their senior supervisors (Appendix 6). Any complications were reported via the hospitals DATIX system and investigated by the hospitals governance teams.

QUALITY 2: EFFECTIVE

Patients with rib fractures present at all times of the day and night and any new acute pain service needed to be accessible 24/7. A major challenge of introducing this service was ensuring that there were always trained staff available to perform SAP blocks when needed. The education and training programme was very successful in training a large number of anaesthetic trainees and consultants. However, the trainee doctors would rotate to other hospitals and the consultant anaesthetists had other commitments out of hours. To improve patient access to SAP blocks, focus was given to training the ACCP's who covered the critical care rota out of hours, 7 days a week. The ACCPs already had advanced skills in ultrasound use for the insertion of central venous access along with experience in acute pain management and patient assessment. Once trained the ACCPs were able to train and educate colleagues in SAP block insertion.

QUALITY 3: WELL LED

Regular meetings were held with the anaesthetic, critical care, acute pain and major trauma teams to discuss any aspects of care that were going well or required improvement.

The involvement and leadership from the ACCPs in delivering SAP blocks was vital in the successful running of the service especially out of hours and ensuring that all patients with rib fractures had equal access [51].

QUALITY 4: CARING

A major objective of the new acute pain service was to improve the care and comfort of patients with rib fractures. Local experiences, discussions with patient and public involvement groups (PPI) along with a national survey identified inadequate pain control as major issue for this cohort which this new service aimed to address [27].

QUALITY 5: RESPONSIVE

Regular MDT meetings enabled any areas of service provision that required improvement or adapting to be quickly addressed. A primary challenge was ensuring that enough staff were trained not only in the performance but also the post procedure management of SAP blocks. The e-learning modules enabled the training of health care professionals across a range of different specialities at a time and location that suited. The E-learning could also be updated to reflect any DATIX reports or patient and staff feedback.

Informal feedback from nursing staff and clinicians highlighted that patients with other forms of traumatic injuries did not have the same access to regional anaesthesia as those with thoracic trauma. Work is in progress to expand access with the introduction of a block area in main theatres where a range of regional anaesthetic catheters can be inserted such as fascia iliaca catheters for patients with hip fractures. Additional guidelines are being produced and

the administration of the service led by the Anaesthesia Associates who at UHB are already trained in the performance of ultrasound guided nerve blocks.

AIMS AND OBJECTIVES

Serratus anterior plane blocks (SAP) with their relative ease of insertion, haemodynamic stability and perceived safety are being utilised in protocolised pain pathways, however evidence for their use in patients with rib fractures is lacking[6, 9, 37]. This research aims to better understand the role of SAP analgesia in patients with traumatic rib fractures.

Objectives

(i) Improve understanding of the mechanisms by which SAP blocks produce analgesia in patients with rib fractures.

(ii) Assess the clinical effectiveness and safety of SAP analgesia.

(iii) Evaluate the impact of SAP analgesia on patient outcome.

CHAPTER TWO:

THE USE OF SERRATUS ANTERIOR PLANE (SAP) BLOCKS FOR RIB FRACTURE PAIN: A SYSTEMATIC REVIEW OF CLINICAL SAFETY, PRACTICALITY, AND EFFECTIVENESS.

INTRODUCTION

Rib fractures following chest trauma are painful and can result in respiratory compromise and increased mortality and morbidity for the patient[13, 14]. A multimodal approach with simple analgesics, opioids and regional techniques is advised[37].

The serratus anterior plane (SAP) block has become a popular alternative to the more advanced regional anaesthetic techniques of Paravertebral (PA) and Epidural (TEA) analgesia in the trauma cohort. This is due to its relative ease of insertion, perceived safety with ultrasound guided insertion and ability for the procedure to be performed in the supine position[6]. It is anticipated that the fascial plane blocks will increase trauma patients access to regional anaesthesia. The insertion of PA and TEA analgesia occurs in less than 3% of patients with traumatic rib fractures due in part to the advanced level of skill required for insertion and post procedure monitoring, associated side effects and contraindications [5].

The SAP block works by the injection of local anaesthetic above (superficial) or below (deep) the serratus anterior muscle. The deep SAP block is considered a more advanced technique due to the closer proximity of the pleura and intercostal vessels. Analgesia is a result of anaesthesia of the lateral cutaneous branches of the intercostal nerves along with variable involvement of the long thoracic and thoracodorsal nerves supplying the serratus anterior and

latissimus dorsi muscles. Other mechanisms of action postulated to be involved following thoracic trauma include deep spread of local anaesthetic to the intercostal nerves, a result of fascial plane disruption, direct analgesic effect on nerve endings located in the fascial planes and systemic absorption[6, 52, 53]. These factors coupled with the differing origins of rib fracture pain compared to post-operative surgical pain are why SAP block effectiveness should be restricted to specific patient groups e.g. patients with thoracic trauma and not pooled with post-operative surgical patients[37].

The purpose of this review is to examine the safety, practicality, and analgesic effectiveness, of SAP block in patients with rib fractures following blunt thoracic trauma via a systematic review of the available literature.

OBJECTIVES

1. Determine if SAP analgesia is safe. Are there any complications or adverse effects associated with its use.
2. Evaluate the practicality (utility) of the SAP block for service provision. Are SAP blocks easy to teach and learn, what grade/speciality/seniority of staff can insert them?
3. Assess how effective SAP analgesia is in the treatment of pain caused by thoracic trauma e.g. rib fractures.

METHODS

The methodology was informed by recommendations made in the Cochrane Handbook and MECIR guidance. [54, 55]. A priori protocol was rigorously applied. This study updates a previous unpublished narrative review undertaken in 2018.

Eligibility Criteria:

The 2018 narrative review identified a paucity of data and studies reporting the effects of SAP analgesia in the trauma cohort. For the safety and utility outcomes (Objectives 1&2) SAP blocks inserted in non-trauma patients were included. The technique is the same and increased the available data for examining rare events. Eligible study types included: RCTs, prospective non-randomised comparative studies, cohort studies, retrospective studies, observational studies, case series and case reports.

Studies were excluded if they were non-human, cadaveric or included patients not admitted to hospital. Articles where a translation into English was not available or published only in abstract form where information on participants and intervention was insufficient, were excluded.

Adopting a broad search of the literature including non-trauma patients and non-randomised controlled trials ensured that the most accurate data with regards to adverse events was collected. Adverse outcomes are not always best represented by randomised controlled trials.

SAP block was defined as a single shot injection or catheter insertion into the fascial plane either above (superficial) or below (deep) the serratus muscle using ultrasound. There was no restriction on the dose, volume, or duration of drug administration. If SAP block was combined with other regional techniques e.g. PECs block and it was not possible to ascertain if adverse events or effectiveness relates to SAP then the study was excluded.

A subgroup analysis including only patients with blunt thoracic trauma was performed to address Objective 3, SAP block effectiveness. For this subgroup analysis any studies involving post-operative surgical patients, those with non-traumatic injuries or penetrating trauma, were excluded. This is because of the differing pain origins in trauma versus surgical patients. The study inclusion criteria are show in Table 4.

Population	Adult Patients ≥16 years old Patients admitted to hospital Objective 1&2: To include <u>all</u> patients i.e. trauma and surgical patients. Objective 3: Patients with rib fractures following blunt thoracic trauma <u>*Subgroup analysis:-*</u> Patients admitted to hospital with rib fractures following blunt thoracic trauma. (objective 3). Deep versus superficial SAP block (Objectives 1,2&3)
Intervention	SAP block (deep or superficial) Single injection or catheter insertion with ultrasound Any form or concentration of local anaesthetic/injectate.
Comparator	Standard treatment with multimodal analgesia which includes:- - Simple analgesic e.g. paracetamol, ibuprofen, neuropathic agents - Systemic opioids - Wound infiltration with local anaesthesia. - Thoracic Epidural - Paravertebral Analgesia - Other forms of regional anaesthesia e.g. intercostal blocks, erector spinae block, PECsI/II block.
Outcomes	1. Safety Assessment - Complications/adverse events associated with insertion o Pneumothorax o Bleeding/haematoma o Nerve damage o Failure to insert - Complications/adverse events post procedure o Infection o Displacement o Local anaesthetic systemic toxicity (LAST) o Change in haemodynamic parameters e.g. hypotension o Nausea and Vomiting 2. Practicality Assessment (ease of use) - Who currently performs the blocks? Grade/Speciality - Are there non-anaesthetists undertaking SAP insertion

	- Are there training programmes for the teaching of SAP blocks 3. Effectiveness Assessment: *(subgroup analysis – trauma patients)* - Resting and dynamic pain Scores (numerical rating and visual analogue scales) - Lung Function tests (inspiratory volume, mls) - Duration of mechanical ventilation (days) - Length of stay in hospital / critical care (days) - Discharge destination (home / extended care) - Prevention of complications associated with rib fractures o Pneumonia o Tracheostomy o Acute respiratory distress syndrome o Death - Patient satisfaction

Table 4 PICOS Model

The primary outcomes were:-

Objective 1:- Adverse events (dichotomous – yes/no)

Objective 2:- Grade/level of staff performing the SAP block

Objective 3:- Dynamic and static pain scores measured on the Visual analogue scale (VAS) or numerical rating scale (NRS).

Given the anticipated heterogeneity in reporting outcomes specific time bands of interest to the review were:

- Immediate/during procedure (0hr)
- Post Procedure Acute (0- 48 hours)
- Post Procedure Subacute (48hours – 7 days)
- Post Procedure Chronic (After 7 days)

Search Strategy:

The following databases were searched: MEDLINE, including MeSH terms (January 1946 to 2020), EMBASE (1974 to 2020.), Cumulative Index of Nursing and Allied Health (CINAHL, 1981 to 2020), Cochrane Central Register of Controlled Trials CENTRAL, clinicaltrials.gov (National Institutes of Health) and the World Health Organisation International Clinical Trials Registry Platform. All databases were searched from 2013. SAP block was first described in May 2014. [6] A search of references, citation tracking, and a review of any grey literature was also undertaken. The search terms used had been piloted in an initial unpublished narrative review undertaken in 2018 (Table 5).

	Search Terminology:
Population	No restrictions
Intervention	SERRATUS TERMS:* "serratus" or "SAB" or "SAP" ANALGESIA TERMS “nerve” or “block” or “catheter” or “regional” or “analgesia” or “an$esthesia” or “inject*” or “pain relief” MESH TERMs**:- ANALGESIA ANESTHESIA REGIONAL ANESTHESIA NERVE BLOCK ANESTHESIOLOGICAL PROCEDURE [Serratus Terms] AND [Analgesia Terms]
Comparator	No restrictions
Outcomes	No restrictions
Studies	No restrictions

* No MeSH terms available for SAP block

** MeSH terms will be updated and checked 24hours before search is conducted.

Table 5 Search Terminology

Study Selection:

Following the removal of duplicates, all titles and abstracts were screened and excluded if not relevant. Full text versions of the remaining studies were assessed for eligibility. The

remaining studies were included in the analysis for Objectives 1 and 2 on safety and practicality. Subgroup analysis on SAP effectiveness was performed with non-trauma patients excluded (Objective 3). Search results were reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [56]. All articles were managed in Endnote reference management software.

Data Extraction:

Data extraction was undertaken by the lead author/investigator, any questions related the eligibility of the study were discussed with an independent party experienced in the methodology of systematic reviews.

An adapted version of the Cochrane data extraction form was used to extract data. Information on author, study characteristics including publication year, study type, duration was recorded along with number enrolled, intervention, comparator, outcomes, grade of staff performing SAP block and adverse events.[54]

Appraisal of studies / Risk of Bias:

The methodological quality of the included RCT's was assessed using the Cochrane Collaboration risk of bias summary tool. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to evaluate the strength of recommendations.[57, 58]

Analysis of the results

For continuous outcomes with sufficient studies that used the same intervention, comparator and outcomes on applicable time scales, results were pooled using a quantitative fixed or random effects meta-analysis with standardized mean differences. Heterogenicity was assessed before deciding on random or fixed effect model. For binary outcomes risk ratios were presented using aggregate data. 95% confidence intervals and double sided P values were reported, where $p<0.05$ is considered significant.

When there was insufficient data or the outcome data varied too much to allow meaningful analysis a narrative review of the results is presented. Text and tabular summaries were used to present the main findings.

Subgroups:

1. SAP block effectiveness (Objective 3) was only assessed in the blunt thoracic trauma population.
2. Superficial and deep SAP blocks were reviewed for Objectives 1,2&3.

RESULTS

165 articles were assessed for eligibility. 7 full-text articles were not retrievable. They were all published in foreign languages and translations were not available. The main reason for exclusion of eligible reports was no relevant outcome data on safety, practicality or effectiveness (n=22), unable to identify SAP from combined blocks (n=11), surgically placed SAP (n=6) and data republished from abstract (n=6). Two reports were retracted, and one was

a review article not identified during screening. Figure 10 summarises the results of the literature search.

113 studies were included. 89 for Objective 1 Safety, 83 for Objective 2 Practicality and 26 for Objective 3 Effectiveness. There was some overlap with studies eligible for multiple outcomes. The study characteristics of all included studies are shown in Appendix 9.

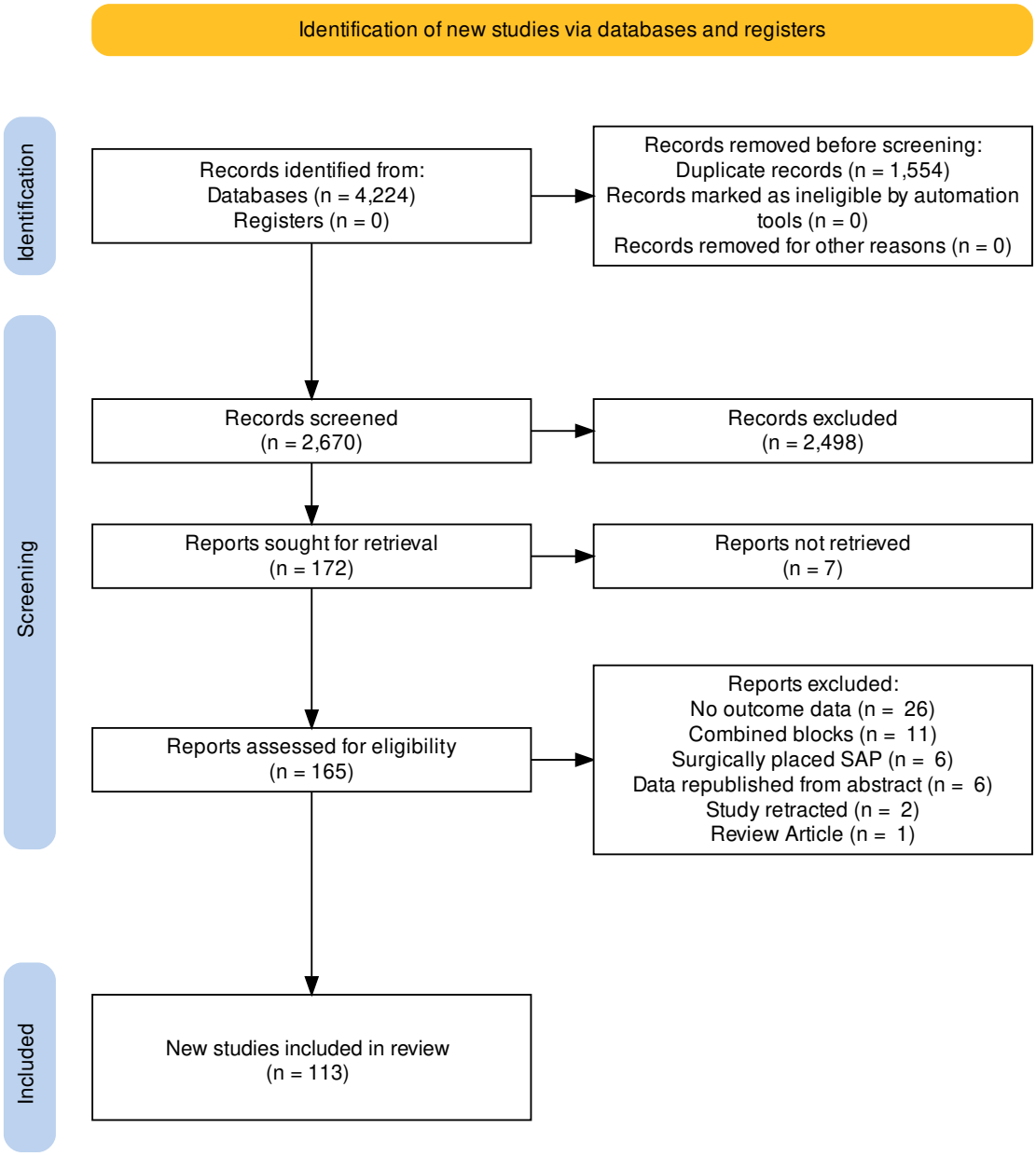


Figure 10 Prisma Flowchart

Objective 1: Safety

From the 89 eligible studies, a narrative review of adverse events of pneumothorax, bleeding, nerve damage, failure, displacement, infection and LAST was undertaken. A metanalysis of hypotensive events and PONV was performed due to a higher event rate and representation in RCTs.

COMPLICATIONS/ADVERSE EVENTS ASSOCIATED WITH INSERTION

73 studies, involving 1587 SAP blocks reported on complications associated with SAP insertion the characteristics of these studies are summarised in Table 6.

	Studies, n (%)	SAP Blocks, n (%)
Study Type		
Experimental (RCT)	22 (30%)	761 (48%)
Quasi Experimental (Non RCT, Time series etc)	20 (27%)	723 (46%)
Observational (Cohort, case series, case report)	31 (43%)	103 (6%)
Indication for SAP		
Breast Surgery	22 (30%)	733 (46%)
Thoracic Surgery	13 (18%)	405 (26%)
Cardiac Surgery	13 (18%)	251 (16%)
Trauma Analgesia	16 (22%)	112 (7%)
Upper Gastrointestinal Surgery	5 (7%)	67 (4%)
Chronic Pain	3 (4%)	8 (0.4%)
Other	1 (1%)	11 (0.6%)
Deep or Superficial SAP Block		
Deep	36 (29%)	737 (46%)
Superficial	28 (39%)	583 (37%)
Unknown	9 (12%)	267 (17%)
Single shot or Catheter Insertion		
Single Shot	48 (66%)	1270 (80%)
Catheter	24 (33%)	283 (18%)
Unknown	1 (1%)	34 (2%)
Follow up Period		
0-2 days (acute)	38 (52%)	1137 (72%)
2-7 days (subacute)	18 (25%)	183 (12%)
≥7 days (chronic)	10 (14%)	161 (10)
Unknown	7 (9%)	106 (6%)

Table 6 Study characteristics (descriptive): Complications associated with insertion

a) Pneumothorax

There was one report of pneumothorax (1/1587, 0.06%). Patient undergoing a wire guided local excision for breast cancer. No previous history of lung disease. Deep SAP block

performed by consultant anaesthetist and shortly after high airway pressures alerted to presence of pneumothorax. Most likely related to SAP block but wire insertion and thoracic wall surgery should be considered as potential cause. [59]

b) Bleeding/haematoma

One SAP block related haematoma was reported (1/1587, 0.06%). A deep SAP catheter was inserted for rib fracture analgesia. No comment was made on the patient characteristics or presence of coagulopathy.[60]

c) Nerve Damage

There were no reports of nerve damage (0/1587, 0%). A case of temporary upper limb nerve deficit was report by Schweizer et all following a superficial SAP catheter insertion for cardiac surgery[61]. The catheter tip was likely placed close to the brachial plexus in the region of the axilla. The motor and sensory deficit recovered within 48hs of the infusion being stopped. Electromyography and Magnetic Resonance Imaging showed no nerve damage.

d) Failure

There were 7 reports of SAP failure (7/1578, 0.45%). One case was due to confirmed placement in the wrong plane. For the other 6 cases it was unclear if the block failure was related to insertion issues or failure of the block to provide adequate analgesia. The authors were contacted for further information, but no response was obtained [62-64]. 3 cases

were from deep SAP injections, 4 unknown, 2 single shot injections and 5 catheter insertions.

COMPLICATIONS/ADVERSE EVENTS POST PROCEDURE.

a) Infection

One reported case (1/1587, 0.06%) of infection reported with a SAP catheter in a patient with thoracic trauma[60]. No further information was given and no response was obtained from the author.

b) Local Anaesthetic Systemic Toxicity (LAST)

There were no cases of LAST (0/1587, 0%)

c) Displacement

Displacement is only applicable to catheter insertions, therefore only studies that reported adverse events in catheter related SAP insertions were included.

21 studies involving 231 SAP catheter insertions (133 deep, 80 superficial and 18 unknown depth). 6 cases of catheter displacement (2.6% 6/231) were reported [65-67]. All deep SAP catheter insertions (1 thoracic trauma, 1 thoracic surgery, 4 cardiac surgery). This may suggest that deep catheters are more likely to displace than superficial, however Fisher Exact Test shows a statistically non-significant difference between deep, superficial, and unknown groups. (Fisher Exact Test, 2 sided, P=0.09).

d) Hypotensive Events

When all study types including case reports were analysed (27 studies, 665 SAP blocks) the incidence of hypotensive events with SAP was 1.35% (9/665). However, general anaesthesia was performed in over 90% of these blocks and a common side effect of general anaesthesia is hypotension. Hypotensive events occurred more frequently than other adverse outcomes and were well represented in RCTs. A meta-analysis of RCTs was performed to report on this outcome more accurately and control for the effect of general anaesthesia, which all the included RCTs utilised. See Appendix 10 for a summary of characteristics of included RCT's for hypotensive events.

Hypotensive event was defined as either a MAP <60mmHg, SBP <80mmHg or the need for intravenous fluids or drug intervention. Clinical heterogenicity between 'other analgesic' methods was suspected and therefore, a subgroup analysis of the different comparative analgesic methods was undertaken grouped into neuraxial (epidural and paravertebral analgesia), opioid based analgesia (no block) and peripheral nerve block (erector spinae plane).

Overall incidence of hypotensive events was 4% (6/145) for SAP and 8.9% (13/145) for 'other analgesia'. There was a statistically non-significant 45% relative risk reduction of a hypotensive event with SAP block compared to other forms of analgesia (P=0.44). The Forrest plot for the result is shown in Figure 11.

A subgroup analysis showed that patients who received SAP had a statistically significant 90% relative risk reduction of hypotensive events when compared to neuraxial analgesia (SAP vs Neuraxial, Risk Ratio 0.1, P 0.03). The Forrest plot for the result is shown in Figure 11.

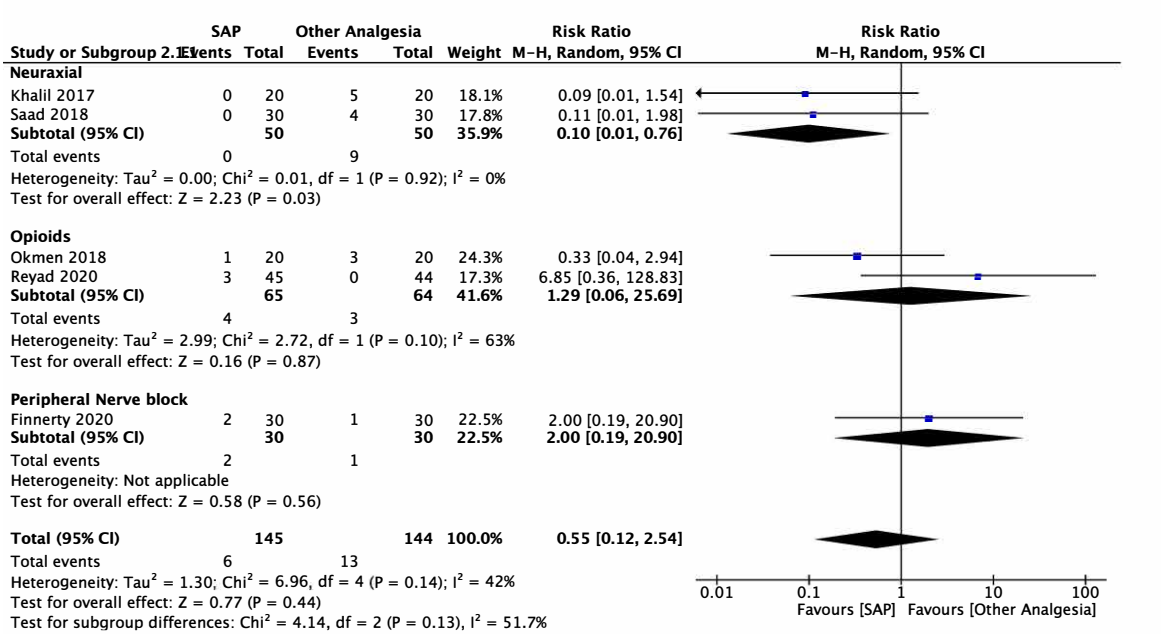


Figure 11 Forrest plot hypotensive events SAP versus other forms of analgesia

The risk of bias for the studies was high and GRADE assessment of the certainty of the result rated as very low. The risk of bias graph and summary are shown in Figures 12 and 13. Risk of bias assessments were undertaken in line with the Cochrane revised risk of bias tool (RoB2)[68]. A summary of results and GRADE assessment of the result are shown in Figure 17. Revman5 publication bias funnel plot is provided in Appendix 11.

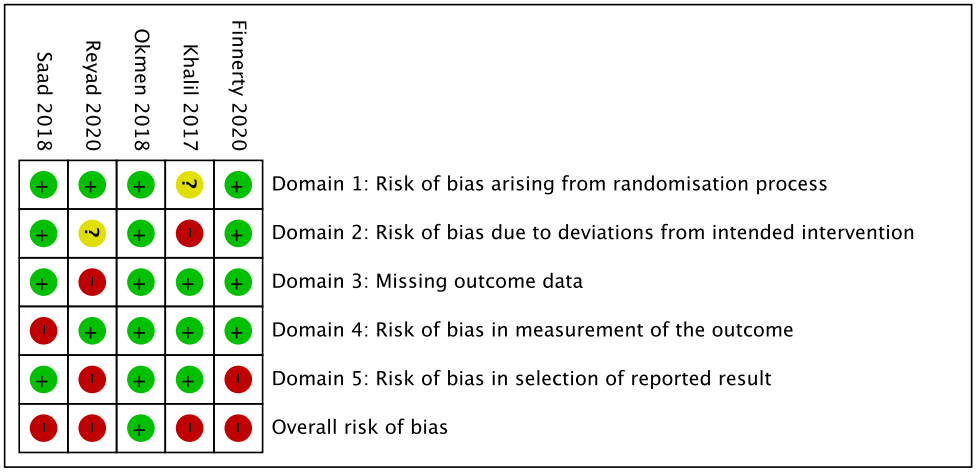


Figure 12 Risk of Bias Summary

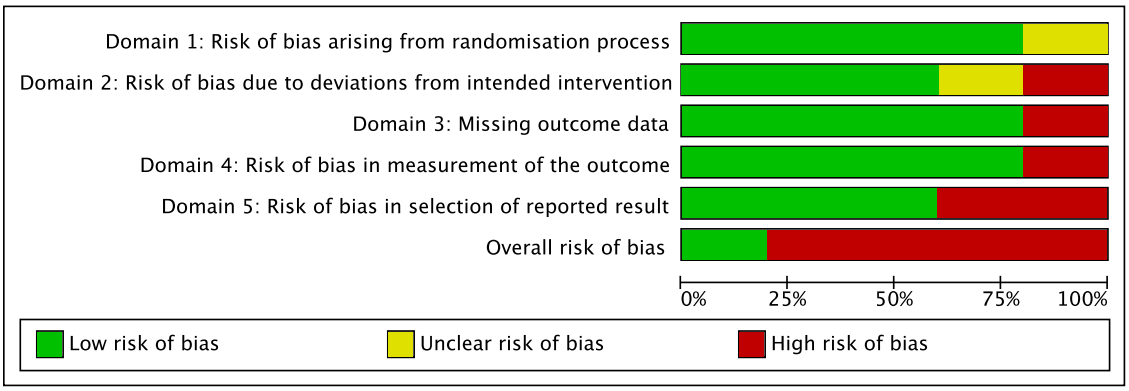


Figure 13 Risk of Bias Graph

e) Post Operative Nausea and Vomiting

When all study types analysed, (39 studies, 1226 SAP blocks) the incidence of PONV was 11% (135/1226). However, general anaesthesia was performed in over 98% of these blocks and a common side effect of general anaesthesia is PONV.

A meta-analysis of RCTs was performed to control for the effect of general anaesthesia. A metanalysis was suitable for this outcome because of a higher event rate and its frequent measurement in RCT's. A fixed effect model was chosen due to a low statistical

heterogenicity (P=0.31, I^2 =13%). See Appendix 12 for a summary of characteristics of included RCT's.

Clinical heterogenicity between 'other analgesic' methods was suspected and therefore, a subgroup analysis of the different comparative analgesic methods was undertaken grouped into neuraxial (epidural and paravertebral analgesia), peripheral nerve block (ESP, wound infiltration, and PEC) and opioid based analgesia (no block). High statistical heterogenicity was also present between subgroups (P = 0.03, I^2 =71.9%) see Figure 14.

Incidence of PONV was 7.8% (36/463) for SAP and 17.3% (82/472) for 'other analgesia'. There was a statistically significant relative risk reduction of PONV by 55% when SAP block was used compared to other forms of analgesia (Risk Ratio 0.45, 95% CI 0.32-0.65, P<0.001). However, the subgroup analysis showed that this significant difference was driven by the no block (opioid only) group which showed a statistically significant relative risk reduction of PONV by 69% when SAP block was used compared to opioid analgesia alone (risk ratio 0.31 95% CI 0.19-0.5, P<0.001). There was no statistically significant difference in PONV between SAP and the neuraxial and peripheral nerve block groups. See Figure 14.

The risk of bias for the studies was high and the GRADE assessment of the certainty of the result rated as low. The risk of bias graph and summary are shown in Figures 15 and 16. A summary of results and GRADE assessment of the result are shown in Figure 17. Revman5 publication bias funnel plot is provided in Appendix 11. Due to the small number of events,

missing data on type of SAP block, high heterogenicity and high bias, subgroup analysis of deep versus superficial SAP blocks was not undertaken.

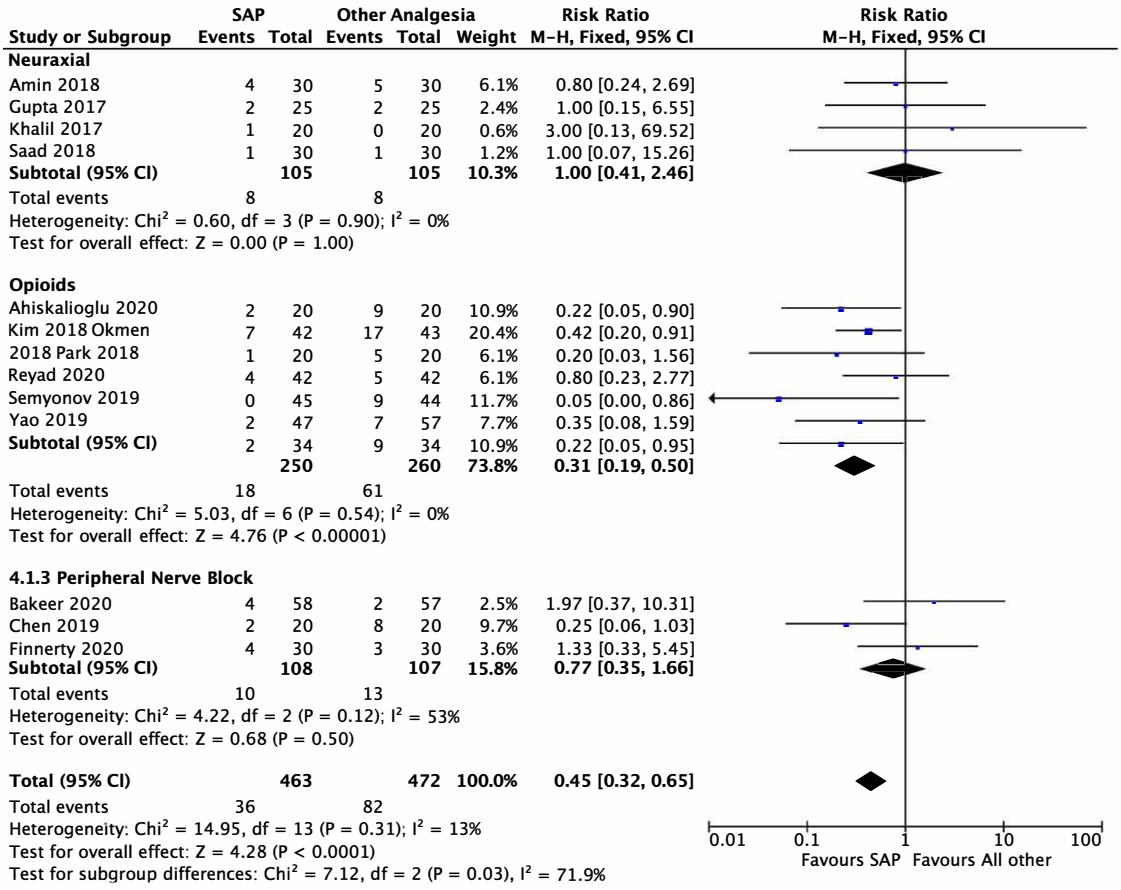


Figure 14 Forrest plot metanalysis results PONV

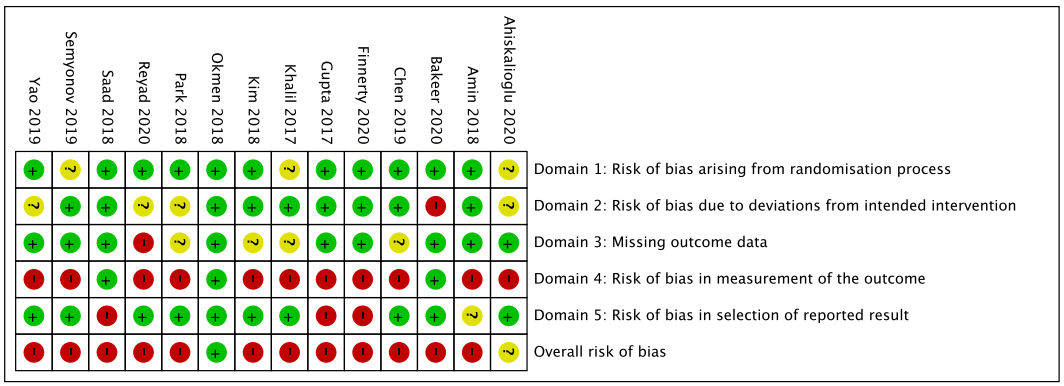


Figure 15 Risk of Bias Summary

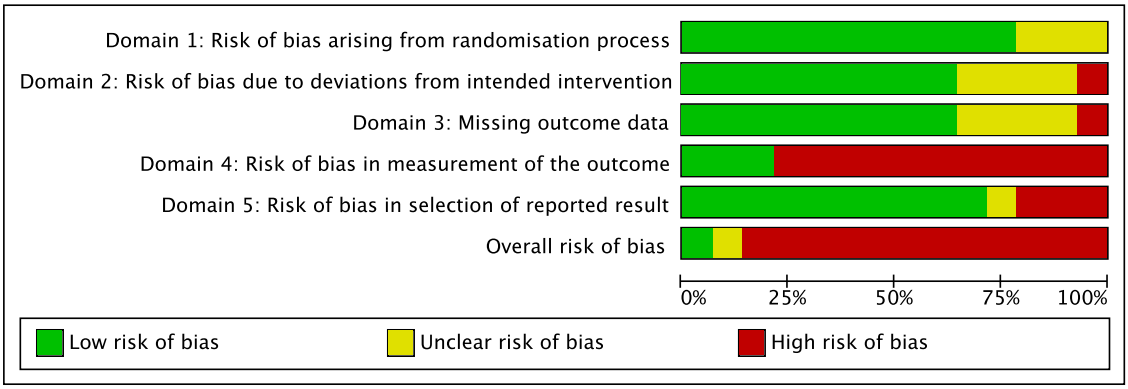


Figure 16 Risk of Bias Graph

[SAP] compared to [Other Analgesia] for [Adverse Events]

Patient or population: All Patients receiving SAP Block
Setting: Any type of surgery
Intervention: SAP
Comparison: Other Analgesia

Outcomes	Anticipated absolute effects* (95% CI) Risk with [Other Analgesia]	Risk with [SAP]	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Pneumothorax	1 case			1587 (73 studies)	-	All study types included to pick up rare event
Bleeding / Haematoma	1 case			1587 (73 studies)	-	All study types included to pick up rare event
Nerve Damage	0 cases			1587 (73 studies)	-	All study types included to pick up rare event
Failure	7 cases			1587 (73 studies)	-	All study types included to pick up rare event
Infection	1 case			1587 (73 studies)	-	All study types included to pick up rare event. May be falsely low due to short follow up period.
Local Anaesthetic Systemic Toxicity	0 cases			1587 (73 studies)	-	All study types included to pick up rare event
Catheter Displacement	6 cases			231 (21 studies)	-	All study types included to pick up rare event
Hypotensive Events	90 per 1,000	**50 per 1,000** (11 to 229)	**RR 0.55** (0.12 to 2.54)	289 (5 RCTs)	⨁◯◯◯ Very low[a,b,c,d]	
Post Operative Nausea and Vomiting	174 per 1,000	**78 per 1,000** (56 to 113)	**RR 0.45** (0.32 to 0.65)	935 (14 RCTs)	⨁⨁◯◯ Low[a,e]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Risk of bias in nearly all trials across different domains
b. Generalisability - only in thoracic surgery patients, ASA 1-3, <70-80years old, fit for thoracic surgery. Also significant subgroup effect with significantly higher number of events in neuraxial group.
c. Optimum sample size calculated at 400. Confidence intervals include RR of 0.75 and 1.25.
d. Publication bias strongly suspected as small trials reporting positive results
e. Generalisability - thoracic surgery and breast surgery patients, ASA1-3, excludes elderly patients. Also significant subgroup effect with significantly higher rates of PONV for patients receiving opioid only treatment.

Figure 17 Summary of Findings: Safety Outcome

*Table made with GradePro software (gdt.gradepro.org)

Objective 2: Practicality Outcome(Utility)

A narrative review has been undertaken to assess this outcome due to a paucity of data.

a) Who currently performs the blocks?

There were 83 studies, representing 1,936 SAP blocks of all study types that reported on the speciality of the doctor performing the block (Table 7).

	Studies, n (%)	SAP Block, n (%)
Speciality		
Anaesthetic Doctor	79 (95%)	1889 (97.5%)
Emergency Medicine Doctor	3 (4%)	9 (0.5%)
Cardiology Doctor	1 (1%)	38 (2%)
Total	83	1936

Table 7 Speciality of physician inserting SAP catheter

Most SAP blocks (97.5%), and all deep blocks and catheter insertions were performed by anaesthetists. Emergency physicians and Cardiologists undertook superficial single shot SAP injections for rib fracture analgesia and the insertion of implantable cardiac devices (Table 8).

	Anaesthetics, n	Emergency Medicine, n	Cardiology, n
Depth of SAP Block			
Superficial	580	7	38
Deep	899	0	0
Unknown	410	2	0
Catheter/Single shot			
Single shot	1408	9	38
Catheter	447	0	0
Unknown	34	0	0

Table 8 SAP block frequency for each speciality.

b.) Are there training programmes for the teaching of SAP blocks

No data on training programmes for the teaching of SAP blocks was identified.

Objective 3: Effectiveness of SAP in patients with thoracic trauma (Subgroup analysis)

26 studies of 237 SAP blocks were analysed for SAP block effectiveness in patients with thoracic trauma. There were no RCTs. Two non-randomised studies presented data on SAP block effectiveness with a comparator either ESP, TEA or PVB[60, 69]. The remaining studies were all case reports or case series often comparing pre and post block pain and respiratory function scores. A narrative review has been performed. Study characteristics are shown in Table 9.

	Studies, n (%)	SAP Blocks, n (%)
Study Type		
Experimental (RCT)	0 (0%)	0 (0%)
Quasi Experimental (Non RCT, Time series etc)	8 (30%)	166 (70%)
Observational (Cohort, case series, case report)	18 (70%)	71 (30%)
Total	*26*	*237*
Indication for SAP		
Trauma Analgesia	26 (100%)	237 (100%)
Deep or Superficial SAP Block		
Deep	10 (38%)	69 (29%)
Superficial	8 (31%)	114 (48%)
Unknown	8 (31%)	54 (23%)
Single shot or Catheter Insertion		
Single Shot	10 (38%)	83 (35%)
Catheter	15 (58%)	120 (50%)
Unknown	1 (4%)	34 (15%)
Follow up Period		
0-2 days (acute)	8 (31%)	84 (36%)
2-7 days (subacute)	8 (31%)	22 (9%)
≥7 days (chronic)	1 (4%)	17 (7%)
Unknown	9 (34%)	114 (48)

Table 9 Characteristics of included studies for effectiveness of SAP in thoracic trauma

PAIN ASSESSMENT

a) Pain scores (static and dynamic)

23 studies of 216 SAP blocks reported on pain scores. A range of scales was used including numerical rating scales (NRS), Visual rating scales (VAS) and verbal rating scales. All studies reported an improvement in static and/or dynamic pain scores post SAP block.

16 studies of 105 SAP Blocks reported static pain scores on a scale of 0-10 (NRS or VAS). From these studies the range of pain scores pre SAP block was 5.5-10, within one hour 0-5 and at 24hours 0-3. Hernadez et al reported a statistically significant reduction in median NRS pain scores from 7 to 3 in the 4hour period following SAP block (P<0.001)[70].

Only one case series of 5 patients reported static VAS pain scores at 48 and 72hours, showing a sustained improvement in pain scores from 8.4 pre block, to 1.2 at 24hours, 2.8 at 48hrs and 3 at 72hours[66].

4 studies of 16 SAP blocks reported on dynamic pain scores on a scale of 0-10 (NRS or VAS). The range of pain scores pre-SAP block was 7-10, within one hour 0-3 and at 24hours 3-4. No studies reported on dynamic pain scores after 24hours.

b) Opioid consumption

5 studies reported opioid consumption involving 50 SAP blocks. All the studies identified a reduction in opioid consumption post SAP block insertion.

Martinez et al showed daily equivalent oral morphine consumption was significantly decreased after SAP from 108 mg (IQR 67 to 120) to 19 mg (IQR 0 to 58) (P = 0.015)[71]. Riley et al also showed a reduction in the daily equivalent oral morphine consumption after SAP from 83.8mg (SD70.6) to 51.3mg (SD 30mg), P=0.05.[60] Jenkins et al reported that

pre SAP 100% patients required IV opioids, post SAP this had reduced to 24% of patients[72].

c) Time rescue analgesia

One study reported on this outcome which compared time to rescue analgesia for SAP block or ESP block in patients with traumatic rib fractures. It showed no significant difference in time to rescue analgesia between the groups, SAP 21.95 hours (SD24.83), ESP 17.54hours (SD 23.11), P=0.6. No studies compared time to rescue analgesia between SAP and no block/opioid only treatment.

d) Compliance with physiotherapy

One case report and one case series identified that patients were better able to tolerate physiotherapy and breathing exercises post SAP block due to improved analgesia. [73, 74]

RESPIRATORY FUNCTION

a) Spirometry

Five studies of 115 SAP blocks all showed an improvement in respiratory function after SAP insertion. The study by Beard et al of 61 SAP blocks which is presented in full in Chapter 4 showed a clinically significant mean increase in inspiratory volume of 825.6 mL (SD 519.8 mL) following SAP catheter insertion[69]. Foley et all showed a 30% increase in inspiratory volumes from baseline following SAP block in 10 patients[75]. Hernandez et all measured incentive spirometry at 4 and 24hours post block and showed a median increase of 150mls and 175mls from baseline in 34 patients ($P<0.001$)[70].

b) Oxygen requirement

3 studies of 40 SAP blocks all reported reductions in oxygen requirements post SAP block. A case report by Wong described a 95year old patient with rib fractures being weaned off oxygen the day after SAP catheter insertion[76]. Mazzocchi et al reported a 20% reduction in fractional inspired oxygen (FiO2) following SAP block administration in 4 trauma patients. Hernadez et al identified that all 34 patients in their study required less oxygen supplementation post SAP block[70].

c) Respiratory Rate

3 studies of 48 SAP blocks all reported improvement in respiratory rate following SAP block. The largest of these studies by Hernandez et al showed a statistically significant decrease in respiratory rate from 24 to 16 breaths per minute ($P<0.01$)[70].

d) Ventilatory Weaning

There is one reported case of a SAP block preventing impending intubation and ventilation of a patient and two cases of SAP catheter insertions assisting with the extubation of ventilated patients[70]. A study comparing ESP and SAP showed no statistically significant difference between SAP and ESP in number of patients requiring ventilatory support (SAP 8/17 patients, ESP 6/17 patients P 0.73)[60].

PREVENTION OF COMPLICATIONS

a) Pneumonia

A study comparing SAP and ESP blocks showed no statistically significant difference in the development of new respiratory complications (pneumonia, pulmonary embolism, respiratory failure) between the groups. The incidence of pneumonia in the SAP group was 35%[60].

b) Length of stay

Beard et al showed that there was no statistically significant difference in length of stay in hospital for patients receiving SAP, TEA or PVB (SAP 22.1 days (16.9) vs TEA 18.3 days (15.6) vs PVB 14.3 days (19.7). Patients in the SAP group had a statistically significantly higher proportion of patients with multiple injuries (polytrauma), endotracheal intubation and head injuries than the PVB group. The full results of this study are presented in Chapter 4.

Riley et al also showed no significant difference in LOS between SAP and ESP for both critical care LOS and hospital LOS (LOScc SAP 0 days (SD3.56) vs ESP 3.88 days (SD9.53) P=0.33, LOShosp SAP 9.76 days (SD5.85) vs ESP 17.94 days (SD 24.98) P 0.21[60].

c) Mortality

No difference in mortality rate between SAP, ESP, PVB or TEA was shown[60, 69]. The incidence of in hospital mortality for SAP was reported as 4.59% and 5.88% by Beard et al and Riley et al respectively. There was no study that compared SAP mortality to no block (opiate only) mortality.

No studies were identified that reported on duration of mechanical ventilation, complications such as tracheostomy and acute respiratory distress syndrome (ARDS), discharge destination or patient satisfaction.

SUBGROUP ANALYSIS: EFFECTIVENESS OF DEEP VS SUPERFICIAL BLOCKS

Both superficial and deep blocks are well represented in all categories of the analysis for pain control i.e pain scores, opiate consumption and inspiratory capacity. An improvement in these parameters was reported for both deep and superficial blocks. It therefore, appears that both deep and superficial SAP blocks work for patients with trauma. It is not possible to comment any further due to the small numbers included and the low level of evidence of provided by the included studies.

DISCUSSION

The incidence of adverse events for SAP insertion were, nerve damage and LAST 0%, pneumothorax, haematoma, infection 0.06% and catheter displacement/failure 0.4%. The Royal College of anaesthetists advises patients that the risk of nerve damage with peripheral nerve blocks is rare at 0.05% and very rare for epidural insertion at 0.01%.[77, 78] In the literature the incidence of LAST following epidural and peripheral nerve block is reported as 0.1%. Pneumothorax following paravertebral analgesia 0.5% and failure in experienced hands 6.8%-10%. For epidural insertion entry site inflammation is reported in the literature as 2.6%, catheter displacement 3.7% and failure rate in clinical practice up to 30%. [34, 79-81] This therefore, suggests that SAP is not associated with any greater risk of adverse event than current regional techniques.

The metanalysis identified that there was a statistically significant 90% relative risk reduction of hypotensive events for SAP when compared to neuraxial analgesia (SAP 0% vs Neuraxial Analgesia 18% Risk Ratio 0.1, P0.03). There was no statistically significant difference in the incidence of hypotensive events between SAP, opiate only analgesia (no block) and peripheral nerve block. The literature reports the incidence of hypotension for epidural and paravertebral analgesia at 4.8% and 4.6% which is lower than the rate of 18% identified in the meta-analysis, this may be because the included studies all utilised epidural analgesia with general anaesthesia which also carries a risk of hypotension[34, 80]. These findings suggest that SAP is a more haemodynamically stable regional anaesthetic technique than epidural or paravertebral analgesia.

The second metanalysis showed that there was a significant relative risk reduction of PONV by 69% when SAP block used compared to opioid only analgesia (risk ratio 0.31 95% CI 0.19-0.5, P<0.001). There was no statistically significant difference between SAP and the neuraxial and peripheral nerve block groups. This finding suggests that it is the opioid sparing effect of SAP that causes the reduction in PONV seen. Available literature suggests that following opioid administration approximately 40% of patients may experience nausea and 15%-25% of patients vomiting. This is in-keeping with the incidence of PONV identified in the opioid only group of 23%.[82]

The adverse incident rates for opioids, peripheral nerve blocks, epidural and paravertebral analgesia reported in the literature are all higher than the figures this systematic review

obtained for SAP insertion. Our findings therefore, support the opinion that SAP insertion is a safe procedure to undertake with no greater incidence of adverse events, compared to currently accepted analgesic methods.

This study showed that the majority (97.5%) of SAP blocks and catheter insertions are performed by anaesthetists. Emergency physicians and cardiologists are performing single shot superficial SAP injections. This suggests that there is scope for non-anaesthetists with ultrasound skills to be trained to insert SAP blocks.

All the studies included in the narrative review for the clinical effectiveness of SAP in patients with blunt thoracic trauma showed that both static and dynamic pain scores were reduced following SAP block insertion, with one case series showing an improvement in pain scores up until day three[66]. Opioid consumption was also shown to be reduced following SAP insertion with Martinez et al showed daily equivalent oral morphine consumption decreased significantly after SAP from 108 mg (IQR 67 to 120) to 19 mg (IQR 0 to 58) (P = 0.015). [71] An improvement in respiratory function was also seen, with all included studies showing an improvement in inspiratory volume, reduced oxygen requirements and a reduction in respiratory rate following SAP insertion. Individual reports of SAP facilitating ventilator weaning and prevention of intubation in patients were also identified.[60, 70] Superficial and deep SAP blocks were well represented in the included studies suggesting that both forms of SAP block and catheter insertion are effective at providing analgesia and improving respiratory function in patients with blunt thoracic trauma with rib fractures.

No difference in LOS in hospital or in-hospital mortality was identified between SAP and other regional techniques of ESP, PVB and TEA. Data on length of stay and mortality is hard to interpret due to the vast number of factors that influences these outcomes and the small number of low-quality studies included in this narrative review. No studies compared hospital LOS and mortality between SAP and opioid only (no block) analgesia.

One of the strengths of this study was its broad search criteria and inclusion of all study types. This resulted in a large exclusion of articles at the initial screening stage. Although time-consuming, due to the heterogenicity of the population and outcome data, narrower search terms would have missed relevant studies, in particular case studies which were vital to the correct reporting of adverse outcomes. Adverse outcomes are not always best reported by randomised controlled trials due to the rarity of the events.

A limitation of the study is that adverse events for any indication i.e breast surgery, thoracic surgery, trauma etc were included. This may impact on the generalisability for some of the adverse outcomes. The pneumothorax rate may be under reported as some patients undergoing thoracic surgery have a chest drain inserted as part of the procedure meaning that pneumothorax recognition following SAP insertion may be under reported. However, patients with thoracic trauma also have pneumothoraces and chest drains prior to SAP insertion so the impact on the data may be minimal. SAP blocks are potentially more challenging in the trauma cohort due to the presence of surgical emphysema from pneumothoraces, chest wall haematomas and tissue oedema from immobility. These factors all degrade the ultrasound image making block performance more difficult compared to when the block is performed on

surgical patients without these conditions. Therefore, the risk of complications may be underestimated by this review for trauma patients having SAP insertion. It appears from the subgroup analysis that PONV was strongly related to opiate administration. All the studies in the meta-analysis included surgical patients. However, the narrative review did show a reduction in opioid consumption for patients receiving SAP for thoracic trauma. Another limitation is that Infection may be under reported in this systematic review as the follow up period for most studies (72%) was less than 48hours. Infection may take longer to present especially in those with SAP catheters. A final limitation was the lack of a priori criteria for the conduction of a meta-analysis and selection of analytical technique (fixed vs random effects).

This study adds evidence to the safety of SAP blocks. However, many of the adverse outcomes are very rare events and our review of 1587 SAPs blocks may include insufficient numbers. The randomised controlled trials only included patients of ASA 1-3, those less than 70-80years and patients deemed fit for surgery. A significant proportion of the trauma population are frail, elderly with multiple comorbidities. Elderly trauma patients are likely to experience more significant issues with hypotension and PONV due to their fragility and so the clinical effect of reducing hypotension and PONV might in fact be greater with SAP in the trauma cohort than reported in the systematic review.

As identified with the GRADE assessment reported in the summary of findings, Table 17 the quality of evidence provided by included studies in the metanalysis was poor due to a high risk of bias being identified in at least one domain for most studies, high statistical and clinical heterogenicity and small sample sizes. Publication bias is very likely because many case reports

and case studies were included which are often only published when a positive or adverse outcome is identified.

The purpose of this review was to identify if SAP blocks were safe, easy to learn and effective in patients with rib fractures. The available data has shown that SAP blocks are safe and not associated with any greater adverse events than currently accepted regional anaesthetic techniques. In fact, SAP may be associated with less hypotension than paravertebral or epidural analgesia. Emergency physicians and cardiologists are already performing SAP blocks and therefore, other health care professions proficient in the use of ultrasonography should be able to be trained to safely perform SAP insertion. It appears from the results of the narrative review that both superficial and deep SAP blocks are effective at providing analgesia, improving respiratory function, and reducing opiate consumption in patients with rib fractures following blunt trauma.

Randomised controlled trials in patients with thoracic trauma are required to better assess the effectiveness of SAP in comparison to current analgesic options, in particular, opioid only analgesia as this is the form of analgesia that many patients with rib fractures receive. Any future studies should also, where possible, include patient reported outcome measures (PROMS) such as quality of life, patient satisfaction, and functional status.

CHAPTER THREE:

HOW DOES THE INSERTION OF TWO SERRATUS ANTERIOR PLANE CATHETERS, ONE DIRECTED MORE POSTERIOMEDIALLY AFFECT INJECTATE SPREAD ACROSS THE HEMITHORAX: A CADAVERIC STUDY

L A Beard, R Sachdeva, S Ramalingam, R G Tunstall, Whitehouse T, F Gao Smith, T Veenith

(Submission to peer review journal in progress)

INTRODUCTION

Fascial plane blocks are considered a feasible alternative to epidural or paravertebral analgesia in patients with multiple ribs fractures (MRFs).[9] This shift is driven by contraindications, positioning requirements for insertion and the risk of complications with Epidural and Paravertebral Analgesia.[83] Superficial serratus anterior plane (SAP) blocks can be inserted with ultrasound guidance in the supine position by suitably trained clinicians, including non-anaesthetists. [3] These factors along with their ease and safety during insertion has led to their incorporation into local guidelines in some institutions.[9, 51]

Innervation of the thorax is complex. The ventral rami of T1-T11 form the intercostal nerves which innervate the ribs, intercostal muscles, skin, pleura and peritoneum of the thorax and abdomen. The intercostal nerves originating from T3-T6 are typical suppling only the thorax. T1, T2, T7-11 are atypical in that they also innervate the skin, musculature and peritoneum of the upper arm and abdomen in addition to the thorax[84, 85].

Each intercostal nerve has several sensory and motor branches

- Cutaneous branches (lateral and anterior) supplying the skin of the anterior-lateral thorax and trunk. The lateral cutaneous branch divides at the mid axillary line.
- Collateral branches that divide at the angle of the rib and supply the rib periosteum, parietal pleura and peritoneum.
- Muscular branches that supply the intercostal muscles[84].

The literature reports that SAP anaesthetises the lateral cutaneous branches of the intercostal nerves that supply the anterior–lateral chest wall between the T2-T9 dermatomes. Variable involvement of other the intercostal nerve branches, long thoracic and thoracodorsal nerves has also been reported.[42, 43] [44, 45]. The long thoracic and thoracodorsal nerves supply the serratus anterior and latissimus dorsi muscles [85].

The origin of pain in patients with multiple rib fractures is multifactorial with nociceptive signals arising from rib periosteum, muscles, fascia, pleura, subcutaneous tissues and skin. Recent fascial plane-based studies have also identified the presence of free nerve endings, contractile units and transmission belts in deep fascial tissues, suggesting the potential for fascia-derived pain. [39, 86, 87]. Therefore, the hypothesis that rib fracture analgesia is mainly from anaesthesia of the lateral cutaneous nerve which supplies the skin of the anterior lateral thorax, does not fully explain the level of analgesia reported.

We hypothesise that paravertebral spread may also contribute to the analgesic effect of SAP blocks. The superficial serratus plane between the serratus anterior and latissiumus dorsi

muscles shows potential for communication with the fascial plane deep to the erector spinae muscle, thereby enabling injectate spread to the paravertebral space, resulting in the anaesthesia of the spinal roots and sympathetic chain, providing analgesia to the hemithorax. [88]

In extensive thoracic trauma, single level SAP injection with or without catheter insertion dominate clinical practice.[9] Studies have demonstrated injectate spread between the third and fifth ribs with a single 20ml SAP injection[89, 90]. This would likely be inadequate for patients with extensive multiple rib fractures (eg. from the second to twelfth rib).

Hydrodissection opens up the fascial plane to facilitate injectate decompression from an area of high to lower pressure, encouraging spread. The catheter over needle insertion technique utilises extensive hydrodissection to enable a suitable length of catheter to be inserted in the plane. This has the potential to increase injectate spread compared to single shot injection [39, 91]. The spread across the fascial planes is also affected by intrathoracic pressure changes, chest wall movements, muscle contractions, effect of gravity, patient positioning, traumatic disruption to the fascial planes and injectate viscosity. [39-41, 43].

This study aims to evaluate whether superficial SAP catheters inserted postero-medially at two different levels on the ipsilateral hemithorax can provide adequate injectate coverage for extensive chest wall injuries that extend the length of the hemithorax (e.g., from rib 1 to 12) and if injectate spread to the paravertebral space occurs.

METHODS

Ethical approval was provided by the Governance for Research Ethics Committee (GAfREC) at University Hospitals Coventry and Warwickshire under the project title 'Revisiting Surgical and General Anatomy' (ID GF0004). Requirement for written consent waived by the ethics committee.

Four fresh frozen cadavers (3 male, 1 female) were used in this study, providing a total of eight hemithoraces. Exclusion criteria included any sign of previous intrathoracic surgery (determined by observation and CT imaging), breast surgery and pacemaker insertion. Accordingly, two hemithoraces were excluded leaving a total of six hemithoraces (5 male, 1 female) in the final analysis. Exclusions were due to one case of previous thoracic surgery and one case of injectate spread outside of the fascial plane due to misplaced catheter.

Two catheters (A and B) were inserted over the lateral thoracic wall. Ultrasound imaging was used to identify the ribs and intercostal spaces in the supine position. Catheter 'A' was inserted at the level of the fourth intercostal space with the catheter tip situated midway between the midaxillary line (MAL) and posterior axillary line (PAL). Catheter 'B' was inserted more posteromedially than catheter A at the level of the seventh intercostal space with catheter tip situated posterior to PAL. A catheter over needle was used to enable accurate positioning of the catheter tip in relation to the anatomical reference lines (Pajunk E-Cath®).

This study attempted to replicate as many factors that can clinically impact the injectate spread. The benefit of the SAP block is attributed from its ability to be inserted in the supine position, without the need for patient repositioning. Hence, the supine position was chosen rather than lateral decubitus. We opted to insert catheter B more posteriorly as the larger circumference of the chest and clearance from the axilla and upper limbs at the 7th ICS allows for this.

SAP catheters were inserted under ultrasound guidance by experienced clinicians. The needle and catheter were directed in an anterior-posterior direction. Anterior-Posterior insertion is the chosen practice in our institution and also the method originally described by Blanco. We also hoped an anterior-posterior approach would encourage more posterior spread than a caudal to cranially placed catheter.[92] An initial saline injectate (10 ml) was used to hydrodissect the superficial fascial plane between latissimus dorsi and serratus anterior after which 2-4 cm of the catheter was left within the fascial plane. A baseline Computerised Tomography (CT) scan was performed (Discovery CT750 HD scanner, GE Medical Systems, USA, Single X Ray source, constant angle acquisition, Tube voltage 120 kVp, X-Ray tube current 100 mA, Helical mode, Rotation time: 0.7 sec, Pitch factor: 0.98 ratio, Single collimation width 0.625mm, Total collimation width 40mm, Convolution Kernel: Soft, Filter type: Body) to identify the catheter tip and any underlying thoracic pathology (Figures 18A, 19), after which an injectate consisting of 19 ml of 0.25% bupivacaine and 1 ml Omnipaque (iohexol; 300mg I/ml) was infused, the dilution followed manufacturers recommendations.[93, 94] This formulation was selected to limit the impact of the increased viscosity of the contrast agent on the spread of injectate in the fascial plane[43, 95, 96]. Cadavers were then intubated and ventilated with

a Mapleson C circuit at a rate of 15 breaths per minute for 15 minutes, after which a contrast CT scan was performed to assess injectate spread (Figure 18).

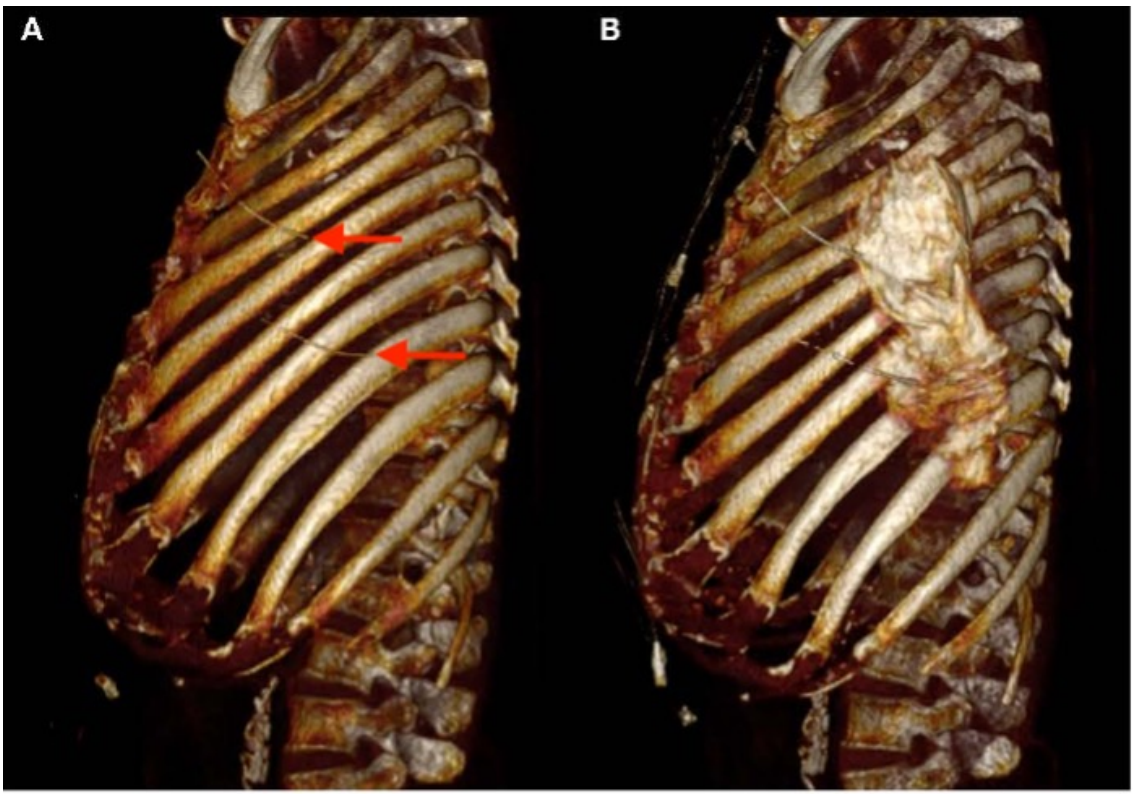


Figure 18 3D volume rendered CT images of the same hemithorax. (A) Baseline CT showing catheter tip position (red arrows); and (B) contrast CT scan showing the spread of 20 ml of injectate.

Outcomes:

The primary outcome was the extent (maximum) of the spread of injectate craniocaudally (in millimeters) and the injectates relation to the nearest rib and or intercostal space. The secondary outcome was whether more posteriomedially directed catheters (Catheters B versus Catheters A) resulted in the spread of injectate to the paravertebral space. The spread (maximum) of injectate in the anterior-posterior direction was also recorded (in millimetres).

Imaging analysis: All images were stored and analysed using the Horos medical image viewer (v3.3.5) for MacOS 11.5. 3D Multi-planar reconstruction (MPR) and 3D volume rendering

modes were used for assessment of contrast spread in the soft tissues. The 3D MPR images were assessed in the default soft-tissue window settings (window level, 50 HU; window width, 350 HU). The 3D volume rendering mode segments the CT image data on the basis of voxel attenuation. Visualization of data is then based on transfer function that maps measured attenuation to colours and opacities. To perform accurate and reproducible quantitative assessment of contrast spread, the *in-situ* catheter was used as the reference object for image calibration. The transfer function was adjusted to display the catheter with same diameter and the level of opacity across all scans.[97] All contrast spread measurements were taken in parallel (craniocaudal) or perpendicular (anterior-posterior) to the scanning table, at a fixed point.

The surface anatomical landmark of the MAL is not visible on CT. A radiological thoracic midpoint was therefore required to permit comparison of catheter tip locations. We termed the radiological thoracic mid point the mid-thoracic line (MTL). The MTL was identified using the 3D MPR mode of the baseline CT (Figure 19). The transverse and sagittal planes were aligned at the level of the catheter tip being studied. The median sagittal plane was aligned with the midline of the vertebral bodies and sternum. The transverse (axial) line was aligned to the same inclination as the nearest vertebral body. The anterior-posterior width of the hemithorax was measured and the coronal line moved to the middle point. The coronal line represented the mid-thoracic line (MTL). The distance of the catheter tip from the MTL (coronal line) was measured in millimetres (Figure 19). Positive measurements represent catheter tips anterior to the MTL and negative measurements posterior to the MTL. This process was

repeated for all catheters (Catheters A and B). 3D volume rendering of the baseline CT (Figure 18A) were used to approximate catheter tip locations to the nearest rib or intercostal space.

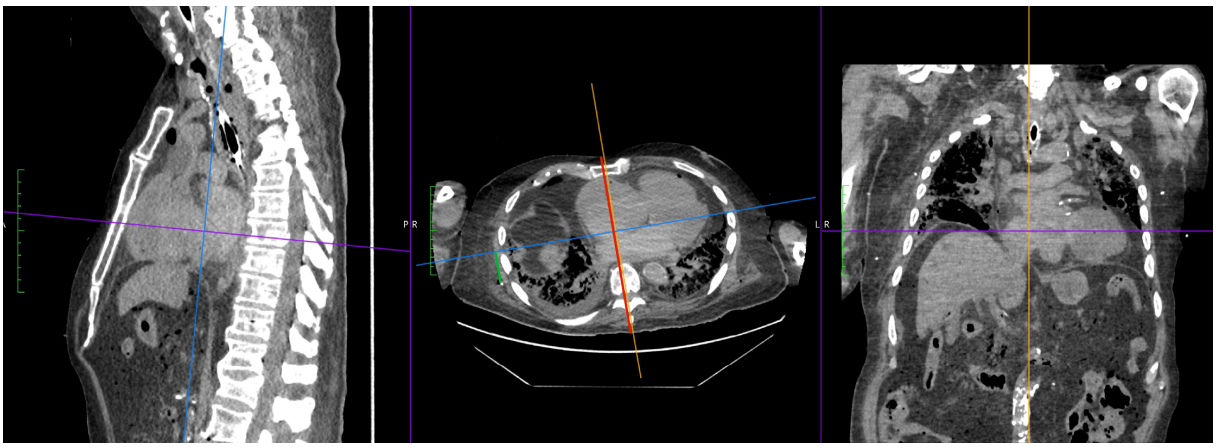


Figure 19 3D Multi-planar reconstruction mode (MPR). Median sagittal line (orange line), transverse (axial) line (purple line), coronal line or mid thoracic line (blue line), anterior-posterior width of the thorax (red line), measurement of the distance between coronal line and catheter tip (green line).

3D volume rendering of the contrast CT scan allowed assessment and measurement of injectate spread in the craniocaudal (vertical) and anterior-posterior (horizontal) directions. Figure 20 shows how the measurements for anterior-posterior and cranial-caudal spread were taken. The volume of contrast was also measured.

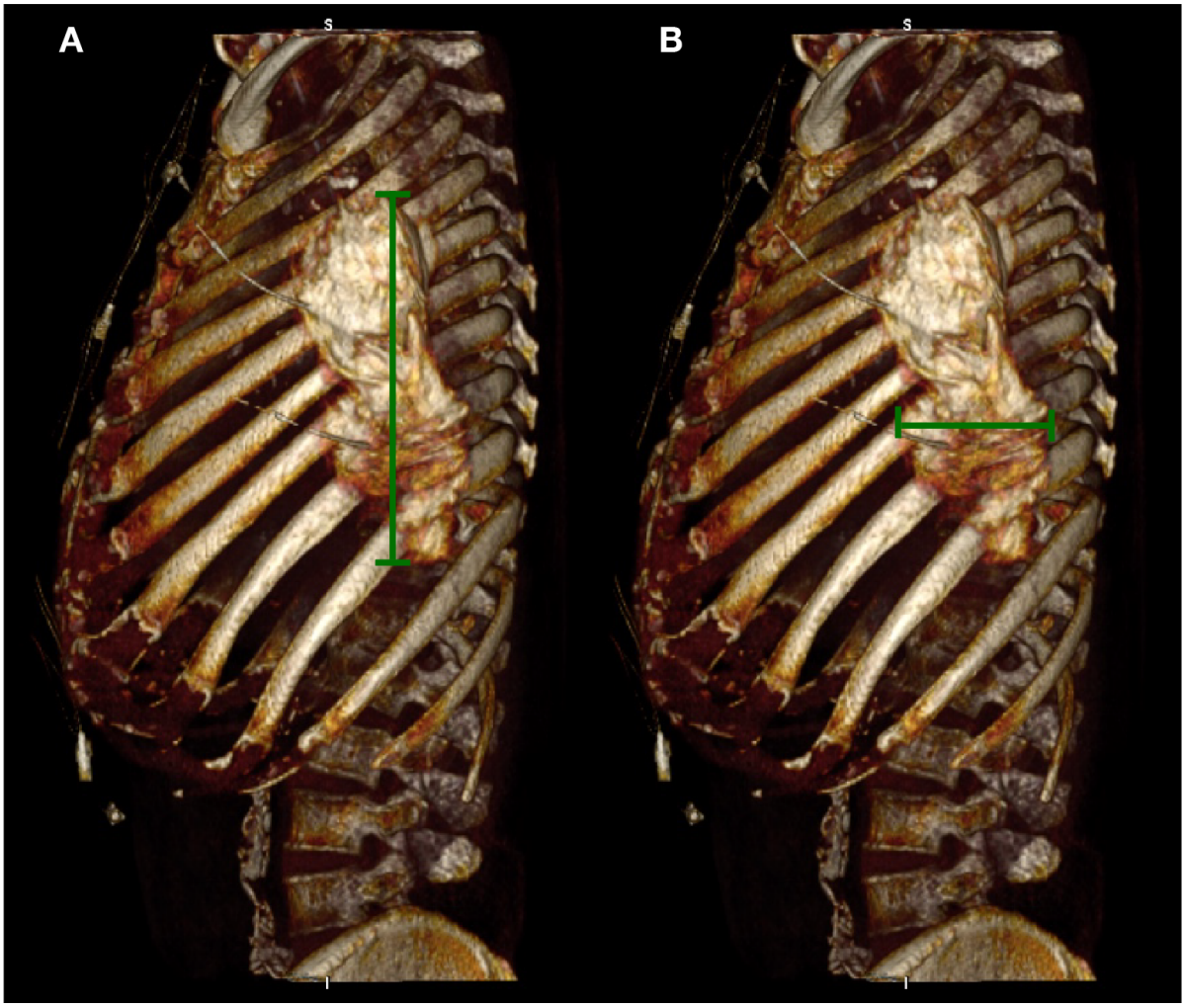


Figure 20 Figure 3: 3D reconstruction of contrast CT showing measurement of maximal injectate spread in the craniocaudal (A) and anterior-posterior (B) directions (green).

Statistical analysis: All types of spread were measured three times, with the imaging parameters reset each time. All the data were tested for normal distributions with Shapiro-Wilk tests. For parametric data, the dispersions are presented as mean ± SD (standard deviations) and for non parametric data as median ± range. Differences between groups were assessed using Mann-Whitney and Fishers exact test as appropriate. Statistical analysis all performed in SPSS.

	Hemithorax						
	1	2	3	4	5	6	Overall
Median spread of injectate(mm) [Range]							
Craniocaudal	162 [160-164]	191 [188-194]	297 [295-297]	191 [189-193]	177 [175-178]	229 [228-233]	191 [160-297]
Anterior-Posterior	80 [79-80]	87 [87-90]	139 [138-140]	80 [80-86]	81 [80-84]	59 [58-60]	81 [58-140]
Anatomical injectate spread							
Most superior anatomical location	Rib 3	Rib 2	ICS 2	ICS 2	Rib 3	Rib 2	Rib 2
Most inferior anatomical location	ICS 9	ICS 9	Rib 11	Rib 10	ICS 9	Rib 10	Rib 11
Median distance of catheter tip from MTL (mm) [Range]							
Catheter A	5 [4-7]	6 [6-12]	-39 [-36 - -39]	-4 [-4 - -3]	-36 [-36 - -37]	-55 [51 - -57]	-20 [-57 - 12]
Catheter B	-33 [-34 - -34]	-24 [-23 - -28]	-90 [-90 - -92]	-27 [-26 - -27]	-72 [-72 - -80]	-71 [-66 - -75]	-50 [-23 - -92]
Spread to PVS							
Catheter A	No	No	No	No	No	No	No
Catheter B	No	No	No	No	No	No	No

mm = millimeter, MTL = Mid Thoracic Line, PVS = Paravertebral Space, ICS = intercostal space
Median distance from MTL = positive (+) measurements denote catheter tips anterior to MTL, negative (-) measurements denote catheter tips posterior to MTL.

Table 10 Spread of injectate

(a) Injectate Spread:

The median craniocaudal spread across the hemithorax from the two catheters was 191 mm (range 160-297 mm). The median anterior-posterior spread was 81mm (range 58-140 mm). Injectate spread is shown in Figure 21 for all cadavers. Anatomically, the most superior spread was to rib 2 and most inferior to rib 11 (Table 10). Figure 22 shows a graphical representation of this spread. The volume of contrast measured for each hemithorax ranged between 94.7 cm^3 and 115.1 cm^3.

(b)Spread to paravertebral space:

There was no spread of injectate to the paravertebral space (PVS) for any of the catheters, see Table 1. Catheters inserted more posteriorly (Catheters B) did not influence the spread of

injectate to the PVS. Fisher's Exact Test was not performed. The median distance of catheter tips from the MTL in catheter group A was -20mm and catheter group B -50mm, a difference of 30mm. There was no statistically significant difference in catheter tip distance from the MTL between the groups (p = 0.15).

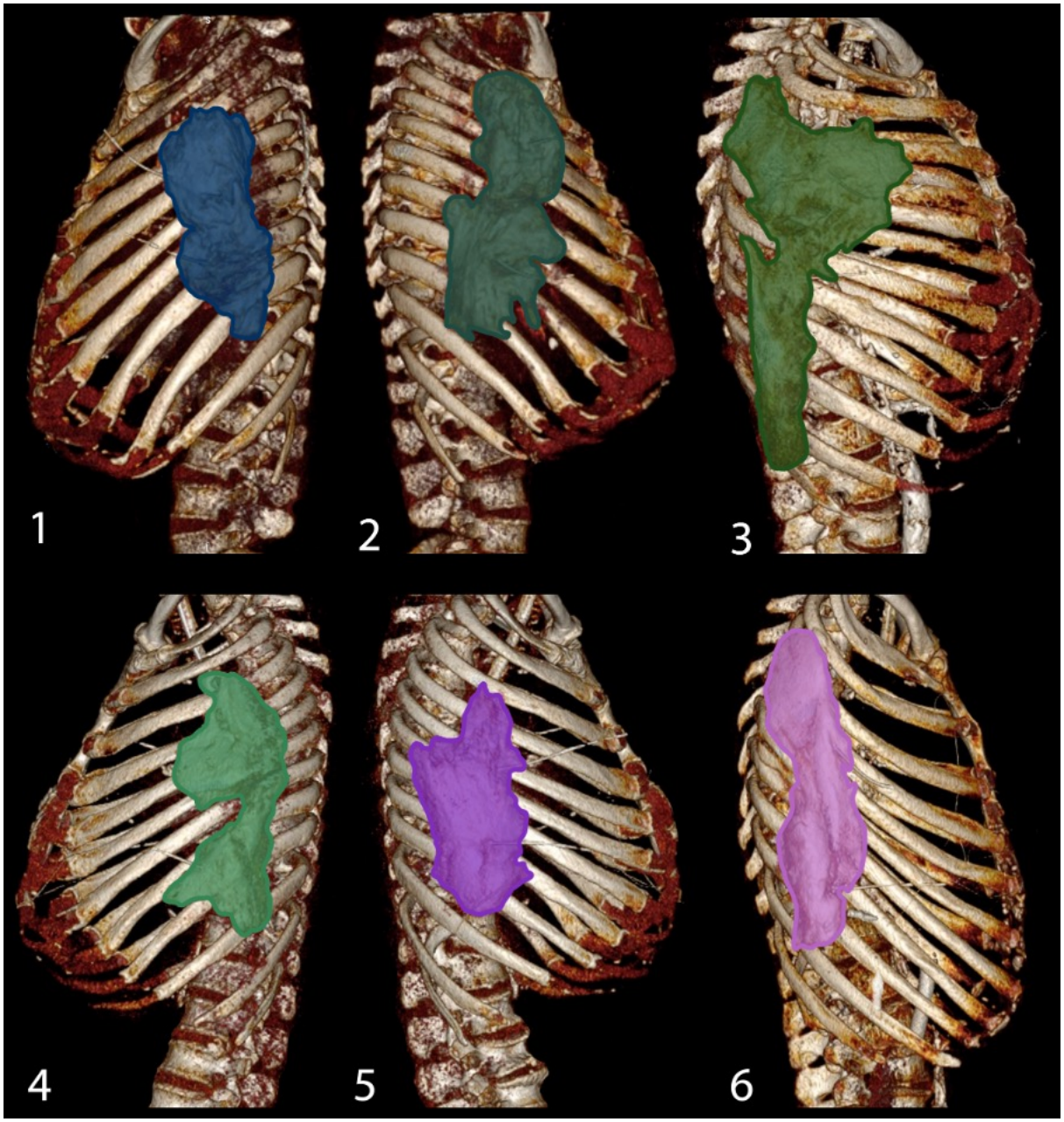


Figure 21 Spread of injectate for each hemithorax, Hemithoraces 1,2 and 4,5 are from the same cadavers.

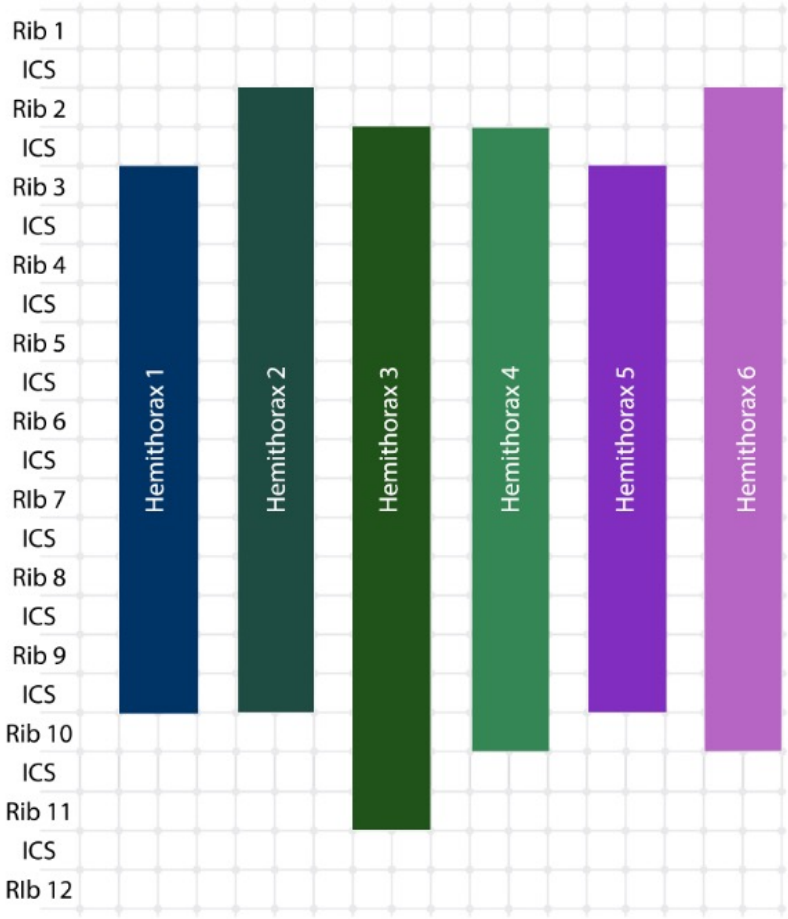


Figure 22 Anatomical spread of craniocaudal injectate spread for each hemithorax. (ICS = Intercostal space)

DISCUSSION

The insertion of two catheters resulted in a median craniocaudal spread of 191mm[range 160-297mm] and anterior-posterior spread 81mm[range 58-140mm]. There was coverage of the lateral hemithorax from ribs 2-11. There was no spread of injectate to the paravertebral space.

There are few other studies on hemithorax spread with two ipsilateral superficial SAP blocks. Biswas utilised single shot injections (caudal to cranial needle direction) and lateral rather than supine position. We decided that it will ultimately be more comfortable for patients to not have to move into an uncomfortable position. The insertion of a catheter allows deposition of local

anaesthetic which can subsequently be topped up. Biswas concluded that it was the number of injections and volume of injectate that influence spread rather than if the SAP block was performed deeply or superficial. [5] Biswas reported a maximum craniocaudal spread of up to 8 ribs (ribs 1-8 covered) when two 20 ml superficial SAP injections were performed at the level of ribs 3 and 5. Our study showed craniocaudal spread of up to 9 ribs with injections at the 4th and 7th ICS (ribs 2-11 covered).

Our increased craniocaudal spread may be due to differences in cadaver preparation, positioning, and injectate composition. However, it may also reflect more optimal positioning of the two catheters at the 4^{th} and 7^{th} ICS, improved injectate spread from hydrodissection and the effect of ventilation and/or chest wall movement. Our most superior spread was to rib 2 suggesting that more superior SAP insertion at the third rib or caudal to cranial needle insertion as seen with Biswas' study may be suggested to cover higher thoracic levels. Our study supports lower levels of SAP catheter insertion with wider spacing of the catheters to cover a larger and lower area of the hemithorax.

The anterior-posterior spread of 81 mm (median) is slightly less than that reported in the literature of between 98 mm and 104 mm[43, 98]. This may be due to ventilation increasing the craniocaudal spread at the expense of anterior posterior spread, however, it may also be due to how spread was measured. Measurements in Horos are made on two dimensional images, whereas the chest wall is curved (3D) in the anterior-posterior direction. Consequently, the anterior-posterior measurements might underestimate the true extent of spread.

However, an important determinant of clinical effect is the number of rib levels covered, and this can be reliably measured on CT images.

Single site SAP injections provide coverage of between 3 and 5 ribs. [89, 90] Our study supports the use of two superficial SAP catheters to provide coverage of up to 9 ribs, which would be necessary to provide adequate analgesia for those with trauma to multiple rib levels. Catheter insertion would be advisable clinically, rather than single site injection, due to the prolonged duration of analalgesia that can be provided without the need for repeated injections, particularly into anatomical planes that may have been disrupted by previous injection or injury.

One limitation of this study is that the thoracic size of the participants varied, meaning that 100mm spread craniocaudally may cover more rib levels in one cadaver compared to another. We, therefore, presented the craniocaudal results in terms of spread of between ribs or ICS along with millimetre measurements for comparison. Another limitation effecting the generalisability of the results is that fresh frozen cadavers were used rather than living participants. The lower body temperature of the fresh frozen cadavers may have increased injectate viscosity and reduced spread. Tissue properties such as compliance may also be affected by the lower temperatures and freezing process, further impacting injectate spread.

Another challenge of this study was relating the anatomical MAL to a radiological measurement the MTL. All catheter distances from the MTL were measured three times with the coronal,

transverse and sagittal planes reset each time. The narrow ranges in these measurements show that the MTL is a reproducible radiological landmark.

We accounted for the effects of thresholding/windowing and thoracic position on contrast measurements by utilising fixed points such as the scanning table for measurements and a constant catheter diameter and opacity for setting the threshold/window levels between scans[97]. The narrow range of all contrast spread measurements supports the use of this approach.

This study was limited by small sample size (n=6) and lack of a control/comparison group. We did consider a comparison group however, due to the small sample size and access to the CT scanner we wanted to maximise our ability to describe spread across the hemithorax from two catheters. We felt that injectate spread from one catheter had been well described in the literature and we wished to use the first of two CT scans to identify catheter tip location. Our main aim was to assess inject spread from two catheters, the coverage that could be achieved and if posterior spread to the paravertebral space occurred. However, despite a lack of control group we have shown that CT imaging can be successfully used to create reproducible results of injectate spread across the hemithorax. Using CT imaging rather than dissection reduces the risk of the dissection process altering injectate spread, reduces gross observational error and means cadavers can be repurposed, resulting in reduced costs and potentially making this type of study more accessible and affordable than dissection. Other strengths of this study include the control of factors that may influence injectate spread such as ventilation and chest wall

movement, cadaver position and hydrodissection of the fascial plane with catheter insertion[40].

Future research investigating the analgesic impact of two ipsilateral SAP catheters in patients with multiple rib fractures are advised in order to confirm that the increased spread seen with two catheters in cadavers equates to improved analgesia in clinical practice. Further investigation into how thoracic trauma may affect injectate spread though disruption of the fascial planes, the influence of fascial nociceptive receptors and the impact of systemic absorption of local anaesthetic would also add to the knowledge base of how SAP blocks exert their clinical effects in patients with thoracic trauma[99].

In conclusion, this study has demonstrated that the insertion of two catheters at intercostal spaces 4 and 7 resulted in consistent coverage of the hemithorax. Our results are in keeping with previous studies that suggest SAP is likely to be most effective for lateral fractures due to there being no spread of injectate to the paravertebral space. [43] The findings of this study will also be applicable to patients undergoing thoracic wall surgery that involves multiple levels.

CHAPTER FOUR:

EFFECTIVENESS OF SERRATUS ANTERIOR PLANE CATHETERS COMPARED WITH OPIOID ONLY ANALGESIA IN PATIENTS WITH MULTIPLE TRAUMATIC RIB FRACTURES ADMITTED TO CRITICAL CARE

INTRODUCTION

Rib fractures are present in 10% of those admitted to hospital following trauma and up to 50% of these patients will require intensive care admission.[1] These patients are at a high risk of developing significant long-term disabilities and mortality. This can be a consequence of the primary injury or a result of secondary complications such as pneumonia, acute respiratory distress syndrome and sepsis.[12, 16]

Factors that increase the risk of mortality include patient age, number of rib fractures, bilateral rib fractures, presence of flail, polytrauma and pre-existing comorbidities.[1] Mortality is approximately 10% however, this increases to 33% in the elderly and those with polytrauma.[2] Pneumonia develops in nearly a third of all patients with rib fractures and this is associated with a mortality rate as high as 65%.[17, 100, 101]

It is recognised that pain contributes to the development of pneumonia.[100] Aggressive and optimum analgesia is, therefore, one of the treatment goals for these patients to encourage deep breathing, coughing and patient mobility to reduce the risk of developing respiratory complications. A variety of analgesic approaches exist, including conservative methods based on opioid analgesic regimes and invasive regional techniques. Regional techniques utilise

traditional methods of thoracic epidural (TEA) and paravertebral catheters (PA) along with novel thoracic wall fascial plane blocks that include serratus anterior plane (SAP) and erector spinae plane blocks (ESP).[6, 9, 100]

Thoracic epidural analgesia (TEA) is commonly seen as the gold standard. However, systematic reviews and metanalysis of the current literature although showing improvement in pain fail to show any significant change in patient outcome with their use.[100, 102] TEA and PA are advanced regional anaesthetic technique performed only by experienced anaesthetists. TEA insertion is also contraindicated in patients with hypotension, hypovolemia, coagulopathy and patients with significant spinal or traumatic brain injuries. These limitations meant that in 2017 less than 3% of patients in England and Wales received TEA or PA analgesia for MRFs[5].

The increased popularity of the thoracic fascial plane blocks has been driven by their ease of insertion, safety due to the use of ultrasound guidance, minimal contraindications and few side effects. SAP catheters with their superficial insertion site and ability to be performed in the supine position make them suitable for trauma patients with abnormal coagulation or movement restrictions. Case reports and case series have demonstrated a reduction in opioid consumption, pain scores and improvement in inspiratory volumes in patients who receive SAP for MRFs.[103-105]

This study aims to compare SAP analgesia to a opioid only 'no block' group in patients admitted to critical care with MRFs following trauma. One limitation of this type of study, is selection bias i.e., those patients with certain characteristics are more likely to receive one type of treatment

over another. Such confounding can be addressed through the use of multivariable regression analysis, but the statistical literature points to several problems with this method, including violation of statistical assumptions between covariates and exposure and errors when the number of cases per covariate is low.[106-108] Thus, this study uses 'matching procedures' instead. These aim to equate (or balance) the distribution of covariates in the experimental and control groups. One way to do this, is using propensity scores, which express how likely participants are to be selected into a treatment condition given observed covariates. Participants in the 'treatment group' are then paired or 'matched' to those with similar scores in the 'control' group.

AIM:

To investigate whether SAP blocks are associated with reduced opioid consumption, improved analgesia and outcomes compared to when opioid-based treatments are used alone in patients admitted to critical care with multiple rib fractures following trauma.

Primary research question is:

1. Is the use of SAP catheters for the analgesia of traumatic rib fractures associated with a reduction in opioid consumption?

Secondary research questions include:

2. Is the use of SAP catheters associated with a reduction in the following outcomes?

Analgesic Effects

a. Highest daily pain score

b. number of hours per day a patient reports severe pain

Respiratory Effects

a. Development of pneumonia

b. Oxygen requirement

Cardiovascular Effects

c. Inotrope consumption

d. Mean arterial (MAP) blood pressure

e. Daily fluid balance

Mortality and Length of Stay

f. Hospital LOS

g. Critical care LOS

h. Mortality

METHODS

Design

Single centre retrospective observational study with propensity score matching and adjustment of baseline covariates. Institutional approval was obtained (CARMS 13906).

Treatment group: SAP block with opioid analgesia

Control group: Opioid based analgesia only (no block group)

Recruitment/participants

Patients admitted between January 2016-September 2019 to the Queen Elizabeth Hospital Intensive Care Unit (ICU) were included in the study with the following inclusion and exclusion criteria:

SAP catheter insertion commenced in February 2018. The 'no block group' was taken from the period before this (January 2016-January 2018). This was to reduce selection bias and ensured a suitable sample size to propensity match.

- SAP group: February 2018 – September 2019
- Opioid group: January 2016 – January 2018

INCLUSION CRITERIA

1. Adult Patients ≥16years
2. ≥3 Rib fractures following trauma
3. Admitted to intensive care
4. Received SAP or opioid only treatment

EXCLUSION CRITERIA

1. Death within 24hours
2. Transfer from another hospital
3. Additional form of regional anaesthesia not SAP i.e. TEA, PA, ESP
4. Missing Data
    a) No CT scan or CT report available to categorise and score injuries.

b) All observation and medication data from ICU admission unavailable. *The electronic system was introduced across ICU units in a staggered approach in 2016 meaning that not all patients admitted in 2016 had their data recorded electronically.

5. SAP removed within 24hours insertion
6. SAP not inserted within 7 days

Figure 23 shows the number of patients that were included in the analysis. The justification for removal of SAP within 24hours was increased resistance to injection (n=1), patient request/self discharge (n=2), removed in theatre for surgical access and not replaced (n=1), reason not documented (n=1).

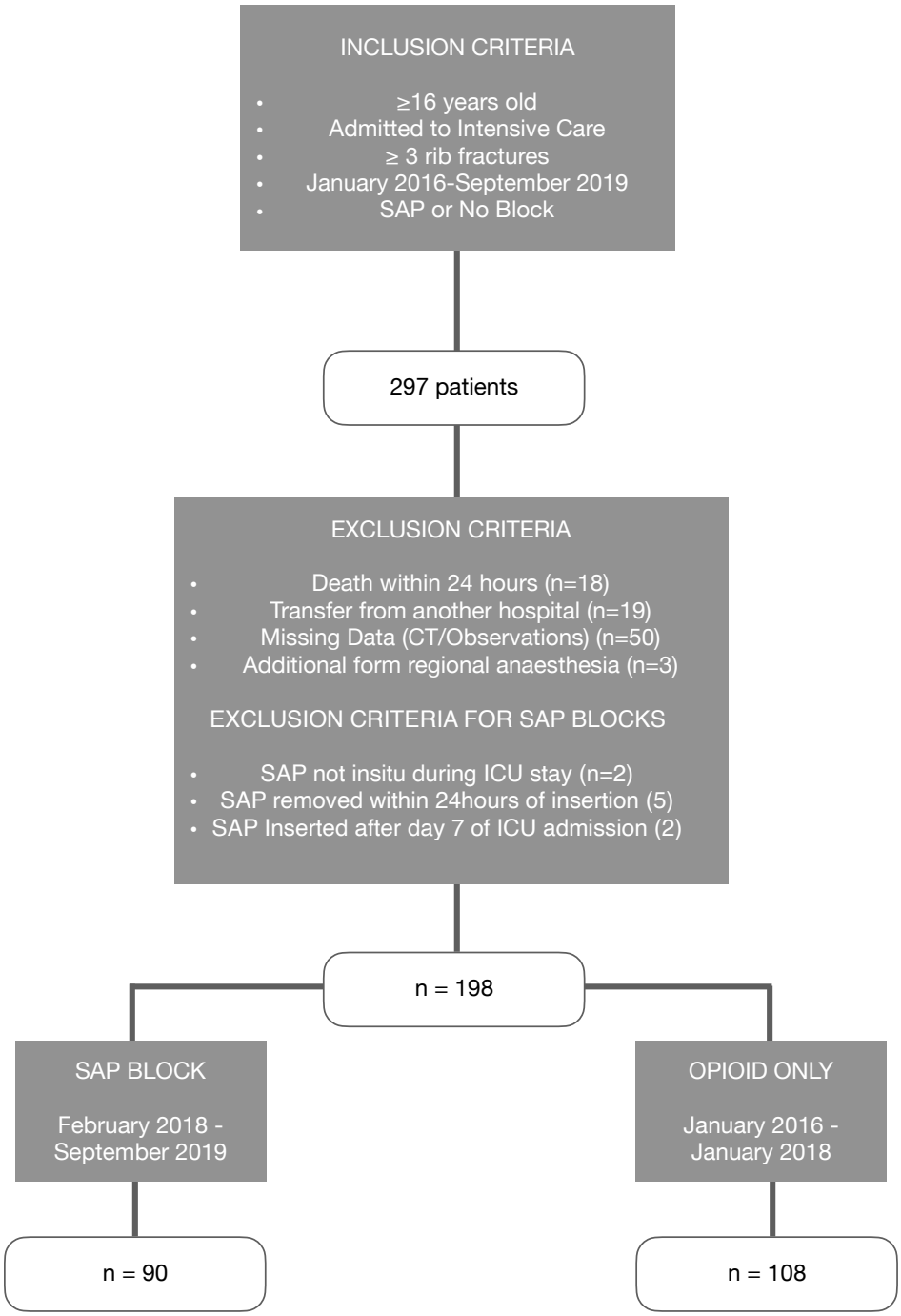


Figure 23 Inclusion and Exclusion Criteria

Data Collection

Data was collected from the Trauma Audit Research Network (TARN) database and the hospitals electronic patient record (PICs/Clinical Portal) for the Queen Elizabeth Hospital

Intensive Care Unit (ICU). The Queen Elizabeth Hospital is a level 1 trauma centre specialising in the management in severe trauma and chest injuries.

Patient parameter data was collected from the electronic patient record for the first 14 days of their critical care stay. Day 1 commenced on their admission to ITU. If patients were discharged from ICU before the 14 days, data collection ceased on the last day that data was available for the 24hours. The time and date of SAP catheter insertion was recorded.

A standardised data collection form was used to reduce any variation in data record keeping amongst the team. All those collecting data were blinded as to the treatment group.

PRIMARY DEPENDENT VARIABLE

Daily oral morphine equivalent (OME) - calculated from oral morphine, IV morphine (PCA and bolus), codeine and tramadol doses as per guidance from the Faculty of Pain Medicine of the Royal College of Anaesthetists [109].

SECONDARY DEPENDENT VARIABLES

Analgesic Effects

- Daily Highest pain score (Numerical rating scale, NRS, 0-10)
- Number of hours per day patients report severe pain (hours)

Respiratory Effects

- Pneumonia development during hospital admission (yes/no). Pneumonia diagnosis was collected from information provided by clinical coding about the patient's inpatient stay. Codes relating to respiratory infection and pneumonia were used.
- Daily highest oxygen requirement (fractional inspired oxygen, FiO_2, %)

Cardiovascular Effects

- Noradrenaline requirements (mg/kg/day)
- Daily lowest MAP (mm/Hg)
- Daily fluid balance (mls/24hrs)

Mortality and Length of Stay

- Mortality in hospital at 30 days
- Length of stay in hospital, LOSHosp (days)
- Length of stay in critical care, LOScc (days)

COVARIATES

Randomised controlled trials can balance known and unknown confounders via a process of randomisation. For observational studies this is not possible. Propensity score matching can be used to obtain a quazi-randomisation, to limit the unbalance of covariates between groups, minimise bias and better estimate true treatment effects.[110, 111]

Propensity score matching is preferred to regression adjustment alone. With propensity score matching it is simpler to ascertain if the propensity score model has been adequately specified. It also allows the design of the study to be separated from the analysis, with participants scored and matched before any analysis of treatment outcome. With regression adjustment the

outcome is known, and subtle adjustments can be made until a desired association is seen. In this study the use of regression was specified prior to analysis and used to help eliminate any residual imbalance in prognostically important covariates.[111]

Propensity score matching methodology was used for this study. 1:1 Nearest neighbour was performed where patients in the treatment and control groups with the most similar propensity scores were matched and their outcomes compared.[111-113]

Matching is dependent on sample size and so careful consideration was given as to what covariates to include. Including unnecessary covariates could result in poor matching across groups and therefore loss of participants. Thus, covariates were chosen based on previous research where there was a known association with group assignment and/or the primary outcome of interest.[110, 112]

Participants were matched according to Age, Sex, Injury severity score (ISS) and Rib Fracture score(RFS). We know from the literature that trauma patient outcomes are affected by sex, age, the severity of the trauma given by the ISS score and also the degree of chest trauma reflected in the RFS.[1, 9, 114-116] Sex plays a role in acute pain, with women demonstrating a lower threshold and tolerance for pain but greater analgesic efficacy than male subjects.[114, 117] This is thought to be a consequence of hormonal effects, differences in anatomy and physiology and genetic factors.[114, 118] These four factors are also likely to impact on patient assignment to the treatment group.[110]

Following propensity matching, adjustments were made for other covariates. This was to reduce the effect of other cofounding variables not yet accounted for. Due to the small sample size, covariates were adjusted if their standardised absolute mean difference (SMD) was >0.1.[119] Covariates included were; Isolated chest injury or polytrauma, Surgical rib fixation, Charleston comorbidity index (CCI), most severely injured body region (Head, Chest, Abdomen, Limbs, other) and if an additional surgical procedure was performed during admission.

Other covariates were collected but not included in the propensity score matching or adjustments. This is either because there was no evidence in the literature for an association with the treatment allocation/outcome or the data did not directly reflect the clinical picture. For example, a tracheostomy can be inserted for severe head injuries or respiratory failure. The data, however, assisted with the interpretation of results.

Additional covariates not matched or adjusted for:

- Rib fracture pattern (anterior/lateral/posterior)
- Mechanism of injury (fall, traffic collision)
- Tracheostomy

ANALYSIS

All data was analysed in R with alpha set to 0.05. All tests were two tailed. Missing data was handled using a pairwise deletion approach.

Propensity matching was undertaken for the primary and secondary outcome measures. As discussed above participants were matched on Age, Sex, ISS, RFS. Adjustments when indicated were made for Isolated chest injury or polytrauma, Surgical rib fixation, CCI, most severely injured body region and if an additional surgical procedure was performed during admission.

Data was analysed using generalised linear models. They specified the negative binomial family with log link function (negative binomial regression) for ordinal outcomes. Negative binomial models were used instead of Poisson regression due to the likely presence of overdispersion. For binary outcomes we used a log-binomial model and reported relative risks (RR). For continuous outcomes we specified the Gaussian family (similar to traditional linear regression). All model assumptions were assessed and data transformations applied where necessary. Propensity matching and regression was undertaken under the guidance of Dr Emma Beard, Department of Epidemiology and Public Health, UCL, University College London, London, UK.

RESULTS

Data were collected on 198 participants with an average age of 55.5 years (SD 19.8). Table 11 shows the characteristics of included participants. Table 12 shows the characteristics of inserted SAP blocks.

Variable	Opioid Only (n=108)		SAP Block (n=90)	
Gender %(n)				
Male	75.9	(82)	74.4	(67)
Female	24.1	(26)	24.6	(23)
Age M(SD)	52.4	(19.2)	59.3	(20.0)
Mechanism of injury %(n)				
Fall	33.3	(36)	41.1	(37)
RTC	63.0	(68)	52.2	(47)
Other	3.7	(4)	6.7	(6)
Isolated/polytrauma %(n)				
Isolated chest injury	8.3	(9)	17.8	(16)
Polytrauma	91.7	(99)	82.2	(74)
Injured body region %(n)				
Chest				
Abdo	35.2	(38)	51.1	(46)
Head	4.6	(5)	2.2	(2)
Limbs	25.00	(27)	11.1	(10)
Spline	6.5	(7)	5.6	(5)
Multiple	0.9	(1)	0.0	(0)
Other	27.8	(30)	30.0	(27)
ISS M(SD)	32.3	(12.9)	28.8	(11.2)
CCI M(SD)	1.5	(1.7)	2.3	(2.2)
Rib Fracture Score M(SD)	12.8	(10.2)	16.9	(10.5)
Surgical fixation of ribs %(n)	6.5	(7)	18.9	(17)
Rib fracture location % (n)				
Anterior	11.0	(9)	7.6	(5)
Lateral	4.8	(4)	6.1	(4)
Posterior	16.6	(14)	12.2	(8)
Ant/Lat	19.0	(16)	13.6	(9)
Post/Lat	16.6	(14)	24.2	(16)
Ant/Post	7.0	(6)	13.6	(9)
Ant/Post/Lat	25.0	(21)	22.7	(15)
Missing Data		(24)		(24)
Surgical procedure %(n) *	47.2	(51)	50.0	(45)
Tracheostomy %(n)	37.0	(40)	20.0	(18)
Highest level of care %(n)				
Level 2	42.6	(46)	65.5	(59)
Level 3	57.4	(62)	34.5	(31)
Pneumonia during admission %(n)	35.2	(38)	26.7	(24)
Mortality in hospital at 30days	9.3	(10)	6.7	(6)
LOS hospital M(SD)	29.5	(24.6)	25.3	(19.0)
LOS critical care M(SD)	11.6	(12.0)	9.04	(10.4)

* *within 28days of admission i.e Laparotomy, neurosurgery, orthopaedic surgery, plastic surgery and other - not including rib fracture surgery*

Table 11 Descriptive statistics for baseline variables.

Variable	SAP Block (n=90)	
Grade of person performing block %(n)		
ACCP	31.2	(28)
Doctor in training (ST2-7)	50.0	(45)
Consultant	15.5	(14)
Unknown	3.3	(3)
Time of insertion after ICU admission (days)		
Mean (SD)	0.98	(1.26)
Range	-1.3 – 5.1	
Duration of block (days)		
Mean (SD)	5.6	(2.24)
Range	1.09-11.25	
Complication %(n)		
None	88.9	(80)
Displaced*	5.6	(5)
Block deemed inadequate **	2.2	(2)
Leaking***	2.2	(2)
Infection ****	1.1	(1)
Swelling/Haematoma	0.0	(0)
Drug infused %(n)		
Infusion (0.125% levobupivocaine 10-20mls/hr)	80	(72)
Bolus' (0.125-0.25% levobupivocaine)	20	(18)
Bilateral blocks %(n)	15.6	(14)
Intubated at time of block %(n)		
No	71.1	(64)
Yes	25.6	(23)
Unknown	3.3	(3)

** 3 patients pulled out catheters due to confusion. Catheter duration between 1.75-8.5 days*
***removed days 2.55 and 2.82, both polytrauma patients.*
**** Started leaking days 4.8-7.4 when removed*
***** Some discharge from around catheter, no growth from catheter tip, mixed organism on swab, no reported sepsis, requirement for antibiotics post removal. Duration of catheter 8.2 days.*

Table 12 Characteristics of inserted SAP blocks.

Propensity Matching

180 participants (90 in each group) were matched. Figure 24 shows reasonably similar distributions of propensity scores in the two groups, while figure 25 shows that the propensity score matching improved the similarity between groups on the measurements of interest.

Participants were matched according to Age, Sex, Injury severity score (ISS) and Rib Fracture score(RFS). Adjustments were made for the following covariates: isolated chest injury or

polytrauma, Surgical rib fixation, Charleston comorbidity index (CCI), most severely injured body region (Head, Chest, Abdomen, Limbs, other) and if a surgical procedure was performed during admission.

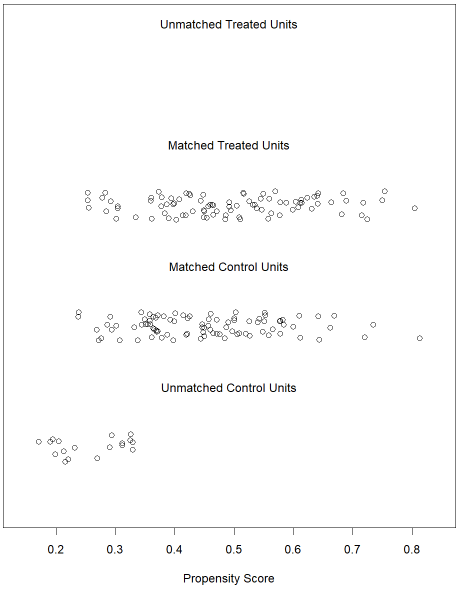


Figure 24 Distribution of propensity scores

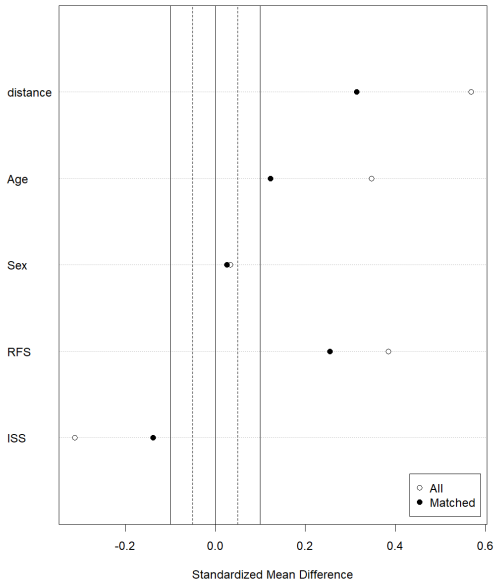


Figure 25 Standardised mean difference overall for each variable and as a function of matched participants

PRIMARY ANALYSIS

Opioid Consumption (OME)

The average OME as a function of group across the 14 days is given in table 13 for the participants included in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was no statistically significant difference in OME across the 14 days

between groups (B=-4.6 95%CI -28.1 to 19.0, P=0.702). A similar finding was found after adjusting for the confounders (B=6.4 95%CI -16.7 to 29.4, P=0.607). Moderation effects with time were assessed, these indicated a statistically significant interaction on days 2, 6, 7, 8, 9, 11, 12 (P<0.05).

	OME (mg/day)		Highest Pain Score (NRS)		Reporting severe pain (hrs)	
Day	Opioid Only Mean(SD)	SAP Block Mean (SD)	Opioid Only Mean(SD)	SAP Block Mean (SD)	Opioid Only Mean(SD)	SAP Block Mean (SD)
1	94.9 (169.4)	103.3 (87.9)	5.14 (2.19)	6.25 (2.38)	1.04 (2.38)	2.35 (4.36)
2	107 (223)	82.4 (84.0)	3.52 (2.64)	4.56 (2.64)	0.38 (1.05)	1.59 (4.21)
3	86.9 (192)	65.2 (77.7)	3.50 (2.50)	4.02 (2.24)	0.50 (1.61)	0.68 (2.61)
4	93.0 (186)	66.9 (93.6)	3.45 (2.63)	2.94 (2.62)	0.55 (1.84)	0.51 (1.37)
5	92.4 (191)	73.8 (122)	3.00 (2.40)	3.17 (2.88)	0.74 (3.65)	1.41 (4.65)
6	90.8 (166)	44.4 (65.9)	2.39 (2.60)	1.81 (2.43)	0.75 (2.75)	0.04 (0.20)
7	92.2 (163)	49.1 (104)	1.30 (1.58)	2.00 (2.43)	0.00 (0.00)	0.38 (1.41)
8	67.7 (135)	40.0 (80.8)	2.00 (2.79)	2.50 (2.65)	0.10 (0.40)	0.40 (1.56)
9	61.7 (103)	23.1 (36.5)	1.14 (2.01)	2.33 (2.26)	0.42 (1.59)	0.40 (1.68)
10	69.6 (125)	36.3 (110)	2.36 (2.33)	2.81 (3.41)	0.11 (0.43)	0.60 (1.68)
11	81.6 (145)	22.4 (26.7)	2.41 (3.14)	3.24 (2.75)	0.96 (3.06)	1.12 (3.09)
12	55.6 (83.1)	18.6 (19.1)	2.07 (2.67)	1.31 (1.75)	0.34 (0.18)	0.00 (0.00)
13	53.3 (78.3)	15.5 (17.4)	1.12 (1.74)	2.50 (2.41)	0.00 (0.00)	0.28 (1.69)
14	43.4 (62.2)	15.2 (15.9)	1.21 (2.50)	1.69 (1.60)	0.33 (1.27)	0.00 (0.00)

NRS, Numerical Rating Scale

Table 13 Average OME, highest pain score (NRS 0-10), and hours patients reporting severe pain (NRS ≥7) each day given across the 14 days as a function of group assignment.

SECONDARY ANALYSIS

Pain Assessment

Daily Highest Pain Score

Daily highest pain score as a function of group across the 14 days is given in Table 13 for the participants included in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was a statistically significant difference in pain scores across the 14 days

between groups in both the adjusted and unadjusted (unadjusted B=0.6 95%CI 0.04 to 1.13, P=0.035, adjusted B=0.9 95%CI 0.3 to 1.5, P=0.004). The SAP group reported greater highest daily pain scores on average over the 14days than the opioid only group. Moderation effects with time were assessed, these indicated a statistically significant interaction only on days 5 and 6 (P<0.05)

Number of hours each day patient reports severe pain (NRS ≤7)

Daily number of hours reporting severe pain as function of group across the 14 days is given in Table 13 for the participants involved in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was a statistically significant difference in the number of hours patients reported severe pain each day across the 14 days between groups if both the adjusted and unadjusted models (unadjusted B=0.5 95%CI 0.03 to 0.92, P=0.035, adjusted B=0.7 95%CI 0.2 to 1.1, P=0.009). The SAP group reported more hours of severe pain on average over the 14days than the opioid only group. Moderation effects with time were assessed, these indicated a statistically significant interaction on days 3 and 6 (P<0.05).

Day	Highest FIO_2 (%)		Lowest MAP (mmHg)		Fluid Balance	
	Opioid Only Mean(SD)	SAP Block Mean (SD)	Opioid Only Mean(SD)	SAP Block Mean (SD)	Opioid Only Mean(SD)	SAP Block Mean (SD)
1	48.4 (22.3)	47.1 (22.7)	67.4 (10.8)	71.2 (10.5)	609 (1936)	-107 (1222)
2	43.4 (19.2)	43.3 (17.5)	70.3 (11.1)	71.7 (11.4)	948 (1956)	95.3 (1636)
3	46.2 (21.1)	45.4 (18.9)	70.0 (11.9)	72.9 (12.4)	359 (1831)	-1.27 (1320)
4	42 (16.9)	43.2 (16.8)	70.8 (10.8)	71.9 (12.0)	279 (1737)	-168 (1122)
5	47.2 (22.2)	42.1 (15.6)	74.0 (13.2)	73.0 (12.6)	136 (1676)	-325 (1175)
6	41.5 (15.2)	43.6 (21.1)	73.5 (14.1)	74.1 (13.6)	102 (1137)	-53 (1455)
7	43.7 (20.6)	41 (17.8)	72.3 (11.3)	76.7 (11.1)	140 (1439)	-228 (1288)
8	43 (16.2)	38.4 (11.0)	72.7 (11.4)	73.1 (14.0)	-103 (1298)	-347 (1186)
9	43.6 (16.3)	37 (9.91)	73.2 (12.4)	69.8 (12.2)	-266 (1561)	-291 (1318)
10	43.6 (14.8)	41.9 (19.2)	71.8 (10.5)	72.6 (12.8)	-276 (1248)	-578 (1179)
11	43.1 (16.9)	40.7 (11.4)	75.3 (13.8)	70.6 (11.4)	-105 (1211)	-241 (1300)
12	40.4 (16.9)	44.9 (18.1)	73.4 (10.9)	66.1 (13.9)	95 (1445)	178 (1203)
13	41.3 (18.9)	40.5 (14.7)	73.5 (11.3)	70.6 (13.4)	-94.5 (1212)	329 (1837)
14	39.4 (19.6)	38.4 (7.97)	72.6 (9.9)	68.8 (10.7)	42.4 (1099)	234 (1452)

Table 14 Average highest Fio2, lowest MAP and daily fluid balance given across the 14 days as a function of group assignment.

Respiratory Assessment

Pneumonia development during hospital admission

Thirty-five percent (n=38) had pneumonia in the opioid group and 26.7% (n=24) in the SAP group. Following propensity matching there was not a statically significant difference between groups in the odds of having pneumonia during admission for the unadjusted or adjusted model (unadjusted OR 0.72, 95% 0.4 to 1.4, P=0.325, adjusted OR 0.9 95%CI 0.4 to 1.9, P=0.799).

Daily highest oxygen requirement: fractional inspired oxygen (FiO2)

The highest FiO_2 as a function of group across the 14 days is given in Table 14 for the participants included in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was no statistically significant difference in the highest Fio2 across the

14 days between groups for the unadjusted and adjusted models with propensity matching (unadjusted B=-1.4 95%CI -5.1 to 2.2, P=0.437, adjusted B=-0.2 95%CI -4.3 to 3.9, P=0.935). Moderation effects with time were assessed, these indicated no statistically significant interaction (P>0.05).

Cardiovascular Assessment

Lowest Daily MAP

The lowest MAP as a function of group across the 14 days is given in Table 14 for the participants included in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was no statistically significant difference in the lowest MAP across the 14 days between groups in both the adjusted and unadjusted models (Unadjusted B=1.0 95%CI -1.9 to 4.0, P=0.488, Adjusted B=0.2 95%CI -3.0 to 3.5, P=0.891).. Moderation effects with time were assessed, these indicated a statistically significant interaction only on day 11 (P<0.05).

Noradrenaline requirements (mg/kg/day)

The average noradrenaline requirements (mg/kg/day) for the opioid group was 0.12mg/kg/day (SD 0.23) and among the SAP group 0.04mg/kg/day (SD 0.16). The mean was not significantly different following propensity matching (unadjusted model B -0.04 95%CI -0.09 to 0.01. P=0.126). The same non-significant findings were found in the adjusted model (IRR=0.9=01 95%CI -0/04 to 0.05, P=0.748).

For reference 0.12mg/kg/day and 0.04mg/kg/day are equivalent to 0.08mcg/kg/min and 0.03mcg/kg/min which are both clinically low infusion rates[120].

Daily Fluid Balance

Daily fluid balance as a function of group across the 14 days is given in Table 14 for the participants included in propensity matching.

After adjusting for time and including a random intercept to account for repeated measurements, there was a statistically significant difference in the fluid intake across the 14 days between groups following propensity matching (unadjusted B=-359.4 95%CI -661.8 to -56.4, P=0.020) with the SAP groups having on average a lower daily fluid balance. This was not significant after adjusting for confounders (adjusted B=-290.3 95%CI -600.5 to 15.4, P=0.074). Moderation effects with time were assessed, these indicated no statistically significant interaction (P>0.05).

Mortality and Length of Stay Measures

Mortality in hospital at 30days

At 30days 9.3% (n=10) of the opioid group had died while 6.7% (n=6) of the SAP group had died. Following propensity matching there was not a statically significant difference between groups in the odds of mortality during admission for the unadjusted model (unadjusted OR 1.8, 95% 0.6 to 5.3, P=0.300). The adjusted model did not converge.

Length of stay critical care

The average LOS in stay in critical care among the opioid group was 11.6days (SD 12.0) and among the SAP group 9.0days (SD 10.4). The expected count was significantly lower in the SAP group in the unadjusted model (IRR=0.8 95%CI 0.8 to 0.9 P<0.001). This was non-significant in the adjusted model (IRR=0.9 95%CI 0.8 to 1.0, P=0.052).

Length of hospital stay

The average LOS in stay in hospital among the opioid group was 29.5 (SD 24.6) and among the SAP group 25.3 (SD 19.0). The expected count was significantly lower in the SAP group in the unadjusted model (IRR= 0.9 95%CI 0.9 to 1.0 P=0.002). The same findings were found in the adjusted model (IRR=0.9 95%CI 0.9 to 1.0, P=0.046).

DISCUSSION

The primary analysis showed that there was significant reduction in opioid consumption (OME) for the SAP group on days 2,6,7,8,9,11 and 12. SAP catheters were inserted 1 day before ICU admission up until day 5 (mean 0.98days) and remained in situ for between 1 and 11 days (mean 5.6days). Table 13 shows that apart from day 1 the mean daily OME for the SAP group was always lower than the opioid only 'no block' group. The lack of statistically significant difference on days 1,3,4,5 may reflect the SAP catheter not yet being in situ, the impact of other injuries and surgical procedures not being fully accounted for by adjustment and/or underpowering. The results suggest that SAP catheters may be associated with a reduction in opioid consumption during critical care admission. This is supported by the literature where

Riley et all identified daily equivalent oral morphine consumption was significantly reduced following SAP block insertion from 83.8mg (SD70.6) to 51.3mg (SD 30mg, P=0.05)[60].

The rate of catheter displacement was 2.2% (n=2). This is in line with SAP catheter displacement rate of 2.6% and epidural displacement rate of 3.6% as reported in the current literature[65-67, 81]. The entry site infection rate was 1.1% (n=1) which is lower than the epidural entry site infection/inflammation reported rate of 2.6% [81]. This supports the assumption that SAP catheters are safe to insert with no greater risk of complications than traditional catheter techniques.

Our study adds evidence to the view that SAP blocks are cardiovascularly stable. No significant difference overall or with time effects was identified for noradrenaline requirements, lowest MAP or daily fluid balance between the groups. A similar finding was reported by Okmen et all where no significant difference in hypotension between a SAP group and opioid only group was identified (P=0.157)[121].

In relation to pain assessment, the opioid only group had significantly lower values for the outcomes of 'highest pain score' and 'number of hours severe pain reported' over the 14-day period for both unadjusted and adjusted models. However, when moderation with time was assessed, for both outcomes there was only a statistically significant interaction for two of the days ($P<0.05$). For 'highest pain score' the daily means between the groups varied by less than 1point on the NRS days 2-14 (table 13). For 'number of hours severe pain reported' the difference between the mean scores was always less than 1.3hours (table 13). Therefore,

although a statistically significant difference was found overall the clinical relevance of these results is negligible.

A significantly lower LOS in hospital was identified in the SAP group compared to the opioid only group (SAP 25.3days, SD 19.0 vs Opioid Only 29.5days SD 24.6, adjusted model P=0.046). This may be a true reflection of the impact of SAP on LOS in hospital. However, there was no significant difference in critical care LOS. It may, therefore, represent factors that were not fully accounted for in matching and adjustment and external factors that affect LOS such as staffing provisions, social circumstances and discharge destinations. For example, the opioid only group had a higher incidence of tracheostomy insertion 37% versus 20% in the SAP group, this may have impacted on the patients length of stay in hospital and eventual discharge destination.

There were limitations to this study. The first limitation being its retrospective design. Although propensity matching and adjustment attempted to account for this it cannot fully replicate the conditions of a prospective randomised controlled trial[111]. Secondly underpowering is likely to be a factor for some of the non-significant results due to the large variance reported for some of the results. Thirdly, for any retrospective study the results are only as accurate as the recorded data. We tried to account for this with our inclusion and exclusion criteria along with using a protocol to standardise data collection but missing data may still impact the results despite these measures. Finally, there are many factors that impact on oral morphine consumption, pain scores, LOS and mortality. We tried to account for this with propensity matching and adjustment for major cofounders. However, there are likely many other external factors that influence these outcomes that cannot be fully adjusted for or even measured. This

may in part explain why identifying differences in patient outcomes with pain interventions alone is challenging.

Prospective randomised controlled trials are required to better assess the effectiveness of SAP catheters in patients with thoracic trauma. Increased emphasis should be given to patient reported outcomes such as mobility, engagement with physiotherapy and quality of life. Prospective studies should also assess the clinical impact of opioids such as constipation and delirium which are difficult to assess retrospectively. This would more clearly delineate the relevance of the opiate sparing effects of SAP catheters to patients. Objective measures of analgesic adequacy e.g. vital capacity along with an assessment of pain tolerability may provide a more accurate overview of analgesic effectiveness than the measurement pain scores alone which are subjective[122].

In conclusion, SAP catheters are likely associated with reduction in opioid consumption. They appear to be a safe technique with no greater complication rate than currently utilised pain catheter techniques and have minimal cardiovascular effects. However, further prospective randomised controlled trials reporting objective measures of pain assessment and patient reported outcome measures are needed to better assess the effectiveness of SAP catheters in patients with thoracic trauma against traditional pain management techniques.

CHAPTER FIVE:

A MULTI-CENTRE LONGITUDINAL CROSS-SECTIONAL STUDY COMPARING SERRATUS ANTERIOR PLANE, PARAVERTEBRAL AND THORACIC EPIDURAL FOR THE ANALGESIA OF MULTIPLE RIB FRACTURES.

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Article presented in its unaltered form below.

ABSTRACT

Background:

There is a paucity of data comparing effectiveness of various techniques for pain management of traumatic rib fractures. This study compared the quality of analgesia provided by serratus anterior plane (SAP) catheters against thoracic epidural (TEA) or paravertebral catheters (PA) in patients with multiple traumatic rib fractures (MRFs).

Methods:

354 patients who received either SAP, TEA or PA at two tertiary referral major trauma centres in the UK were included (2016-2018). Primary outcomes were change in inspiratory volumes and pain scores. Secondary outcomes included in-hospital mortality, along with the length of stay in hospital and critical care. Data were analysed using linear, log-binomial and negative binomial regression models.

Main Results:

Across all blocks, there was a mean (SD) increase in inspiratory volume post block of 789.4mls (479.7). Ninety-eight percent of all participants reported moderate/severe pain prior to regional analgesia, which was reduced to 34% post block. There was no significant difference in the change in inspiratory volume or pain scores between the TEA, PA or SAP groups. Overall crude mortality was 13.2% (95% CI 7.8 to 18.7). In an adjusted analysis and compared to TEA, in-hospital mortality was similar between groups (RR 0.38, 95% CI 0.14 to 1.01) and (RR 0.54, 95% CI 0.18 to 1.64) for SAP and PA respectively.

Conclusion:

SAP, TEA, and PA all appear to offer the ability to reduce pain scores and improve respiratory function.

INTRODUCTION

Patients with thoracic trauma are at significant risk of morbidity and mortality from their initial thoracic injury or as a consequence of secondary insults such as atelectasis, pneumonia, and acute respiratory distress syndrome. Pneumonia, as a complication of multiple rib fractures

(MRFs), is diagnosed in 11-31% of patients and associated with increased mortality.[1, 2, 17] Effective analgesia has been shown to reduce the risk of respiratory complications by enabling the patient to deep breath, cough and facilitate early mobilisation.[12-14]

Regional analgesic techniques such as thoracic epidural (TEA) and paravertebral catheters (PA) have long been used as the "gold standard" method in the multimodal approach of pain management. Their use, however, is limited due to concomitant injuries (such as spinal and head injuries), contraindications (such as trauma-related coagulopathy and anticoagulant medications), multi-morbidity (e.g. ageing trauma population) and inability to position the patient during the acute phase. Current literature reports TEA use between 9.9% and 18.4% in this group, with opioid analgesia, dominant.[1-4]

Thoracic wall fascial plane blocks with their ease of insertion, absence of beta-blockade effect with haemodynamic stability and safety are a welcome addition to the analgesic armamentarium in patients with MRFs.[6] Many fascial plane techniques have been described, they include the serratus anterior plane (SAP), erector spinae plane (ESP), and rhomboid intercostal blocks, although high quality data on their efficacy is lacking.[123] Some blocks, such as the erector spinae plane, paravertebral and thoracic epidural, require patient cooperation in a lateral or sitting position during block insertion. This is often impossible in patients with significant thoracic, head or pelvic injuries after polytrauma. SAP blocks can be performed in the supine position with minimal repositioning. The evidence base for SAP analgesia in those with multiple rib fractures is limited to mainly case reports and case series.

Pain scores can be static (when the patient is at rest) or dynamic (on movement and coughing). Dynamic pain scores are more pertinent in patients with MRFs as this would determine their ability to breathe deeply, cough and mobilise when they are most vulnerable to develop respiratory complications. [1, 124] For these reasons, we believe that a functional physiological assessment of analgesic adequacy assessed by measuring inspiratory volumes (incentive spirometry) should be a mandated outcome measure along with standard pain scores. This combined approach provides a better reflection of analgesic adequacy in this cohort.

The primary aim of this study was to compare the quality of analgesia, assessed by dynamic pain scores and inspiratory volumes, between SAP, TEA and PA catheters in a group of patients with traumatic MRFs. The secondary aim was to investigate if there was a difference in patient outcome between the three groups by analysing the length of stay and mortality data. Although systematic reviews have analysed studies comparing TEA, PA, intercostal nerve blocks and opiate based treatments, to our knowledge this is the first study to compare the effectiveness of SAP to PA or TEA.[100, 102]

METHODS

Design:

We included all consecutive adults with multiple rib fractures who received SAP, TEA or PA catheters and were admitted to hospital between 2016 and 2018 in two tertiary referral major trauma centres in the UK. Patients who had more than one type of regional anaesthesia or who died within 24 hours of admission to hospital were excluded. Outcome data were collected from existing pain databases and patient records. This was merged with data from a high-

quality national database provided by the Trauma Audit Research Network (TARN). Institutional approval was obtained from both sites (GF0223 / CARMS14833)

Measures:

Primary outcome

The primary outcome measure was block effectiveness defined by a change in inspiratory volumes (mls) and dynamic pain scores, recorded before and after block insertion (within 90 minutes). Inspiratory volumes were measured with an incentive spirometer (mls). Pain scores were measured by a 4-point Likert Verbal Rating Scale (VRS) using standardised categories. [125] Pain scores of 0-3 were recorded, where 0 = no pain, 1 = mild pain, 2 = moderate pain and 3 = severe pain. The four-point pain score was selected as this was the adopted practice in participating sites. Previous studies have shown that responses to the VRS yield similar precision and reliability as Visual Analogue Scales (VAS) and are often viewed as simpler to complete.[126, 127]

Secondary outcomes

Secondary outcome measures included the overall length of stay in hospital (LOS), LOS in critical care (LOSCC) and in-hospital mortality.

Covariates

Covariates included demographic data on age, sex, comorbid state as assessed by Charlson Comorbidity Index (CCI), injury severity score (ISS), abbreviated injury score (AIS) for each body system and outcome (dead/alive). Data on mortality is provided from in-hospital patient deaths

before discharge. Rib fracture score (RFS) was captured from the electronic patient records, if not available the investigators calculated it from the trauma CT scan (RFS = (number of breaks x side factor) + age factor)[14]. Surgical rib fixation and intubation status at the time of regional anaesthesia was also documented.

Statistical Analysis

Data were analysed in R studio. Alpha was set to 0.05. All tests were two-sided, thus the null hypothesis reflected a belief that associations could be in either direction. Given that this is an exploratory analysis, we did not adjust for multiple comparisons. Differences in participant characteristics were assessed with ANOVA and chi-squared tests for categorical variables. Post-hoc analyses were conducted for any significant omnibus results using the Tukey Honest Significant Differences (Tukey HSD) for ANOVA and standardised residual for chi-square.

Missing data were handled using a pairwise deletion approach. Missing data were as follows for sample overall who had either a PA, TEA or SAP catheter (n=354): Age n=3, ISS n=8, RFS n=31, CCI score n=2, sex n=3, isolated or polytrauma n=3, mechanism n=20, mechanism type n=20, most severely injured body region n=20, AIS score for the head, face, thorax, abdomen, spine, pelvis, limbs and other n=20, pre and post inspiratory volume n=231, pre and post pain score n=155. Missing pain scores and inspiratory volumes were a result of patient inability to perform the tests due to intubation (n=50), confusion/reduced conscious level (n=8) and patient refusal (n=2). The remaining missing data had no reason provided. Figure 26 shows the inclusion criteria for each stage of the analysis.

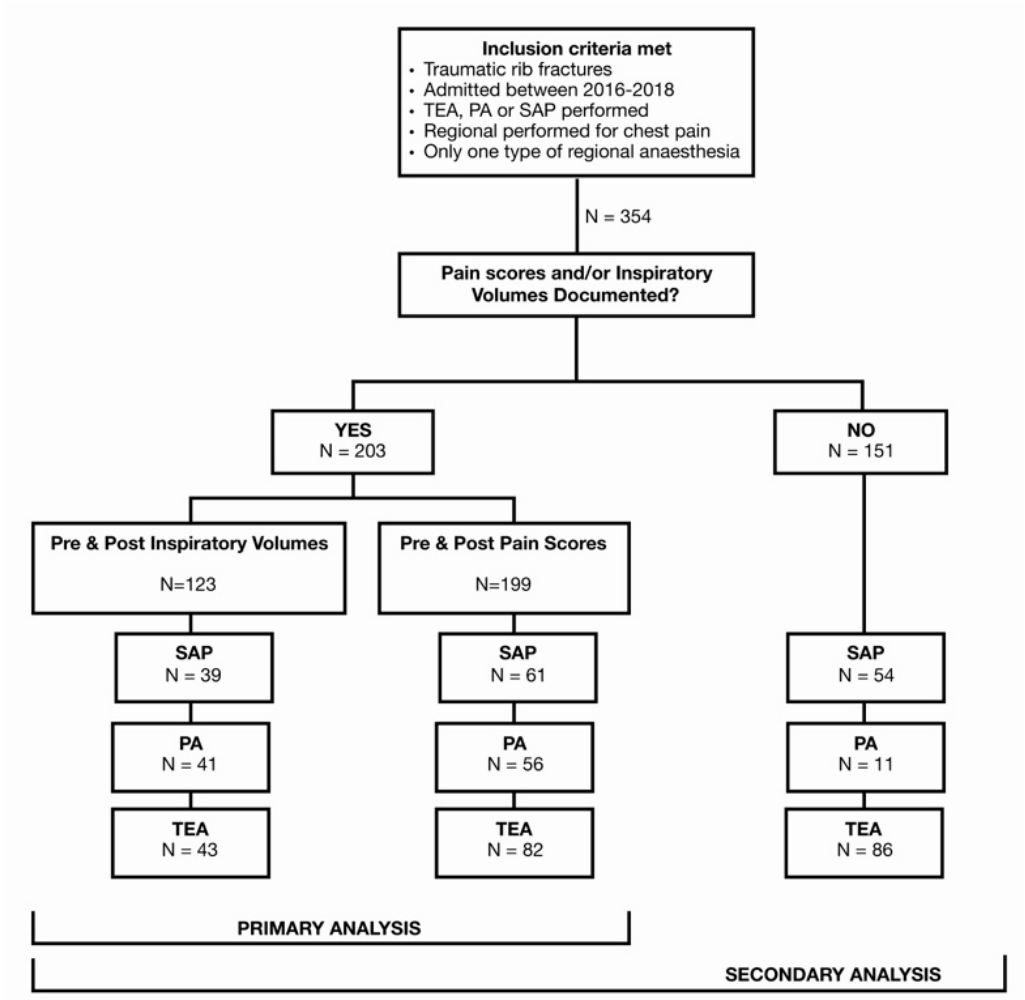


Figure 26 Inclusion criteria for each stage of the analysis. PA, paravertebral catheter; SAP, serratus anterior plane; TEA, thoracic epidural.

Generalised Linear models specifying the binomial family and log link function (Log binomial regression) was used to assess difference in the number of participants moving from reporting severe/moderate pain pre-block to mild/no pain post-block and in-hospital mortality. Generalised linear models specifying the Gaussian family and identify link function (similar to linear regression) was used to assess differences in change in inspiratory volume from the pre to post-block measurement. Finally, generalised linear models specifying the negative binomial family with log link function (negative binomial regression) was used to assess differences in

length of stay in hospital/critical care among the three groups. Negative binomial models were used instead of Poisson regression due to the presence of overdispersion. Poisson and negative binomial models are recommended when predicting length of stay as data are often skewed[128-130].

Unadjusted and adjusted models are reported for each outcome. We adjusted for confounders that were chosen a priori, based on their expected associations with multiple rib fractures (MRFs). For pain and inspiratory volumes the following covariates were adjusted for: age, gender, ISS and RFS score. For in-hospital mortality and length of stay, the following covariates were adjusted for: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest, other), surgical rib fixation and isolated chest injury versus polytrauma.

RESULTS

Data were collected on 354 patients who had either SAP (n=117), PA (n=68) or TEA (n=169). Table 15 shows the characteristics of participants overall and as a function of the block type they received. Differences were assessed using chi-square tests and ANOVAs.

The PA group had a significantly lower proportion of patients with multiple injuries (polytrauma), endotracheal intubation and significant head injuries. The PA group also had significantly lower rib fracture (RFS) scores representing less severe chest trauma. The patient characteristics in the SAP and TEA groups were more comparable. However, the SAP group did have significantly more patients with severe head injuries compared to TEA and PA. The adjusted models selected aimed to account for these differences.

	Overall	SAP	PA	TEA	P-value [y]
Age Mean (SD)	61.3 (18.4)	70.0 (18.4)	65.5 (17.0)	59.9 (18.8)	0.50
ISS score (Mean (SD)	23.9 (11.2)	26.9 (12.7)	18.2 (8.2)	24.1 (10.2)	0.10
RFS Mean (SD)	15.5 (9.5)	15.1[a] (9.1)	11.1[b] (4.8)	17.6[a] (10.6)	0.02
CCI Mean (SD)	2.6 (2.3)	2.5 (2.4)	3.1 (2.3)	2.5 (2.2)	0.95
AIS scores Mean (SD)					
Head	0.8 (1.6)	1.2 [a] (1.9)	0.4 [b] (1.0)	0.7[b] (1.5)	0.02
Face	0.2 (0.6)	0.4 (0.8)	0.1 (0.4)	0.2 (0.6)	0.06
Thorax	3.8 (0.6)	3.7[a] (0.7)	3.6[a] (0.7)	3.96[b] (0.6)	0.01
Abdomen	0.6 (1.2)	0.7 (1.3)	0.5 (1.1)	0.6 (1.1)	0.58
Spine	0.8 (1.2)	1.1 (1.2)	0.5 (0.9)	0.9 (1.1)	0.23
Pelvis	0.5 (1.2)	0.6 (1.4)	0.3 (1.00.)	0.5 (1.2)	0.62
Limbs	1.0 (1.1)	1.2 (1.2)	0.5 (0.9)	1.2 (1.1)	0.80
Other	0.1 (0.3)	0.1[a] (0.4)	<0.1[b] (0.2)	<0.1[a] (0.2)	0.02
					P-value [z]
Gender n (%)					
Female	98 (27.9)	27 (23.5)	29 (42.65)	42 (25.00)	
Male	253 (72.1)	88 (76.5[a])	39 (57.35[b])	126 (75.00[a])	0.01
Trauma type n (%)					
Polytrauma	258 (73.5)	90 (78.3)	38 (55.88)	130 (77.38)	
Isolated	93 (26.5)	25 (21.7[a])	30 (44.1[b])	38 (22.6[a])	<0.01
Surgical rib fixation n (%)					
Yes	74 (22.)	22 (19.6)	14 (23.3)	38 (25.0)	
No	250 (77.2)	90 (80.4)	46 (76.7)	114 (75.0)	0.59
Intubated at time of block n (%)					
Yes	50 (24.8)	24 (28.9)	1 (4.0)	25 (26.6)	
No	152 (75.3)	59 (71.1[a])	24 (96.0[b])	69 (73.4[a])	0.04
Mechanism n (%)					
Fall < 2m	107 (32.)	35 (32.1 [a])	32 (48.5 [b])	40 (25.2[b])	
Fall >2m	55 (16.5)	16 (14.7)	11 (16.7)	28 (17.6)	
Vehicle	148 (44.)	53 (48.6 [a])	18 (27.3 [b])	77 (48.4[b])	
Other	24 (7.2)	5 (4.6)	5 (7.6)	14 (8.8)	0.02
Most severely injured n (%) region					
Chest	247 (4.0)	64 (58.7 [a])	57 (86.4 [b])	126 (79.3 [b])	
Head	26 (7.8)	15 (13.8[a])	2 (3.0 [b])	9 (5.7[b])	
Other	61 (18.3)	30 (27.5[a])	7 (10.6 [b])	24 (15.1[b])	<0.001

Abbreviations: SD = standard deviation; n = sample size; % = percentage; AIS = Abbreviated injury score; CCI = Charlson Comorbidity Index; ISS = Injury Severity Score; PA = Paravertebral; RFS = Rib Fracture Score; SAP = Serratus Anterior Plane; TEA = Thoracic Epidural

If letters differ [(a/b)] they indicate significant differences in the post-hoc comparisons at alpha 0.05

[y] : p value from ANOVA

[z] : p value from chi-squared test

Table 15 Characteristics of participants overall and as a function of block type

Inspiratory volumes

All groups saw a clinically significant mean increase in inspiratory volume over time of 789.4mls (SD 479.7mls). The mean increase for each block type individually was; SAP 825.6mls (SD519.8mls), PA 790.2mls (SD515.4mls) and TEA 755.8mls (SD 410.6mls). There was no statistically significant difference in the magnitude of this change between the TEA and the PA or SAP groups (see Figure 27).

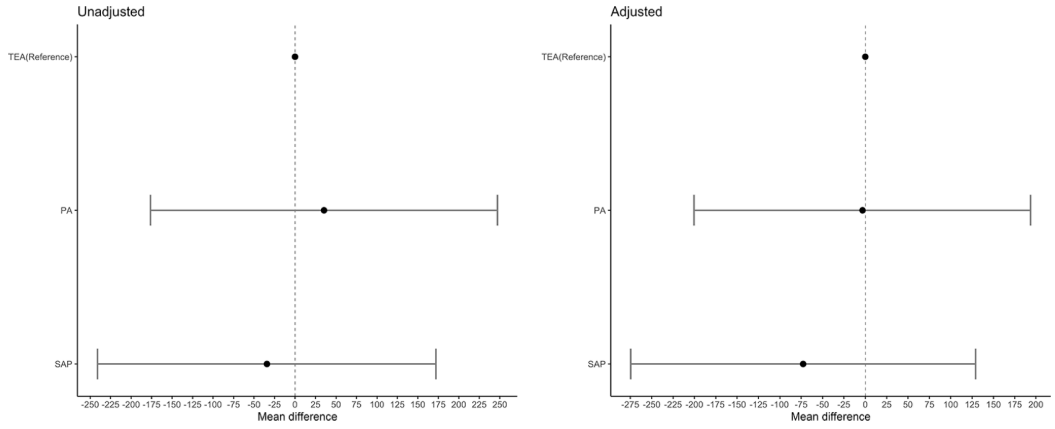


Figure 27 Mean difference (CIs) in inspiratory volume changes between block types for the unadjusted and adjusted linear regression models. Adjusted covariates: age, gender, ISS and RFS score. ISS, injury severity score; RFS, rib fracture score.

Pain Scores

Table 16 shows the pre and post pain scores overall and as a function of block type. Across all blocks, approximately 98% of all participants reported moderate/severe pain prior to regional analgesia, which was reduced to 34% following block placement. Of those who had moderate/severe pain in the pre-block period, 55.17% (n=32) in the Serratus block group, 50.00% (n=28) in the paravertebral and 40.74% (n=33) in the epidural group reported no

pain/mild pain post block. The probability of changing from higher to lower levels of pain did not differ between groups (Figure 28).

	Pre-block	Post-block
Overall n (%)		
No pain	1 (0.5)	20 (10.1)
Mild pain	3 (1.5)	111 (55.8)
Moderate pain	42 (21.1)	66 (33.2)
Severe pain	153 (76.9)	2 (1.0)
SAP n (%)		
No pain	1 (1.6)	7 (11.5)
Mild pain	2 (3.3)	27 (44.3)
Moderate pain	10 (16.4)	25 (41.0)
Severe pain	48 (78.7)	2 (3.3)
PA n (%)		
No pain	0 (0.0)	2 (3.6)
Mild pain	0 (0.0)	36 (64.3)
Moderate pain	13 (23.2)	18 (32.1)
Severe pain	43 (76.8)	0 (0.0)
TEA n (%)		
No pain	0 (0.0)	11 (13.4)
Mild pain	1 (1.2)	48 (58.5)
Moderate pain	19 (23.8)	23 (28.1)
Severe pain	62 (75.6)	0 (0.0)

Abreviations: n = sample size; % = percentage; SD = standard deviation; PA = Paravertebral; SAP = Serratus Anterior Plane; TEA = Thoracic Epidural

Table 16 Pre and Post pain scores overall and as a function of block type

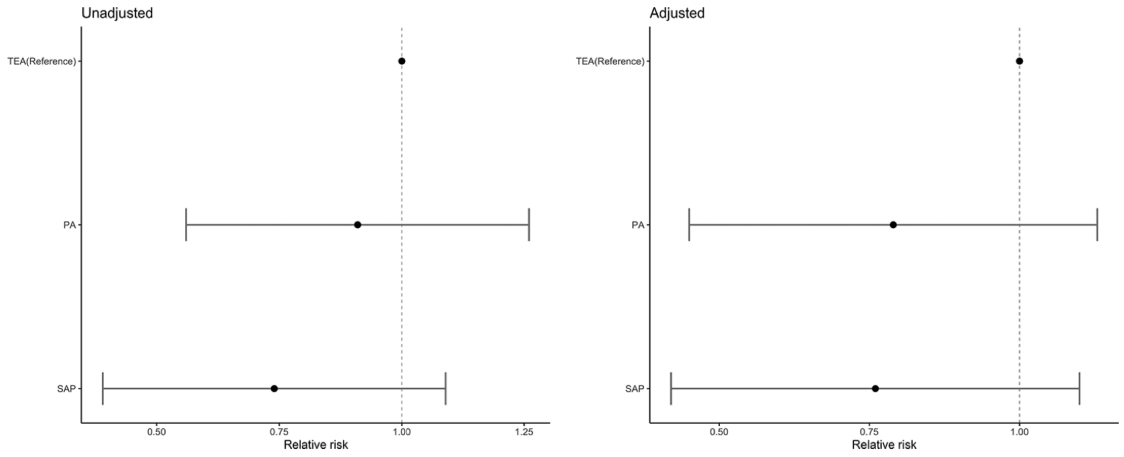


Figure 28 Relative risks (CIs) for the unadjusted and adjusted log binomial models comparing the number of participants reporting a change in their pain scores from severe/ moderate to mild/none. Adjusted covariates: age, gender, ISS and RFS score.

Mortality

The overall mortality rate was 13.2%% (95% CI 7.8 to 18.7), 4.59% (n=5) of participants died in the SAP group, 4.55% (n=3) in the PA group and 7.56% (n=12) in the TEA group. In the adjusted model, there were no differences in mortality across block types (Figure 29).

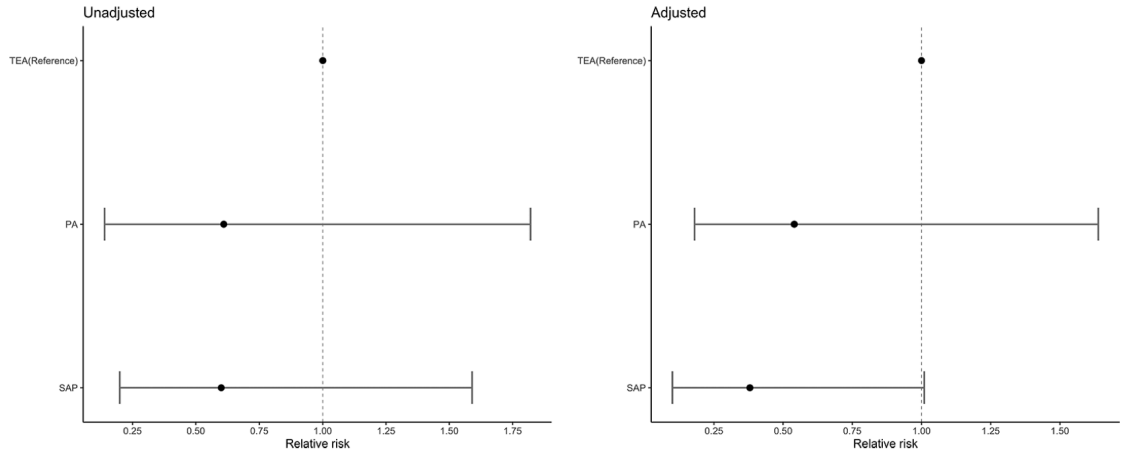


Figure 29 Relative risks (CIs) for the unadjusted and adjusted log binomial models comparing in-hospital mortality risk. Adjusted covariates: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest and other), surgical rib fixation and isolated chest injury versus polytrauma.

Length of stay in hospital and critical care

The overall length of stay in critical care mean (SD) was 7.8days (7.5) and in hospital LOS was mean (SD) 18.2days (17.4). The mean [SD] length of stay in critical care was highest in the TEA group (9.6days [9.3]), followed by SAP (9.4days [10.0]), and lowest in the PA group (4.3days [3.2]). The mean [SD] hospital LOS was highest in the SAP group (22.1days [16.9]), followed by TEA (18.3days [15.6]) and lowest in the PA (14.3days [19.7]). In an adjusted model, no significant differences were found between groups with respect to hospital LOS (Figure 30). The PA group compared to TEA had a significantly shorter critical care stay (Figure 31).

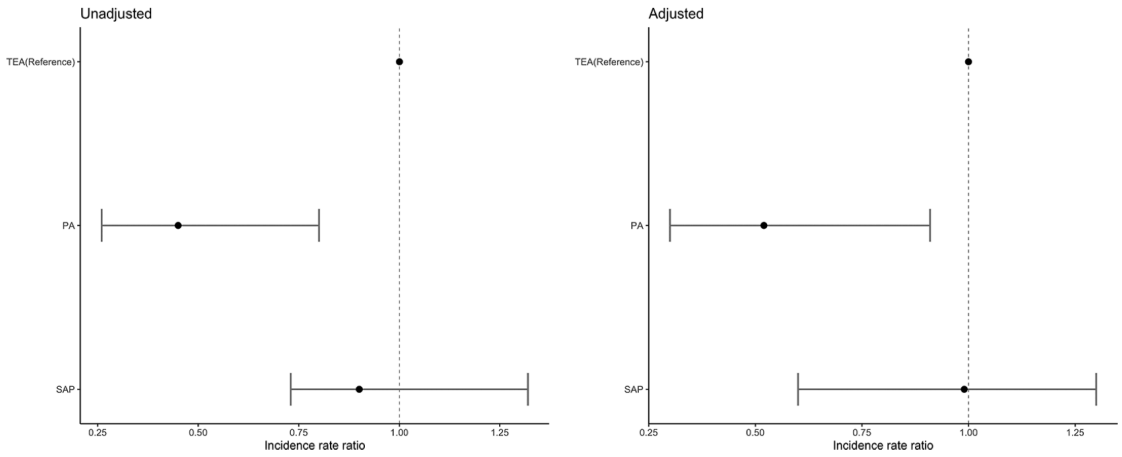


Figure 30 Incidence rate ratio (CIs) for the unadjusted and adjusted negative binomial model comparing length of stay hospital. Adjusted covariates: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest and other), surgical rib fixation and isolated chest injury versus polytrauma.

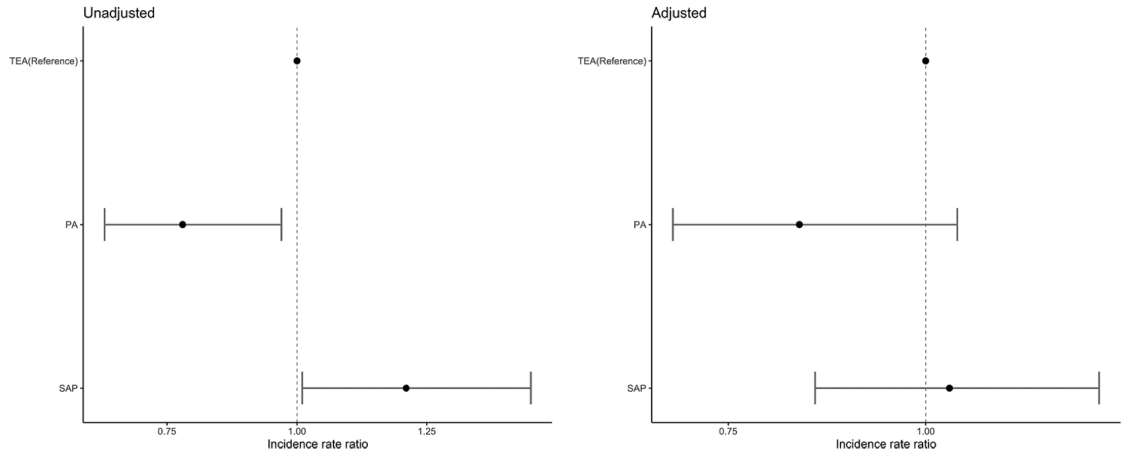


Figure 31 Incidence rate ratio (CIs) for the unadjusted and adjusted binomial model comparing length of stay in critical care. Adjusted covariates: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest and other), surgical rib fixation and isolated chest injury versus polytrauma.

The complete results of the adjusted and unadjusted models with associated P-values are available in the supplementary material for inspiratory volumes and pain scores (supplementary Table 1), mortality (supplementary Table 2) and length of stay in critical or hospital (supplementary Table 3) see Appendix 13.

DISCUSSION

Our study suggests that all three techniques of regional anaesthesia contributed to reductions in pain and improvements in respiratory function, and that post insertion SAP is likely to be comparable to TEA or PA when used for the analgesia of multiple rib fractures. This is the first pragmatic study which has assessed analgesic adequacy in those receiving SAP, TEA or PA and so adds to the growing body of literature that has detailed a significant improvement in pain scores and inspiratory volumes following SAP analgesia. [11][72, 104]

Previous systematic reviews comparing traditional analgesic modalities have not reported significant differences in mortality or LOS. [100, 102] Our findings of a reduced rate of critical care LOS in the PA group should be interpreted with caution given the possibility of unmeasured confounding, lack of adjustment for multiple comparisons, and secondary outcome metric status.

From a population health standpoint, our SAP block findings are encouraging given the current under-utilisation of traditional techniques (i.e. TEA or PA) in the setting of trauma. For example, it has been reported that fewer than 3% of patients in England and Wales in 2017 with rib fractures received TEA or PA. [5] This is likely due to contra-indications, associated side effects such as hypotension and the advanced level of skill required for the insertion of PA and TEA analgesia. The fascial plane techniques (i.e. SAP/ESP block), in comparison, are presumed to be safe and technically easy to insert given the superficial location and availability of ultrasound guidance. Although not examined in our study, SAP blocks have also been shown to reduce

opioid consumption, which would be anticipated given the analgesic benefit demonstrated herein. [131, 132] SAP analgesia should not produce sympathetic block which accounts for its anticipated haemodynamic stability. Finally, given the superficial nature of the block, liberalisation of anticoagulation rules for placement may be in order.

Our study has significant limitations. The heterogeneous nature of this cohort means that recommending a gold standard of analgesia is not possible.[37, 133] Given the observational nature of the data and inherent limitations of retrospective reviews, our data should be interpreted with caution due to the possibility of unmeasured confounders, multiple comparisons performed, and small sample size for rare outcomes such as death. With respect to the heterogeneity of the data, the decision on the type of regional catheter used was left to the treating clinician.[9] Additionally, we did not track or adjust for differences in bolus and infusion rates by block type.

Our study did not make comparison to a non-block group. Therefore, we are unable to comment on whether or not a block relative to pharmacological methods such as opioids adds value or improves outcomes. Despite these limitations, our study has several strengths including data collection across multiple sites and the paired nature of the data with respect to analgesic assessment and changes in respiratory mechanics.

Conclusion

In two large tertiary care hospitals in the UK, regional anaesthesia appears to result in improvements in analgesia and respiratory mechanics in patients suffering from traumatic rib

fractures. Given inherent limitations of TEA and PA blocks, SAP blocks may represent an attractive analgesic option for these patients.

CHAPTER SIX

CONCLUDING CHAPTER

This research aimed to better understand the role of SAP analgesia in patients with traumatic rib fractures, by increasing our understanding of the mechanisms by which SAP blocks provide pain relief and evaluating their safety, clinical effectiveness, and impact on patient outcomes.

MECHANISMS

The origin of pain in patients with multiple rib fractures is multifactorial with nociceptive signals arising from rib periosteum, muscles, fascia, pleura, subcutaneous tissues, and skin. Current opinion is that SAP rib fracture analgesia is mainly from anaesthesia of the lateral cutaneous nerve which supplies the skin of the anterior lateral thorax [42,45]. Variable involvement of other intercostal nerve branches, long thoracic and thoracodorsal nerves has also been reported.[42, 43] [44, 45]. This, however, does not fully explain the level of analgesia reported by patients.

The study presented in Chapter 3 hypothesised whether there was injectate spread to the paravertebral space with posterior-medially inserted SAP catheters. This would provide a greater level of analgesia. It also investigated the extent of hemithorax injectate spread with two posteriorly directed SAP catheters. The study controlled for factors that affect injectate spread in the thoracic fascial planes such as intrathoracic pressure changes with ventilation, injectate viscosity, and patient positioning [39-41, 43].

Two SAP catheters provided coverage of the lateral hemithorax from ribs 2-11 (median craniocaudal spread of 191mm and anterior-posterior spread 81mm). However, no injectate spread to the paravertebral space was identified.

Further research is required to assess other mechanisms of SAP analgesia such as the significance of fascial plane nociceptive receptors, how traumatic disruption of the fascial planes affects deep injectate spread and the impact of systemic absorption of local anaesthesia. Clinical correlation is required to confirm that the increased spread seen with two catheters in cadavers equates to improved patient analgesia.

SAFETY

Due to its superficial insertion site, distance from neuraxial structures and utilisation of in plane ultrasound techniques SAP block is considered a relatively safe analgesic technique. Our systematic review of the literature supported this view.

The systematic review (Chapter 2) identified the incidence of adverse events for SAP insertion were; nerve damage and LAST 0%, pneumothorax, haematoma and infection 0.06% and catheter displacement/failure 0.4%. These values are all less than the figures quoted by the RCOA and in the literature for epidural and paravertebral insertion[34, 78, 80]. Epidural and paravertebral analgesia are associated with a degree of hypotension due to sympathetic nervous system blockage[34]. The metanalysis identified that there was a statistically

significant 90% relative risk reduction of hypotensive events for SAP when compared to epidural and paravertebral analgesia (SAP 0% vs Neuraxial Analgesia 18% Risk Ratio 0.1, P0.03).

The propensity matched study in Chapter 4 collected data on adverse events related to SAP insertion. The rate of catheter displacement was 2.2% (n=2) and entry site infection 2.6%, no cases of pneumothorax were reported. These values are in line rates reported in the literature[65-67, 81]. The study also supported the view that SAP blocks are cardiovascularly stable as no significant difference overall or with time effects was identified for noradrenaline requirements, lowest MAP or daily fluid balance between the SAP and the Opioid only (no block) group.

These findings endorse the belief that SAP catheters are safe to insert with no greater risk of complications and possibly a lower risk of hypotension than the traditional catheter techniques of epidural and paravertebral analgesia.

EFFECTIVENESS

The propensity matched study presented in Chapter 4 comparing SAP catheters to opioid only (no block) analgesia identified that that there was significant reduction in opioid consumption (OME) for the SAP group on days 2,6,7,8,9,11 and 12. The lack of statistically significant difference on days 1,3,4,5 may reflect the SAP catheter not yet being in situ, the impact of other injuries and surgical procedures not being fully accounted for by adjustment and/or underpowering. No clinically significant difference in pain scores or number of hours the patient was in severe pain was identified between groups.

The multi-centre cross-sectional study in Chapter 5 showed that post insertion SAP analgesia resulted in reduced pain scores and improvements in respiratory function. Inspiratory volume increased by 825.6mls (SD519.8mls) post SAP block. The magnitude of this increase was comparable to the Paravertebral (790.2mls, SD 515.4mls) and Thoracic Epidural groups (755.8mls SD 410.6mls). For patients who had moderate/severe pain in the pre-block period, 55.17% (n=32) in the Serratus block group, 50.00% (n=28) in the paravertebral and 40.74% (n=33) in the epidural group reported no pain/mild pain post block. The study suggests that all three techniques of regional anaesthesia contributed to reductions in pain and improvements in respiratory function, and that post insertion SAP is likely to be comparable to TEA or PA when used for the analgesia of multiple rib fractures.

These results are further supported by the findings of the narrative review in Chapter 2. All the studies included the clinical effectiveness of SAP in patients with blunt thoracic trauma showed that both static and dynamic pain scores were reduced following SAP block insertion. Opioid consumption was reduced following SAP insertion with Martinez et al identifying daily equivalent oral morphine consumption decreased significantly after SAP from 108 mg (IQR 67 to 120) to 19 mg (IQR 0 to 58) (P = 0.015). [71] An improvement in respiratory function was also seen, with all included studies showing an improvement in inspiratory volume, reduced oxygen requirements and a reduction in respiratory rate following SAP insertion. Individual reports of SAP facilitating ventilator weaning and prevention of intubation in patients were also identified.[60, 70] Superficial and deep SAP blocks were well represented in the included studies suggesting that both forms of SAP block and catheter insertion are effective at providing

analgesia and improving respiratory function in patients with blunt thoracic trauma with rib fractures.

It can therefore be summated, that SAP analgesia can provide improvements in analgesia and respiratory mechanics in patients suffering from traumatic rib fractures. Given the inherent limitations of TEA and PA blocks, SAP blocks may represent an attractive analgesic option for these patients.

PATIENT OUTCOMES

Patient outcomes such as pneumonia, mortality and length of stay can be difficult to interpret in this cohort, due to these outcomes not solely being influenced by the pain technique alone but a range of factors such as pre-existing comorbidities, injury patterns, need for additional surgery, pre-morbid mobility level, staffing levels and discharged destination. These factors and many others cannot always be fully accounted or adjusted for.

PNEUMONIA

The propensity matched study (Chapter 4) identified that 35% of patients (n=38) had pneumonia in the opioid group and 26.7% (n=24) in the SAP group. Following propensity matching there was not a statically significant difference between groups in the odds of having pneumonia during admission (adjusted model OR 0.9 95%CI 0.4 to 1.9, P=0.799). This result is supported by the literature where a study comparing SAP and ESP blocks showed no statistically significant difference in the development of new respiratory complications (pneumonia, pulmonary embolism, respiratory failure) between the groups. The incidence of pneumonia in the SAP group was 35% which is similar to our findings[60].

LOS CRITICAL CARE

For the studies presented in Chapters 4 and 5, no significant difference in critical care LOS was found between SAP and the comparison groups of opioid only (no block), TEA and Paravertebral analgesia. The average LOS in critical care for the SAP groups was 9 days (Propensity matched study chapter 4 SAP_{LOSCC} 9.0days [SD 10.4], Multicentre Cross sectional study chapter 5 SAP_{LOSCC} 9.4days [SD 10.0]).

LOS HOSPITAL

The average LOS in stay in hospital for patients receiving SAP analgesia as identified from the studies in Chapters 4 and 5 was between 22 and 25days. There was no statistically significant difference found in hospital LOS between SAP and TEA and PA groups. However, the hospital LOS was lower in the SAP group (25.3days, SD 19.0) compared to the no block, opioid only group (29.5 days, SD 24.6, [adjusted model, IRR=0.9 95%CI 0.9 to 1.0, P=0.046]).

MORTALITY

In hospital mortality for SAP was reported between 4.6% and 6.7% in Chapters 4 and 5. There was no significant difference in mortality between SAP and comparison groups of TEA, paravertebral and opioid only analgesia. These rates are similar to the literature where Riley et al gives a SAP mortality rate of 5.9%.

From these findings SAP does not appear to influence pneumonia development, length of stay or mortality over any other established analgesic technique. Future prospective randomised

controlled trials are needed to collect higher quality data on these outcomes which are challenging to measure and interpret retrospectively.

WHICH PATIENTS SHOULD RECEIVE SAP ANALGESIA?

Both superficial and deep SAP blocks/catheters appear to provide analgesia for patients with multiple rib fractures. There is not enough data from this study or the current literature to advise on one over the other.

From information gathered during this research SAP analgesia can be used for all rib fracture patterns. However, from our current understanding of the mechanism of SAP analgesia being mainly localised to the lateral site of injection with no paravertebral spread. They are likely to be most effective for patients with lateral patterns of rib fracture injury. Two catheters/injections are advised for fractures that cover extent of the hemithorax.

SAP analgesia is particularly useful in patients for whom TEA and paravertebral analgesia is contraindicated such as those that are anticoagulated, hypotensive, or have significant head or spinal injuries where peripheral neurological monitoring is required. The ability of SAP blocks/catheters to be inserted in the supine position would be helpful for patients where remaining supine is advisable e.g. those with significant spinal or pelvic injuries. SAP analgesia could also play role in providing 24/7 access to optimum analgesia as SAP blocks/catheters can be inserted by non-anaesthetic allied health professions who are experienced with ultrasound and local anaesthetic use.

CONCLUSIONS

A review of the current literature and the findings of the studies presented in this thesis support the opinion that SAP analgesia is a safe technique that contributes to improved analgesia and respiratory mechanics in patients with multiple rib fractures.

The effectiveness of thoracic epidural and paravertebral analgesia is not disputed; however, SAP analgesia could play a beneficial role in patients for whom these techniques are not available for, because of medical contraindications or service provision. SAP analgesia is of particular benefit to patients with rib fractures for whom rolling laterally or sitting is not advisable due to their traumatic injuries.

Paravertebral and thoracic epidural insertion are advanced anaesthetic techniques performed only by senior anaesthetists. The use of ultrasound for SAP insertion and impressive safety profile due to its distance from neuraxial structures, means there is the potential for SAP blocks and catheters to be inserted by non-anaesthetic ultrasound trained allied health care professional and physicians from other specialties e.g. emergency medicine. This would help with the delivery of 24/7 analgesic services.

More research is needed to evaluate the impact trauma has on injectate spread in the fascial planes along with how fascial nociceptors and systemic absorption contribute to SAP analgesia. Prospective randomised controlled trials that also report on patient reported outcome measures (PROMS) are required to better assess the impact of SAP analgesia on thoracic pain, respiratory mechanics, and patient outcomes.

FUTURE DIRECTIONS

The research presented in this thesis utilises retrospective data and smaller scale sample sizes with a higher risk of bias. Despite these limitations it is evident that SAP analgesia is a safe technique which contributes to improved analgesia and respiratory mechanics in patients with multiple rib fractures. The findings of this thesis have helped to inform a study conceived between the Birmingham Clinical Trials Unit (BCTU) and the National Institute for Health and Care Research (NIHR) for which I am a co-applicant, the ERASER Trial (**E**arly **R**ib **A**nalgesia with **Ser**ratus)[134, 135].

The ERASER trial is a pragmatic, multicentre, randomised controlled trial. It is a phase three trial comparing the cost and clinical effectiveness of SAP analgesia to the current usual care of patients admitted to hospital with MRFs.

Patients are eligible for inclusion if they are more than 16years of age, with three of more rib fractures following blunt thoracic trauma. Full exclusion criteria are available in the full protocol but includes severe traumatic brain injury requiring prolonged ventilation, acute quadriparesis, spinal fracture precluding mobilisation and any conditions that preclude SAP catheter insertion[135].

Patients are randomised on a 1:1 ratio to either the intervention arm; SAP treatment and usual care where a SAP catheter will be inserted and continuous infusion of local anaesthesia started, or the control arm; usual care which includes physiotherapy, multimodal analgesia and rib

fixation. An automated online system will perform randomisation to ensure allocation concealment. The trial is not blinded at the patient or investigator level (open label).

The primary outcome measure is a new diagnosis of pneumonia as defined by a blinded end point review committee using all available trial data and the Clinical Pulmonary Infection Score (CPIS)[136]. A full list of secondary outcomes is available in the full trial protocol but includes pain assessed using a numerical rating scale (0-10), ventilatory function (incentive spirometry and peak flow), requirement for non-invasive/invasive ventilation, opiate consumption, mortality at 30 days and 3months, complications and safety data associated with SAP and patient reported outcome measures (PROMS) at 1 and 3 months. The PROMs measured include the EQ-5D-5L which assesses patient mobility, self-care, usual activities, pain and depression, the Medical Research Council (MRC) dyspnoea scale and the McGill Pain Questionnaire[135, 137].

The ERASER trial plans to enrol 824 patients by August 2026. The results of this trial will help inform treatment protocols and contribute to a consensus on the optimum analgesic care for patients with multiple rib fractures.

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APPENDICES

APPENDIX 1: REVIEW OF LENGTH OF STAY IN ELDERLY PATIENTS WITH SEVERE CHEST INJURY AT UHB

Author: L A Beard

BACKGROUND:
The LOS for patients with severe chest trauma (ISS>15) over 75years of age is the highest I the region.
This review aimed to:

- Identify the reasons for prolonged stays at UHB in this cohort
- Identify subgroup of patients who are at risk of unnecessarily prolonged hospital stay.

INCLUSION CRITERIA:
* Age >75years
* ISS >15
* Most severely injured body region: Chest

EXCLUSION CRITERIA:
* Missing notes

METHODS:

- Retrospective review of patient notes
- Audit registration and approval received: CARMS-14401

DATA COLLECTED:

- Transfer status
- Trauma Team Presence
- LOS Ward / Hospital / ICU
- AIS scores: Head, face, chest, abdomen, spine, pelvis, limbs
- Reason for delayed discharged: Up to three reasons recorded (1^{st} / 2^{nd}/3^{rd})

RESULTS

- Total 32 cases from 2017 met inclusion criteria
- 8 excluded - unavailability of notes, 24 included in the analysis

DESCRIPTIVE DATA

Variable	Descriptor	Frequency	%
Mechanism	Fall from less than 2m	17	70.8
	Vehicle incident/collision	7	29.2

ISS Scores

N	Min	Max	Mean	SD
24	16	34	21.4	5.02

LOS

	N	Minimum	Maximum	Mean	Std. Deviation
Total LOS	24	2	94	23.9	23.8
ICU LOS	7	1	85	22.4	30.0
Ward LOS	24	1	85	17.3	17.8

LENGTH OF STAY VERSUS ISOLATED CHEST INJURY OR POLYTRAUMA

	Isolated	N	Mean	Std. Deviation	Std. Error Mean	P Value	95% CI
Total LOS	Isolated Chest	7	9.8	3.8	1.4	0.06	-40.8 – 1.13
	Polytrauma	17	29.7	26.3	6.3		

Patients with isolated chest injuries have a shorter mean total LOS compared to those with polytrauma (9.8 days vs 29.7, p=0.06)

POLYTRAUMA VERSUS MECHANISM

Polytrauma occurs in 64% of those who fall from less than 2m (11 out of 17) and 85% (6 out of 7) of those following vehicle collisions.

REASONS FOR DELAYED DISCHARGE

The main reasons for delayed discharge are shown below. 1^{o} is the main reason, 2^{o} second reason and 3^{o} third reason. All cases had a main reason documented. Not all cases had a second and third reason.

Category	**1^{o} Reason** n	**2^{o} Reason** n	**3^{o} Reason** n
Pain	4	2	-
Respiratory complication	3	1	3
Other medical issue	4	1	-
Discharge planning	4	3	-
Transfer to local hospital	3	2	-
Delirium	-	-	3
Physiotherapy delay	-	2	-
Delay ICU discharge	1	1	-
None	5	-	-
Total	24	12	6

Overall: All reasons combined (1^{o} + 2^{o} + 3^{o})

Category	**Overall** n	%
Physiotherapy delay	2	5.4
Delay ICU discharge	2	5.4
Delirium	3	8.1

Other medical issue	5	13.5
Transfer to local hospital	5	13.5
Pain	6	16.2
Respiratory complication	7	18.9
Discharge planning	7	18.9
Total	37	100%

Main delays are due to:

1. Respiratory complications and discharge planning issues

Inadequate pain control is linked to respiratory complications and delirium and increased focus on these aspects may reduce the LOS for these patients. Delays due to awaiting social care, rehab beds and transfers out are easier to quantify and measured from time patient documented as fit for discharge in notes or referral made to other centre until the date they were discharged.

		N	Minimum	Maximum	Mean	Std. Deviation
Discharge home/rehab	Days Delayed	7	3	26	11.00	8.907
Discharge local hospital	Days Delayed	5	4	32	15.40	12.402

On average patients are waiting 11-15 days to be discharged with care packages, to rehab centres or other hospitals. The minimum delay was 3 days and the maximum 32 days. Improvements in these areas are therefore needed.

LIMITATIONS

- Opinion based assessment of notes, risk of bias.
- Small study (n=24)
- Multiple factors contribute to patient delays in discharge and results may not be generalisable to other hospital

SUMMARY

This is a high risk cohort where ISS score does not affect LOS alone. Polytrauma occured in 71% of patients (17/24) and is a result most commonly of falls from less than 2m. As you might expect the polytrauma patients have the longest LOS in hospital (isolated chest injury 9.8 days vs polytrauma 29.7, p=0.06). They are also subjected to the greatest numbers of delays.

RECOMMENDATIONS

Improvements in pain provision may reduce respiratory complications, delirium and importantly improve patient comfort. 25% of patients reported significant pain that prevented discharge. Delays due to discharge planning and referrals to rehab, care homes and local hospitals caused considerable delays ranging between 3 and 32 days.

It is the patients with severe chest trauma and associated injuries that experience the majority of these delays (67.5%) and therefore this cohort should have increased vigilance with regards to early discharge planning, organisation of the referral process and pain management.

APPENDIX 2: ANALGESIA OF PATIENTS WITH MULTIPLE RIB FRACTURES IN CRITICAL CARE: A SURVEY OF HEALTHCARE PROFESSIONALS IN THE UK.

Full citation:
L Beard, B Holt, C Snelson, C Parcha, F Gao Smith, T Veenith. Analgesia of Patients with Multiple Rib Fractures in Critical Care: A Survey of Healthcare Professionals in the UK. Indian Journal Critical Care Medicine 2020; 24(3): 184-189.[27]

Abstract

Introduction: Good analgesia has been shown to reduce the risk of pneumonia, chronic pain, and mortality in patients with multiple rib fractures (MRFs). This survey explores the current analgesic practice in the UK, protocol use, barriers to provision, and physician preferences.

Materials and methods: A web-based survey was distributed nationally to an enriched cohort of clinicians working in UK trauma units with an interest in MRF management.

Results: Seventy-nine healthcare professionals responded. A third (31.4%) reported that their department had a rib fracture pain protocol, 52.9% did not, and 15.7% were unsure. Significantly more respondents reported adequate pain control when a hospital protocol was present compared to when not (χ^2, $p < 0.01$). Inadequate analgesia, a poor cough, and inability to breathe deeply were the commonest complications reported by 81.4, 78.6, and 65.7%, respectively. Patient-controlled analgesia (PCA) was the most commonly used form of analgesia (38.6%) followed by thoracic epidural (TEA) (30.0%) and continuous opioid infusion (18.6%). However, TEA was the preferred method of analgesia among respondents (37.1%) followed by serratus block (21.4%), paravertebral block (17.1%), and PCA (14.3%).

Discussion: There is considerable variation among physicians in their current use of analgesic modalities, with opiate-based methods predominating despite a physician preference for regional techniques. Thoracic epidurals are preferred by physicians but of limited use as a result of contraindications, time pressures, and staff skill mix. Pain control is reported to be better handled when protocols are present. Further research focusing on currently utilized regional techniques is required in order to produce a validated standardized national protocol that is informed by the current practice, the evidence base, and limitations to service provision.

Keywords: Analgesia, Critical care, Pain relief, Rib fractures, Thorax trauma.

Key messages: There is considerable variation among physicians in their current use of analgesic modalities. Opiate-based methods dominate for thoracic trauma despite a physician preference for regional techniques, which can be challenging in this cohort due to contraindications, staff skill mix, and time pressures. Inadequate analgesia is common but is better managed when pain management protocols are available.

Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23375

Introduction

Multiple rib fractures (MRFs) are commonly associated with blunt trauma present in approximately 10% of those with all types of trauma and up to 80% of those with significant thoracic injury.[1,2] These patients form a high-risk cohort with a mortality as high as 33%. The risk of mortality doubles in those above 65 years of age.[3,4] Complications include pneumonia, pulmonary effusion, acute respiratory distress syndrome, lobar collapse, and a requirement for noninvasive or invasive ventilation.[5–7] Currently 11 to 31% of patients with MRFs will develop pneumonia,[6,7] with odds of mortality nearly four times that of those without.[8]

Good analgesia allows these patients to cough, deep breathe, and participate in their physiotherapy sessions. These factors have been shown to reduce the risk of pneumonia and mortality.[5,9] It also has a role in improving patient comfort and reduces the development of chronic pain.[10,11] A multidisciplinary clinical pathway targeting pain-control services for these high-risk trauma patients decreased rib fracture-associated morbidity and mortality.[12] Rib fracture scoring systems offer a unique clinical utility to identify high-risk patients and have been combined with pain pathways to ensure that the pain of high-risk patients is managed aggressively.[11,13]

Over the last decade, the specialist societies[14] have downgraded the usage of epidural as the gold standard for MRF pain. Their advice was adjusted following further review of available literature after the exclusion of postoperative surgical patients. The overall consensus is that the current evidence base regarding the optimal analgesic method in this cohort is limited and of low quality.[14] Current regional techniques in use for patients with MRFs include TEA, paravertebral catheters (PVB), intrapleural infusion, and the more recent thoracic wall fascial plane techniques such as the serratus anterior plane (SAP) and erector spinae plane (ESPB) blocks. Patients with MRFs represent a large high-risk cohort in whom it is essential that pain is managed rapidly and aggressively.

[1,3,4,6]Department of Anesthesia and Critical Care, Queen Elizabeth Hospital Birmingham, Birmingham, UK

[2]Department of Anesthesia and Critical Care, Leeds Teaching Hospitals NHS Trust, Leeds, UK

[5]Birmingham Acute Care Research Group, University of Birmingham, Birmingham, UK

Corresponding Author: Laura Beard, Department of Anesthesia and Critical Care, Queen Elizabeth Hospital Birmingham, Birmingham, UK, Phone: +44 (0)7825778064, e-mail: laura.beard@nhs.net

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Conflict of interest: None

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However, achieving adequate analgesia can be challenging due to the presence of associated thoracic spine injury, comorbidities, trauma-related coagulopathy and prior anticoagulant use.[15]

We designed this survey to explore the current analgesic practice in the UK, the use of analgesic protocols, barriers to analgesic provision, and physician analgesic preferences. The results of the survey would be used to help inform further research into the analgesic management of this cohort and the development of a standardized validated national analgesic protocol.

Materials and Methods

We distributed the survey nationally to an enriched cohort of clinicians working in trauma units with an interest in MRF management over a 6-week period in 2018 (April/May). To make the survey generalizable, we asked various members of the trauma clinical team, including intensivists, anesthetists, surgeons, and advanced critical care practitioners (ACCPs). No incentive was provided to encourage participation.

Survey Design

This survey was designed by members of the intensive care unit (ICU) using a web-based platform. Questions were selected to identify the respondents' demographics (role, specialty, and region), local practices of managing rib fracture-associated pain, their attitudes toward these practices, and any barriers they have experienced in providing analgesia for MRF patients. In order to prevent the formation of an excess of data categories during analysis, respondents were presented with a series of answers to select from which had been deemed relevant by practitioners in the design team. Respondents were also permitted to specify their own answers where appropriate as free text. Answer choices were determined based on the question posed. A range of discrete options were used to assess demographics and the method of analgesia most commonly employed, and a 5-point Likert scale (always, usually, sometimes, rarely, never) was used to assess the frequency of adherence to protocols where present. Statistical analysis involved a Chi-square test to determine the relationship between using an analgesic protocol and adequacy of analgesia. A p value of <0.05 was considered significant.

Table 1: Demographics of survey respondents by staff role, specialty, area of interest in intensive care unit, and type of hospital

		n	%
Staff role	Consultant	26	37.1
	Specialty trainee/registrar	15	21.4
	Foundation/core trainee	2	2.9
	Nontraining doctor	1	1.4
	Nurse	5	7.1
	ACCP	20	28.6
	Other	1	1.4
Specialty	Anesthetics	20	28.6
	Emergency medicine	1	1.4
	ICU	26	37.1
	ICU and anesthetics	16	22.9
	ICU and general medicine	4	5.7
	Surgery (with trauma)	3	4.3
	Surgery (without trauma)	0	0.0
Area of ICU	General (surgery)	3	4.3
	General (medical)	0	0.0
	General (mixed)	44	62.9
	Cardiothoracic	6	8.6
	Liver	4	5.7
	Neuro	8	11.4
	Burns	1	1.4
	Other	4	5.7
Type of hospital	Tertiary center with regional trauma center	58	82.9
	Tertiary center without regional trauma center	2	2.9
	Tertiary pediatric center with trauma	0	0.0
	Tertiary pediatric center without trauma	0	0.0
	District general hospital	9	12.9
	Single specialty hospital	1	1.4

Results

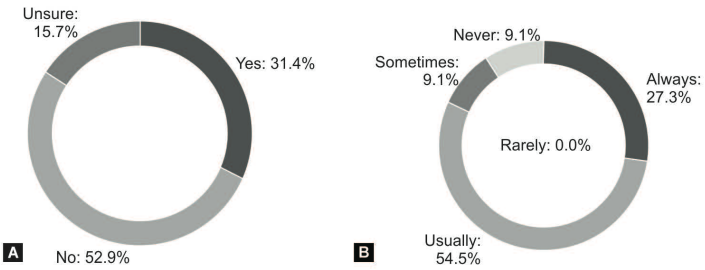
Seventy-nine healthcare professionals completed the survey. Nine of these surveys were incomplete and thus excluded.

Demographics of Respondents

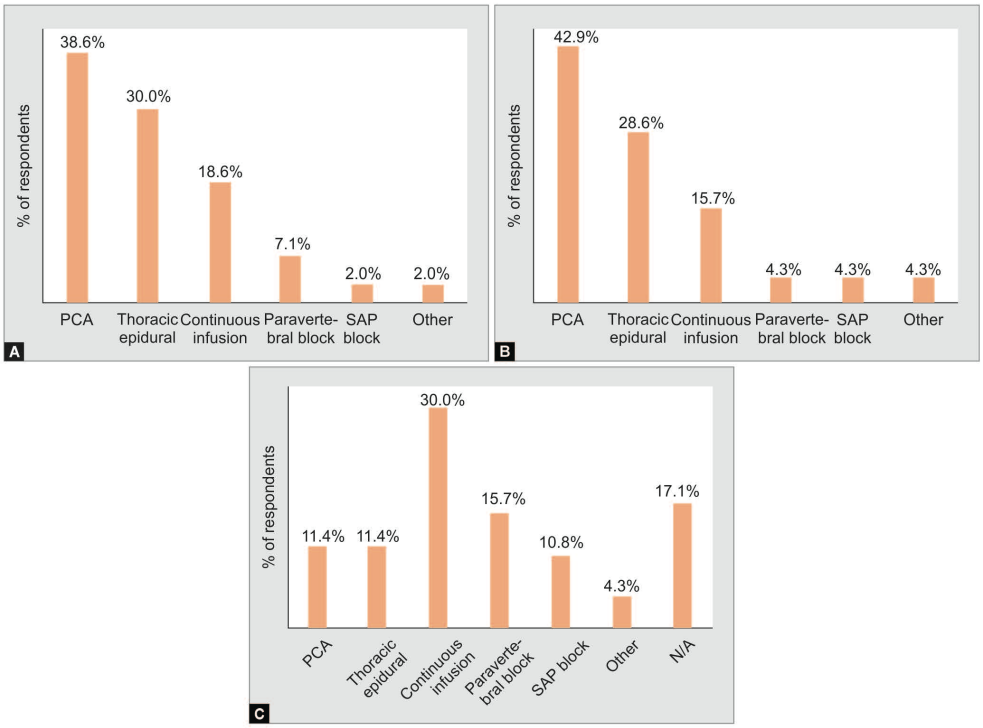
The majority of respondents were physicians ($n = 44$) at varying stages of training: consultants, specialty trainees, foundation or core trainees, and nontraining doctors, accounting for 26, 15, 2, and 1 of the respondents, respectively. The remaining respondents consisted of 20 ACCPs, 5 nurses, and 1 unspecified staff role (Table 1). Of all the specialties surveyed, the respondents mostly worked in intensive care in some capacity ($n = 46$, 65.7%), primarily mixed, followed by anesthesia ($n = 20$, 28.6%), surgery with an interest in trauma ($n = 3$, 4.3%), and emergency medicine ($n = 1$, 1.4%). The majority of respondents worked in a tertiary center with regional trauma facilities available also known as a major trauma center [MTC (82.9% $n = 58$)]. In UK, the MTCs were introduced in 2012 to standardize and improve the immediate care and rehabilitation services for patients who experience life- or limb-threatening traumatic injuries. The MTCs are usually located within larger hospitals in major cities and have immediate access to computed tomography scanners, operating theaters, and critical care services. Of the respondents, 92.3% were from England where the majority of MTCs are located, with the remainder located in Wales and Scotland.

Of the respondents, 31.4% reported that their department has a protocol in place for the analgesia of patients with rib fractures, 52.9% stated their department did not, and 15.7% were unsure (Fig. 1A). Of those that did have a protocol in their place of work, 27.3% reported they always used the protocol, 54.6% reported they usually used the protocol, 9.1% used it sometimes and 9.1% never (Fig. 1B).

In addition to paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), and morphine, Patient-controlled analgesia (PCA) was the most commonly used form of analgesia for 38.6% of respondents, followed by TEA (30.0%) and continuous infusion of drugs such as morphine, alfentanil, or ketamine (18.6%) (Fig. 2A). Patient-controlled analgesia was also the second most commonly used form of analgesia, popular among those who do not use it first-line.



Figs 1A and B: Access to and usage frequency of analgesia protocols for managing rib fracture-associated pain among respondents; (A) Accessibility; (B) Usage frequency among those with access



Figs 2A to C: Most frequently used methods of analgesia for rib fracture-associated pain in intensive care; (A) Most commonly used; (B) Second most commonly used; (C) Third most commonly used

Paravertebral catheters and SAP were not commonly used as first- or second-line methods, together accounting for 9.1% and 8.6% of these, respectively (Figs 2A and B). Their usage collectively increased to 26.5% when the respondents considered the third most commonly used method (Fig. 2C).

In the presence of no contraindications, TEA was the preferred method of analgesia for rib fractures among respondents, which was opted for by 37.1% vs 14.3% for PCA. Paravertebral catheters and SAP were also more frequently used in the absence of contraindications, being the method of choice for 17.1% and 21.4% of respondents, respectively (Fig. 3).

Attitudes Concerning the Efficacy of Analgesia

When asked whether they thought the pain of patients with rib fractures was adequately managed in the ICU, no respondents reported that pain was "always" controlled; 42.9% reported it was

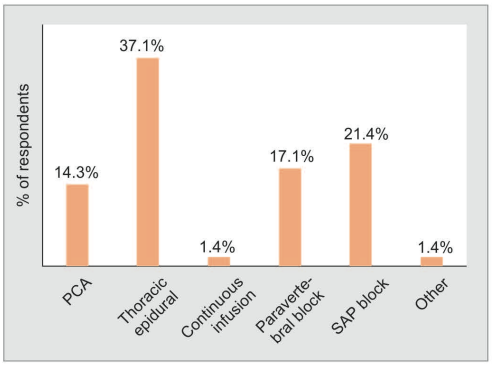


Fig. 3: The respondents' preferred method of choice for managing pain secondary to rib fractures in the absence of any contraindications

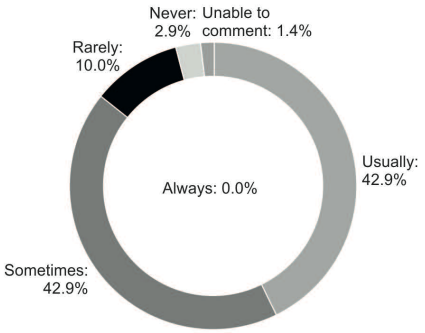


Fig. 4: Frequency of adequate analgesia being achieved for multiple rib fracture patients in intensive care

Table 2: Adequacy of pain control with and without the presence of pain management guidelines

How often do you feel pain is adequately managed?							
Do you have a guideline?	*Number of responses*	*Always*	*Usually*	*Sometimes*	*Rarely*	*Never*	*Unable to comment*
Yes	23	0	18	4	0	0	0
No	41	0	8	23	6	1	3

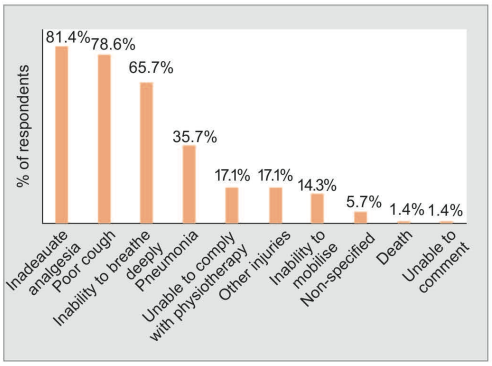


Fig. 5: Most frequent complications of rib fractures seen by respondents in intensive care (up to three complications selected per respondents)

"usually" controlled, 42.9% "sometimes," 10.0% "rarely," and 2.9% "never"; 1.4% was unable to comment (Fig. 4).

A comparison of the adequacy of analgesia was made between those who responded that they had a protocol compared to those that did not (Table 2). Respondents who were uncertain about the presence of a hospital protocol were excluded. Adequate pain control was taken to be "always" and "usually" and inadequate pain control "sometimes," "rarely," and "never."

For those with a hospital guideline, adequate pain control was reported by 78.3% and inadequate by 17.4%, compared to those without a hospital protocol in which adequate pain control was reported by 21.1% and inadequate control by 78.9%. Significantly more respondents who had a hospital protocol said they achieved adequate pain control compared to those without (χ^2, $p < 0.01$).

Respondents were also asked which three complications of rib fractures they most often encountered in their ICU. These were found to be inadequate analgesia (81.4%), a poor cough (78.6%), and inability to breathe deeply (65.7%); (Fig. 5).

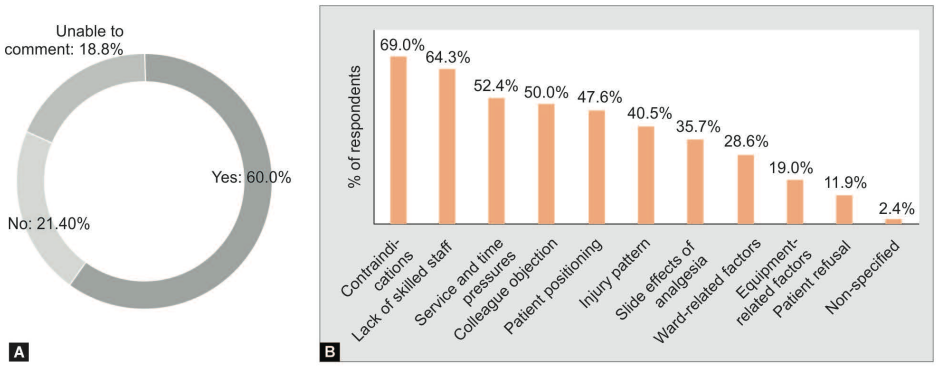
Barriers to Analgesia

Nearly two thirds of respondents (60.0%) reported challenges or barriers to analgesic options for MRF patients in the ICU. A fifth (21.4%) experienced neither of these, while the remainder (18.6%) were unable to comment (Fig. 6A). Each respondent selected up to five reasons for this. Contraindications provided the majority of challenges (69.0%), closely followed by a lack of skilled staff (64.3%), service and time pressures (52.4%), colleague objection (50.0%), and patient positioning (47.6%) (Fig. 6B). These barriers were in respect to all methods of analgesia collectively.

Discussion

Current Practice

These results demonstrate that there is considerable variation among physicians in their current use of analgesic modalities for patients with MRFs. Opiate-based methods predominate, with PCAs and continuous infusions still the mainstay of analgesic treatment for these patients. This is supported by the current literature. A retrospective review of patients admitted with rib fractures recorded that 63% of patients received opiate-based PCA analgesia and 18% TEA.[16] Other studies report TEA use between 9.9 and 18.4%.[6,7,17] In this study when no contraindications are present, physicians preferred method of analgesia was TEA, closely



Figs 6A and B: (A) The percentages of respondents who have or have not experienced barriers to or challenges in providing analgesia for patients with rib fractures; (B) The most common barriers and challenges experienced by respondents in intensive care

followed by SAP and PVB (37.1%, 21.4%, and 17.1%), thus revealing an overwhelming preference for regional anesthesia where possible.

This is perhaps understandable, given the benefits of regional anesthesia in other cohorts. These advantages include superior analgesia and the avoidance of adverse effects associated with opioid use such as nausea and vomiting, constipation, sedation, and delirium.[18]

Barriers to Analgesia

This study found that barriers to the provision of analgesia were experienced by 60.0% of respondents. Contraindications to analgesic choice, lack of skilled staff and service and time pressures were the top three barriers to providing analgesia (69.0%, 64.3%, and 52.4%). Thoracic epidural use can be problematic in this cohort as up to 90% of patients with MRFs have associated injuries such as spinal and head injuries which, in addition to preexisting comorbidities, hypotension, and coagulopathy, may preclude their use.[6] This might also explain why TEA usage in the literature and this study is limited despite being the preferred choice by physicians. Opioid-based analgesia, though less favored by physicians in this study, is the most commonly used analgesic method. This is due to its noninvasive nature, ease of administration, and ability for it to be provided by a range of healthcare professionals.

Alternative techniques such as the novel thoracic wall blocks will potentially play a larger role in the management of pain secondary to MRFs. Serratus anterior plane and ESPB are less susceptible to the barriers mentioned above. Their insertion site is away from the epidural space, increasing the access of patients with MRFs to regional techniques due to a reduced contraindication profile. There is also the potential for nonanesthetists to perform the SAP catheter insertion because of its superficial insertion site and reduced complication risk compared to PVB and TEA.[19] Serratus anterior plane can also be performed in the supine position, negating the need for patient repositioning. These factors would be significant where time and staff skill mix are the limitations. Barriers aside, the regional technique that is superior for managing rib fracture pain is yet to be determined.[14] Thoracic epidural has long been considered the gold standard of thoracic analgesia but associated adverse effects and complications detract from its merits.

A recent study demonstrated SAP provides an equivalent level of analgesia to TEA postthoracotomy while maintaining hemodynamic stability.[20] Similarly, a meta-analysis of PVB vs TEA postthoracotomy found no significant difference in reported pain scores.[21] Evidence suggests PVB may provide superior analgesia to SAP. A recent trial comparing these two regional blocks following breast surgery observed a prolonged duration of analgesia and reduced opioid usage associated with PVB.[22] However, PVB is a more difficult technique to perform with the potential for greater complications.[11,23] Further high-quality studies are required to fully investigate the efficacy of the novel SAP and ESPB techniques compared to the more traditional regional approaches of TEA and PVB in the trauma cohort.

Guideline Adoption

It is concerning that no respondents felt that patient's pain was "always" controlled. Inadequate pain control was the most common complication reported (81.4%), closely followed by poor cough (78.6%) and inability to deep breathe (65.7%), both exacerbated by inadequate analgesia. Previous studies demonstrated the effectiveness of multidisciplinary patient pathways to improve outcomes for patients with MRFs.[12] Witt and Bulger also showed the benefits of clinical scoring systems and early multimodal analgesia.[4]

The use of guidelines and protocols with associated severity scoring systems to assist with the escalation of pain management is essential. Approximately one third (31.4%) of respondents had a protocol for analgesia in their place of work, with 81.8% of respondents stating they always or usually followed the protocol, suggesting that protocols are well utilized when present.

This study revealed the pain relief of patients with MRFs was perceived to be significantly better managed when a hospital protocol was present compared to not ($\chi^2, p < 0.01$).

Conclusion

These results show that the current analgesic practice for patients with MRFs is inadequate. Uptake of protocols that provide escalation strategies[11] is not universally adopted. However, protocol use in this cohort is associated with improved analgesia and patient outcomes. Regional anesthetic techniques such as TEA are preferred over opiates by physicians but opiate use predominates in those with thoracic injuries as a result of contraindications to TEA use,

service and time pressures, and staff skill mix. The novel thoracic wall blocks with their reduced side effect profile, ease of insertion, and limited contraindications may herald a new approach to the analgesic management of patients with MRFs. Further research into the efficacy of these thoracic wall blocks is needed.

Although it is recognized that regional analgesia is very important for the pain management of patients with thoracic trauma, there is still an important role for PCA morphine, especially in those with polytrauma and also to allow the patient autonomy over their analgesic regime. In patients with multiple injuries, morphine PCA and regional analgesia should be seen as complementary techniques aiming to improve pain, patient satisfaction, and reduce opiate consumption.

We suggest future research should focus on currently utilized regional techniques of TEA, PVB, SAP, and ESPB. In the UK, the use of pleural infusions and intercostal nerve catheters as mentioned in some specialty guidance is a rarity.[14] The aim of such research would be to produce a validated standardized national protocol that is informed by current practice, the evidence base, and current limitations to service provision.

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APPENDIX 3: ACUTE PAIN ALGORITHM

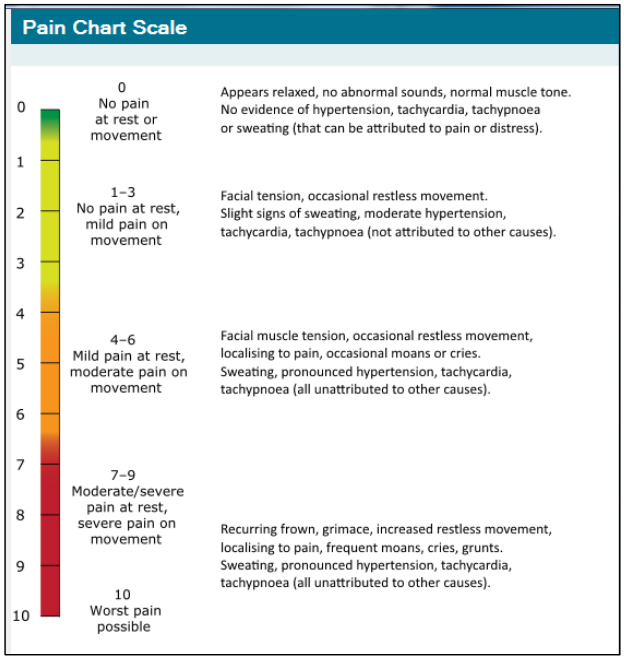
Authors: L Beard, D Bennett, M Knowles

MANAGEMENT OF ACUTE PAIN IN PATIENTS WITH RIB FRACTURES

INTRODUCTION:

Rib fractures are present in up to 10% of patients who are admitted to hospital with traumatic injuries. Respiratory complications are common and include pneumonia, atelectasis, acute respiratory distress syndrome (ARDS) and need for invasive and non-invasive ventilation[1]. Pneumonia occurs in 11-31% of patients with rib fractures, these individuals have nearly four times the odds of mortality than those who do not develop the infection [2-4].

Optimal pain control enables the patient to deep breathe, cough, and comply with physiotherapy. This assists in the clearance of secretions and prevention of atelectasis, reducing the risk of developing pneumonia. Aggressive and rapid pain management is therefore essential in this large high-risk cohort in order to reduce the risk of respiratory complications.



PAIN ASSESSMENT

Pain needs to be assessed not only at rest but also during activities such as deep breathing, coughing and movement.

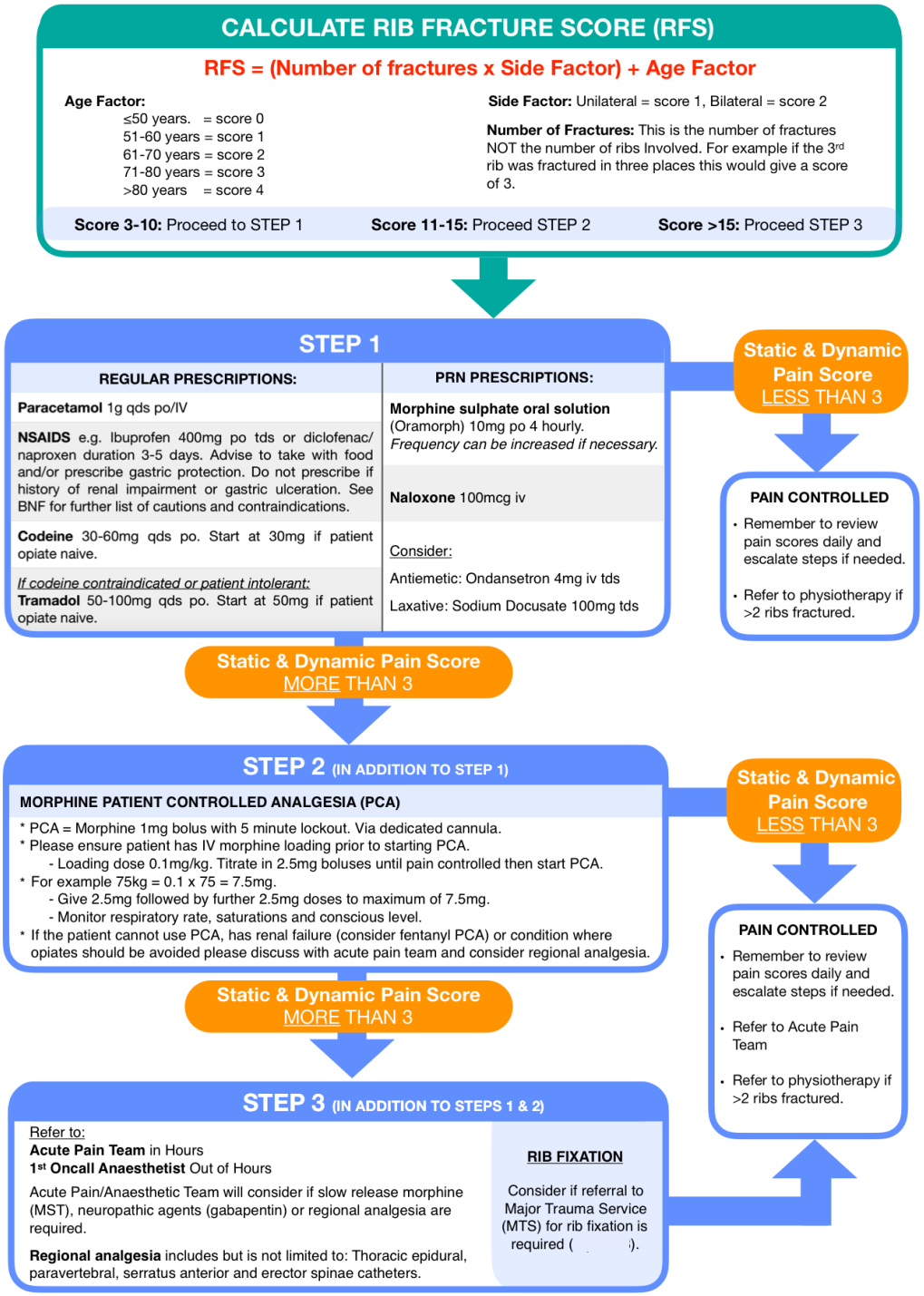
Static Pain Score = Pain at rest

Dynamic Pain Score = Pain on deep breathing and coughing

Please follow the assessment and treatment flowchart below. The Flowchart is modified from the guidelines used at the University Hospitals Coventry and Warwickshire (UHCW) that they published in the the BJA 2016 on 'Rib Fracture Management'.[1].

Doses listed in the Algorithm need to be adjusted for patients weighing less than 50Kg.

Please consult BNF for further advice regarding contraindications and cautions.



Doses listed in the Algorithm need to be adjusted for patients weighing less than 50Kg. Please consult BNF for further advice regarding contraindications and cautions.

*Modified from the University Hospitals Coventry and Warwickshire (UHCW) protocol published in the BJA 2016 covering 'Rib fracture management'.[1]

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University Hospitals Birmingham NHS
NHS Foundation Trust

CONTROLLED DOCUMENT

Management of Thoracic Wall Blocks:

Serratus Anterior Plane (SAPC) & Erector Spinae (ESPC) Catheters

CATEGORY:	Clinical Guidelines
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1. GUIDELINE SUMMARY

- This guideline has been developed to assist with the safe management of thoracic wall fascial plane catheters: serratus anterior plane catheters (SAPC) and erector spinae catheters (ESPC)
- SAPC and ESPC can be used to assist with the analgesic management of patients with multiple rib fractures (MRFs) and for post-operative analgesia following thoracic wall procedures including but not limited to thoracotomy, thoracoscopy and breast surgery.
- The guideline is designed to reduce variations in practice and provide information for staff on who to contact if there are any concerns or questions regarding this analgesic technique. It covers the management of thoracic fascial plane catheters at the Queen Elizabeth Hospital Birmingham (QEHB) and Heartlands, Good Hope and Solihull Hospitals (HGS). Site specific differences are highlighted in the text and appendices.

2. PURPOSE

- Pain in patients with MRFs or those who have undergone thoracic surgery can be difficult to manage.
- Inadequate analgesia results in an inability to deep breathe, clear secretions and comply with physiotherapy. This increases the patient's risk of complications such as pneumonia, need for invasive ventilation and acute respiratory distress syndrome (ARDS).
- Prompt and effective analgesia is therefore vital in this cohort.
- Serratus anterior plane catheters (SAPC) allow local anaesthetic to be infiltrated around the nerves that supply the lateral chest wall. The lateral divisions of the intercostal nerves T2-T9 (lateral cutaneous nerves) are anaesthetised providing analgesia with minimal side effects. In some cases, the long thoracic, intercostal and thoracodorsal nerves will also be blocked.
- Erector spinae catheters (ESPC) sit in the paraspinal fascial plane, their analgesic action is believed to result from the diffusion of local anaesthetic anteriorly to the ventral and dorsal rami of the spinal nerves. Further studies investigating paravertebral spread are ongoing.

3. INDICATION & PATIENT SELECTION

- ***Surgical Patients:*** Patient selection will be decided by the Consultant Anaesthetist undertaking or supervising the anaesthesia.
- ***Rib Fractures:*** Current limited evidence tentatively suggests that the SAPC technique is perhaps more effective in patients with anterior-lateral fractures. However, patients with posterior fractures have obtained improved analgesia at QEHB and University Hospital Coventry and Warwickshire (UHCW) with a SAPC. Please note that ESPC is a new type of regional anaesthesia and performed by a very limited number of anaesthetists.
- If further assistance is required in deciding if a fascial plane catheter is required please consult the following:
    - The consultant overseeing the patient's care and the Acute Pain Team.
    - APPENDIX A: PATIENT SELECTION ALGORITHM provides further information about patient selection for SAPC in those with rib fractures.
    - If you require further advice or information please refer to the contact list in SECTION 14. Please try to ascertain if named staff members are in work that day before contacting via phone.

- All referrals for thoracic fascial plane catheters by non-anaesthetic staff for patients with MRFs should be via the Acute Pain (UCAP) Team who will assess the suitability of the request and current analgesia.

4. CONTRAINDICATIONS

- Patient refusal
- History of local anaesthetic allergy/anaphylaxis
- Local infection at the site of serratus block performance
- Distorted anatomy making identification of ultrasound anatomy impossible. This could be due to previous thoracic surgery, extensive trauma or surgical emphysema.
- Abnormal Coagulation / Infection – these are relative contraindications and should be assessed on a case by case basis following discussion with the patients treating consultant.

5. PATIENT CONSENT

Risks that should be discussed include: *(Please complete the trusts relevant paper consent form)*

- Failure
- Inadequate analgesia
- Damage to surrounding structures e.g. nerve damage, vascular puncture
- Catheter displacement resulting in localised swelling
- Infection
- Bleeding and haematoma formation
- Local anaesthetic toxicity
- Pneumothorax (very rare)

6. STOP BEFORE YOU BLOCK

- Please ensure that before every catheter insertion the appropriate WHO/LocSSIPs checklist is undertaken in accordance with local policy.
- This is particularly important in areas outside of theatres such as Critical Care and Resus where regional blocks are not performed as frequently.
- For more information on 'Stop before you Block" please view the Royal College of Anaesthetists (RCOA) website on wrong site blocks: https://www.rcoa.ac.uk/standards-of-clinical-practice/wrong-site-block

7. BLOCK PERFORMANCE

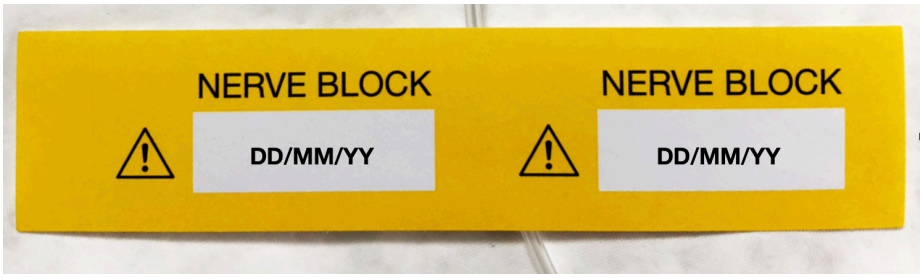
- All SAPC insertions should be performed in a suitable environment with monitoring and access to emergency drugs and equipment if needed. Recommended locations include but are not limited to Critical Care, HDU, Emergency Department Resus Area, Theatres and Theatre Recovery.
- Please check the ward that the patient is returning to is able to manage the catheter and infusion regime. Please contact the site manager if there are any issues regarding this.
- The same monitoring requirements for any peripheral nerve block apply e.g Intravenous access, pulse oximetry, cardiac monitoring (3 lead ECG), blood pressure cuff.
- Resuscitation equipment should be available and the nearest store of Intralipid should be identified.

- Patient consent and pre procedure checklists should be completed as detailed in sections 5 and 6.
- For training on how to perform SAPC/ESPC please refer to the contact list in SECTION 14.
- At QEHB a regional block trolley is located by the main nursing station on Critical Care Area B and contains the equipment needed to perform a SAPC. Please ensure that it is returned to its location on Area B after use. At HGS, the necessary equipment is located in the main theatre areas.

8. DOCUMENTATION AND PRESCRIPTION

LABELLING OF THE CATHETER:

- Please label the serratus catheter with the yellow *'nerve* block' sticker provided in the E-Cath Kit or other suitable alternative.
- Please document the date of insertion on the sticker.



PROCEEDURE DOCUMENTATION

QEHB: Please document all blocks and catheters on PICS:

- Procedures ---> Local anaesthetic nerve block.

HGS: Please document on the Peripheral Nerve Catheter Infusion Chart, example in APPENDIX B.

PLEASE REFER PATIENT TO THE ACUTE PAIN TEAM ONCE CATHETER INSERTED. This can be done via PICS at QEHB or for HGS, please refer to the contact list at the end of the document.

PRESCRIPTION

QEHB: Please prescribe all infusions and boluses on PICS.

HGS: Please prescribe all infusion and boluses on the relevant peripheral nerve catheter infusion chart (appendix B) and on the electronic prescription (EP) or paper chart if in critical care.

INITIAL BOLUS:

- Following catheter insertion a bolus of 20-30mls of 0.25% (levo) bupivacaine should be administered.

MAINTAINENCE:

- A continuous infusion of 0.125% levobupivacaine (QEHB) or 0.1% Bupivacaine (HGS) at 10mls/hr should be started.
- At QEHB this will be administered via the Yellow Cadd Solaris Pumps please see below for further information.
- AT HGS, this will be administered via the yellow McKinley pumps which are also used for epidurals.

BREAKTHROUGH PAIN

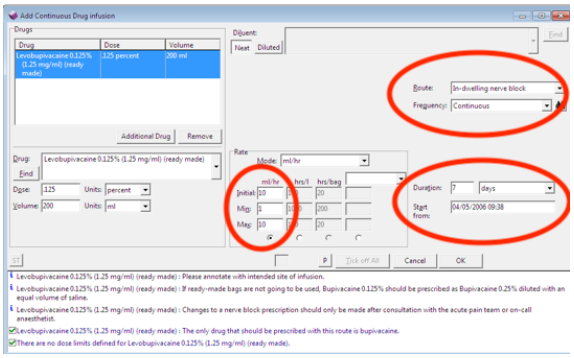
- If the patient experiences an increase in their rib fracture pain a PRN bolus should be considered.
- 5-10mls 0.125% levobupivacaine or 0.1% bupivacaine PRN, maximum of 6 hourly when an infusion is running.
- The bolus can be given via the Cadd Solaris Pump or McKinley pump, if the bolus function on the pump is not available a syringe top up should be administered. See section 8 “Catheter top ups” for more information.
- If repeated boluses are required the infusion rate could be increased to a maximum of 15mls/hr of 0.125% levobupivacaine (QEHB) or 0.1% bupivacaine (HGS). Patient weight, total local anaesthetic dose, top ups and additional sources of local anaesthetic should be taken into consideration as discussed below.

LOCAL ANAESTHETIC MAXIMUM RATES AND LIMITS

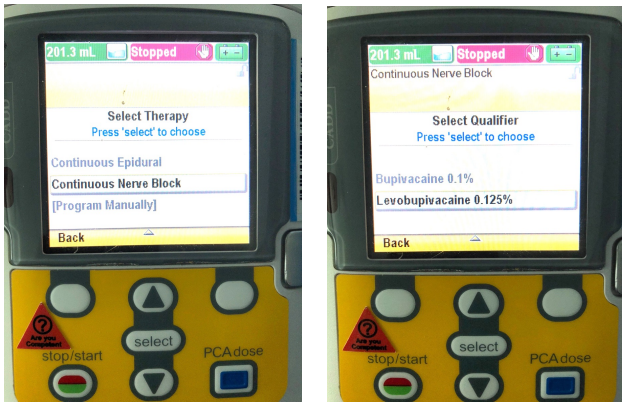
- Maximum single bolus dose of bupivacaine is 2mg/kg.
- Consider dose reduction of 10-20% in patients with renal impairment, hepatic dysfunction or cardiac failure. Caution with dosing at extremes of body weight.
- Adjust bolus dose and infusion concentration/rate if bilateral catheters used or there is an additional source of local anaesthetic running.
- THE BNF recommends a maximum (levo)bupivacaine dose of 12.5–18.75 mg/hour; maximum 400 mg per day via continuous **epidural** infusion in adults. There are no recommend 24/hr limits for peripheral nerve or fascial plane infusions. However, the BNF recommendations should be taken into consideration and suggest caution if the infusion rate is increased above 10mls/hr or where the bolus frequency or concentration is increased.

QEHB PICS PRESCRIPTION & PUMPS

Please ensure administration route is via indwelling nerve block not epidural on PICS.



The Yellow Cadd Solis Infusion Pumps can be used to administer the continuous infusion. Please select the continuous nerve block option and levobupivacaine 0.125%.



HGS PUMPS

The McKinley pumps can be used to administer the continuous infusion. Please select the same program as for the epidural.

BILATERAL CATHETERS:

- If bilateral SAPCs are present then a 'Y tube' can be used at QEHB to connect the two E-Cath filters to one infusion line. Levobupivacaine 0.125% via continuous infusion can then be run via this single line at a rate of 10-15mls/hr. Please see maintenance section above for local anaesthetic daily limits.
- Please see APPENDIX C 'SET UP OF CONTINUOUS INFUSION FOR BILATERAL SERRATUS BLOCKS AT QEHB' for more information.

9. CATHETER TOP UPS

- Boluses are only to be performed by a doctor or appropriately trained health care professional.
- Can be performed on the ward as long as resuscitation equipment and monitoring is available.

- Following a top up either via the pump or by syringe a set of observations is required every 5 minutes for 20 minutes after top up. If stable, subsequent observations can return to their previous frequency.

Bolus Administration:

- Confirm the patient's identity and allergy status.
- Ensure that the patient has IV access and is in bed.
- Check for signs of catheter migration, leakage and infection.
- Check that the filter is still in situ.
- Perform a 5ml bolus of 0.125% Levobupivacaine (QEHB) or 0.1%bupivocaine (HGS) via the Cadd Solis Pump or the McKinley pump.
- Monitor for signs of local anaesthetic toxicity. Please review SECTION 13:- COMPLICATIONS.
- If required a further 5mls can be administered in the same way 5mins after the initial bolus.
- Please 'admin' the bolus on PICS at QEHB or EP at HGS.

If a bolus is to be given via syringe please follow these additional steps.

- Non sterile gloves should be worn and injection carried out using a non-touch technique (ANTT).
- Wipe the filter cap with alcohol and chlorhexidine swab, allow to dry for 30 seconds and remove.
- Attach syringe and ensure negative aspiration prior to top up.
- If blood is present on aspiration do not inject, inform senior anaesthetist or critical care doctor.
- If negative aspiration:-
    - Inject 5ml bolus
    - Check for signs of local anaesthetic toxicity. Please review SECTION 13:- COMPLICATIONS.
    - If further bolus required wait 5mins after first bolus and ensure negative aspiration before administering the next 5ml bolus.
- Once complete replace the filter cap and sign the prescription chart.

10. NURSING CHECKS

- At the start of every shift please ensure the following:
    - The tegaderm dressing is intact and dry
    - There is no sign of leakage or infection
    - The infusion line is intact and firmly connected. Any inadvertent disconnection means the infusion is no longer sterile.
    - There is no new localised swelling around the site of the catheter
    - The catheter has been in for less than 7 days.
    - The filter has been changed every 72hours.
    - If the filter or infusion line becomes disconnected please stop the infusion and organise urgent review. In critical care speak to the registrar or consultant on for the unit, for ward patients contact the acute pain team or on-call anaesthetic team if unavailable.
- Catheters should be clearly labelled with the yellow 'nerve block' sticker or suitable alternative.

- Please ensure care is taken when dressings around the SAPC site are removed or changed. Chest drain dressings are often in close proximity to the SAPC. Please remind other members of nursing and medical staff that extra caution is required when removing chest drains to ensure the SAPC infusion line is not accidently cut or damaged.
- If you have concerns about any of these parameters please discuss with the nurse in charge and escalate to the doctor looking after the patient.
- For more information on who to contact if there are any concerns please refer to SECTION 14: CONTACTS.

11. DISCHARGE TO THE WARD

- On the critical care discharge form please document that the catheter should be removed by day 7.
- **QEHB:** - Please complete a referral to the acute pain team on PICS on discharge from the critical care/recovery/theatres to the ward. Please advise the ward nursing staff to contact the acute pain/outreach (UCAP) team if there is any concern.
- **HGS: -** Please refer the patient to the acute pain team on discharge from the critical care area/recovery/theatres to the ward. Please advise the nursing staff to contact the first-on anaesthetist (bleeps BHH 0201 and GHH 8170) out of hours or the acute pain team in hours if there is any concern at these sites.

12. CATHETER DURATION AND REMOVAL

Duration:

- Catheters can remain for up to 7 days.
- The filter should be changed every 72hrs (QEHB: available on the Regional Trolley in Critical Care Area B: infusion drawer)
- The catheters should be removed if there are any signs of infection, swelling, leakage or blood on aspiration.
- Regular analgesia should be prescribed prior to removal.

Removal:

- Please consider/check the anticoagulation status of the patient prior to removal.
- Using an aseptic non-touch technique remove the dressing and sutures securing the E-Cath to the skin. Apply gentle traction to the catheter. If there is any resistance stop traction and inform the acute pain team or anaesthetic team (SECTION 14: CONTACTS).
- Send tip for MC&S only if infection is suspected.
- Cover site with non-occlusive dressing which can be removed after 24hours.

Disconnections

- If the catheter and filter become disconnected urgent review by the acute pain team or anaesthetist is required.
- The infusion of local anaesthetic should be stopped and no further boluses given.
- The exact location of the disconnection (patient side vs infusion side) and whether the disconnection was witnessed will impact on whether the catheter can continue to be used or needs removing.

13. POTENTIAL COMPLICATIONS OF SAPC

- Failure / inadequate analgesia
- Damage to surrounding structures e.g. nerve damage, vascular puncture
- Pneumothorax and need for chest drain
- Systemic local anaesthetic toxicity
- Catheter displacement resulting in local swelling and inadequate analgesia
- Infection
- Bleeding and haematoma formation

LOCAL ANAESTHETIC TOXICITY

Can occur if there is rapid absorption into the blood stream or administered intravenously. It is rare but the consequences can be life threatening.

MOST COMMON SIGNS AND SYMPTOMS OF LOCAL ANANESTHETIC TOXICITY		
Mild	**Moderate**	**Severe**
• Restlessness / confusion • Dizziness / light headed • Numbness of tongue and lips (lip smacking) • Tingling around the mouth • Metallic taste in mouth • Ringing in ears • Double vision/ blurred vision	• Heaviness of limbs • Muscle twitches	• Alteration in mental status • Severe agitation • Change in level of consciousness • Convulsions • Cardiac arrhythmias • Brady and tachycardias • Hypotension • Respiratory arrest • Cardiac arrest

- Treatment of toxicity
    - STOP local anaesthetic infusion or injection
    - Get urgent help.
        - If mild/moderate features contact the oncall anaesthetist for urgent review, if unavailable contact the ITU team covering the wards or outreach.
        - If severe features or patient unstable put out '2222' call.
    - Attach monitoring – ECG, BP, oxygen saturations
    - Administer additional oxygen.
    - Commence CPR if in cardiac arrest.
    - **Fetch nearest supply of intralipid.**

Please refer to the AAGBI guidelines regarding the management of Severe Local Anaesthetic Toxicity found in APPENDIX D or via the following link (https://www.aagbi.org/sites/default/files/la_toxicity_2010_0.pdf)

14.) CONTACT DETAILS

For review of SAPC:-

	QEHB	HGS
3rd Oncall Anaesthetist	Blp	-
2nd Oncall Anaesthetist	Blp	BHH
1st Oncall Anaesthetist	Blp	BHH GHH SHH
Acute Pain team (UCAP)	Blp	BHH GHH SHH
Outreach (UCAP)	Blp	
Intensive Care Registrar	Level 3 Level 2	

Acute Pain Team Consultants:

QEHB	HGS

For further advice regarding SAP catheters and patient selection please contact:

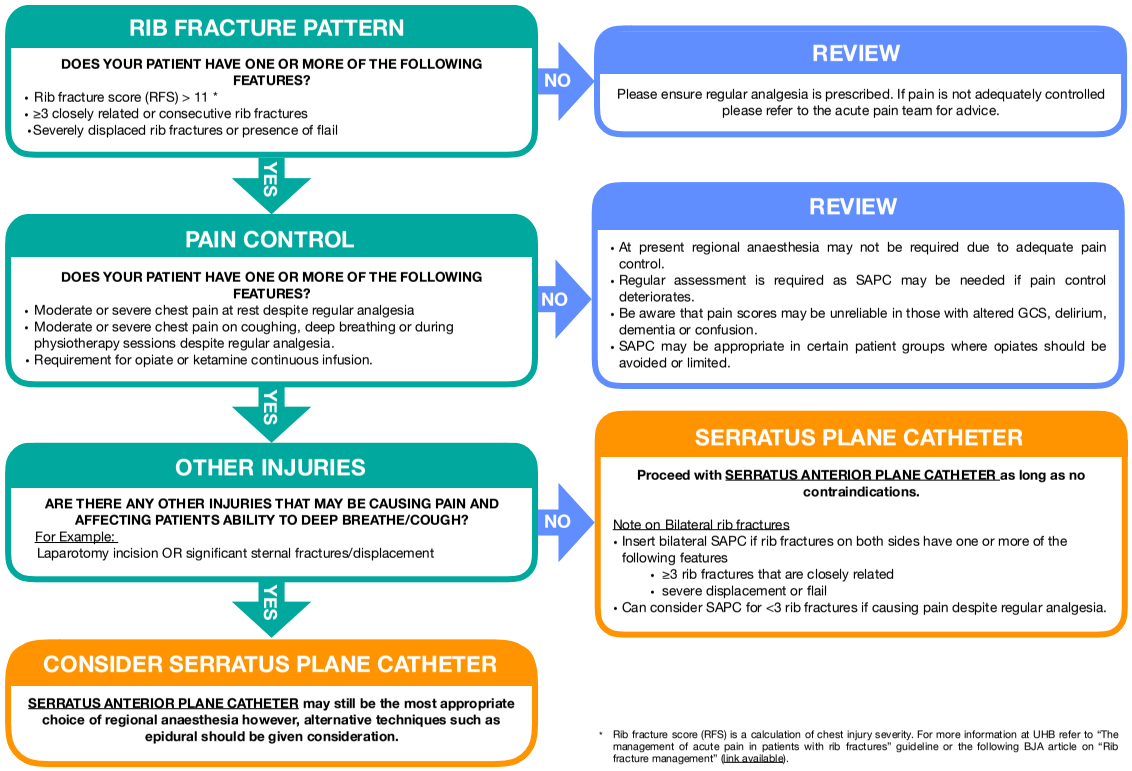
QEHB	HGS

For additional information and/or training:

QEHB	HGS

APPENDIX A: SERRATUS ANTERIOR PLANE CATHETER - PATIENT SELECTION ALGORITHM

SERRATUS ANTERIOR PLANE CATHETER (SAPC) :- PATIENT SELECTION ALGORITHM

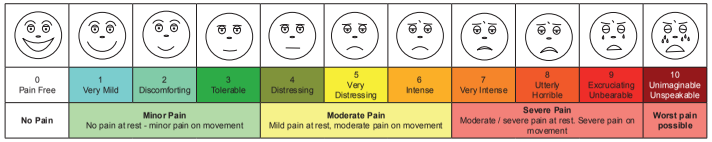


* Rib fracture score (RFS) is a calculation of chest injury severity. For more information at UHB refer to "The management of acute pain in patients with rib fractures" guideline or the following BJA article on "Rib fracture management" (link available).

APPENDIX B: PERIPHERAL NERVE CATHETER INFUSION CHART AT HGS

Escalation Pathway

NEWS² 1-4 Or Patient causing CLINICAL concern	NEWS² 5 or more Or Patient causing CLINICAL concern	NEWS² 7 or more Or Patient causing CLINICAL concern
Please check if there is a ReSPECT form and any limitations of treatment documented which may have implication for ongoing care		
▶ Inform nurse in charge. ▶ Increase frequency of observations and document frequency required. ▶ Consider escalation of care if required. ▶ Assess patient and consider cause of clinical concern ▶ Initiate treatment within scope of practice. ▶ Consider Sepsis Screen ▶ Document any actions in the patient's notes. **For ED only** ▶ Notify co-ordinator	▶ Inform nurse in charge. ▶ Assess patient, initiate treatment within scope of practice. ▶ Consider cause of clinical concern ▶ Screen for sepsis & commence Sepsis Pathway if appropriate. ▶ **Contact Junior Doctor to review patient within 30 minutes. If unable to attend inform senior doctor to review.** ▶ **Inform CCCOT.** **For ED only** ▶ Liaise with middle / senior grade clinician to prioritise patient ▶ Request speciality review if required. ▶ Patient should be reviewed within 10 mins ▶ Repeat patient observations every 30 mins until NEWS2 is below 5, unless otherwise advised ▶ If no improvement in patient's condition and senior team not available contact on call Consultant via switchboard ▶ Document all action in patient's notes	▶ Inform nurse in charge. ▶ Assess patient, initiate treatment within scope of practice. ▶ Consider cause of clinical concern. ▶ Screen for sepsis & commence Sepsis Pathway if appropriate. ▶ **Immediate call to Junior Doctor and CCCOT. If unable to attend Senior Doctor to review.** ▶ **Ensure patient is reviewed by SpR or Consultant within 1 hour of NEWS2 score - 7 or above.** **For ED only** ▶ Liaise with middle / senior grade clinician to prioritise patient ▶ Request speciality review if required. ▶ Patient should be reviewed within 10 mins ▶ Repeat patient observations every 30 mins until NEWS2 below 5 unless otherwise advised. ▶ Consider transfer to higher level of care if appropriate ▶ If no improvement in patient's condition and senior team not available contact on call consultant via switchboard ▶ Document all action in patient's notes.
NEWS² 3 in a single parameter ▶ Inform nurse in charge. ▶ **Contact Junior Doctor to review patient in 30 mins to decide whether escalation of care is necessary.** ▶ Repeat observations based on clinical assessment. ▶ Screen for sepsis & commence Sepsis Pathway if appropriate. ▶ Document all action in patient's notes		



University Hospitals Birmingham
NHS Foundation Trust

Peripheral Nerve Catheter Infusion Chart

Name: _____
Hospital No: _____
D.O.B: _____
Male / Female _____

Ward _____
Anaesthetist _____
Surgeon _____
Operation _____
Date _____

DRUGS AND FOOD ALLERGIES (or "none known" or "none declared" if appropriate)			
Date of writing	DRUG/FOOD	REACTION DETAILS	SIGN
WEIGHT	kg	DATE	

Local anaesthetic: Bupivacaine 0.1% / Levobupivacaine 0.125% / Other .....

ABDOMINAL	**Rectus sheath / TAP (10-15mls/hr Total for bilateral catheters)**	
THORAX	**Paravertebral / serratus / erector spinae / subpectoral (10-15mls/hr)**	
UPPER LIMB	**Interscalene / supraclavicular/ infraclavicular (1-5mls/hr)**	**DELETE AS APPROPRIATE**
LOWER LIMB	**Femoral / fascia iliaca / popliteal / sciatic (5-10mls/hr)**	
Other	_____	

Prescriber: Sign _____ **Print** _____
Date _____ **Time** _____ **(24hr clock)**

NB: Adjust infusion rate if bilateral catheters used. Consider dose reduction of 10-20% in patients with renal impairment, hepatic dysfunction or cardiac failure. Caution with dosing at extremes of body weight.

Post-Operative Initial Assessment

Resps **BP**
HR **Sedation Score** **Pain Score**

Bag	1	2	3	4
Start Date				
Start Time				
Set up By				
Date finish				
Time finish				
Remaining mls				
Checked by				

Nursing Instructions:-
- Observe for signs of catheter site infection e.g. redness, pain, etc
- Nerve block infusions do not normally cause hypotension. If blood pressure is low consider other causes.
- It is not possible to measure a block height with peripheral nerve blocks.

Medical / Anaesthetic advice should be sought if:-
- Pain score of more than 7
- The patient has severe pain call the Anaesthetist on call or Pain Team
- Systolic blood pressure is less than **90mmHg**
- Local anaesthetic toxicity suspected (Be aware of nearest Intralipid™ supply)

Any doubt about any aspect of PCA, please ask the Pain Team or Anaesthetist on call:-

BHH	**Pain Team**	**Bleep 2774 / 2432**	**or**	**Anaesthetist 1st on**
SOL	**Pain Team**	**Bleep 0199**	**or**	**Anaesthetist 1st on**
GHH	**Pain Team**	**Bleep 8118**	**or**	**Anaesthetist 2nd on**

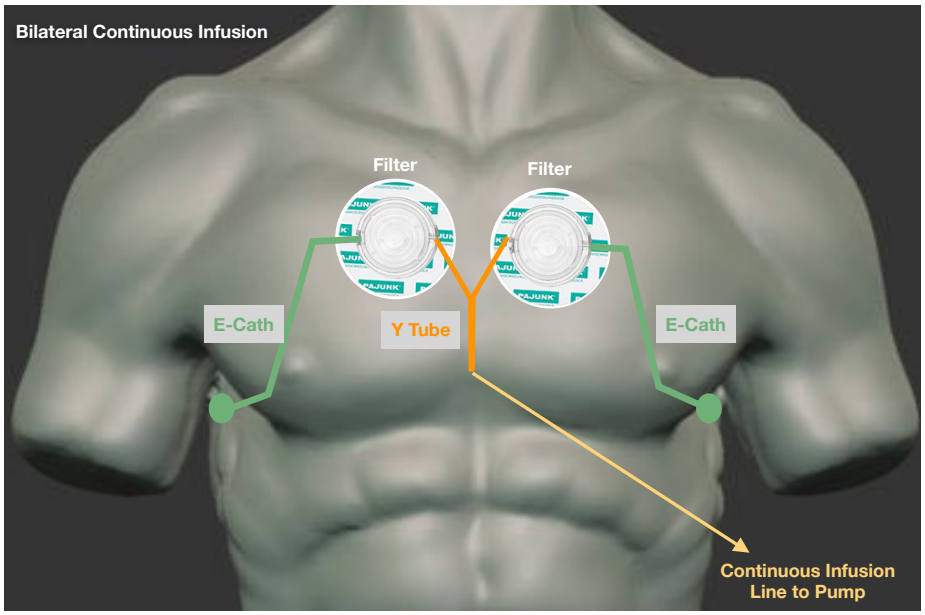
Local Anaesthetic Toxicity

Patients with continuous regional analgesia must be observed for signs of local anaesthetic toxicity which include;
- Change in level of consciousness
- Tingling around the mouth
- Metallic taste in the mouth
- Ringing in ears
- Dizziness
- Blurred Vision
- Muscle twitches

If any of these symptoms occur:
- **STOP the local anaesthetic infusion**
- **Get urgent help:**
- **Contact inpatient Pain Team / on-call anaesthetist**

Fetch nearest Intralipid™

APPENDIX C: SET UP OF CONTINUOUS INFUSION FOR BILATERAL SERRATUS BLOCKS AT QEHB

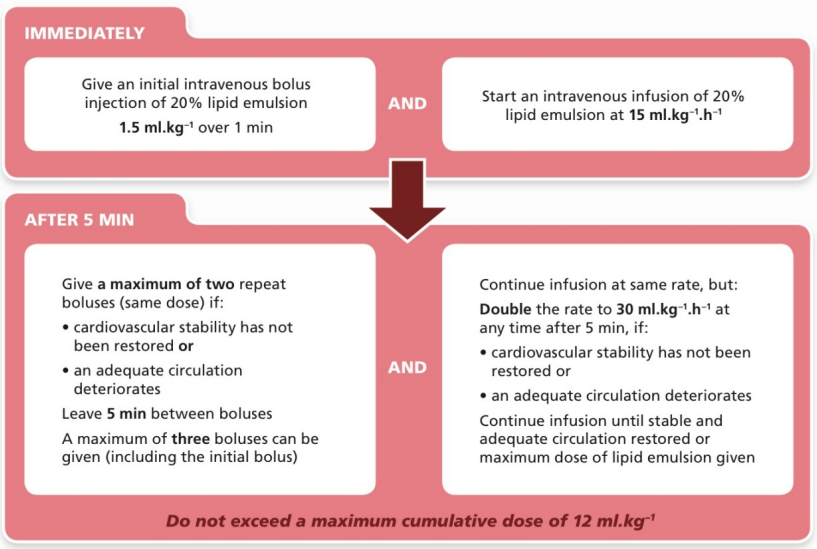


This configuration allows the bolus of individual catheters via a dedicated filter if required.

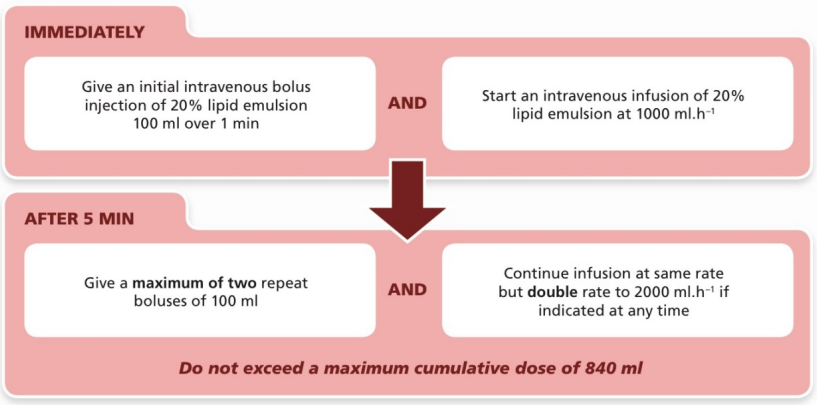
Y-Tube:
Location: Infusion drawer of regional block trolley on critical care area B



APPENDIX D: AAGBI LOCAL ANAESTHETIC TOXICITY



An approximate dose regimen for a 70-kg patient would be as follows:



This AAGBI Safety Guideline was produced by a Working Party that comprised:
Grant Cave, Will Harrop-Griffiths (Chair), Martyn Harvey, Tim Meek, John Picard, Tim Short and Guy Weinberg.

This Safety Guideline is endorsed by the Australian and New Zealand College of Anaesthetists (ANZCA).

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AAGBI Safety Guideline

Management of Severe Local Anaesthetic Toxicity

1 Recognition

Signs of severe toxicity:

- Sudden alteration in mental status, severe agitation or loss of consciousness, with or without tonic-clonic convulsions
- Cardiovascular collapse: sinus bradycardia, conduction blocks, asystole and ventricular tachyarrhythmias may all occur
- Local anaesthetic (LA) toxicity may occur some time after an initial injection

2 Immediate management

- Stop injecting the LA
- Call for help
- Maintain the airway and, if necessary, secure it with a tracheal tube
- Give 100% oxygen and ensure adequate lung ventilation (hyperventilation may help by increasing plasma pH in the presence of metabolic acidosis)
- Confirm or establish intravenous access
- Control seizures: give a benzodiazepine, thiopental or propofol in small incremental doses
- Assess cardiovascular status throughout
- Consider drawing blood for analysis, but do not delay definitive treatment to do this

3 Treatment

IN CIRCULATORY ARREST

- Start cardiopulmonary resuscitation (CPR) using standard protocols
- Manage arrhythmias using the same protocols, recognising that arrhythmias may be very refractory to treatment
- Consider the use of cardiopulmonary bypass if available

GIVE INTRAVENOUS LIPID EMULSION
(following the regimen overleaf)

- Continue CPR throughout treatment with lipid emulsion
- Recovery from LA-induced cardiac arrest may take >1 h
- Propofol is not a suitable substitute for lipid emulsion
- Lidocaine should not be used as an anti-arrhythmic therapy

WITHOUT CIRCULATORY ARREST
Use conventional therapies to treat:

- hypotension,
- bradycardia,
- tachyarrhythmia

CONSIDER INTRAVENOUS LIPID EMULSION
(following the regimen overleaf)

- Propofol is not a suitable substitute for lipid emulsion
- Lidocaine should not be used as an anti-arrhythmic therapy

4 Follow-up

- Arrange safe transfer to a clinical area with appropriate equipment and suitable staff until sustained recovery is achieved
- Exclude pancreatitis by regular clinical review, including daily amylase or lipase assays for two days
- Report cases as follows:
  - in the United Kingdom to the National Patient Safety Agency (via **www.npsa.nhs.uk**)
  - in the Republic of Ireland to the Irish Medicines Board (via **www.imb.ie**)

If Lipid has been given, please also report its use to the international registry at **www.lipidregistry.org**. Details may also be posted at **www.lipidrescue.org**

Your nearest bag of Lipid Emulsion is kept .....

This guideline is not a standard of medical care. The ultimate judgement with regard to a particular clinical procedure or treatment plan must be made by the clinician in the light of the clinical data presented and the diagnostic and treatment options available.

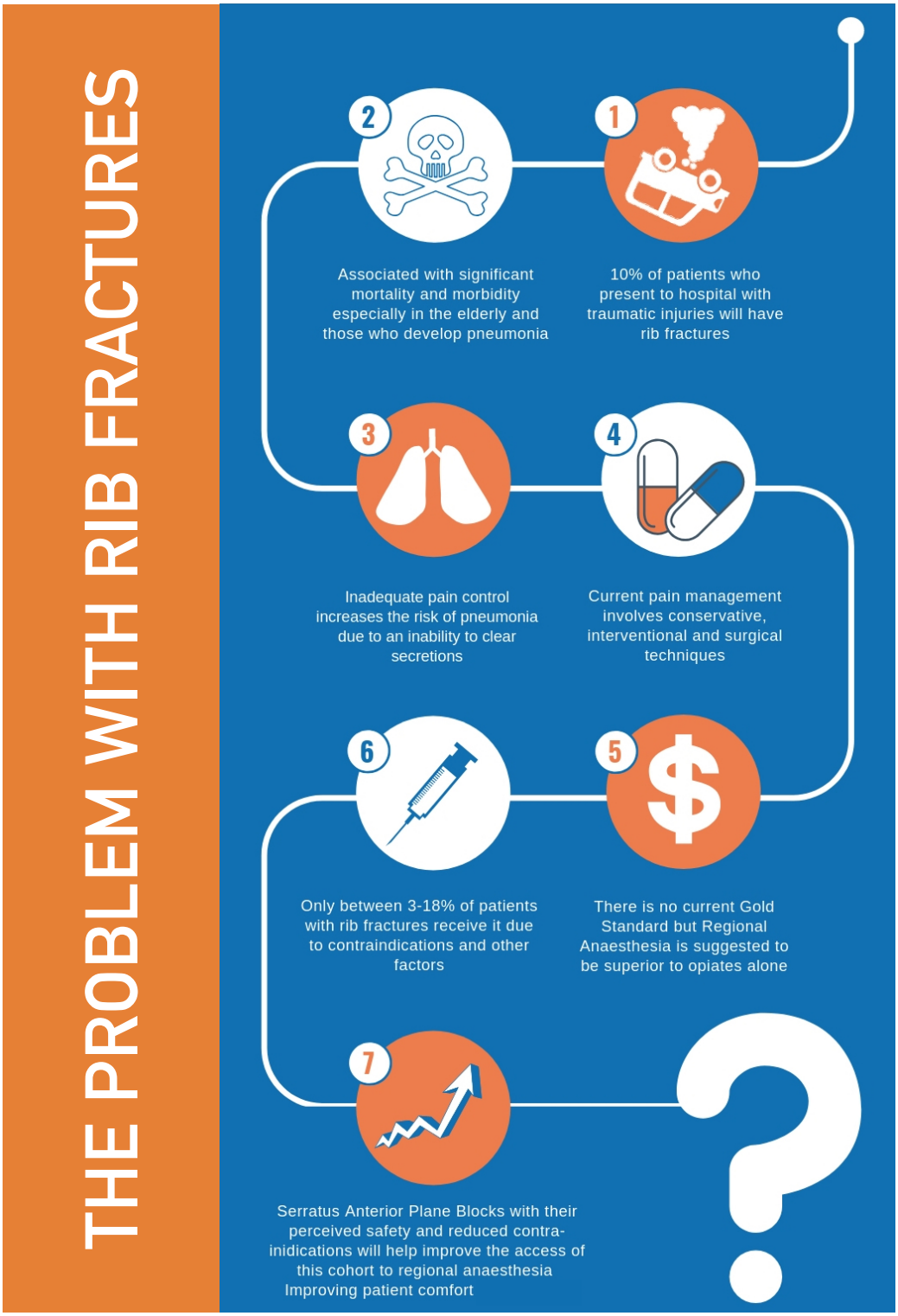
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APPENDIX E: REFERENCES

- Blanco R, Parras T, McDonnell J et al. Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia 2013, 68, 1107–1113.
- A Gaur. Serratus anterior plane block for multiple rib fratures. Pain physician 2014;17:E651-662.
- Mayes M, Davison E, Patten D et al. An anatomical evaluation of the serratus anterior plane block. Anaesthesia 2016, 71, 1064–1069.
- May L, Hillerman C et al. Rib Fracture Management. BJA Education 16 (1): 26–32 (2016).
- Royal Cornwall Hospitals NHS trust. Clinical Guideline For The Use of Rectus Sheath Catheters For The Management of Pain Following Laparotomy. (Guideline)
- Worcestershire Acute Hospitals NHS trust. Rectus Sheath and wound infiltration catheters. (Guideline)
- https://www.asra.com/asra-news/article/39/how-i-do-it-erector-spinae-block-for-rib

APPENDIX 5: INFOGRAPHIC - THE PROBLEM WITH RIB FRACTURES

Author: L Beard



APPENDIX 6: ADVANCE CRITICAL CARE PRACTITIONER SAP PROCEDURE COMPETANCY.

University Hospital NHS Foundation Trust Department of Anaesthesia & Critical Care

Name of Advanced Critical Care Practitioner (ACCP): _____

REGIONAL ANAESTHESIA: SERRATUS ANTERIOR BLOCK

ASSESSMENT OF COMPETENCY

Before practical skills competency is assessed, the ACCP must have completed the assessment of supporting knowledge (online resource). Assessment can be made and signed off only by a consultant anesthetist; or trained ACCP/ SpR as appropriate. A minimum of 10 successful blocks must be performed during training before sign-off – however, this is only a minimum and does not automatically indicate competence. Performance of bilateral blocks on the same patient should be recorded as two separate blocks.

ASSESSMENT OF SUPPORTING KNOWLEDGE	PASS	DEFER	SIGNATURE
Has undertaken ALS training and holds a valid ALS certificate			
Understands indications for performing serratus anterior blocks.			
Awareness of contraindications to the performance of serratus anterior blocks.			
Knowledge of anatomy (surface and ultrasound) required for safe serratus anterior block performance.			
Practical knowledge of pharmacology of drugs used for regional anaesthesia and treatment of common complications.			
Understands the physiological effects of regional anaesthesia and potential complications of serratus anterior blocks.			
Able to recognise and manage complications of serratus anterior blocks.			
Familiar with Trust Policy on Drug Administration and accurate prescription for procedure/addendum on Drug Administration			

Supporting knowledge satisfactory YES / NO

SIMULATION SESSION WITH PHANTOM	COMPLETED	SIGNATURE
Has completed a session using the phantom model to practice in-plane needing technique.		
Has completed the 'cannula' challenge (See Laura Beard)		

Simulation satisfactory YES / NO

Signature of Assessing Doctor: ……..

Print Name: …….. Grade: …….. Date……

LOGBOOK:

NO	DATE	PATIENT ID	SUCCESSFUL Y/N	COMMENTS	SIGN OFF SIGNATURE/PRINT
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

	PASS	FAIL	SIGNATURE
Completed minimum of 10 successful Serratus Anterior blocks under direct supervision			

PRACTICAL SKILLS SIGN OFF: TO BE COMPLETED DURING ONE BLOCK PERFORMANCE

PRACTICAL SKILLS COMPETENCY	PASS	DEFER	SIGNATURE
Identification of correct patient.			
Anaesthetic pre-assessment performed including awareness of contraindications			
Explanation of procedure (where able) to patient and informed consent obtained			
Communicates with nurse- WHO completed			
Prepares appropriate drugs Inc. emergency drugs			
Ensures appropriate monitoring in place			
Establishes IV access			
Appropriate positioning of patient for procedure			
Uses full aseptic technique with handwashing & correct personal protective equipment i.e. surgical hat, sterile gloves			
Correct preparation of skin with alcoholic chlorhexidine			
Clean technique maintained throughout procedure			
Safe administration of local anaesthetic for patient comfort			
Performs regional anaesthetic using ultrasound and an appropriate technique to safely identify ultrasound anatomy			
Safe disposal of sharps post procedure			
Documents procedure in notes, PICS & database			
Monitors patient during onset of block and post procedure			
Responds appropriately to any adverse effects of regional anaesthesia e.g. hypotension, bradycardia, inadequate block, Intravascular breach			

Signature of Assessing Doctor: ……

Print Name……..Grade…… Date……..

COMPLETED OVERALL COMPETENCY SIGN OFF:

Signature of Advanced Critical Care Practitioner: ……..

Print Name…….Grade…….Date…….

Competent to perform Serratus Anterior block YES / NO

Signature of Clinical Lead……..

Print Name: ……..……..Date……

THORACIC WALL FASCIAL PLANE CATHETERS

BACKGROUND

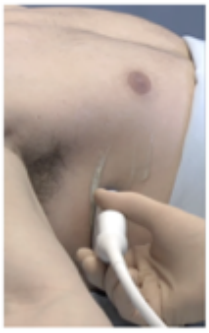
ONE OF THE MOST COMMONLY USED FASCIAL PLANE CATHETERS AT QEHB IS THE SERRATUS ANTERIOR PLANE (SAP) CATHETER USED FOR RIB FRACTURE ANALGESIA. ERECTOR SPINAE AND PARASTERNAL CATHETERS ARE ALSO USED AND ARE MANAGED IN THE SAME WAY. THESE CATHETERS CAN ALSO BE USED FOR POST OPERATIVE ANALGESIA.

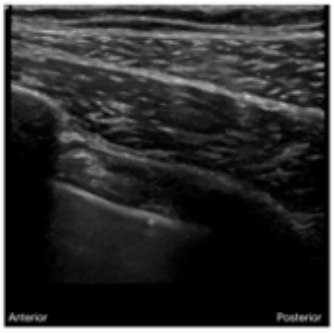
OVER 10% OF PATIENTS WITH TRAUMATIC INJURIES WILL HAVE RIB FRACTURES. APPROXIMATELY 33% OF THESE PATIENTS WILL DEVELOP PNEUMONIA WHICH INCREASES THE RISK OF DEATH.

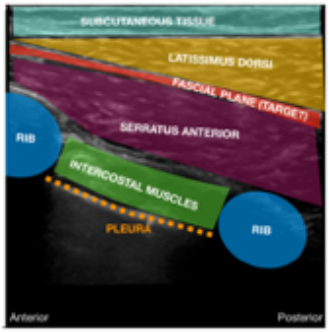
EFFECTIVE ANALGESIA WITH THE USE OF REGIONAL ANAESTHESIA REDUCES THE RISK OF PNEUMONIA BY ENABLING THE PATIENT TO DEEP BREATHE, COUGH AND COMPLY WITH PHYSIOTHERAPY.

WHAT IS A SAP BLOCK?

LOCAL ANAESTHESIA IS DEPOSITED BETWEEN TWO MUSCLES (SERRATUS ANTERIOR AND LATISSIMUS DORSI) ON THE SIDE OF SIDE OF THE CHEST WALL IN WHAT IS CALLED THE 'FASCIAL PLANE' USING ULTRASOUND.







WHAT DOES IT ANAESTHETISE

SAP ANALGESIA PROVIDES PAIN RELIEF TO THE ANTERIOR-LATERAL CHEST WALL. SPINAL, SCAPULA AND CLAVICLE FRACTURES WILL THEREFORE NOT BE COVERED BY THE BLOCK. IN THE MAJORITY OF CASES ADDITIONAL ANALGESIA IN THE FORM OF PARACETAMOL, NSAIDS, CODEINE OR TRAMADOL AND OPIATES IN THE FORM OF ORAL PRN OR IV PCA WILL BE REQUIRED.



COMPLICATIONS	
LOCAL ANAESTHETIC TOXICITY (LAST)	HAEMATOMA / BLEEDING
PNEUMOTHORAX	FAILURE
CATHETER DISPLACEMENT / SWELLING	INFECTION

MOST COMMON SIGNS AND SYMPTOMS OF LOCAL ANANESTHETIC TOXICITY		
Mild	**Moderate**	**Severe**
• Restlessness / confusion • Dizziness / light headed • Numbness of tongue and lips (lip smacking) • Tingling around the mouth • Metallic taste in mouth • Ringing in ears • Double vision/ blurred vision	• Heaviness of limbs • Muscle twitches	• Alteration in mental status • Severe agitation • Change in level of consciousness • Convulsions • Cardiac arrhythmias • Brady and tachycardias • Hypotension • Respiratory arrest • Cardiac arrest

COMPLICATIONS

THE RISK OF COMPLICATIONS IS VERY SMALL HOWEVER, IF YOU ARE CONCERNED THE ACUTE PAIN TEAM SHOULD BE CONTACTED OR '2222' CALLED IF THE PATIENT IS UNSTABLE.

IF THERE IS A CONCERN ABOUT LOCAL ANAESTHETIC TOXICITY THE INFUSION SHOULD BE STOPPED, INTRALIPID OBTAINED FROM THE RESUS TROLLEY AND THE EMERGENCY TEAM WHO ARRIVE INFORMED OF THE RISK.

THORACIC WALL FASCIAL PLANE CATHETERS

HOW ARE THEY MANAGED



CONTINUOUS INFUSION: 200MLS PLAIN LEVOBUPIVACAINE 0.125% AT 10MLS/HR
THE RATE REMAINS UNCHANGED BUT A BOLUS OF 5-10MLS VIA THE CADD SOLARIS PUMPS CAN BE GIVEN BY APPROPRIATELY TRAINED STAFF FOR BREAKTHROUGH PAIN. PLEASE CONTACT THE ACUTE PAIN TEAM IF YOU FEEL THE PATIENTS PAIN IS NOT CONTROLLED. MORPHINE PCA CAN BE RUN ALONGSIDE THIS PLAIN LEVOBUPIVACAINE BAG IF REQUIRED.

NURSING CHECKS

PLEASE CHECK THE FOLLOWING AT THE START OF EVERY SHIFT

- TEGADERM DRESSING IS INTACT AND DRY
- THERE IS NO SIGN OF LEAKAGE OR INFECTION
- THERE IS NO SWELLING AROUND THE SITE OF THE CATHETER
- THE INFUSION LINE IS INTACT AND FIRMLY CONNECTED TO THE FILTER
- THE FILTER HAS BEEN CHANGED EVERY 72 HOURS

PLEASE ENSURE THAT CARE IS TAKEN WHEN DRESSINGS ARE CHANGED OR CHEST DRAINS REMOVED AS THE CATHETER AND INFUSION LINE ARE IN CLOSE PROXIMITY.

DISCONNECTIONS

IF THE INFUSION LINE BECOMES DISCONNECTED PLEASE STOP THE INFUSION, CAP OFF BOTH ENDS AND CONTACT THE ACUTE PAIN TEAM. THE CATHETER MAY NEED TO BE REMOVED DEPENDING ON WHERE, WHEN AND HOW THE DISCONNECTION OCCURED.

DURATION AND REMOVAL

CATHETERS CAN REMAIN IN FOR UP TO 7 DAYS. THEY SHOULD BE REMOVED BEFORE IF THERE ARE ANY SIGNS OF INFECTION, SWELLING OR BLEEDING. IF THE PATIENT IS KNOWN TO HAVE ABNORMAL CLOTTING OR BE ON ANY FORM OF ANTICOAGULATION THIS SHOULD BE DISCUSSED WITH THE ACUTE PAIN TEAM AND CLOTTING REPEATED IF REQUIRED PRIOR TO REMOVAL. PLEASE ENSURE REGULAR ANALGESIA IS PRESCRIBED.

THE ACUTE PAIN TEAM CAN ASSIST IN THE REMOVAL OF THE CATHETERS AND REPLACING FILTERS. THE E-CATH IS SECURED WITH TWO SUTURES IN ITS WINGS. THE SITE SHOULD BE COVERED WITH A NON OCCLUSIVE DRESSING. SEND THE TIP FOR MC&S ONLY IF INFECTION SUSPECTED.

CONTACT

THE ACUTE PAIN TEAM WILL USUALLY BE THE FIRST POINT OF CONTACT. A GUIDELINE FEATURING ALL OF THIS INFORMATION IS NOW AVAILABLE ON THE INTRANET.

Acute Pain team / Outreach (UCAP)	Blp XXX
3rd Oncall Anaesthetist	Blp XXXX Ext XXXXX
2nd Oncall Anaesthetist	Blp XXXX
1st Oncall Anaesthetist	Blp XXXX
Intensive Care Registrar	Level 3 and above Blp XXXX / Phone XXXXX Level 2 and below Blp XXXX / Phone XXXXX

APPENDIX 8: REGIONAL ANAESTHETIC TROLLEY



APPENDIX 9: STUDY CHARACTERISTICS OF ALL INCLUDED STUDIES

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Abdallah 2017	75	Breast Surgery	Canada	0-2 days	Quasi Experimental	SAP (Both)	Single	PEC1	Safety Utility
Abdallah 2018	166	Breast Surgery	Canada	0-2 days	Quasi Experimental	SAP (Both)	Single	SAP (superficial)	Safety Utility
Abdallah 2019	25	Thoracic Surgery	Egypt	0-2 days	Experimental	SAP (Superficial)	Catheter	SAP (superficial)	Safety Utility
Abouelmagd 2017	2	Trauma Analgesia	UK	2-7 days	Quasi Experimental*CA	SAP (Superficial)	Catheter	None	Safety Effectiveness
Ahiskalioglu 2017	1	Pain Procedure	Turkey	0-2 days	Observational	SAP (Superficial)	Single	None	Safety Utility
Ahiskalioglu 2020	20	Breast Surgery	Turkey	0-2 days	Experimental	SAP (Superficial)	Single	Saline	Safety Utility
Allain 2019	15	Thoracic Surgery	France	0-2 days	Quasi Experimental	SAP (Superficial)	Catheter	TPVB	Safety Utility
Amin 2018	30	Breast Surgery	Egypt	0-2 days	Experimental	SAP (Deep)	Single	TPVB	Safety Utility
Anderson 2019	2	Cardiac Surgery	USA	Unknown	Observational	SAP (Superficial)	Catheter	None	Safety Utility
Arora 2016	20	Breast Surgery	India	0-2 days	Experimental*CA	SAP (Deep)	Single	TPVB	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Arumugam 2015	25	Thoracic Surgery	USA	Unknown	Observational	SAP (Deep)	Catheter	None	Safety Utility
Arumugam 2016	25	Thoracic Surgery	USA	Unknown	Quasi Experimental*CA	SAP (Unknown)	Single	TEA	Safety Utility
Bakeer 2020	58	Breast Surgery	Egypt	Unknown	Experimental	SAP (Deep)	Single	PECSII	Safety Utility
Bashandy 2016	20	Thoracic Surgery	Egypt	0-2 days	Quasi Experimental*CA	SAP (Superficial)	Catheter	TEA	Safety Utility
Bashandy 2016	25	Breast Surgery	Egypt	0-2 days	Experimental*CA	SAP (Unknown)	Single	TPVB	Safety Utility
Beard 2020	61	Trauma Analgesia	UK	Unknown	Quasi Experimental	SAP (Superficial)	Catheter	TEA	Safety Utility
Berthoud 2018	1	Cardiac Surgery	France	Unknown	Observational	SAP (Deep)	Single	None	Safety Utility
Berthouf 2018	20	Cardiac Surgery	France	0-2 days	Quasi Experimental	SAP (Deep)	Single	Wound Infiltration	Safety Utility
Bhatt 2019	3	Cardiac Surgery	USA	0-2 days	Observational	SAP (Deep)	Single	None	Safety Utility
Bhoi 2016	1	Breast Surgery	India	2-7 days	Observational	SAP (deep)	Single	None	Safety Utility
Blanco 2013	8	Other Surgery	Uk	0-2 days	Quasi Experimental	SAP (Both)	Single	SAP (deep)	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Bossolasco 2017	1	Trauma Analgesia	Italy	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Utility Effectiveness
Brunet 2019	13	Trauma Analgesia	France	0-2 days	Quasi Experimental*CA	SAP (Deep)	Catheter	None	Safety Effectiveness
Camacho 2018	1	Trauma Analgesia	Portugal	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Effectiveness
Chen 2019	20	Thoracic Surgery	China	0-2 days	Experimental	SAP (Superficial)	Single	Wound Infiltration	Safety Utility
de Waroux 2017	7	Cardiac Surgery	Belgium	0-2 days	Quasi Experimental*CA	SAP (Superficial)	Single	Opioid	Safety
Dept 2016	11	Other Surgery	Korea	0-2 days	Experimental	SAP (Deep)	Single	None	Safety Utility
Dept 2016	8	Breast Surgery	Japan	>7 days	Observational	SAP (Superficial)	Single	None	Safety Utility
Dept 2017	42	Breast Surgery	Japan	0-2 days	Experimental	SAP (Unknown)	Single	SAP (unknown)	Safety
Desai 2019	1	Breast Surgery	UK	0-2 days	Observational	SAP (Deep)	Single	None	Safety Utility
Droghetti 2018	12	Cardiac Surgery	Italy	>7 days	Observational	SAP (Superficial)	Single	None	Safety

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Durant 2017	2	Trauma Analgesia	USA	0-2 days	Observational	SAP (Both)	Single	None	Safety Utility Effectiveness
Ekinci 2020	30	Thoracic Surgery	Turkey	0-2 days	Experimental	SAP (Deep)	Single	ESP	Safety Utility
EL- Sherif 2020	40	Breast Surgery	Egypt	0-2 days	Experimental	SAP (Deep)	Single	SAP (deep)	Safety Utility
Fernandez 2018	8	Gastrointestinal Surgery	Spain	Unknown	Observational	SAP (Deep)	Single	None	Safety Utility
Fernandez 2018	52	Gastrointestinal Surgery	Spain	0-2 days	Quasi Experimental	SAP (Deep)	Single	None	Safety Utility
Finnerty 2020	30	Thoracic Surgery	Ireland	>7 days	Experimental	SAP (Deep)	Single	ESP	Safety Utility
Foley 2017	9	Trauma Analgesia	USA	Unknown	Observational	SAP (Both)	Single	None	Safety Effectiveness
Fu 2017	1	Trauma Analgesia	USA	0-2 days	Observational	SAP (Superficial)	Catheter	None	Safety Effectiveness
Fusco 2017	1	Trauma Analgesia	Italy	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Effectiveness
Gaballah 2019	30	Thoracic Surgery	Egypt	0-2 days	Experimental	SAP (Superficial)	Single	ESP	Safety Utility
Gautam 2020	50	Cardiac Surgery	India	0-2 days	Experimental	SAP (Deep)	Catheter	Saline	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Gedefa 2018	2	Trauma Analgesia	Africa	0-2 days	Observational	SAP (Deep)	Single	None	Safety Effectiveness
George 2018	1	Cardiac Surgery	USA	2-7 days	Observational	SAP (Deep)	Single	None	Safety Utility
Giordano 2018	1	Trauma Analgesia	Italy	Unknown	Observational	SAP (Superficial)	Catheter	None	Safety
Goldsmith 2020	1	Pain Procedure	USA	0-2 days	Observational	SAP (Superficial)	Single	None	Safety Utility
Gupta 2017	25	Breast Surgery	India	2-7 days	Experimental	SAP (Superficial)	Single	TPVB	Safety Utility
Hammerbeck 2017	5	Breast Surgery	UK	0-2 days	Quasi Experimental*CA	SAP (Unknown)	Single	None	Safety Utility
Hanley 2019	20	Thoracic Surgery	Ireland	0-2 days	Experimental	SAP (Deep)	Catheter	TPVB	Safety Utility
Hernandez 2015	10	Trauma Analgesia	USA	0-2 days	Observational	SAP (Deep)	Single	None	Safety Effectiveness
Hernandez 2019	34	Trauma Analgesia	USA	0-2 days	Quasi Experimental	SAP (Deep)	unknown	None	Safety Utility Effectiveness
Huang 2020	60	Breast Surgery	China	0-2 days	Experimental	SAP (Deep)	Single	SAP (deep)	Safety Utility
Ilic 2019	12	Trauma Analgesia	Serbia	Unknown	Observational	SAP (Superficial)	Single	None	Safety Effectiveness

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Indira 2020	40	Thoracic Surgery	India	0-2 days	Experimental*CA	SAP (Unknown)	Catheter	TEA	Safety Utility
Jenkins 2018	17	Trauma Analgesia	UK	Unknown	Quasi Experimental	SAP (Unknown)	Single	None	Safety Effectiveness
Kazior 2019	10	Cardiac Surgery	USA	Unknown	Quasi Experimental	SAP (Unknown)	Single	No Block	Safety Utility
Khalil 2017	20	Thoracic Surgery	Egypt	0-2 days	Experimental	SAP (Superficial)	Catheter	TEA	Safety Utility
Khemka 2019	11	Breast Surgery	India	Unknown	Observational	SAP (Superficial)	Catheter	None	Safety Utility
Kim 2018	42	Thoracic Surgery	Korea	0-2 days	Experimental	SAP (Superficial)	Single	Saline	Safety Utility
Kim 2020	27	Thoracic Surgery	Korea	Unknown	Experimental	SAP (Unknown)	Single	Intercostal nerve block	Safety Utility
Kubodera 2020	21	Breast Surgery	Japan	Unknown	Quasi Experimental	SAP (Superficial)	Single	PECS	Safety Utility
Kunhabdulla 2014	1	Trauma Analgesia		>7 days	Observational	SAP (Deep)	Catheter	None	Safety Utility
Lee 2019	23	Thoracic Surgery	Korea	Unknown	Experimental	SAP (Superficial)	Single	No Block	Safety
Lin 2020	6	Trauma Analgesia	USA	Unknown	Observational	SAP (Superficial)	Single	None	Safety Utility Effectiveness

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Madabushi 2015	1	Gastrointestinal Surgery	India	>7 days	Observational	SAP (Unknown)	Catheter	None	Safety Utility
Malik 2015	11	Trauma Analgesia	Uk	0-2 days	Quasi Experimental*CA	SAP (Superficial)	Single	None	Safety Effectiveness
Manson 2017	2	Cardiac Surgery	USA	0-2 days	Observational	SAP (Both)	Single	None	Safety Utility
Martinez 2020	10	Trauma Analgesia	France	2-7 days	Observational	SAP (Superficial)	Single	None	Safety Utility Effectiveness
Mazzinari 2019	28	Breast Surgery	Spain	0-2 days	Experimental	SAP (Deep)	Single	No Block	Safety Utility
Mazzocchi 2019	4	Trauma Analgesia	Itaky	Unknown	Observational	SAP (Unknown)	Single	None	Safety Effectiveness
Mbuvah 2019	1	Trauma Analgesia	USA	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Effectiveness
Migliore 2020	38	Cardiac Surgery	It	>7 days	Quasi Experimental	SAP (Superficial)	Single	None	Safety Utility
Millerchip 2014	3	Trauma Analgesia	UK	Unknown	Observational	SAP (Unknown)	Catheter	None	Safety Utility Effectiveness
Okmen 2017	20	Thoracic Surgery	Turkey	0-2 days	Quasi Experimental	SAP (Deep)	Single	PCA	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Okmen 2018	20	Thoracic Surgery	Turkey	0-2 days	Experimental	SAP (Deep)	Single	PCA	Safety Utility
Oksuz 2018	20	Thoracic Surgery	Turkey	0-2 days	Quasi Experimental	SAP (Unknown)	Single	Intercostal nerve block	Safety Utility
Oksuz 2019	24	Thoracic Surgery	Turkey	0-2 days	Quasi Experimental	SAP (Superficial)	Single	PCA	Safety Utility
Park 2018	42	Thoracic Surgery	Korea	0-2 days	Experimental	SAP (Deep)	Single	No block	Safety
Parras 2015	11	Trauma Analgesia	UK	0-2 days	Quasi Experimental*CA	SAP (Superficial)	Catheter	None	Safety Effectiveness
Perez 2017	35	Breast Surgery	Spain	>7 days	Quasi Experimental*CA	SAP (Deep)	Single	No Block	Safety Utility
Perez 2018	40	Breast Surgery	Spain	>7 days	Quasi Experimental*CA	SAP (Unknown)	Single	Opioid	Safety Utility
Perez 2018	4	Gastrointestinal Surgery	Spain	>7 days	Quasi Experimental*CA	SAP (Deep)	single	None	Safety Utility
Petrucci 2015	1	Breast Surgery	Italy	Unknown	Observational	SAP (Deep)	Single	No Block	Safety Utility
Piracha 2017	7	Breast Surgery	USA	0-2 days	Observational	SAP (Deep)	Single	None	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Rahimzadeh 2018	30	Breast Surgery	Iran	0-2 days	Experimental	SAP (Unknown)	Single	No block	Safety Utility
Reyad 2020	45	Thoracic Surgery	Egypt	>7 days	Experimental	SAP (Deep)	Single	PCA	Safety Utility
Riley 2020	17	Trauma Analgesia	Australia	>7 days	Quasi Experimental	SAP (unknown)	Catheter	ESP	Safety Effectiveness
Rose 2019	1	Trauma Analgesia	Canada	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Effectiveness
Rose 2019	5	Trauma Analgesia	Canada	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Effectiveness
Saad 2018	30	Thoracic Surgery	Egypt	0-2 days	Experimental	SAP (Superficial)	Single	TPVB	Safety Utility
Sami 2019	2	Trauma Analgesia	Turkey	>7 days	Observational	SAP (Deep)	Single	None	Safety
Santambrogio 2015	10	Breast Surgery	Italy	0-2 days	Quasi Experimental*CA	SAP (Unknown)	Single	None	Safety Utility
Saravanan 2020	20	Breast Surgery	India	0-2 days	Experimental*CA	SAP (Unknown)	Single	No block	Safety Utility
Schweizer 2019	1	Cardiac Surgery	France	2-7 days	Observational	SAP (Superficial)	Catheter	None	Safety Utility
Segura 2018	8	Thoracic Surgery	Portugal	0-2 days	Observational	SAP (Superficial)	Single	None	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Semyonov 2019	47	Thoracic Surgery	Isreal	0-2 days	Experimental	SAP (Both)	Single	No Block	Safety Utility
Shokri 2017	23	Breast Surgery	Egypt	0-2 days	Experimental	SAP (Deep)	Single	Wound Infiltration	Safety Utility
Tao 2020	1	Gastrointestinal Surgery	China	0-2 days	Observational	SAP (Deep)	Catheter	None	Safety Utility
Teniola 2017	1	trauma Analgesia	USA	Unknown	Observational	SAP (Unknown)	Catheter	None	Safety
Tiwari 2019	2	Gastrointestinal Surgery	Australia	2-7 days	Observational	SAP (Deep)	Catheter	None	Safety Utility
Tore 2019	50	Thoracic Surgery	Turkey	2-7 days	Quasi Experimental	SAP (Superficial)	Single	PCA	Safety Utility
Toscano 2020	33	Cardiac Surgery	Italy	0-2 days	Quasi Experimental	SAP (Deep)	Catheter		Safety Utility
Vasco-Blázquez 2019	1	Breast Surgery	SPain	2-7 days	Observational	SAP (Deep)	Single	None	Safety Utility
Vig 2019	10	Thoracic Surgery	india	2-7 days	Quasi Experimental	SAP (Deep)	Catheter	None	Safety Utility
Viti 2020	46	Thoracic Surgery	Italy	0-2 days	Experimental	SAP (Deep)	Catheter	No Block	Safety Utility
Wang 2019	41	Thoracic Surgery	China	2-7 days	Quasi Experimental	SAP (Superficial)	Single	TPVB	Safety Utility

Study	SAP blocks (n)	Setting	Country	Follow up period	Study Type	Intervention	Single shot/ catheter	Comparator (if applicable)	Outcome Assessed
Watts 2018	5	Trauma Analgesia	UK	Unknown	Observational	SAP (Unknown)	Catheter	None	Safety
Wong 2017	1	Trauma Analgesia	USA	Unknown	Observational	SAP (unknown)	Catheter	None	Safety Effectiveness
Wong 2019	1	Trauma Analgesia	USA	Unknown	Observational	SAP (Unknown)	Catheter	None	Safety Effectiveness
Yao 2019	34	breast Surgery	China	0-2 days	Experimental	SAP (Superficial)	Single	SAP (saline)	Safety Utility
Yoon 2019	1	Breast Surgery	Korea	0-2 days	Observational	SAP (Superficial)	Single	None	Safety Utility
Ziacchi 2020	91	Cardiac Surgery	Italy	0-2 days	Quasi Experimental	SAP (Superficial)	Single	No block	Safety
Zocca 2017	8	Breast Surgery	USA	0-2 days	Observational	SAP (Superficial)	Single	None	Safety

*CA Conference Abstract, SAP Serratus anterior plane block, TPVB Thoracic Paravertebral Block, ESP Erector spinae plane block, PCA patient controlled analgesia, TEA Thoracic epidural analgesia, PEC Pectoralis block

Experimental = Randomised controlled trial, Quasi Experimental = Non randomised controlled trial, time series etc, Observational = cohort, case control, case series, case report.

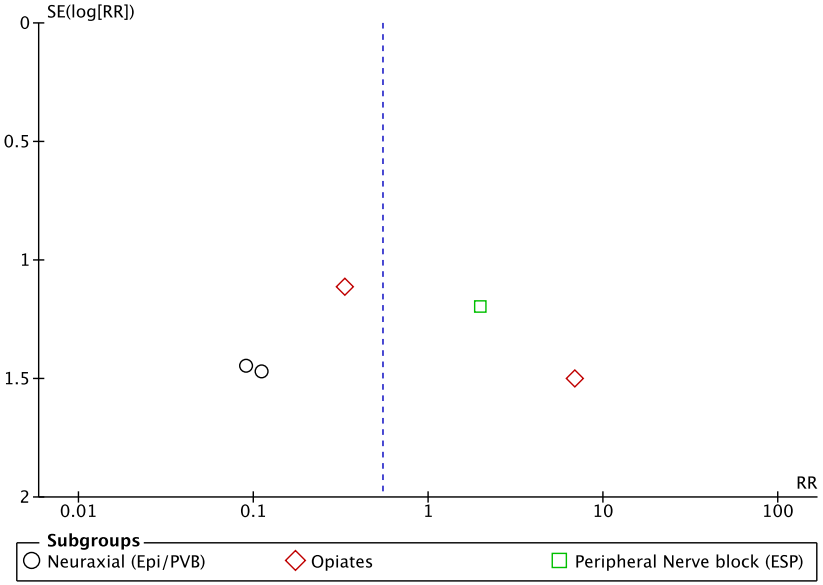
APPENDIX 10: TRIAL CHARACTERISTICS FOR HYPOTENSIVE EVENTS

Study	n	Setting	Country	Duration of inclusion (days)	Inclusion Criteria (Population)	Exclusion Criteria (Population)	Intervention	Comparator	Outcomes
Finnerty 2020	60	Thoracic Surgery	Ireland	30	ASA 1-3 18-80 years Unilateral MITS	Infection block site Contraindication regional anesthesia History opiate abuse Chronic pain Cognitive dysfunction	SAP Block (Deep)	ESP Block	Quality of Recovery-15 Pain (VRS) Time to first IV Opioid 24hr opioid consumption Highest and Lowest BP Hypotension (IVI / Drugs) PONV Block Complications
Khalil 2017	40	Thoracic Surgery	Egypt	1	Thoracic Surgery	Chronic Pain Opioid dependence Unable to communicate Bleeding disorder	SAP Block (Superficial)	TEA	Pain scores (VAS) Hypotension (SBP<80) PONV
Okmen 2018	40	Thoracic Surgery	Turkey	1	ASA 1-3 18-70 years VATS	Opioid use preoperatively Allergy local anaesthesia Systemic infection Uncontrolled hypertension Diabetes mellitus	SAP Block (Deep)	PCA Tramadol	Pain (VAS) Quantity Tramadol Use Sedation (RSS) Additional Analgesic use PONV Respiratory depression Hypotension (MAP <60mmhg)
Reyad 2020	89	Thoracic Surgery	Egypt	84	Elective thoracotomy >18 years ASA 2-3	Allergy to local anaesthesia Allergy to NSAIDS Allergy to Opioids Obesity (BMI >40) Significant cardiac, liver, renal disease Chronic pain History of drug abuse Neuropsychiatric diseases Recurrent chest malignancies	SAP (Deep)	PCA Morphine	Chronic Pain (PTPS) Pain (VAS) QOL ADL Opioid consumption PONV Hypotension (IVI administration) Sedation Constipation Urinary retention
Saad 2018	60	Thoracic Surgery	Egypt	1	40-60 years ASA 1-2 Lung lobectomy	Local infection at insertion site Coagulopathy Cognitive disorders	SAP (Superficial)	TPVB	Pain (VAS) Time first recue analgesic Total opioid dose Respiratory depression Hypotension PONV Bradycardia

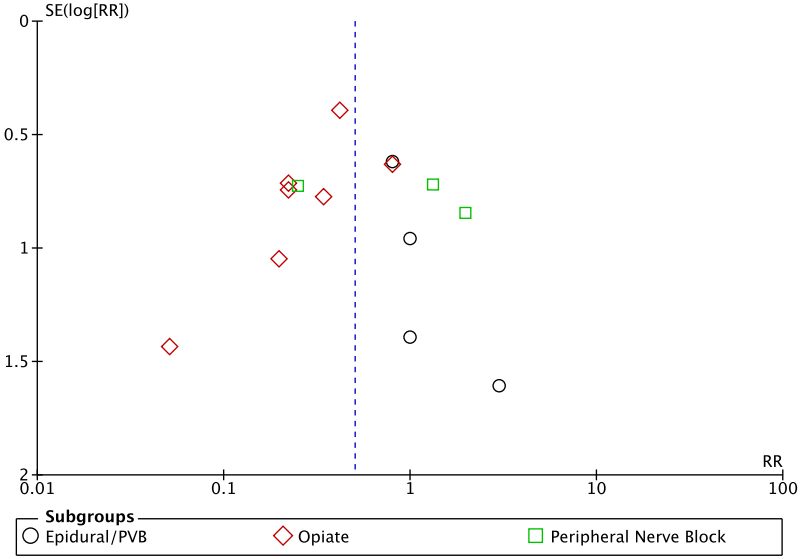
*MITS Minimally invasive thoracic surgery, SAP Serratus Anterior Plane Block, ESP Erector Spinae Plane Block, VRS Verbal Response Score, PONV Post operative nausea and vomiting, TEA Thoracic Epidural Analgesia, VAS Visual Analogue Scale, VATS Video Assisted Thoracoscopic Surgery, RSS Ramsay Sedation Scale, NSAIDS Non steroids Anti-inflammatory Drug, BMI Body mass index, PTPS Post thoracotomy pain syndrome, QOL Quality of life, ADL Activities of daily living, TPVB Thoracic paravertebral block, IVI Intravenous fluid infusion.

APPENDIX 11: REVMAN5 FUNNEL PLOTS FOR RISK OF PUBLICATION BIAS HYPOTENSIVE EVENTS(A) AND PONV (B)

(A) Hypotensive events



(B) PONV



APPENDIX 12: SUMMARY OF CHARACTERISTICS FOR INCLUDED RCTS: POST OPERATIVE NAUSEA AND VOMITING (PONV)

	Number of participants in trial	Setting	Country	Duration of inclusion (days)	Inclusion Criteria (Population)	Exclusion Criteria (Population)	Intervention	Comparator	Outcomes
Ahiskalioglu 2020	40	Breast Surgery	Turkey	1	Breast reduction surgery ASA1-2 18-60 years	Cardiac, renal, haematological disease History of peptic Ulcer History of gastrointestinal bleed Allergy analgesic medications Chronic Pain Routine analgesic use Neurological disease Coagulopathy or anticoagulant use Uncooperative patients	SAP (Superficial)	PCA Fentanyl	Pain (VAS) Opioid consumption Time to first analgesic PONV
Amin 2018	60	Breast Surgery	Egypt	1	Mastectomy 30-60 years ASA 1-2	Obesity (BMI>40 kg/m^2) Renal insufficiency Chronic analgesic therapy Diabetes with polyneuritis Generalised or local infection Chronic pain Inability to communicate	SAP (Deep)	TPVB	Opioid consumption 24hours Time to first analgesic Pain (VAS) PONV Blood pressure Heart rate
Bakeer 2020	115	Breast Surgery	Egypt	1	18-60years ASA 2 Mastectomy	Coagulopathy or bleeding disorder Drug allergy Opioid dependence Local infection Psychiatric illness	SAP (Deep)	PECs Block	Opioid consumption Pain (VAS) Time first rescue analgesic Sedation (RSS) Heart rate PONV (Scale 0-3) Patient satisfaction Other complications
Chen 2019	40	Thoracic Surgery	China	2	ASA 1-2 18-65 years VATS	Allergy Severe cardiovascular disease Hepatorenal insufficiency Coagulation disorder Infection at injection site Obesity (BMI>40 kg/m^2)	SAP (Superficial)	Local Anaesthetic Wound Infiltration	Pain (VAS) Opioid consumption PONV Pulmonary complications Length hospital stay
Finnerty 2020	60	Thoracic Surgery	Ireland	30	ASA 1-3 18-80 years Unilateral MITS	Infection block site Contraindication regional anesthesia History opiate abuse Chronic pain Cognitive dysfunction	SAP Block (Deep)	ESP Block	Quality of Recovery-15 Pain (VRS) Time to first IV Opioid 24hr opioid consumption Highest and Lowest BP Hypotension PONV Block Complications
Gupta 2017	50	Breast Surgery	India	3	18-60 years ASA 1-2	Contraindications to nerve block	SAP (Superficial)	TPVB	Duration of analgesia Opioid consumption

	Number of participants in trial	Setting	Country	Duration of inclusion (days)	Inclusion Criteria (Population)	Exclusion Criteria (Population)	Intervention	Comparator	Outcomes
					Mastectomy	Significant neurological, cardiac, renal, hepatic or respiratory disease			Pain (VAS) PONV
Khalil 2017	40	Thoracic Surgery	Egypt	1	Thoracic Surgery	Chronic Pain Opioid dependence Unable to communicate Bleeding disorder	SAP Block (Superficial)	TEA	Pain scores (VAS) Hypotension (SBP<80) PONV
Kim 2018	85	Thoracic Surgery	Korea	2	ASA 1-2 20-65years VATS	Allergy to local anaesthesia Coagulopathy Local infection Neurological deficit Psychiatric illness Severe cardiovascular or liver disease Renal failure Chronic opioid use Pregnancy Inability to communicate	SAP (Superifical)	Opioid	Quality of recovery – 40 Pain (NRS) Opioid consumption Length of stay PONV Pulmonary complications
Okmen 2018	40	Thoracic Surgery	Turkey	1	ASA 1-3 18-70 years VATS	Opioid use preoperatively Allergy local anaesthesia Systemic infection Uncontrolled hypertension Diabetes mellitus	SAP Block (Deep)	PCA Tramadol	Pain (VAS) Quantity Tramadol Use Sedation (RSS) Additional Analgesic use PONV (Scale 0-3) Respiratory depression Hypotension (MAP <60mmhg)
Park 2018	84	Thoracic Surgery	Korea	1	VATS ASA 1-2 20-80 years	Renal impairment History of drug abuse Chronic pain Allergy to local anaesthetic	SAP (Deep)	Opioid	Opioid consumption Pain (NRS) PONV Pruritis Respiratory rate Patient satisfaction
Reyad 2020	89	Thoracic Surgery	Egypt	84	Elective thoracotomy >18 years ASA 2-3	Allergy to local anaesthesia Allergy to NSAIDS Allergy to Opioids Obesity (BMI >40 kg/m^2) Significant cardiac, liver, renal disease Chronic pain History of drug abuse Neuropsychiatric diseases Recurrent chest malignancies	SAP (Deep)	PCA Morphine	Chronic Pain (PTPS) Pain (VAS) QOL ADL Opioid consumption PONV Sedation Constipation Urinary retention Itching
Saad 2018	60	Thoracic Surgery	Egypt	1	40-60 years ASA 1-2 Lung lobectomy	Local infection at insertion site Coagulopathy Cognitive disorders	SAP (Superficial)	TPVB	Pain (VAS) Time first recue analgesic Total opioid dose Respiratory depression

	Number of participants in trial	Setting	Country	Duration of inclusion (days)	Inclusion Criteria (Population)	Exclusion Criteria (Population)	Intervention	Comparator	Outcomes
Semyonov 2019	104	Thoracic Surgery	Israel	3	>18 years VATS ASA1-3	Cognitive disorder Caogulopathy Haemodynamic instability Opioid abuse Allergy local anaesthetic or opioid	SAP (Deep)	Opioid	Hypotension PONV (Scale 0-3) Bradycardia Pain (VAS) Opioid consumption PONV Block complications
Yao 2019	68	Breast Surgery	China	1	ASA 1-2 18-60years Unilateral breast surgery	Allergy to local anaesthetics Coagulation disorder Local infection Chronic opioid use Inability to communicate	SAP (Superfical)	Opioid	Quality of recovery - 40 Pain (VAS) Opioid consumption PONV Dizziness Post anesthesia discharge time

*MITS Minimally invasive thoracic surgery, SAP Serratus Anterior Plane Block, ESP Erector Spinae Plane Block, VRS Verbal Response Score, PONV Post operative nausea and vomiting, TEA Thoracic Epidural Analgesia, VAS Visual Analogue Scale, VATS Video Assisted Thoracscopic Surgery, RSS Ramsay Sedation Scale, NSAIDS Non steroids Anti-inflammatory Drug, BMI Body mass index, PTPS Post thoracotomy pain syndrome, QOL Quality of life, ADL Activities of daily living, TPVB Thoracic paravertebral block, PECs Pectoralis Nerve Block, NRS Numerical rating scales

APPENDIX 13: SUPPLEMENTARY DATA

Supplementary Table 1: Adjusted and unadjusted models comparing change scores in inspiratory volume and the number of participants reporting a change in their pain scores from severe/moderate to mild/none

	Unadjusted			Adjusted		
Inspiratory volume	Mean difference [a]	95%CI	P Value	Mean difference [a]	95%CI	P Value
TEA	Reference			Reference		
PA	35.4	-176.3 to 247.1	0.74	-3.3	-200.4 to 193.8	0.97
SAP	-34.4	-241.0 to 172.1	0.75	-72.7	-274.5 to 129.2	0.48
Male				Reference		
Female				-396.2	-578.3 to -214.1	<0.001
ISS score				-2.6	-13.7 to 8.5	0.65
RFS score				-7.1	-17.8 to 3.6	0.20
Age				-7.5	-12.43 to -2.65	0.003
Pain scores	RR [b]	95%CI	P Value	RR [b]	95%CI	P Value
TEA	Reference			Reference		
PA	0.9	0.6 to 1.3	0.58	0.8	0.5 to 1.1	0.17
SAP	0.7	0.4 to 1.1	0.09	0.8	0.4 to 1.1	0.12
Male				Reference		
Female				1.2	0.9 to 1.5	0.25
ISS score				1.0	1.0 to 1.0	0.07
RFS score				1.0	1.9 to 1.0	0.83
Age				1.0	1.0 to 1.0	0.01

Abbreviations: RR=relative risk; CI=confidence interval; ISS = Injury Severity Score; PA = Paravertebral; RFS = Rib Fracture Score; SAP = Serratus Anterior Plane; TEA = Thoracic Epidural
Alpha set to 0.05
a: Mean difference (B coefficient) calculated from linear regression models - Mean difference reflects the difference in means between groups
b: RR (exp(B) coefficient) calculated from log binomial models - RR reflects the difference in risk between groups.
Adjusted covariates: age, gender, ISS and RFS score.

Supplementary Table 2: Adjusted and unadjusted models comparing in-hospital Mortality risk

	Unadjusted			**Adjusted**		
	RR	**95%CI**	**P**	**RR**	**95%CI**	**P**
TEA	Reference			Reference		
PA	0.6	0.1 to 1.8	0.42	0.5	0.2 to 1.6	0.28
SAP	0.6	0.2 to 1.6	0.34	0.4	0.1 to 1.0	0.05
Gender – Male				Reference		
Gender – Female				0.4	0.2 to 1.1	0.07
ISS score				1.0	1.0 to 1.1	0.55
RFS score				1.0	0.9 to 1.0	0.49
Age				1.1	1.0 to 1.1	<0.01
CCI				1.3	1.0 to 1.5	0.02
Injured region– chest				Reference		
Injured region – head				0.4	<0.1 to 3.8	0.43
Injured region – other				0.2	<0.1 to 1.5	0.11
Surgical rib fixation – no				Reference		
Surgical rib fixation – yes				0.6	0.1 to 2.9	0.55
Isolated				Reference		
Poly trauma				1.7	0.6 to 4.6	0.29

Abbreviations: RR=relative risk; CI=confidence interval; CCI = Charlson Comorbidity Index; ISS = Injury Severity Score; PA = Paravertebral; RFS = Rib Fracture Score; SAP = Serratus Anterior Plane; TEA = Thoracic Epidural
Alpha set to 0.05
a: RR (exp(B) coefficient) calculated from log binomial models - RR reflects the difference in risk between groups.
Adjusted covariates: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest, other), surgical rib fixation and isolated chest injury versus polytrauma

Supplementary Table 3: Adjusted and unadjusted models comparing length of stay in critical care and hospital

	Length of stay in critical care						Length of stay in hospital					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	IRR	95%CI	P-value [a]	IRR	95%CI	P-value [a]	IRR	95%CI	P-value [a]	IRR	95%CI	P-value [a]
TEA	Reference			Reference			Reference			Reference		
PA	0.5	0.3 to 0.8	0.01	0.5	0.3 to 0.9	0.07	0.8	0.6 to 1.0	0.03	0.8	0.7 to 1.0	0.10
SAP	0.9	0.7 to 1.3	0.88	1.0	0.6 to 1.3	0.95	1.2	1.0 to 1.5	0.04	1.0	0.9 to 1.2	0.77
Gender – Male				Reference						Reference		
Gender – Female				0.9	0.7 to 1.3	0.73				1.6	1.1 to 1.6	<0.01
ISS score				1.0	1.0 to 1.0	0.98				1.0	1.0 to 1.0	0.07
RFS score				1.0	1.0 to 1.0	0.01				1.0	1.0 to 1.0	<0.01
Age				1.0	1.0 to 1.0	0.90				1.0	1.0 to 1.0	0.64
CCI				1.2	1.1 to 1.4	<0.001				1.2	1.1 to 1.2	<0.001
Injured region– chest				Reference						Reference		
Injured region – head				1.5	0.9 to 2.6	0.09				1.8	1.3 to 2.5	<0.01
Injured region – other				0.8	0.53 to 1.2	0.21				1.2	0.9 to 1.6	0.08
Surgical rib fixation – no				Reference						Reference		
Surgical rib fixation – yes				1.4	1.0 to 1.9	0.03				1.3	1.1 to 1.6	<0.01
Isolated				Reference						Reference		
Poly trauma				1.5	1.0 to 2.3	0.07				1.1	0.9 to 1.4	0.25

Abbreviations: IRR=Incidence Rate Ratio; CI=confidence interval; CCI = Charlson Comorbidity Index; ISS = Injury Severity Score; PA = Paravertebral; RFS = Rib Fracture Score; SAP = Serratus Anterior Plane; TEA = Thoracic Epidural

Alpha set to 0.05

a: IRR (exp(B) coefficient) calculated from negative binomial models - IRR reflects the difference in incidence of events between groups.

Adjusted covariates: age, gender, ISS, RFS score, CCI, most severely injured body region (head, chest, other), surgical rib fixation and isolated chest injury versus polytrauma.