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Optimizing perioperative analgesia for patients undergoing operative fixation of hip fractures

Szilárd Szűcs

MD, DESA

A Thesis presented to the National University of Ireland, Cork for the Doctor of Philosophy (Anaesthesia)

Research conducted in the Department of Anaesthesia, Intensive Care and Pain Medicine, Cork University Hospital

Submitted in October 2013

Head of Department

Professor H.P. Redmond, MCh

Supervisors

Professor G.D. Shorten, PhD

Dr. G. Iohom, PhD

Acknowledgement

I would like to express my gratitude to my two supervisors, Professor George Shorten and Dr. Gabriella Iohom for offering this wonderful opportunity to carry out this research. They were most excellent supervisors. Both were always interested in the work and were very supportive of me at all times.

I would also like to thank to Dr. Brian O'Donnell who advised me on how to start working in Research and introduced me to ultrasound guided regional anaesthesia.

Dedication

I dedicate this work to my family and sons - Botond and Balázs - for giving me perspective and all the important things.

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Declaration

I certify that this thesis submitted to the University College Cork, for examination for the degree of Doctor of Philosophy, is my own work and has not been submitted for another degree, either at University College Cork or elsewhere.

_____

Dr. Szilárd Szűcs

Glossary of Terms

ANOVA- Analysis of variance between groups

ASA- American Society of Anesthesiologist physical status

BMI- Body mass index

CFNB- Continuous femoral nerve block

CI- Confidence interval

CRP- C-reactive protein

CSA- Continuous spinal anaesthesia

CVP- Central venous pressure

DHS- Dynamic hip screw

ED 50%- Effective dose, for 50% of people given it

FNB- Femoral nerve block

FNF- Fractured neck of femur

IL-6- Interleukine- 6

IMHS- Intramedullary hip screw

LA- Local anaesthetic

LEGS- Lower extremity gain scale

MHz- MegaHertz

MLAD- minimum effective local anaesthetic dose

PCA- Patient controlled analgesia

QOR- Quality of recovery score

SA- Spinal anaesthesia

SAP- Systolic arterial blood pressure

SD- Standard deviation

SVR- Systemic vascular resistance

UGFNB- Ultrasound guided femoral nerve block

VAS- Visual analogue scale

VRS- verbal rating score

Original application and subsequent changes

Application for MD degree by Thesis in Anaesthesia and Intensive Care Medicine was approved by the Faculty of Medicine at University College Cork in October 2009.

The thesis proposal was entitled: " Perioperative analgesia in fractures".

Original MD Thesis proposal

Perioperative analgesia in fractures

Dr. Szilard Szucs

Supervisor: Dr. Gabriella Iohom Department of Anaesthesia, Intensive Care and Pain Medicine
Cork University Hospital

Location: Cork University Hospital

Overall Objectives

The research sets out to explore different perioperative analgesic regimes in elderly patients with fractured neck of femur.

We propose to use conventional therapy, continuous femoral nerve block and single dose dexamethasone.

Specific Aims

i. To compare analgesia provided by two different regimes in the perioperative period.

ii. To evaluate the analgesic efficacy of single dose dexamethasone on postoperative analgesia.

Background and Significance

Fractured neck of femur is a common cause of admission to hospital in elderly patients and requires operative fixation. Preoperative pain is an important distressing factor. Regional anaesthesia is effective in alleviating pain due to trauma, and it has the advantage of producing localized but complete pain relief, while avoiding the side effects of systemic analgesics or anaesthetics (1). Continuous catheter techniques were developed after the initial attempts of Ansboro in 1946 (2). Femoral nerve blockade prior to positioning for spinal anaesthesia provides excellent pain relief and is a well tolerated procedure (3-6). With the use of a specialized needle (Contiplex®, BBraun), a catheter can be placed adjacent to the femoral nerve and a continuous infusion of local anaesthetic ensures good pain relief in the preoperative period.

The analgesic efficacy of continuous femoral nerve block will be evaluated in the clinical setting of fractured neck of femur perioperatively.

Proximal femur fracture in old patients is known to carry substantial mortality and high morbidity. It is possible that it contributes to this deterioration through its catabolic effects. Not only may it retard wound healing and fracture repair (7) but it also appears to increase net protein breakdown in uninjured muscle and thereby hinder mobilization in individuals with already poor muscle function (8).

Patients with proximal femur fracture show a prolonged adrenocortical response to injury. By 2-3 weeks plasma cortisol is higher than in younger patients with similar or more severe injuries or healthy elderly controls (9). The increase in cortisol is substantial and these differences continue for at least eight weeks (10).

Serum concentration of C-reactive protein and cytokine increase drastically postoperatively in hip-fracture elderly patients and are predictive of complications and impaired mental function (11). Higher IL-6 levels are adversely associated with recovery of lower extremity function after hip fracture (12).

Dexamethasone has the potential of inhibiting cortisol secretion (by inhibiting the primary hypothalamo-pituitary-adrenal axis at the pituitary level and by a mechanism involving changes in transcription) (13,14). In addition, preoperative glucocorticoids may improve analgesia and decrease opioid consumption with reduction in associated side effects in a variety of clinical settings (15-18).

Study Design

1. study

Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur

Prospective, randomized controlled trial.

It is planned to recruit 40 patients in total, 20 in each group.

Inclusion Criteria

Above 60 years

ASA I to III (see below appendix 2)

Exclusion Criteria

Patient refusal

Outside Age Range

Coagulation disorders

Depression

Cushing syndrome

Endocrine disorders

Corticosteroid treatment in the last 4 months

Head injury or other associated injuries

More than 10 mg morphine administered before arrival to hospital

Loss of consciousness and signs of acute coronary syndrome

Mini-Mental Score < 25 (see appendix 3)

Geriatric depression scale > 10 points (see appendix 4)

Allergy to bupivacaine, morphine, paracetamol, diclofenac sodium

Skin lesions/infection at site of injection

Renal dysfunction

Sepsis

Methods

Forty patients will be enrolled having obtained appropriate consent and will be randomized using sealed envelopes to two groups.

Group I will receive standard medical treatment im morphine prn, paracetamol 1g po/pr 6 hourly and for the patients below the age of 70 years diclofenac 50 mg po/pr 8 hourly

depending on creatinine clearance.

Group II will receive a perineural catheter, with 10 ml 0.5% bupivacaine + 10 ml 2% lignocaine as bolus followed by a continuous infusion of 0.25% bupivacaine 5 ml/h delivered via an elastomeric pump. Patients will also receive paracetamol and diclofenac around the clock similar to patients in Group I. Rescue medication in this group will consist of morphine 10 mg prn. The perineural catheter will be retained for 72 hours.

Pain severity will be recorded by the patient on a visual analogue scale (0–10 cm: 0 cm, no pain; 10 cm, worst pain imaginable) on arrival to the Accident and Emergency Department, 30 minutes after first medication/catheter insertion and 6 hourly thereafter. VAS scores will be recorded at rest and after passive movement (30 degree flexion of thigh). At the same time points nausea and vomiting (0-no nausea, 1-nausea only, 2-nausea and vomiting), pruritus (1-no itch, 2-itching but tolerable, 3-severe itch needing chlorpheniramine, Piriton 5 mg im) and sedation scores (1-awake, 2-drowsy, 3-asleep, easily rousable, 4-asleep, hard to rouse) will be recorded. In the operative theatre patients in the second group will receive a lignocaine bolus (10 ml 1% lignocaine) 15 minutes prior to positioning for spinal anaesthesia. Cumulative analgesic consumption will be noted.

Before leaving the operative theatre patients will be asked about the satisfaction regarding pain control; recorded using a 100 mm linear visual analogue scale. Patients in Group II will also be asked if they would choose the same analgesic modality again. Adverse events will be recorded by the attending anaesthetist on a dedicated data sheet. Such sheets will be filed safely and discussed at weekly research group meetings.

2. study

Effects of a single dose of dexamethasone in patients undergoing operative fixation of proximal femur fracture

Prospective, randomized, placebo-controlled clinical trial.

It is planned to recruit 40 patients, 20 in each group.

Inclusion criteria

above 60 years

ASA I to III

Exclusion criteria

patient refusal

outside age range

coagulation disorders

depression

Cushing syndrome

endocrine disorders

corticosteroid treatment in the last 4 months

head injury or other associated injuries

Mini-Mental Score < 25

Geriatric depression scale > 10 points

Renal dysfunction

Sepsis

Methods

Following ethical approval and having obtained written informed consent from each, 40 patients scheduled to undergo operative fixation of proximal femur fracture under spinal anaesthesia will be randomized using sealed envelopes to two groups.

Group 1 will receive a single dose of 0.1 mg/kg dexamethasone i.v. on arrival to theatre prior to positioning for spinal anaesthesia.

Group 2 will receive the same volume (2 ml) of normal saline i.v.

On arrival to anaesthesia induction room two 18G cannulae will be inserted; one for i.v. fluid administration and one for repeated blood sampling. Spinal anaesthesia will be performed using appropriate doses of hyperbaric bupivacaine (11 mg in patients < 70 kg and 12.5 mg in patients > 70 kg) through a 25 G spinal needle.

All patients will receive paracetamol 1 g six hourly with the first dose given intraoperatively i.v. Rescue analgesia will consist of 5 to 10 mg morphine i.m.

Pain severity at rest and on movement will be recorded on a visual analogue scale (0 cm –no pain; 10 cm-worst pain imaginable) on arrival to theatre, on arrival to recovery, 6, 12, 24, 48, 72 hours and one week postoperatively. Analgesic consumption and associated side effects will also be recorded. Blood samples for estimation of cortisol, CRP and IL-6 will be collected preoperatively, 6 h and 24 h and 48 h postoperatively.

Statistical Analysis

Collected data will be examined for normality. Quantitative data e.g. analgesic consumption and visual analog pain scores will be examined using the student-t test. Categorical data will be analysed using the chi-squared test. $P<0.05$ will be considered significant.

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Extension to PhD by Thesis

At this time point I made an application to upgrade from MD to PhD by Thesis and to carry out three additional research projects. This was approved in October 2012.

Study III

Previous hip fracture studies suggested that using regional anaesthesia had marginally advantage in terms of early mortality(1) and may influence outcome up to one year. For this reason we followed up the patients recruited in the first two studies for a period of one year.

Study IV

Clearly the process of positioning patients prior to performing spinal anaesthesia is one of the most stimulating events of the preoperative period. To minimizing preoperative stress it would be very desirable to minimize discomfort during the positioning to perform spinal anaesthesia. For this reason we studied the analgesic effect of the femoral nerve block with the intention to deposit local anaesthetic in different areas around the femoral nerve, for positioning prior to performing spinal anaesthesia.

Study V

Spinal anaesthesia offers a safe technique for high risk patients. The selection of local anaesthetic dose in the patients is extremely important. Insufficient dose of local anaesthetic results in an insufficient block, on the other side excess of local anaesthetic may have haemodynamic side effects like hypotension, associated with complications. Determination of the effective local anaesthetic dose is necessary to achieve balance in

safety and efficacy, therefore we designed a study to define the initial minimum amount of local anaesthetic dose required for operative fixation of fractured neck of femur with with continuous spinal anaesthesia.

Study VI

Spinal anaesthesia is effective for surgical fixation of hip fracture, but it is associated with the risk of haemodynamic complications, like hypotension and is effective only for a few hours after the surgery. We designed a study to evaluate the efficacy of the periarticular local anaesthetic infiltration during the first postoperative day.

Review article

In addition to the previous original body of work a review article will be published on Femoral nerve blockade highlighting the use of ultrasound guidance.

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1. Urwin SC, Parker MJ, Griffiths R: General versus regional anaesthesia for hip fracture surgery: meta-analysis of randomized trials. *British Journal of Anaesthesia* 2000; **84(4)**:450-55

Publications/presentations arising from or associated with this work

Presentations

- S. Szucs, P. Sajgalik, B. O'Donnell, I. Ahmad, G. Iohom, G.D. Shorten: Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur,

  Oral presentation of interim results - Irish Society of Regional Anaesthesia annual meeting, Dublin, Ireland, 11.05.2009

- S. Szucs, P. Sajgalik, B. O'Donnell, I. Ahmad, G. Iohom, G.D. Shorten: Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur,

  Oral presentation - South of Ireland Association of Anaesthetists annual meeting, Killarny, Ireland, 11.09.2009, Annual Research Grant winner

- S. Szucs, P. Sajgalik, B. O'Donnell, I. Ahmad, G. Iohom, G.D. Shorten: Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur,

  Anesthesia&Analgesia March 2010; **110**(3S Suppl): S 484

  doi:10.1213/01.ANE.0000398215.59935.49

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- S. Szucs, G. Iohom: Functional recovery following operative fixation of fractured neck of femur in the elderly

Regional Anaesthesia & Pain Medicine 2010: -Vol 35-Issue 5- pp E181

doi: 10.1097/AAP.0b013e3181f3582c

Poster presentation - Annual Congress of The European Society of Regional Anaesthesia&Pain Therapy, Porto, Portugal, 09.09.2010

- S. Szucs, A. Broderick, S.F. Sultan, G. Iohom: Single dose of dexamethasone in hip fractures

  Poster presentation - Irish Congress of Anaesthesia, Dublin, Ireland, 21.05.2011

- S. Szucs, D. Morau, S.F. Sultan, G. Iohom: Positioning of local anaesthetic in femoral nerve block

  Oral presentation - Irish Society of Regional Anaesthesia annual meeting, Dublin, Ireland, 21.05.2011

- S. Szucs, A. Broderick, F. Sultan, G. Iohom: Effects of a single preincisional dose of dexamethasone on pain following operative fixation of fractured neck of femur

  Regional Anaesthesia &Pain Medicine 2011: -Vol 36- Issue 5- pp E205

  doi: 10.1097/AAP.0b013e3182302f32

  Poster presentation - Annual Congress of The European Society of Regional Anaesthesia&Pain Therapy, Dresden, Germany, 08.09.2011

- M. O'Sullivan, S. Szucs, F. Loughnane: Continuous Spinal Anaesthesia for Hip Fracture Surgery in Elderly, High-risk Patients

  Regional Anaesthesia &Pain Medicine 2011: -Vol 36- Issue 5- pp 224

  doi: 10.1097/AAP.0b013e3182302f32

  Poster presentation - Annual Congress of The European Society of Regional Anaesthesia&Pain Therapy, Dresden, Germany, 09.09.2011

- S. Szucs, J. Rauf, G. Iohom, G.D. Shorten: Determination of minimum local anaesthetic needed for operative fixation of fractured neck of femur with

continuous spinal anaesthesia

Poster presentation - Irish Congress of Anaesthesia, Dublin, Ireland, 17.05.2013, Best Regional Anaesthesia Poster Award Winner

- S. Szucs, D. McCarthy, T. Hitka, G. Iohom, G.D. Shorten: Postoperative analgesia following surgery for fractured neck of femur: a comparison of periarticular infiltration of local anaesthetic with systemic postoperative analgesics

Regional Anaesthesia &Pain Medicine 2013: -Vol 38- Issue 5- pp 231

doi: 10.1097/AAP.0b013e3182a6a572

Poster presentation - Annual Congress of The European Society of Regional Anaesthesia&Pain Therapy, Glasgow, United Kingdom, 06.09.2013

Original Articles

- S. Szucs, D. Morau, G. Iohom,: Femoral nerve blockade. *Medical Ultrasonography* 2010 Jun; **12(2)**: 139-144 (Appendix 2.)
- S. Szucs, G. Iohom, B. O'Donnell, P. Sajgalik, I. Ahmad, N. Salah, G. Shorten: Analgesic efficacy of continuous femoral nerve block commenced prior to operative fixation of fractured neck of femur. *Perioperative Medicine* 2012, **1**:4 (Appendix 3.)
- Szűcs S, Morau D, Sultan SF, Iohom G, Shorten G: A comparison of three techniques (local anesthetic deposited circumferential to vs. above vs. below the nerve) for ultrasound guided femoral nerve block. *BMC Anesthesiology* 2014, **14**:6
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Chapter 1

Introduction

Optimizing perioperative analgesia for patients

undergoing operative fixation of

hip fractures

1.1 Overall objectives

Fractured neck of femur is a common cause of admission to hospital in elderly patients and requires operative fixation. Perioperative pain is an important distressing factor. Regional anaesthesia is effective in alleviating pain due to trauma, and it has the advantage of producing localized but complete pain relief, while avoiding the side effects of systemic analgesics or anaesthetics (1). Continuous catheter techniques were developed after the initial attempts of Ansboro in 1946 (2). Femoral nerve blockade prior to positioning for spinal anaesthesia provides excellent pain relief and is a well tolerated procedure (3-6).

Old patients with hip fracture have been at risk of significant morbidity and mortality, they are requiring multidisciplinary care, early surgery provides the most effective analgesia(7).

Peripheral nerve blockade should always be considered, therefore, as an adjunct to spinal or general anaesthesia, to extend the period of postoperative non-opioid analgesia(7).

Regional anaesthesia has marginally advantages compared to general anaesthesia for hip fracture patients in terms of early mortality(8), however spinal anaesthesia is associated with higher risk for hypotension(7).

Proximal femur fracture in old patients is known to carry substantial mortality and high morbidity. It is possible that cortisol contributes to this deterioration through its catabolic effects. Not only may it retard wound healing and fracture repair (9) but it also appears to increase net protein breakdown in uninjured muscle and thereby hinder mobilization in individuals with already poor muscle function (10).

Patients with proximal femur fracture show a prolonged adrenocortical response to injury. By 2-3 weeks plasma cortisol is higher than in younger patients with similar or more severe injuries or healthy elderly controls (11). The increase in cortisol is substantial and these differences continue for at least eight weeks (12).

Serum concentrations of C-reactive protein and cytokine increase drastically postoperatively in hip-fracture elderly patients and are predictive of complications and impaired mental function (13). Higher IL-6 levels are adversely associated with recovery of lower extremity function after hip fracture (14).

Dexamethasone has the potential of inhibiting cortisol secretion (by inhibiting the hypothalamo-pituitary-adrenal axis primarily at the pituitary level and by a mechanism involving changes in transcription) (15,16). In addition, preoperative glucocorticoids improve analgesia and decrease opioid consumption with reduction in associated side effects in a variety of clinical settings (17-20).

Our research sets out to explore different perioperative analgesic regimes in elderly patients awaiting operative fixation of fractured neck of femur.

We propose to study the following interventions along the critical care pathway: perioperative continuous femoral nerve block, single dose dexamethasone at induction of anaesthesia, continuous spinal anaesthesia perioperatively and periarticular/wound infiltration by surgeon before closure.

The overall objective is to maximize perioperative analgesia in patients undergoing operative fixation of fractured neck of femur.

To this end we designed a series of studies with specific aims.

1.2 Outlines of the research projects

Study I:

Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur

Is continuous femoral nerve block more effective than the conventional systemic pain therapy in patients admitted to hospital awaiting operative fixation of fractured neck of femur? In the intervention group we inserted a perineural femoral nerve catheter and after a bolus of local anaesthetic we started an infusion for 72 hours. The principal outcome measure was VAS pain score on passive movement six hour after the insertion of the perineural femoral nerve catheter.

Study II:

Effects of a single dose of dexamethasone in patients undergoing operative fixation of proximal femur fracture

Does a single dose of 0.1 mg/kg preoperative dexamethasone have postoperative effect in patients undergoing operative fixation of fractured neck of femur? The principal outcome measure was VRS pain scores at rest six hours after the surgery.

Study III:

Recovery after fractured neck of femur in elderly

Does the interventions mentioned above have any influence on long term functional outcome following operative fixation of fractured neck of femur? A previously validated questionnaire was administered over the telephone to patients in the previous two studies. The primary outcome was their walking ability one year after the surgery.

Study IV:

Optimal positioning of local anaesthetic in femoral nerve block prior to operative fixation of fractured neck of femur

Does the intention to deposit the local anaesthetic in ultrasound guided femoral nerve block have any influence on patient comfort and analgesic efficacy for positioning prior to spinal anaesthesia in patients with fractured neck of femur? The ultrasound guided femoral nerve block was performed using the following endpoints: circumferential spread, anterior or posterior local anaesthetic deposition. The primary outcome measure was VRS at the positioning for performing spinal anaesthesia.

Study V:

Determination of the minimum local anaesthetic dose in fractured neck of femur patients with continuous spinal anaesthesia

What is the minimum intrathecal local anaesthetic dose administered via a spinal catheter required for operative fixation of fractured neck of femur? The primary

outcome measure was the minimum dose of local anaesthetic needed to achieve a satisfactory sensory block prior to incision.

Study VI:

Postoperative analgesia following surgery for fractured neck of femur: a comparison of periarticular infiltration of local anaesthetic with systemic postoperative analgesics

Does periarticular infiltration of local anaesthetic have any benefits in terms of postoperative analgesia in fractured neck of femur patients when added to a conventional analgesic regimen? The periarticular infiltration with local anaesthetic was administered by the surgeon before closing the wound. The primary outcome measure was VRS pain scores 12 hours after the surgery.

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Review article

Femoral nerve blockade

2.1 Abstract

Femoral nerve blockade is the most widely performed lower limb block. Methods of femoral nerve blockade are briefly reviewed with particular reference to ultrasound guidance.

Keywords: femoral nerve, anaesthetic block, ultrasonography

Rezumat

Blocajul anestezic al nervului femural este cel mai frecvent blocaj efectuat al nivelului membrului inferior. Sunt trecute în revistă metodele de blocaj anestezic ale nivelului femural, cu referire în particular la ghidajul ecografic.

Cuvinte cheie: nervul femural, blocaj anestezic, ecografie

2.2 Introduction

Femoral nerve blockade is widely practiced by physicians in a variety of circumstances, i.e. analgesia for femur fractures in pre-hospital medicine (1), in the accident and emergency departments and in clinical settings of perioperative care (2). Femoral nerve blockade is likely to be the most widely performed lower limb block.

2.3 Anatomy

The femoral nerve is a terminal branch of the lumbar plexus (3). It arises from the ventral rami of the second, third and fourth lumbar nerves and it descends through the substance of the psoas major muscle, emerging from the muscle at the lower part of its lateral border. It runs in the gutter of the iliopsoas muscle under the fascia iliaca, it then passes behind the inguinal ligament and enters the femoral triangle. At this level the fascia along the internal aspect of the iliopsoas thickens to form the iliopectineal band that separates the femoral vessels from the nerve.

The femoral nerve divides into superficial and deep terminal branches in the femoral triangle (4). The superficial branches includes the lateral musculocutaneous nerve which innervates the sartorius muscle and the skin of the anterior thigh; and the medial musculocutaneous nerve which divides to innervate the pectineus muscle, the articular surface of the acetabulum and the skin of the medial thigh.

The deep branches comprise the saphenous nerve and the branches which innervate the quadriceps muscles - rectus femoris, vastus lateralis, vastus medialis, and vastus intermedius muscles. The saphenous nerve is sensory only and supplies the skin of the medial leg as far as the medial malleolus. In the thigh it descends with the nerve to the vastus medialis muscle.

Applied anatomy

Dermatomal innervation

Femoral nerve blockade results in anaesthesia of the skin of the antero-medial thigh (femoral nerve), knee (femoral nerve) and the medial border of the leg (saphenous

nerve).

Myotomal innervation

The main muscles innervated by the femoral nerve are the sartorius, quadriceps femoris (rectus femoris, vastus lateralis, intermedius and medialis), as well as the iliopsoas and pectineus muscles.

The femoral nerve innervates the anterior wall of the hip joint, the anterior aspect of the femur and the antero-medial walls of the knee joint.

Indications

Analgesia in the following scenarios

Fractured neck/shaft of femur

Hip joint (following total hip replacement)

Knee joint (following anterior cruciate ligament repair, total knee replacement)

Anaesthesia. Alone: skin graft from the anterior aspect of the thigh, muscle biopsy

In combination with a popliteal block (any procedure on the foot and lower leg), with high sciatic and obturator blocks (any procedure on the lower limb).

2.4 Targeted femoral nerve block

The femoral nerve is situated most superficially at the level of inguinal crease, although its relative depth may vary (3). Femoral nerve blockade has been attempted blindly in the past, with a sharp needle, 1-1.5 cm laterally from the femoral pulse. Paresthesia technique followed, based on elicited paresthesia in the femoral innervation area. Peripheral nerve stimulation technique have the added benefit of targeting more precisely the nerve while minimizing potential nerve injury. The classic endpoint for injection in the case nerve stimulator guided femoral block is the ‘ dancing patella’ sign, i.e. quadriceps contraction (2).

Fascia iliaca (iliacus) compartment block - an indirect femoral nerve block

Following an injection under the fascia iliaca in the inguinal region (iliacus or fascia iliaca block), anaesthetic solution is distributed to the femoral nerve (>90%), lateral femoral cutaneous nerve (>85%) and occasionally to the genito-femoral nerve.
The fascia iliaca block is very similar to the femoral nerve block in terms of extent of blockade, although the lateral femoral cutaneous nerve (sometimes called the lateral cutaneous nerve of the thigh) is blocked more consistently with this approach compared with femoral block (3).
The fascia iliaca block was initially described in children and then extrapolated to adults. The main landmark for its performance is the inguinal ligament outlined by a line connecting the anterior superior iliac spine and the pubic tubercle. The needle insertion point is approximately one cm below of the junction between the outer on-

third and the inner two-third of this line. Block performances is based on the highly unreliable ‘two pop’ feel as a result of piercing the fascia lata and the fascia iliaca (5).

Sonoanatomy

The femoral nerve block is ideally suited for ultrasound guidance with a high frequency (>10 MHz) linear probe because of the relatively superficial position of the femoral nerve (6,7). Distal to the inguinal ligament, the femoral nerve lies lateral to the femoral artery, deep to the fascia iliaca, on the anterior aspect of the iliopsoas muscle (Fig. 1.). The artery is easily located due to its pulsation and/or flow identified by doppler (Fig. 2., Fig. 3.) The femoral nerve is often found within a triangular hyperechoic region, lateral to the femoral artery and superficial to the iliopsoas muscle. The femoral nerve may be quite thin and flat in this region as the nerve fans out into multiple branches. The nerve may also appear as a biconvex or oval hyperechoic structure.

From superficial to deep, the fascia lata is first encountered, then the fascia iliaca (hyperechioc line). Inguinal lymph nodes may appear as hyperechoic cortex with echogenic hilum and hence may be confused with the nerve in the short axis view. A nerve is a continuous structure that can be traced (by scanning proximally and distally) while a lymph node is not and can seen only in a discrete location.

The ultimate aim is to deposit local anaesthetic solution adjacent to the femoral nerve in order to ensure a successful block. Similarly to other ultrasound guided blocks, an aggressive and a more conservative approach may be described. The first would typically aim to surround the femoral nerve with a pool of local anaesthetic (often referred to as the ‘doughnut sign’) and would correspond to the classical femoral nerve block (Fig. 4.). Ultrasound guidance, through a more precise injection has allowed for a

reduction of the effective local anaesthetic dose. The conservative approach would correspond to the classic fascia iliaca block, i.e. injecting at a distance from the nerve under the fascia iliaca and observing the spread of the local anaesthetic solution towards the femoral nerve. Due to contrast enhancement, following injection of the hypoechoic local anaesthetic, often the hyperechoic femoral nerve becomes more prominent (Fig. 5.).

Ultrasound guidance may facilitate peripheral nerve blockade in many ways, including visualization of the neural target and its surrounding structures, assessment of adequate needle-tip position, observation of local anaesthetic spread around the target nerve, identification of anomalous anatomy or pathology. Ultrasound guidance holds the potential to minimized complications associated with peripheral nerve blockade such as nerve injury on inadvertent intravascular injection of local anaesthetics. However, no clinical studies exist to confirm or refute these potential advantages of ultrasound guidance and both nerve injury and intravascular injection has occurred despite its use. In addition the technique is highly operator dependent (8).

Visualization of the nerves with ultrasound depends on the operator's ability to properly locate the nerve, handle the transducer, maximize the ultrasound machine capability (e.g., the choice of transducer frequency, proper adjustment of depth, focus and gain and the use of compound imaging). Needling requires considerable hand-eye coordination (9).

Single shot

Out of plane needle insertion technique

A 5 cm 22 G insulated needle (preferable with an echogenic tip design) is inserted perpendicular to the transducer and the ultrasound beam (Fig. 6A). In this case, only the

cross section of the needle shaft (a white dot) may be observed during needle advancement. It can be technically challenging to track the location of the needle tip during out of plane needle insertion. Gentle scanning over the needle may prove useful. Injection of a small amount of fluid e.g., glucose 5% or local anaesthetic (hydrolocalisation) may expand the femoral triangle and the hypoechoic fluid collection can bring the hyperechoic nerve and the fascia iliaca into view (7). Correct needle tip location may be confirmed by electrical stimulation aiming for patellar movement.

In plane needle insertion technique

The in plane approach is most commonly used for femoral nerve block by aligning the block needle with the ultrasound beam (Fig. 2,3,5,7). The needle shaft and tip can be visualized distinctly but it may take a longer time to align the needle with the beam compared with the out of plane approach. Also, depending on the depth of femoral nerve, longer needle may be required.

Fascia iliaca block

In essence this is an indirect femoral nerve block (Fig.7). Traditionally, a blunt needle has been used to perform a 'two pop' technique at the junction of lateral one-third and medial two-thirds of the inguinal ligament. With ultrasound, whether using in plane or out of plane approach at couple of centimeters laterally from the neurovascular bundle, the aim is to pierce both fascia lata and fascia iliaca and observe the spread of local anaesthetic solution medially towards the femoral nerve. Higher volumes of local anaesthetic solution may be necessary (5).

Catheter technique

Duration of analgesia may be extended beyond the pharmacologic effect of the single shot injection using perineural indwelling catheters through which local anaesthetic solution may be administered up to 72 hours (10). Regiments include repeated boli, continuous infusion or patient controlled boli with or without a background infusion of local anaesthetic solutions. Risk of infection may be minimized by strictly adhering to sterility guidelines (mask, sterile gown, gloves, ultrasound probe sheat and gel, antiseptic solution, etc).

Several techniqual issues are specific to continuous perineural catheter placement (11,12). The optimal method is still unknown. Herein we illustrate the technique most often used at our institution (Fig. 6.) whereby the nerve (in short axis) is approached through an out of plane needle insertion using a catheter through needle technique (Fig. 6A). Local anaesthetic solution may be injected at this point to dilate the perineural space. This will facilitate further visualization of the nerve and the actual catheter insertion and advancement. The next manouvre is to turn the ultrasound probe aiming to visualize both the nerve in long axis and the needle in plane (Fig. 6B,C, 8). In this view the catheter may be visualized appearing through the needle tip and positioning itself alongside the nerve (Fig. 9). A small volume of air may be injected to confirm the location of the catheter tip (Fig. 10). The ultimate confirmation, although not performed routinely, is opacification of the catheter (Fig. 6D). Alternatively, the catheter may be inserted blindly through the needle and its position subsequently confirmed using ultrasound as described (Fig. 11.12).

2.5 Future directions

Currently, research is ongoing with regards to minimal efficient local anaesthetic dose and volume, with regards to the effect of different distribution patterns of local anaesthetic around nerves, finding the best delivery, dosing strategy and drug combinations for perineural infusions to mention but a few. Similarly, the ideal local anaesthetic is still awaited, to provide prolonged selective sensory blockade with no motor block.

In conclusion, a simple technique is described to perform a femoral nerve block using ultrasound guidance. With increasingly available ultrasound machines it is conceivable that this technique will become standard practice in the near future. However, adherence to standard monitoring, asepsis, prevention of complications and immediate availability of emergency drugs should not be underestimated.

2.6 Figures

Figure 1. Scout scan of the left femoral nerve (short axis) at the level of inguinal crease (lateral to femoral artery, deep to fascia lata, superficial to iliopsoas muscle).

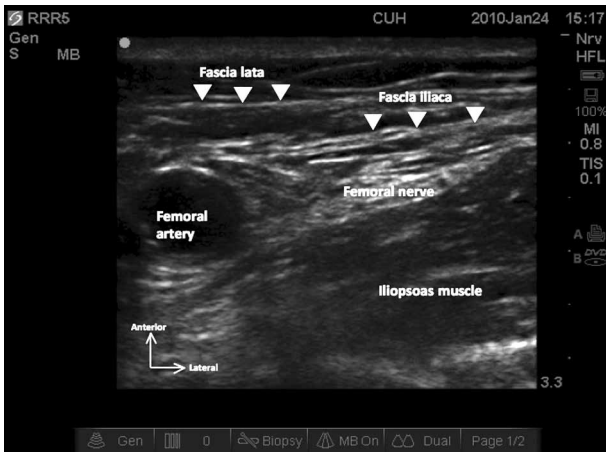


Figure 2. Doppler identification of intravascular flow; needle in plane.

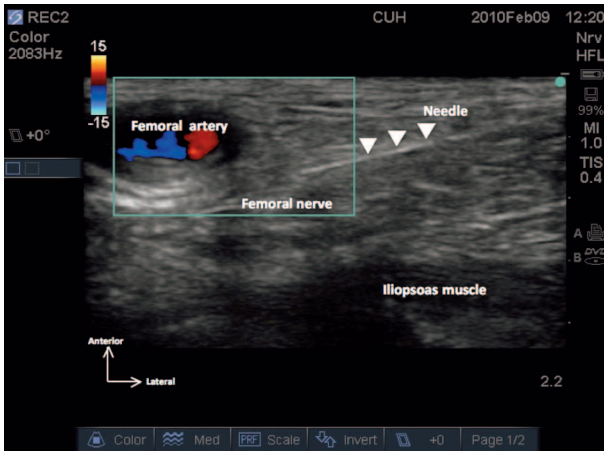


Figure 3. Circumferential spread of local anaesthetic solution following injection between femoral artery and nerve (aggressive approach). Doppler used to avoid intravascular injection.

LA-local anaesthetic solution

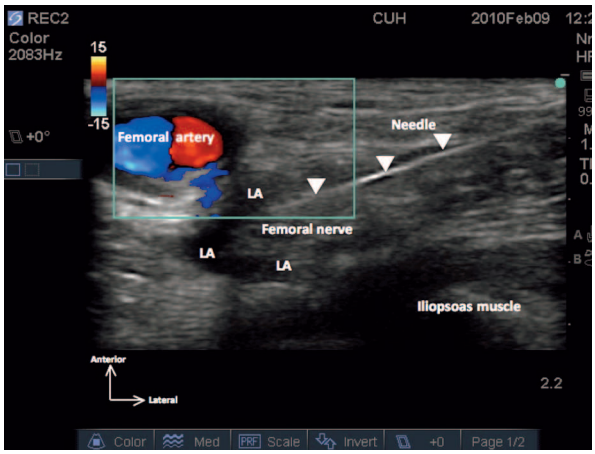


Figure 4. Femoral nerve surrounded by local anaesthetic solution following needle withdrawal.

LA-local anaesthetic solution

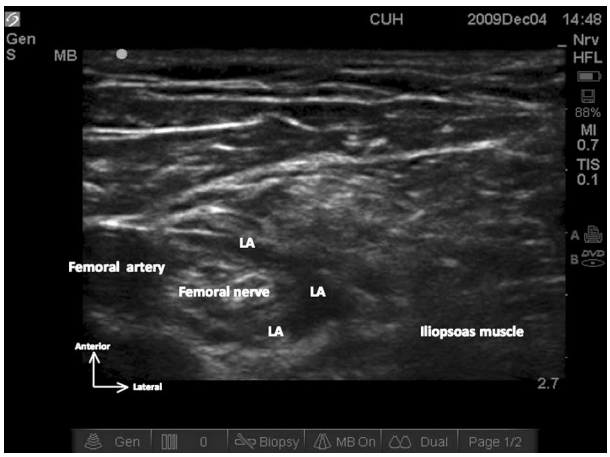


Figure 5. Left femoral nerve (short axis) more visible following injection of some local anaesthetic solution around it. The needle is approaching in plane.

LA-local anaesthetic solution

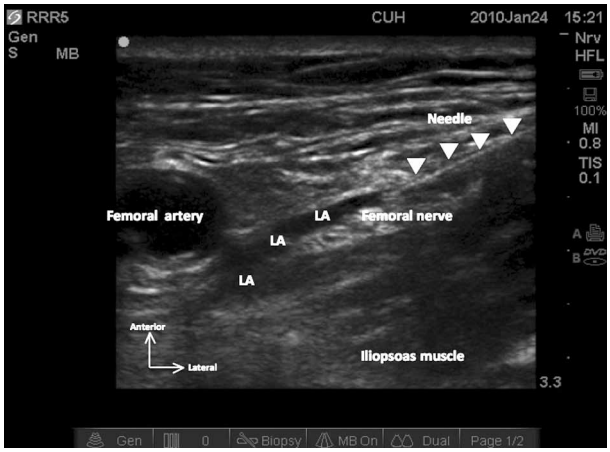


Figure 6. Sequence of catheter insertion; a) top left: out of plane puncture adjacent to femoral nerve; b) top right: probe turned to visualize nerve in long axis, catheter inserted through needle appears alongside the nerve; c) bottom left: catheter tip confirmed by injecting 1 ml of air; d) bottom right: correct position of catheter confirmed with opacification.

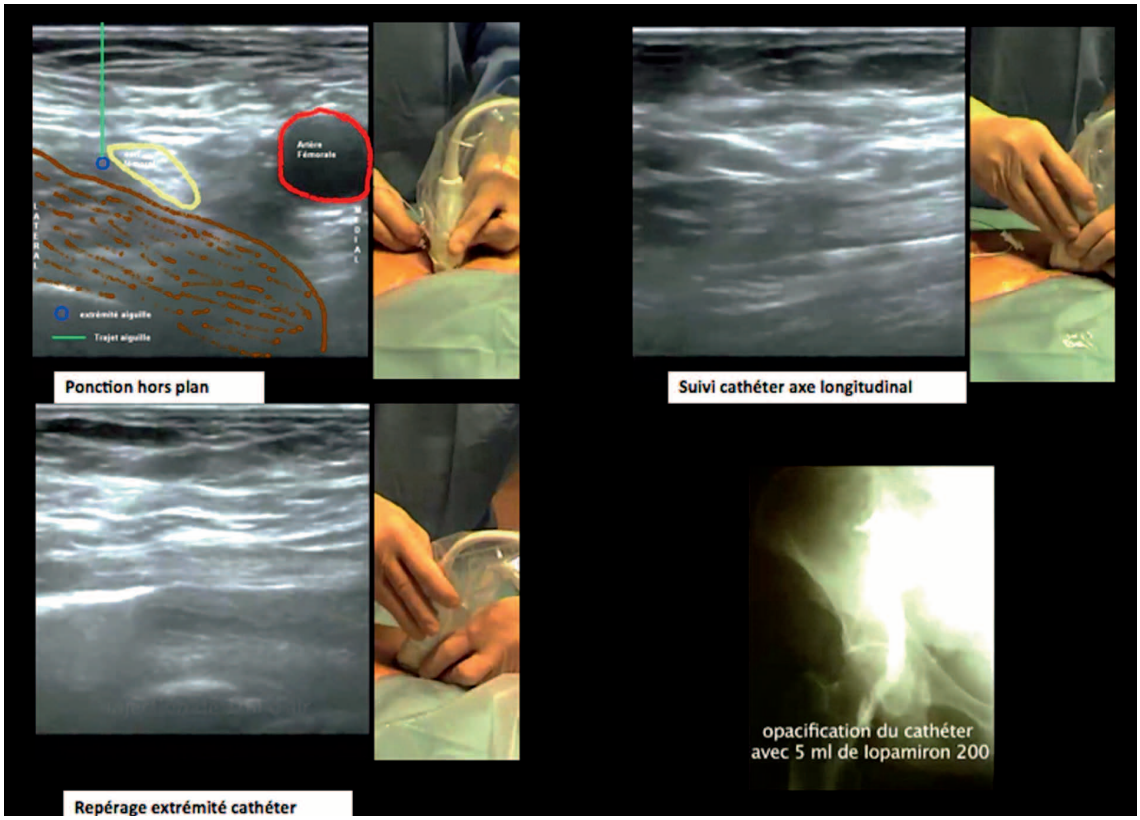


Figure 7. Needle in plane, femoral nerve in short axis, local anaesthetic being deposited around it (needle tip at distance from nerve, conservative approach).

LA-local anaesthetic solution

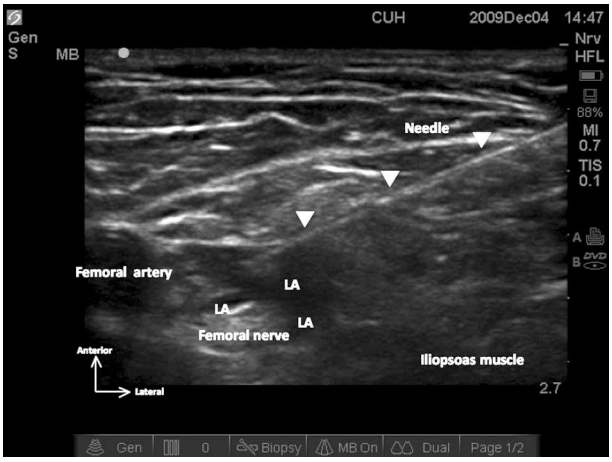


Figure 8. Needle approaching in plane, femoral nerve visualized in long axis.

LA-local anaesthetic solution

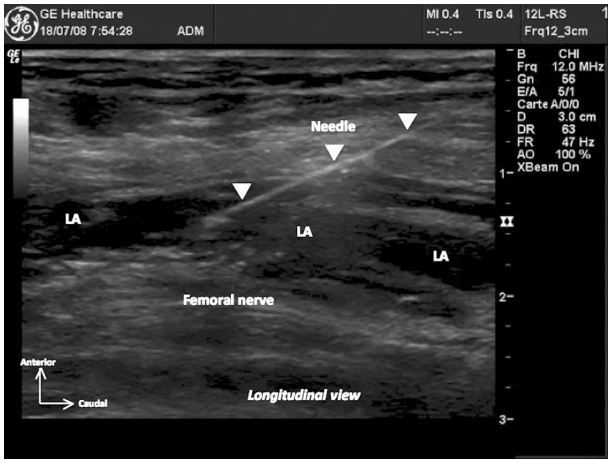


Figure 9. The echogenic catheter parallel to femoral nerve in longitudinal view.

LA-local anaesthetic solution

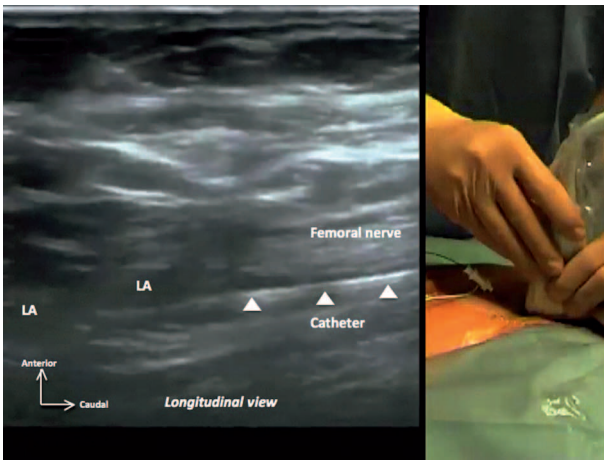


Figure 10. Correct position of catheter tip verified by injection of an air bubble.

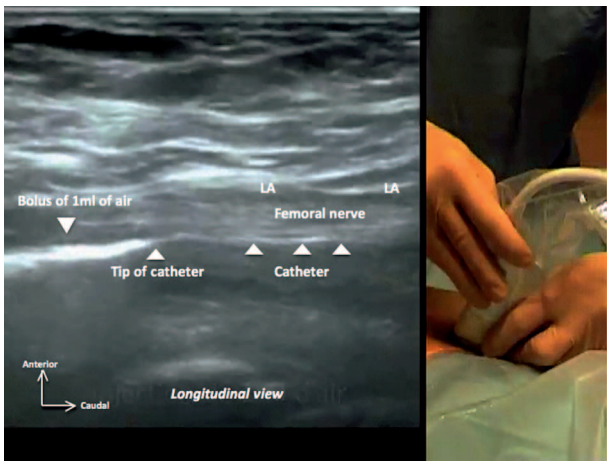


Figure 11. Catheter crossing the femoral nerve and disappearing in the pelvis alongside the nerve.

LA-local anaesthetic solution

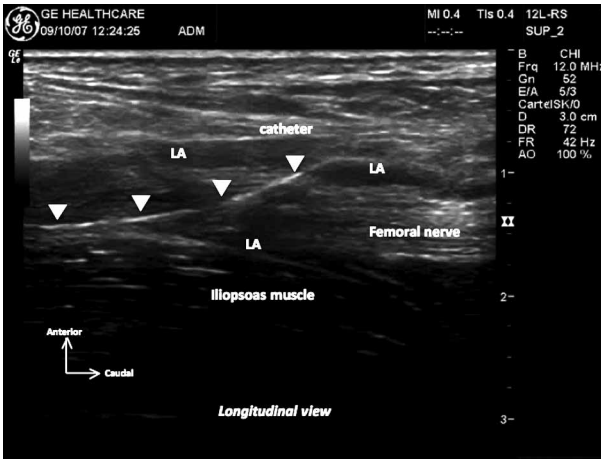
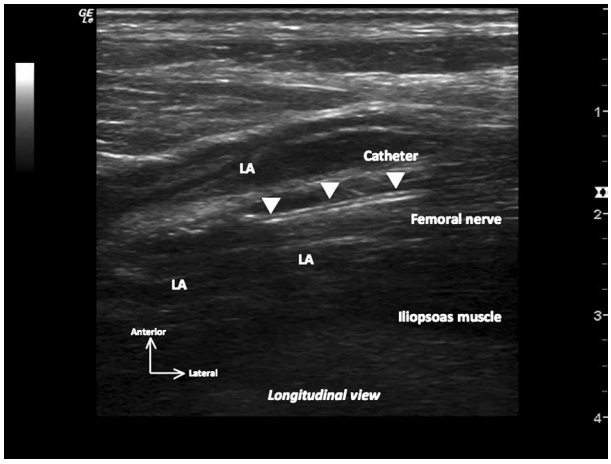


Figure 12. Catheter adjacent to femoral nerve in long axis surrounded by local anaesthetic solution.

LA-local anaesthetic solution



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Chapter 3

Study 1

Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur

3.1 Abstract

Background: Peripheral nerve blocks are effective in treating acute pain, thereby minimizing the requirement for opiate analgesics. Fractured neck of femur (FNF) is a common, painful injury. The provision of effective analgesia to this cohort is challenging but an important determinant of their functional outcome. We investigated the analgesic efficacy of continuous femoral nerve block (CFNB) in patients with FNF.

Methods: Following institutional ethical approval and with informed consent, patients awaiting FNF surgery were randomly allocated to receive either standard opiate-based analgesia (Group 1) or a femoral perineural catheter (Group 2). Patients in Group 1 received parenteral morphine as required. Those in Group 2 received a CFNB comprising a bolus of local anaesthetic followed by a continuous infusion of 0.25% bupivacaine. For both Groups, rescue analgesia consisted of intramuscular morphine as required and all patients received paracetamol regularly. Pain was assessed using a visual analogue scale at rest and during passive movement (dynamic pain score) at 30 min following first analgesic intervention and six hourly thereafter for 72 hours. Patient satisfaction with the analgesic regimen received was recorded using verbal rating scores (0-10). The primary outcome measured was dynamic pain score from initial analgesic intervention to 72 hours later.

Results: Of 27 recruited, 24 patients successfully completed the study protocol and underwent per protocol analysis. The intervals from recruitment to the study until surgery were similar in both groups [31.4(17.7) vs 27.5(14.2) h, P=0.57]. The groups were similar in terms of baseline clinical characteristics. For patients in Group 2, pain

scores at rest were less than those reported by patients in Group 1 [9.5(9.4) vs 31(28), P=0.031]. Dynamic pain scores reported by patients in Group 2 were less at each time point from 30 min up to 54 hours [e.g at 6 h 30.7(23.4) vs 67.0(32.0), P=0.004]. Cumulative morphine consumption over 72 h was less in Group 2. Patient satisfaction scores were greater in Group 2 [9.4(1.1) vs 7.6(1.8), P=0.014].

Conclusions: Continuous femoral nerve block provides more effective perioperative analgesia than a standard opiate-based regimen for patients undergoing fixation of fractured neck of femur. It is associated with lesser opiate use and greater patient satisfaction.

Keywords: perioperative pain relief, hip fractured neck of femur, continuous femoral nerve block

3.2 Introduction

Fractured neck of femur (FNF) is a common, painful reason for hospital admission in elderly patients (1). Proximal femur fracture in elderly patients is associated with substantial mortality and high morbidity, all cause mortality in the first three month after hip fracture was 5.75% in women and 7.95% in men (2). Pain management in the elderly can be challenging due to the presence of co-morbidities, altered pharmacokinetics and pharmacodynamics. Despite clinical guidelines favoring surgical repair of FNF within 24 hours of injury (3) patients may wait considerable periods of time for their turn in the operating room. In this context, preoperative pain is an important distressing factor.

Proximal femur fracture can be classified as intracapsular or extracapsular fractures. Intracapsular fractures are subcapital or transcervical fractures. Extracapsular fractures include per-, inter- and sub-trochanteric. In the case of basal cervical fracture the lines tend to be approximately at the level of the insertion of the joint capsule, and they behave as extracapsular fractures.(3)

Approximately 77 000 hip fractures occur in the UK annually with a median postoperative length of stay of 23 days and a 30-day. The majority of the proximal femur fractures occur in patients over the age of 60 and 75% occurring in females. Among the patients, 90% of hip fractures occur after a simple, mechanical fall from standing height in patients with osteoporotic bone(4).

The sensory innervation of the proximal femur and a variable portion of the intra-capsular neck of femur arises from the femoral nerve (5). Femoral nerve block is

effective in providing analgesia for femur factures, and has been previously described in FNF (6). Perineural catheter placement permits the provision of continuous peripheral nerve block, thereby extending the duration of analgesia. Continuous femoral nerve block (CFNB) may therefore have a role in the provision of high quality analgesia in patients awaiting surgery for FNF. Such regional analgesia techniques may improve the quality of pain relief and potentially limit both opiate use and associated opiate-related side effects (7).

It is not known whether CFNB improves analgesic outcomes in elderly patients presenting acutely with FNF. We conducted a study to compare the analgesic efficacy of CFNB and conventional parenteral opiate analgesia in this patient group. Our hypothesis was that continuous femoral nerve block provides better peri-operative analgesia than standard parenteral opiate analgesia in patients awaiting surgery to repair FNF.

3.3 Methods

Ethical approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Written, informed consent was obtained from all patients. Patients presenting via the emergency room of Cork University Hospital with fractured neck of femur, American Society of Anesthesiologists grades I to III and aged above 60 years, were invited to participate in the study. Exclusion criteria included patient refusal, the presence of more than one fracture; Mini-Mental Score <22 (Table. 1, reference 6.); coagulation disorders; head injury; loss of consciousness; 10 mg or more morphine administration pre-hospital; acute intercurrent heart disease; allergy to bupivacaine, morphine or paracetamol; skin lesions/infection at block site; and renal dysfunction. Patients with evidence of systemic infections (clinically defined or elevated C-reactive protein levels, leucocytosis, or body temperature higher than 37.8^{O} C) were also excluded.

On recruitment to the study, patients were randomized using a random number sequence and sealed envelopes. Those randomized to Group 1 received standard analgesia consisting of parenteral morphine as required, paracetamol 1g enterally 6 hourly and below the age of 70 diclofenac 75 mg 12 hourly.

Patients in Group 2 received 10 ml of 2 % lidocaine and 10 ml of 0.5% bupivacaine via a perineural femoral catheter followed by 0.25% bupivacaine infused at 4 ml per hour for 72 hours. They also received paracetamol 1g enterally 6 hourly and below age of 70 diclofenac 75 mg 12 hourly. Breakthrough pain in Group 2 was treated with

intramuscular morphine as required. Fifteen minutes prior to positioning for spinal anaesthesia, a lidocaine bolus (10 ml 1% lidocaine) was administered through the catheter. On positioning for spinal anaesthesia (fractured limb dependent in view of using weight/height appropriate dose of hyperbaric bupivacaine), analgesia for this patient group was provided at the discretion of the attending anaesthetist.

Continuous Femoral Block Technique

Having attached standard monitoring (non-invasive blood pressure, oxygen saturation and electrocardiography) and inserted a peripheral intravenous cannula, the femoral catheter was placed using nerve stimulation. The needle insertion point was first determined using predefined landmarks. A skin mark was placed one centimeter caudal to the inguinal ligament and one centimeter lateral to the point of maximal palpable pulsation of the femoral artery.

The skin of the anterior thigh was prepared aseptically and a sterile drape was placed. The skin was anaesthetised using a 25G hypodermic needle and 1% lidocaine. The block needle (Contiplex, BBraun, Melsungen, Germany) was attached to a nerve stimulator set at 1mA at 2Hz with a pulse duration of 0.1ms. Appropriate needle position was determined by the presence of quadriceps contractions resulting in patellar movement at a current of 0.4mA. On attaining this endpoint the needle was immobilized, and following negative aspiration 10 ml 2% lidocaine was injected. The Contiplex cannula was then advanced over the needle, the needle withdrawn and the catheter placed through the cannula 3 cm in cephaled direction. Finally the cannula was removed and the catheter secured to the skin using an adhesive, transparent dressing.

The patient received 10 ml 0.5 % bupivacaine, following which a continuous infusion of 0.25% bupivacaine was commenced at 4 ml per hour, delivered via an elastomeric pump (Acemedical, AutoFuser).

Primary Outcome

The primary outcome measure was pain assessed using visual analogue score (VAS 0-100) on passive movement (30 degree flexion) of the injured limb at 6 hours following recruitment.

Secondary Outcomes

Visual analogue scores for pain were measured at rest and passive movement at recruitment, 30 minutes after recruitment and 6 hourly for the next 72 hours. Pain on positioning for spinal anesthesia was also recorded (Verbal Rating Score 0-10). Satisfaction with the analgesic regimen received was measured at the end of the assessment period using a 100 mm visual analog scale. Opiate analgesic consumption, side effects (nausea and vomiting; sedation; pruritis) and haemodynamic variables (heart rate, blood pressure) were recorded during the three-day study period.

Adverse events were recorded by the attending anaesthetist on a dedicated data sheet.

Statistical Analysis

Our study was powered to detect a 50 % reduction in VAS pain score six hour after recruitment. With alpha error rate of 0.05 and power of 0.80, it was estimated that 24 patients would be required. Assuming 15 % exclusion rate, we planned to recruit 27 patients. Statistical analysis were performed by using EpiInfo™ 2002 (Centers for

Disease Control and Prevention) statistical software. Data was examined for normality. Quantitative data was analyzed using ANOVA or Fisher exact test. Categorical data was examined by Kruskal-Wallis test. Summary data are presented as mean (SD) or median [range] where appropriate.

3.4 Results

Fifty-seven patients were approached, 27 met the inclusion criteria and thus were recruited to the study (12 to Group 1; 15 to Group 2). Three patients were excluded leaving 24 patients for final analysis (12 patients in Group 1; 12 patients in Group 2). Patients were excluded for the following reasons: (1) elastomeric pump failure, (2) patient confusion with subsequent pump disconnection after 12 hours, (3) late diagnosis of a complicating acetabular fracture.

There were no differences in baseline characteristics between Group 1 and 2 (Table 2).

Pain on passive movement at 6 hours was significantly less in Group 2 compared to Group 1 [30.7(23.4) vs 67.0(32) mm, p=0.004]. Pain measured during passive movement was significantly less in Group 2 at each time point up to 54 hours (Figure 1). Similarly, pain measured at rest was consistently less in Group 2 at all time points, reaching the statistical significance level 30 minutes, six and 42 hours after recruitment (Figure 2). Cumulative morphine consumption was lower in Group 2 at each time point except at 30 minutes and 24 hours after recruitment. (Figure 3.)

Haemodynamic parameters were not different between the group perioperatively up to 66 hours post recruitment. At 66 and 72 hours patients in Group 2 had higher heart rate compared to those in Group 1[81.71(7.29) vs 74.09(6.70) bpm, P=0.03 and 84.88(9.84) vs 73.27 (11.03) bpm, P=0.02, respectively). (Figure 4)

Respiratory rate was higher in Group 1 compared to Group 2 at 12 h [(17.81 (1.40) vs 16.16 (2.16) per minute, P=0.04] and 30 h post recruitment [18.36(1.74) vs 16.18(2.04) per minute, P=0.01]. (Figure 4)

The intervals from the recruitment to the study until surgery is similar to intervals reported in a previous study(9) and were similar in both groups [27.1(13.6) h vs. 31.5(17.9), P=0.25]. Pharmacological agents used for sedation and analgesia for positioning of patients in Group 1 were fentanyl (1 instance), fentanyl plus midazolam (3 patients), propofol plus fentanyl (2 patients). No medication was administered for this purpose to patients in Group 2.

The incidence of nausea/vomiting [3/12 (25%) vs. 4/12 (33%) in Group 1 and 2 respectively], pruritus [2/12 (16.6%) vs. 1/12 (8.3%) in Group 1. and 2. respectively] were similar in the two groups (P<0.05). The incidence of excessive sedation was also similar in the two groups [1/12 (8.3%) vs 1/12 (8.3%) in both group].

A trend towards lesser pain sensation (VRS) was identified in Group 2 vs. Group 1 at positioning for spinal anaesthesia [3.7(3.2) vs. 5.4(2.7), P=0.10] although this did not reach statistical significance.

Scores for patients satisfaction with analgesia overall were greater in Group 2 [9.4(1.1) vs 7.6(1.8), P =0.014].

3.5 Discussion

The most important finding of our study was that continuous femoral nerve blockade offered superior analgesia compared to systemic opioids in the period around operative fixation of fractured neck of femur. In addition, continuous femoral nerve block it was associated with greater patient satisfaction.

Best practice review of the care of patients with fractured neck of femur included a continuous femoral nerve block as analgesia in the Emergency Department (10), however this is not common practice. When performed at all, single shot femoral nerve block is administered by physicians in the emergency department (11) or in the prehospital setting (12).

Our study demonstrated feasibility of continuous femoral nerve block in this clinical context. The femoral perineural catheter was successfully placed in each of the 15 patients randomized to Group 2.. The true economic input of the use of perineural catheters and elastomeric pumps requires further evaluation.

Opioid consumption was not eliminated by the presence of a continuous perineural catheter. A logical explanation for this is contribution of the sciatic nerve to the femur and the lateral cutaneous nerves innervation of the surgical incision. This may account for the presence of morphine associated side effects in this group. Our chosen continuous infusion regime, while limiting local anaesthetic dose and potential toxicity, may have decreased the spread of local anaesthetic towards the lateral cutaneous nerve of the thigh.

In our study, the average intervals between initial analgesic intervention and surgery were 27.1 and 31.5 hours (Group 1 and 2 respectively). Therefore the first bolus of 10 mls of bupivacaine probably had minimal effect at the time of surgery. We believe that one of the benefits of the combined bolus+ continuous infusion is that it is suitable in a setting in which the duration of the need for potent analgesia is variable and unpredictable (such as for patients with FNF). Cuvillon et al.(13) have demonstrated that the duration of a single bolus of bupivacaine 0.5% 20 mL for FNB is 22 h (range 15-32). Thus the analgesic benefits (in the 72 hour study interval defined for this investigation) of the CFNB technique were of greater importance preoperatively.

There are several limitations to this study. For ethical and economical reasons, it was not possible to use a double-blinded methodology. The authors considered it to be ethically unacceptable to insert a placebo femoral nerve catheter for blinding purpose only. At our institution, the standard dressing employed for securing a femoral nerve catheter comprises a transparent adhesive layer (usually Tegaderm™ Film, 3M). This made it unfeasible to apply a "dummy" catheter to the groin. A patient controlled analgesia (PCA) pump would have allowed a more precise measurement of parenteral opioid consumption. Analgesia for positioning prior to spinal anaesthesia was not standardized, and may account for the observed measures. Outcomes such as time to mobilization, postoperative respiratory or cardiovascular compromises and time to achieved discharged criteria were not assessed. One cohort of patients, the confused elderly, which might be expected to benefit most from this intervention were not studied for ethical reasons (difficult ensuring that consent was informed). The interval for initiating analgesic management until surgery were similar in the two Groups. As we arbitrary selected a cut-off time of 72 hours for the continuous perineural blockade, our

results contain both pre- and postoperative parameters. We did not specifically address whether any benefits associated with the catheter occurred pre- or postoperatively.

Although ultrasound guidance was not used in this study, we believe that it would enhance the benefits of CFNB technique. Specifically it may minimize the patient discomfort associated with use of peripheral nerve stimulation during the nerve block procedure and, in expert hands, may decrease the likelihood of block failure of nerve injury.

Our study reflects other available evidence substantiating the use of continuous peripheral nerve block analgesia in FNF (14). Whether analgesia influences early mobilization or long-term rehabilitation requires further research.

We conclude that, compared with systemic opiate based regime, continuous femoral nerve blockade provides superior perioperative analgesia for patients undergoing operative fixation of fractured neck of femur.

3.6 Tables

Table 1. Mini Mental Scale

Mini Mental Examination

Score	Section	Task
	Orientation	
5		**What is- year, season, date, day, month**
5		**Where are we- country, county, town, hospital, floor**
	Registration	
3		**Name 3 objects, 1 second to say each, ask patient to recall all 3.**
5		**Serial 7's, (100-7, 93-7 etc.) Stop after 5 correct**
3		**Ask for the aforementioned 3 objects**
	Language	
2		**Name pencil and watch**
1		**Repeat the following 'No ifs, ands, or buts'**
3		**Follow three stage command 'TAKE PAPER IN YOUR HAND, FOLD IT AND PUT IT ON YOUR LAP'**
3		**Read and obey 'CLOSE YOUR EYES'**

Score Results

>25 Normal

>22 Borderline Cognitive Dysfunction

>20 Marked Cognitive Dysfunction

<17 Severe Dementia

Table 2. Baseline characteristics

	Group 1	Group 2
	N=12	**N=12**
Age (year), mean (SD)	**80.2 (+/- 5.1)**	**76.0 (+/- 13.7)**
Female/Male	**10/2**	**6/6**
FNF side left:right	**4/8**	**8/4**
Hours waiting for surgery, mean(SD)	**27.0(+/- 13.6)**	**31.45(+/-17.9)**
VRS before spinal anaesthesia, mean(SD)	**6.44(+/- 2.7)**	**3.72(+/-3.2)**
Satisfaction with pain control, mean(SD)	**7.4(+/-2.2)**	**9.62(+/-0.9)***

**p<0.05 refers to between group comparisons*

Data displayed as mean(SD) or number of cases

Table 3. Cumulative cyclizine consumption, at significant difference time points

	Group 1	Group 2
30 minutes after recruitment, mean(SD)	**39.08(34.15)**	**12.66(19.92), P=0.03**
6 hours after recruitment, mean(SD)	**45.33(39.85)**	**12.66(19.92)**
	Kruskal Wallis test H=5.77 degree of freedom 1, P=0.01	
12 hours after recruitment, mean(SD)	**48.50(42.71)**	**16.09(22.51), P=0.03**
24 hours after recruitment, mean(SD)	**58.91 (50.91)**	**16.09(22.51)**
	Kruskal Wallis test H=5.99 degree of freedom 1, P=0.01	
30 hours after recruitment, mean(SD)	**65.16 (56.27)**	**16.09(22.51)**
	Kruskal Wallis test H=6.13 degree of freedom 1, P=0.01	
36 hours after recruitment, mean(SD)	**65.16 (56.27)**	**22.90(29.19)**
	Kruskal Wallis test H=4.13 degree of freedom 1, P=0.04	

Data displayed as mean(SD)

2.7 Figures

Figure 1. VAS pain scores at passive movement

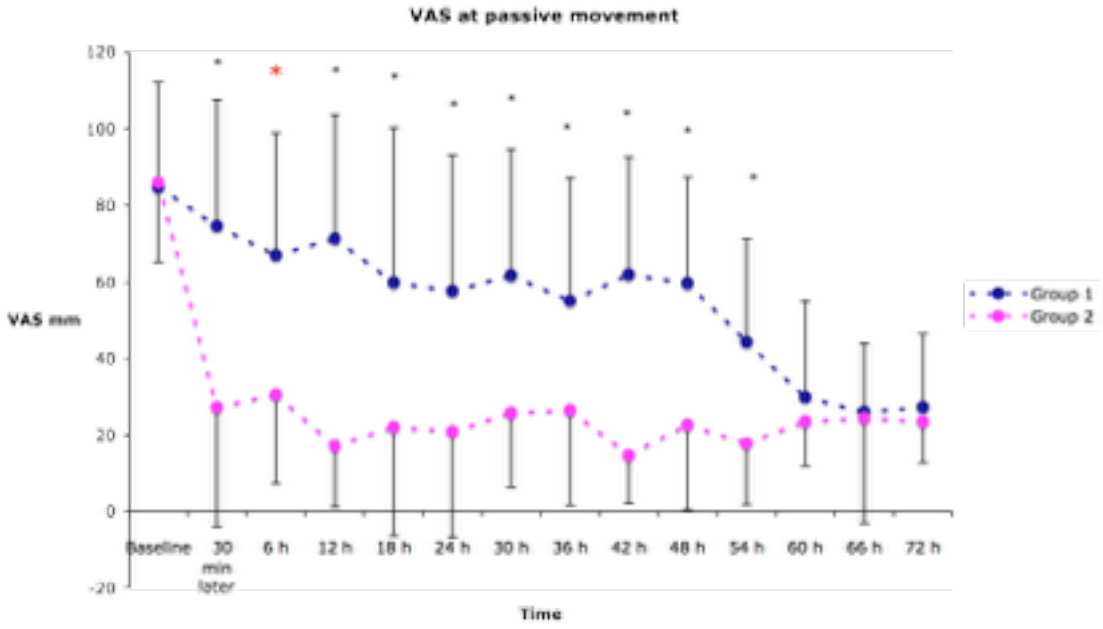


Figure 2. VAS pain scores at rest

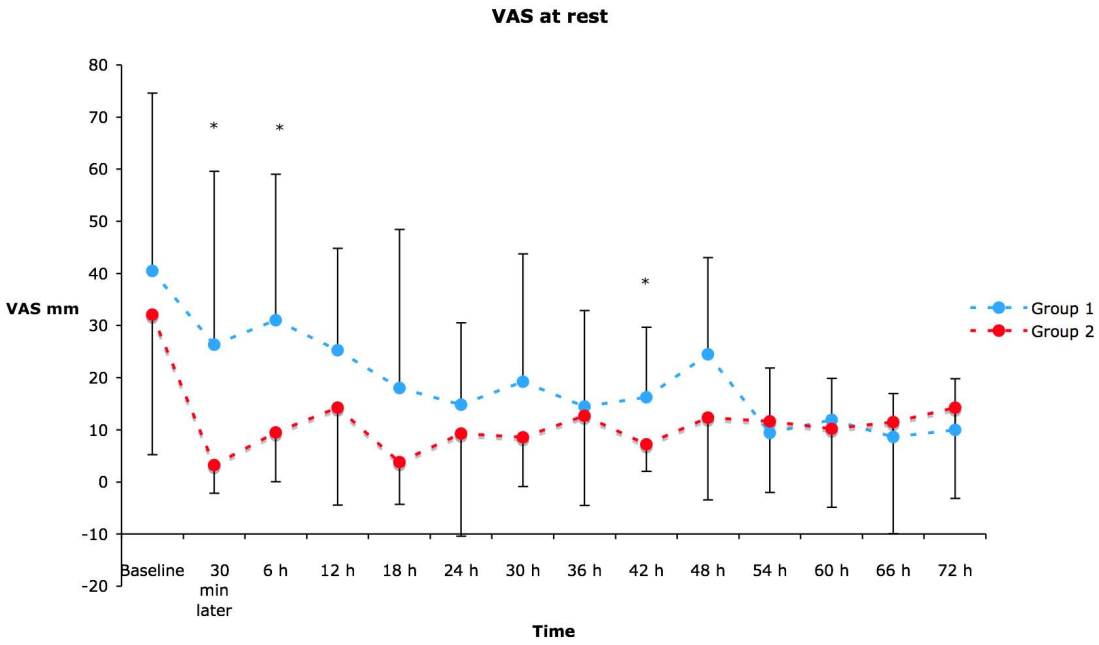


Figure 3. Cumulative morphine consumption

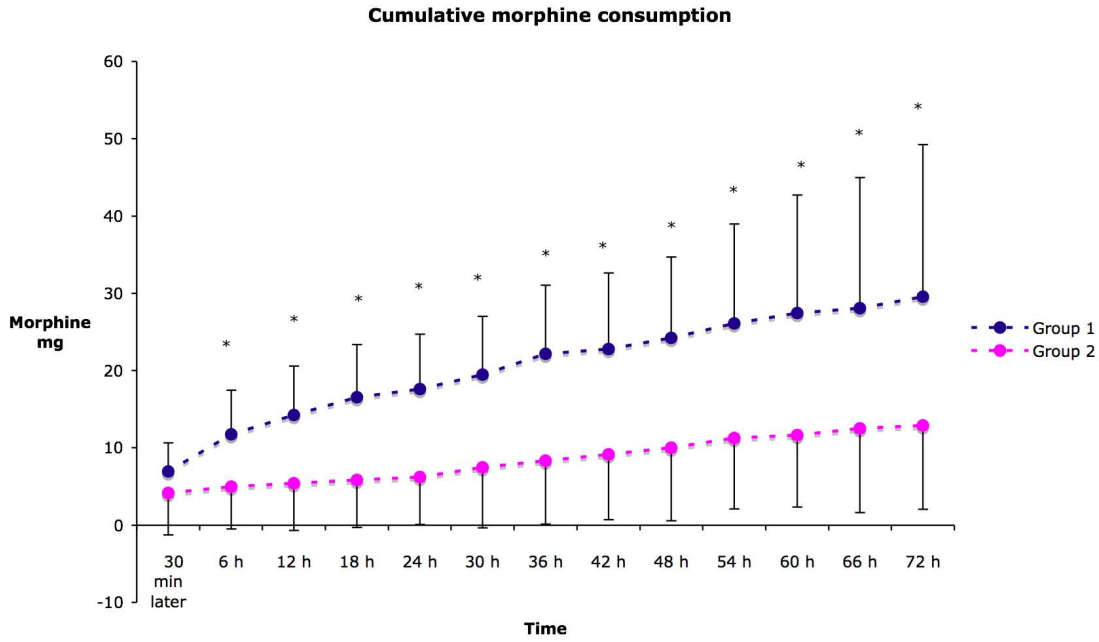
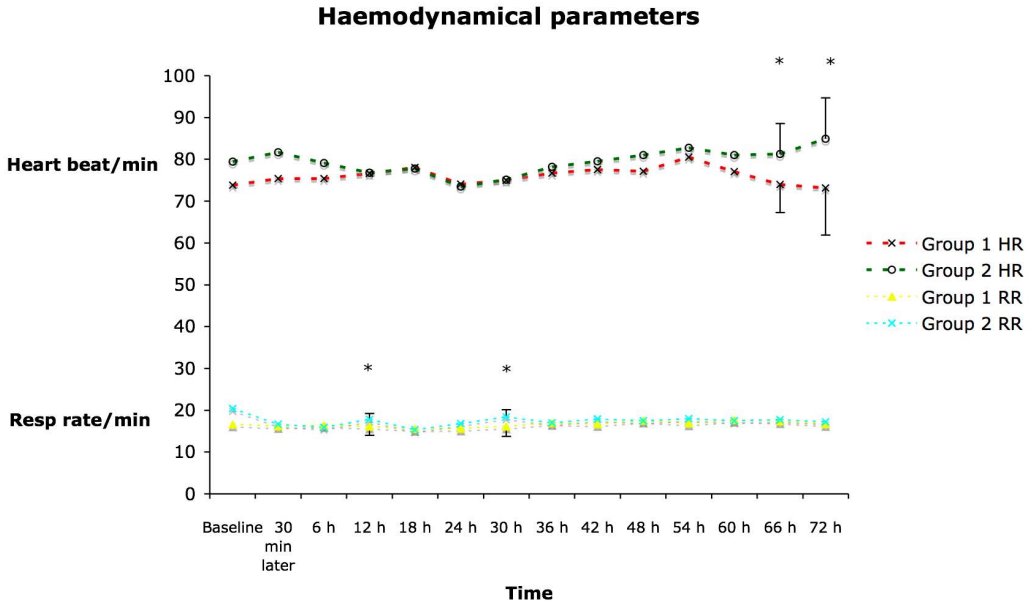


Figure 4. Haemodynamical parameters



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Chapter 4

Study 2

Pain relief effect of a single dose of dexamethasone after operative fixation of proximal femur fracture: randomized, double blinded clinical trial

4.1 Abstract

Background: Fractured neck of femur is a common cause of hospital admission in the elderly and usually requires operative fixation. Administration of dexamethasone has the potential to inhibit a patient's endogenous secretion of cortisol. In a variety of clinical settings, preoperative glucocorticoid administration has improved analgesia and decreased opioid consumption and the associated adverse effects (10-11). Our hypothesis was that a single dose of dexamethasone administered immediately preoperatively enhances postoperative analgesia in patients undergoing operative fixation of fractured neck of femur (FNF).

Methods: With institutional ethical approval, and having obtained written informed consent from each, 37 patients were studied. Participating patients (scheduled to undergo operative fixation of FNF) were randomly allocated to one of two groups (Dexamethasone or Placebo). Patients in the dexamethasone group received a single dose of 0.1 mg/kg dexamethasone i.v. immediately preoperatively. Patients in the placebo group received the same volume of normal saline. Patients underwent operative fixation of FNF using standardized anaesthetic and surgical techniques. The primary outcome was pain score (VRS) at rest six hours after surgery.

Results: Thirty seven patients were recruited and data from 30 patients were analysed. The groups were similar in terms of demographic characteristics. Pain scores at rest six hours after the surgery was significantly lower in the dexamethasone group compared with the placebo group [0.84(1.34) vs. 3.94(2.94), mean(SD), significancy level is 0.0012, p=0.0004]. Pain scores on passive movement six hours after the surgery tended to be lower in the dexamethasone group [3.25(2.63) vs. 5.55(3.76), mean(SD) p=0.055].

Cumulative morphine consumption 24 hours after the surgery tended to be lower in the dexamethasone group [7.72(8.34) vs. 15.12(9.4), mean(SD) p=0.04].

Conclusion: Intravenous dexamethsone (0.1 mg/kg) administered immediately before operative fixation of fractured neck of femur improves the early postoperative analgesia.

4.2 Introduction

Fractured neck of femur (FNF) is a common cause of hospital admission in the elderly, requires operative fixation and have 5-8 % mortality in three month time (1). Patients with femur fracture show a prolonged adrenocortical response to injury. Two-three weeks after the fracture, plasma cortisol is greater in such patients than in younger patients with similar injuries or in healthy elderly controls (2). The increase in plasma cortisol concentration is substantial and these differences continue for at least eight weeks (3).

Dexamethasone can inhibit cortisol secretion by inhibiting the hypothalamo-pituitary -adrenal axis primarily at the pituitary level and by a mechanism involving changes in transcription (4-5). In a variety of clinical settings glucocorticoids administered preoperatively improve analgesia and decrease opioid consumption and their associated adverse effects (6-8).

To date, single dose dexamethasone has not been evaluated for its effects on postoperative pain and the inflammatory response to surgery.

In this study, our hypothesis was that administration of a single dose of dexamethasone 0.1 mg/kg preoperatively enhances postoperative analgesia after the surgery in patients undergoing operative fixation of FNF. The primary outcome parameter was pain score at rest six hours after surgery.

4.3 Methods

With institutional ethical approval [Clinical Research Ethics Committee of the Cork Teaching Hospitals [(ECM 3 (bbbb) 07/07/09.)] and having registered with ClinicalTrials.gov (NCT01550146), a prospective, double-blind, randomized, placebo-controlled trial was undertaken at Cork University Hospital, Cork, Ireland between July 2009 and August 2012. Patients were randomly assigned to receive either preoperative single dose of dexamethasone or the same volume of normal saline as placebo (Dexamethasone D or Placebo P). We used a random number tables and sealed envelopes prepared by one of the co-author (GI). Written, informed consent was obtained from all patients.

Patients admitted on to the Emergency Department at Cork University Hospital with fractured neck of femur, American Society of Anaesthesiologists grades I -III and aged >65 years, were invited to participate in the study. Exclusion criteria were endocrine disorders (including I and II type of Diabetes mellitus), prior diagnosis of depression, corticosteroid treatment (in any form) within the previous last 4 months, Mini-Mental Score <22, coagulation disorders, head injury, other associated injuries, loss of consciousness, renal dysfunction and sepsis.

Patients in group D received a single dose of dexamethasone 0.1 mg kg -1 (1 mg ml -1) i.v. on arrival to the operating theatre (prior to performance of a femoral nerve block to facilitate positioning for spinal anaesthesia). Patients in group P received the same volume 0.1 ml kg -1 of normal saline i.v on arrival to the operating theatre.

On arrival to the operating theatre 18G cannula were inserted for i.v. drugs and fluid administration. Ultrasound-guided femoral nerve block (15 mls of 2 % lignocaine) was performed to facilitate positioning for spinal anaesthesia, which was performed using hyperbaric bupivacaine (11 mg in patients < 70 kg and 12.5 mg in patients > 70 kg) through a 25 G spinal needle.

All patients received paracetamol 1 g i.v. during surgery and six hourly thereafter for a week. Rescue analgesia consisted of 5 - 10 mg morphine i.m.

An independent blinded observer assessed pain severity at rest and on movement using a verbal rating score (0–no pain; 10-worst pain imaginable) on arrival to the operating theatre, on arrival to recovery, and at 6, 12, 24, 48, 72 hours and one week post-operatively. Blood samples for estimation of cortisol, was collected immediately preoperatively (prior to ultrasound guided femoral nerve block), six h, 24 h and 48 h post-operatively. Salivary cortisol level was measured by radioimmunoassay (9).

Analgesic consumption and associated adverse effects were also recorded.

Statistical analysis

Quantitative data were tested for normality and, as appropriate, analyzed using the unpaired two-tail Student t test corrected for multiple testing using Bonferroni correction as necessary. Categorical data were examined using the chi-squared test (or Fisher's Exact Test as appropriate). $P<0.00125$ was considered significant.

To detect a reduction of 50% in pain scores six hours after the surgery which is in agreement with the study of Chudinov et al. (10) with a two-sided 5% significance level and a power of 80%, a sample size of 17 patients per group was necessary.

4.4 Results

Thirty seven patients were recruited to this study of whom 30 were managed per protocol. Seven patients were excluded: in two cases, the patients mental status deteriorated after recruitment and in five cases, it was elected to perform the surgery under general anaesthesia for reasons unrelated to the study (Figure 1.). Patient characteristics were similar in the two groups (Table 1.).

The pain scores at rest six hour after the surgery were lesser in the dexamethasone group compared with the placebo group [0.84(1.34) vs. 3.94(2.94), mean(SD) p=0.0004] (Figure 2.). Pain scores on passive movement six hours after the surgery tended to be lesser in the dexamethasone group [3.25(2.63) vs. 5.55(3.76), mean(SD) p=0.055](Figure 3.) although this did not achieve statistical significance. Cumulative morphine consumption 24 hours after the surgery was lesser in the dexamethasone group than in the placebo group [7.72(8.34) vs. 15.12(9.4), mean(SD) respectively; p=0.04] (Figure 4.).

Cortisol concentration measured in saliva was significantly lesser in the dexamethasone group on the first postoperative evening [0.74(0.79) vs. 3.78(3.44), mean(SD); p=0.01] (Figure 5.).

Pain scores measured at rest and on passive movements at the other time points studied were similar in the two groups (Figure 2. and 3).

Compared with those in the placebo group, patients in the dexamethasone group had lesser systolic blood pressure (mmHg), six hours postoperatively [112(38) vs. 132(40), mean(SD) p=0.02].

Patients in the two groups were similar in terms of incidence of opioid related side effects, nausea/vomiting, sedation and pruritus..

4.5 Discussion

The results of the study showed that single low dose of dexamethasone have significant analgesic effect in the early postoperative period after operative fixation of fractured neck of femur.

Administration of a single dose of intravenous dexamethasone preoperatively decrease the likelihood for early and late postoperative vomiting in children and of late postoperative vomiting in adults (11) and decreases the incidence of nausea and pain in the early postoperative period after laparoscopic cholecystectomy (12-15). Dexamethasone prophylaxis has been used in dental surgery (16) and thyroidectomy (17-18), and shown to be a safe and effective method to reduce significantly the postoperative analgesic requirement. Similar doses of dexamethasone administered intravenously preoperatively decrease total analgesic requirements in patient undergoing total laparoscopic hysterectomy (19-20). Prior to this study, the potential analgesic benefits of preoperative dexamethasone to patients undergoing fixation of fractured neck of femur had not been studied. We believe that such benefits as we have demonstrated have particular significance in this population in view of their possible contribution to rehabilitation, a critical determinant of overall outcome in this setting. Our results are consistent with previously reported results in various postoperative cases.

Although we did not follow patients in this study to identify subsequent y benefits of preoperative dexamethasone or persistent post-surgical pain (PPSP), we and others have demonstrated that the quality of earl postoperative pain relief is a consistent and

important determinant of the incidence of PPSP (21).

Dexamethasone is a synthetic glucocorticoid with mainly anti-inflammatory effect, it was found to be safe with low risk of potential side effects. Already were showed that corticosteroids suppress the transmission in thin an-myelinated C fibers (22). Anti-inflammatory effect and an inhibitory effect on nociceptive C fiber transmission are potential mechanism for analgesic effect of the dexamethasone.

In the dexamethasone group one patient's preoperative cortisol level was higher than the normal range and the postoperative VRS pain scores were higher than the mean at each time point. This might raise the possibility of patients with high preoperative cortisol levels not benefiting from preoperative low dose dexamethasone. Further research is needed in this field.

Our study has certain limitations. The result is positive in terms of primary outcome; however data were studied from only 13 patients in the dexamethasone group because four patients were excluded. One patient was excluded from the analysis because of mental status deterioration after recruitment and in three cases, surgery were performed under general anaesthesia for clinical reasons independent of the study. This could have contributed to relative under-powering and Type II error in secondary outcomes.

Our findings indicate that single dose dexamethasone 0.1 mg/kg administered immediately preoperatively confers significant analgesic benefit in the early postoperative period after the operative fixation of fractured neck of femur. We have also demonstrated that the patients' saliva cortisol level were lesser on the first postoperative evening, suggesting an inhibitory effect of the intervention on the hypothalamic-pituitary-adrenal axis.

4.6 Tables

Table 1. Patients Demographic Characteristics

	Dexamethasone group	Placebo group	p value
Gender(Female/Male)	8/5	12/5	
Age(years) mean(SD)	74(20.3)	71.95(19.48)	0.38
BMI (kg/m^2) mean(SD)	21.4(7.25)	23.4(7.38)	0.18
Fractured side (Right/Left)	6/7	7/10	

Data displayed as number of cases.

BMI: Body Mass Index

4.7 Figures

Figure 1.

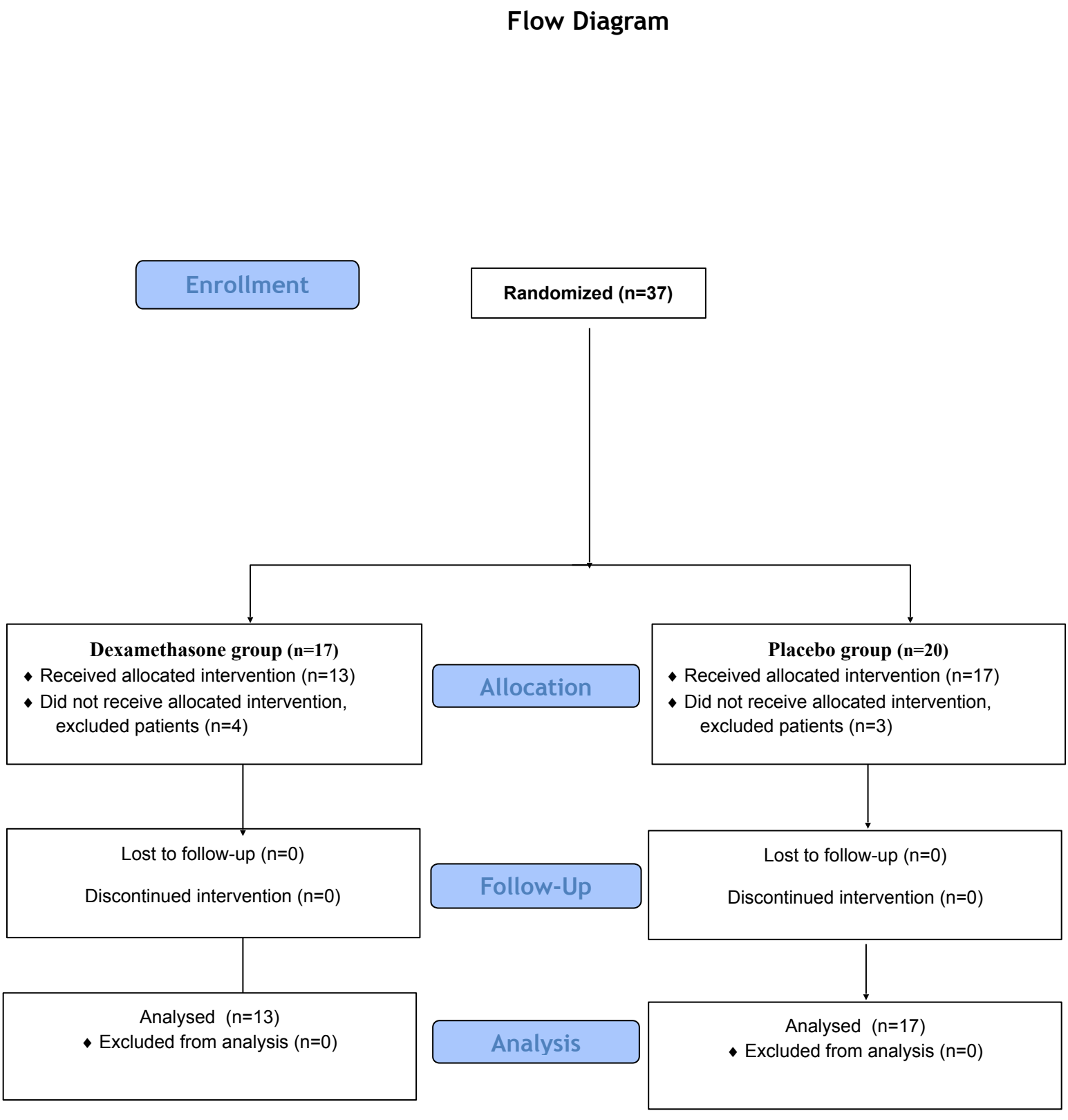


Figure 2. Pain scores at rest (included the primary outcome in the sixth postoperative hour)

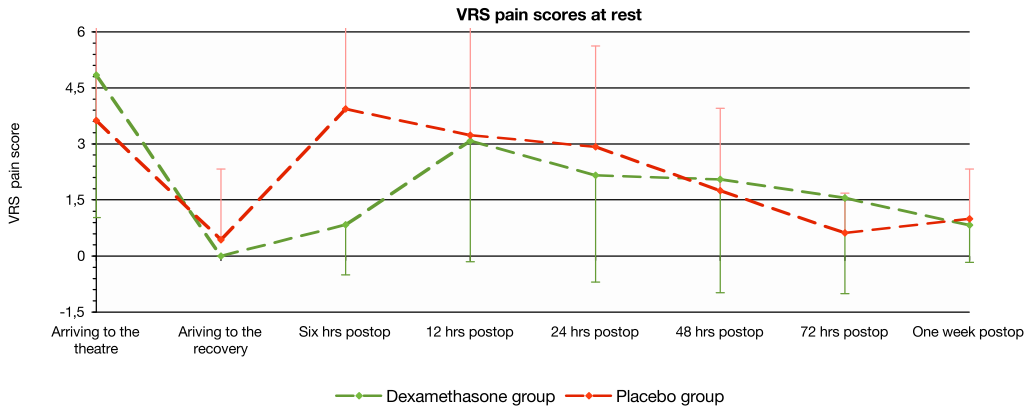


Figure 3. Pain scores on passive movements

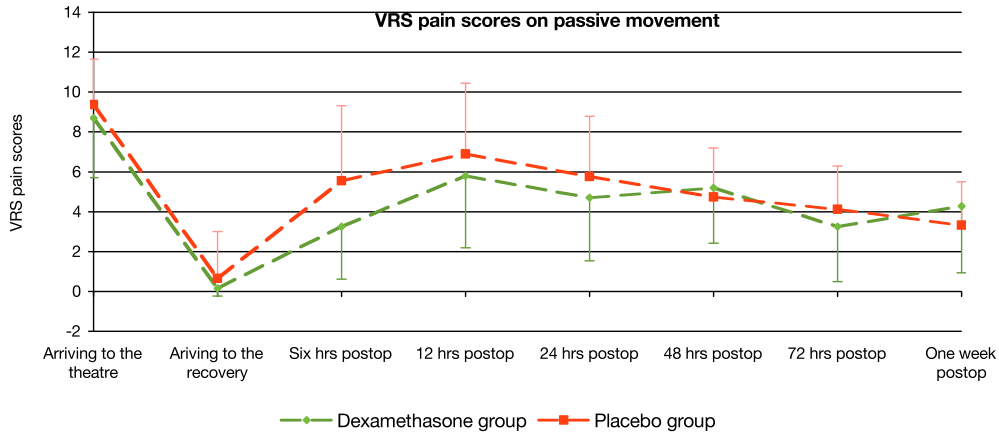


Figure 4. Cumulative morphine consumption

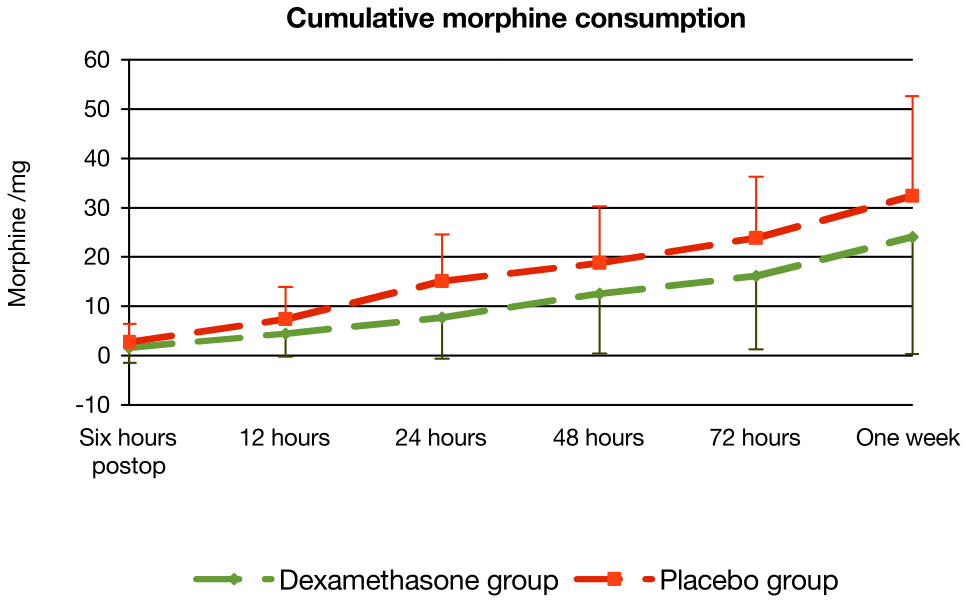
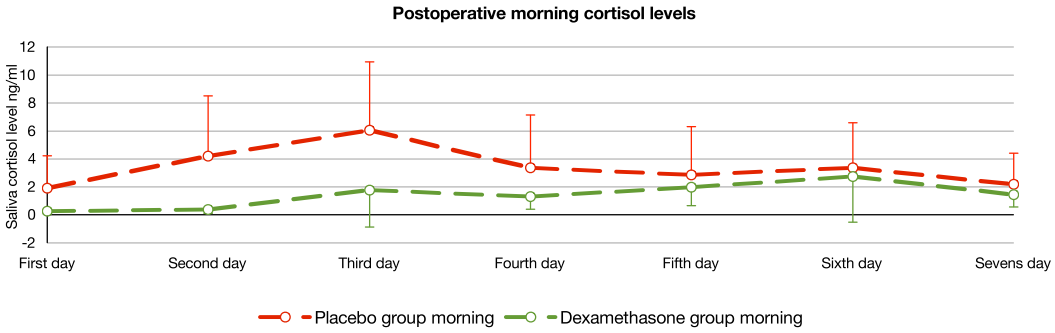
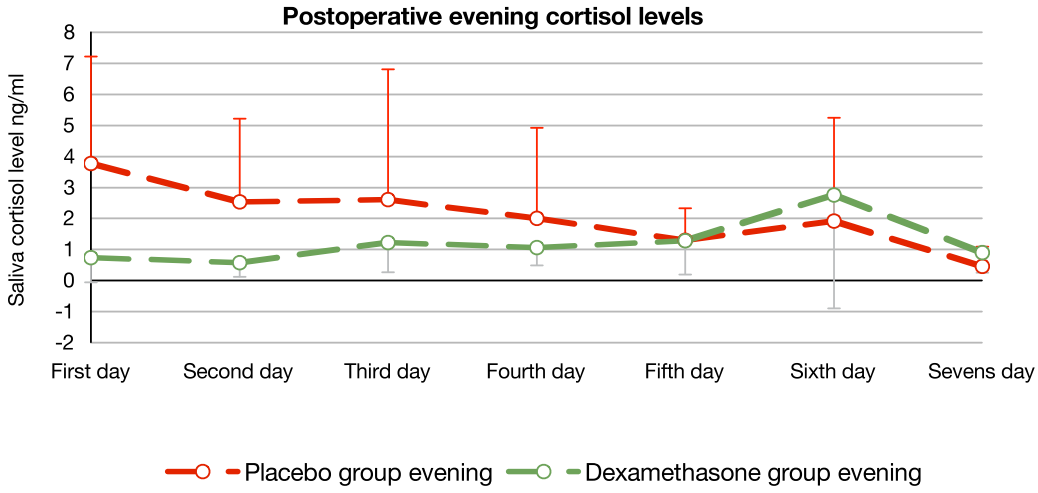


Figure 5. Salivary cortisol concentration vs. time (by group)





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Chapter 5

Study 3

Functional recovery following operative fixation of fractured neck of femur in the elderly

5.1 Abstract, Study I follow up

Background and aims: The aim of our study was to characterize long term functional outcome following operative fixation of fractured neck of femur and to investigate the effect of the analgesic regimen used peri-operatively on this outcome. We followed up patients enrolled in a previous prospective randomized controlled trial looking at the efficacy of two analgesic regimens (continuous femoral nerve blockade vs. systemic opioids) in the immediate peri-operative period.

Methods: Following ethics committee approval, a questionnaire comprising 30 questions was administered by phone at six and 12 months after the surgery. Patients were initially contacted and interviewed by phone. After three unsuccessful attempts a letter containing the questionnaire and a self addressed envelope was sent by post. There is no single unifying scale in widespread use for proximal femoral fracture patients (1). The validity, sensitivity, and responsiveness of self-report measures of physical function are comparable to performance-based measures in a sample of patients followed after fracturing a hip (2). We decided to use a questionnaire from a previously validated Lower Extremity Gain Scale: a performance-based measure to assess recovery after hip fracture study (3) because it can be easily administered by clinicians in a short time as part of care. Association between functional outcome and the peri-operative analgesic regimen was sought post-hoc. Based on previous study (3), data collection were performed at two, six and 12 month time after the surgery.

Results: Out of the 24 patients recruited, 16 answered the questionnaire to date. Of these, 14 reached the 12 month time point. One patient in the conventional group suffered a stroke shortly after discharge home and requires assistance around the clock,

therefore was excluded from the analysis. We wasn't able to contact the rest of the patients by phone or we didn't received the filled questionnaire sent by post at the three postoperative timepoints. Demographic characteristics were similar in the two groups (Table 2.). Although showing a trend of improvement over time, the difference between overall global scores at six [(53 vs. 15(10.9), p=0.15]and 12 months[28.3(31.7) vs. 25.2(16.6), p =0.43] did not reach statistical significance. There was no difference between individual or global scores in the two groups at either time point.

Conclusions: Our results indicate good functional outcome at 12 months post operative fixation of fractured neck of femur with no difference between the two groups.

5.2 Abstract, Study II follow up

Background and aims: The aim of our study was to characterize long term functional outcome following operative fixation of fractured neck of femur and to investigate the effect of the analgesic regimen used perioperatively on this outcome. We followed up patients enrolled in a previous prospective randomized controlled trial looking at the efficacy of two potential analgesic regimens (Single dose of preoperative dexamethasone vs. placebo).

Methods: After obtaining ethics approval a questionnaire comprising 30 questions was administered by phone at two, six and 12 months after the surgery. After three unsuccessful attempts a letter containing the questionnaire and a self addressed envelope were sent by post.

There is no single unifying scale in widespread use for proximal femoral fracture patients (1). The validity, sensitivity, and responsiveness of self-report measures of physical function are comparable to performance-based measures in a sample of patients followed after fracturing a hip (2). We decided to use a questionnaire from a previously validated Lower Extremity Gain Scale: a performance-based measure to assess recovery after hip fracture study (3) because it can be easily administered by clinicians in a short time as part of care and was decided to collect data at two, six and 12 month time after the surgery.

Association between functional outcome and the peri-operative analgesia regime was sought using a post-hoc analysis.

Results: Out of the 37 patients recruited, 18 answered the questionnaire. One patient in the dexamethasone group and one patient in the placebo group died after discharge to

home, therefore was excluded from the analysis. We wasn't able to contact the rest of the patients by phone or we didn't received the filled questionnaire sent by post at the three postoperative timepoints. Demographic characteristics were similar in the two groups (Table 3.).

The difference between overall global score at two, six and 12 month did not reach statistical significance(Figure 2.)

Conclusions: Our results showed no difference in any time point between the two groups.

5.3 Tables

Table 1. LEGS Questionnaire:

1. Walk 3m (10ft) or across room _____
2. Put on socks and shoes_____
3. Put on pants_____
4. Get on and off of bed_____
5. Rise from armless chair_____
6. Wash feet_____
7. Climb stairs_____
8. Get on and off toilet_____
9. Reach for item on ground from sitting position_____
10. Cook_____
11. Tie shoelaces _____
12. Wash entire body_____
13. Walk 1 block_____
14. Do housework_____
15. Do laundry _____
16. Get in and out of the bath or shower _____
17. Get in and out of a car _____
18. Go out of walking distance _____
19. Step down a curb_____
20. Vacuum a rug _____
21. Go shopping _____
22. Step up a curb _____
23. Sit in a bathtub _____
24. Do outdoor yard work_____
25. Get on an escalator_____
26. Get off an escalator_____
27. Put on shirt_____
28. Button shirt _____
29. Feed self _____
30. Groom self_____

Likert type scale

3-Not at all difficult

2-Mildly difficult

1-Difficult

0-Extremely difficult

Table 2. Demographic characteristics

Group	Coventional Th	CFNB	(P value)
Sex (Female/ Male)	6/2	4/2	
Age(years)mean (SD)	81,25(4.2)	79,16(14.9)	(0.30)
FNF side(Left/Right)	3/5	5/1	
Surgery (hemiarhtroplasty)	6/2	4/2	

Data displayed in numbers and mean (SD)

Table 3. Demographic characteristics

Group	Coventional Th	Dexamethasone	(P value)
Sex (Female/ Male)	9/4	5/3	
Age(years)mean (SD)	80.0(5.1)	77,66(9.45)	(0.61)
FNF side(Left/Right)	4/8	3/5	

Data displayed in numbers and mean (SD)

5.4 Figures

Figure 1. LEGS scores

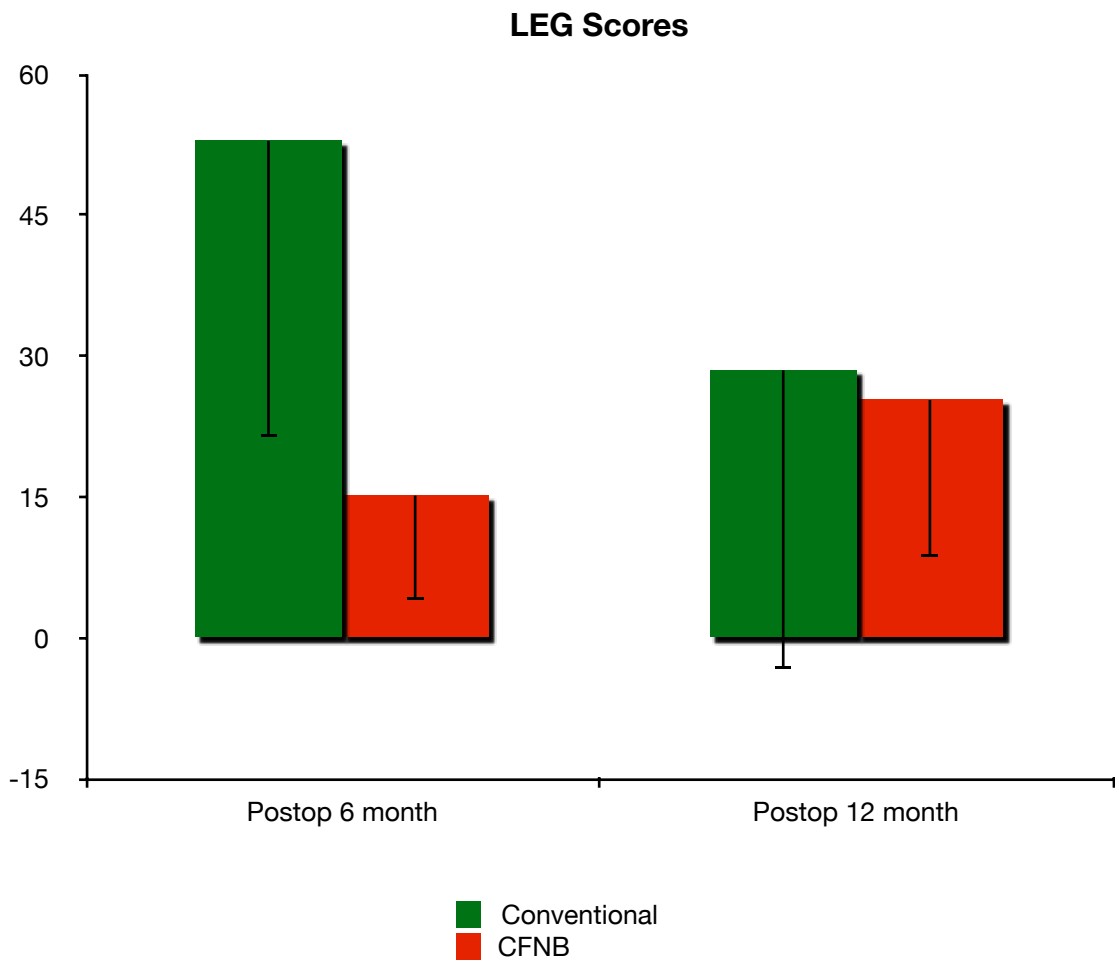
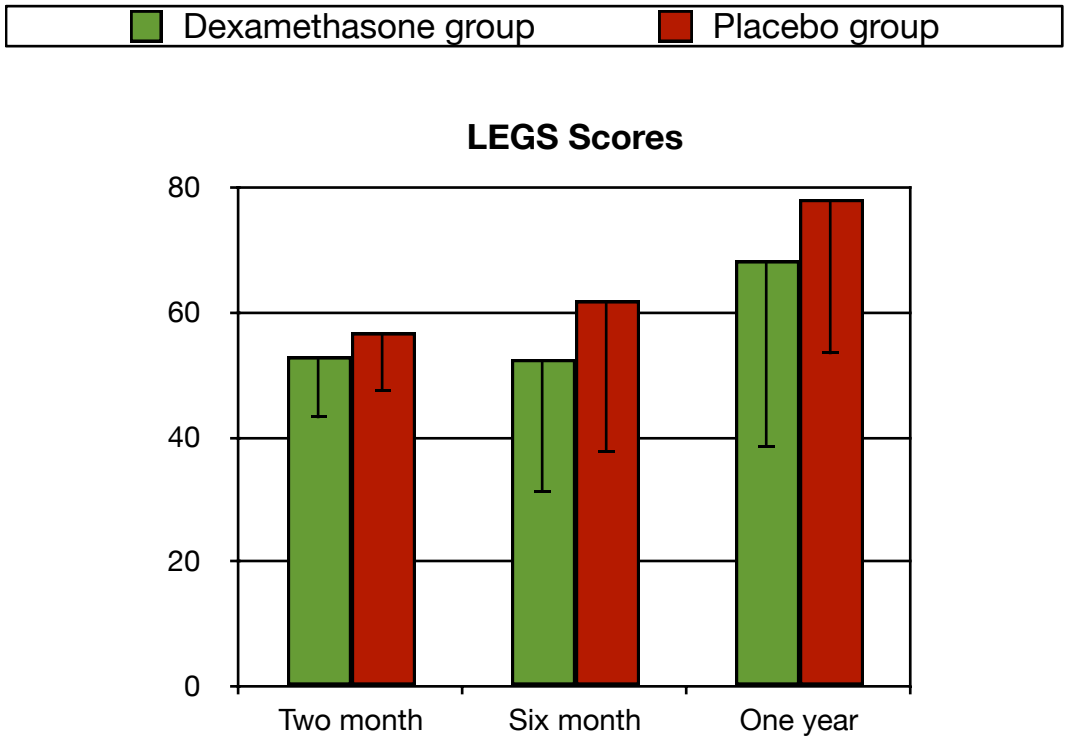


Figure 2. LEGS scores



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Chapter 6

Study 4

Comparing circumferential spread of local anaesthetic with deposition above or below the femoral nerve during ultrasound guided femoral nerve block prior to operative fixation of femoral neck fracture: randomized control trial

6.1 Abstract

Background: Fractured neck of femur (FNF) is a common cause of admission to hospital in elderly patients and requires operative fixation. The combination of femoral nerve block and spinal anaesthesia is a common anaesthetic technique for this procedure. The optimal disposition of local anaesthetic (LA) relative the femoral nerve has not been defined. Our hypothesis was: the deposition of LA around (i.e. circumferential to vs. either above or below) the femoral nerve would result in greater analgesia for positioning of the patient for performance of spinal anaesthesia. The primary outcome was verbal rating (VRS) pain scores 0-10 assessed immediately after positioning for performing spinal anaesthesia.

Methods: With Institutional ethics approval and ClinicalTrials.gov (NCT01527812) registration 52 patients were studied. Patients were randomly allocated to undergo an ultrasound- guided femoral nerve block, with lidocaine 2% (15 ml) injected i. above, ii. below, iii. circumferential to the femoral nerve. A blinded observer assessed i. the sensory nerve block (cold) in the areas of the terminal branches of the femoral nerve and ii. VRS pain scores on passive movement from block completion a 5 minutes intervals for 30 minutes. Immediately after positioning for spinal anaesthesia, the patients VRS pain scores were recorded.

Results: Pain VRS scores during positioning were similar in the three groups [Above group / Below group / Circumferential group: 2(0-9)/0(0-10)/3(0-10), median(range), p: 0.32]. The block was deemed to have failed in 20%, 47% and 12% in the Above group, Below group and Circumferential group respectively. The median number of needle

passes was greater in the Circumferential group compared with the Above group (p: 0-009). Patient satisfaction was greatest in the Circumferential group [mean satisfaction scores in the Above group / Below group / Circumferential group: 83.5(19.8) / 88.1(20.5) / 93.8(12.3), mean(SD), p:0.04]

Conclusions: We conclude that, relative to depositing the LA above the nerve, there is no clinical advantage to intending to deposit LA circumferential during performing femoral nerve block, the intention to deposit the LA above the femoral nerve will be similarly effective.

Keywords: Optimal positioning of the local anaesthetic, femoral nerve block

6.2 Introduction

Fractured neck of femur (FNF) is a common cause of hospital admission in elderly patients and requires operative fixation. Spinal anaesthesia is a technique which is commonly used for these cases and which is performed with the patient in the lateral decubitus position. Positioning the patient prior to administering spinal anaesthesia can be very painful and presents a common clinical problem for anaesthetists.

Regional anaesthesia is effective in alleviating pain due to trauma, and it offers the advantage of producing localized but complete pain relief (1). Femoral nerve blockade (FNB) prior to positioning for spinal anaesthesia can provide excellent pain relief and is generally a well tolerated procedure (2-5). Ultrasound guided femoral nerve block (UGFNB) is a technique which is intended to improve the block success rate and it is widely used in our hospital. Casati and al. compared the use of ultrasound with nerve stimulator to detect the femoral nerve during the peripheral nerve block. They calculated that 15 ml of 0.5% of ropivacaine is the ED 50 for UGFNB and demonstrated a decrease of 42% of effective dose (ED50%) by using ultrasound for localizing the femoral nerve(6). A recent editorial by Sites and al. questioned that the circumferential spread of the local anaesthetic in most of the cases were assumed that ideal, but not defined yet(7). We currently employ different approaches in relation to injection of local anaesthetic (LA) solution close to the femoral nerve. Firstly, one may attempt to position the LA circumferentially, around the nerve. This technique requires several needle passes, which may cause patient discomfort. Another option is to inject the LA either above or below the nerve without changing the position of the tip of the needle, thereby minimizing the number of needle passes and the chance of patient discomfort. It

is not known if this results in an equivalent quality of sensory block. The femoral nerve has separated into branches at this level and we assume that the spread of LA may influence the quality and the distribution of the block.

Our objective was to compare the analgesic efficacy of UGFNB for positioning patients to perform spinal anaesthesia and block success when the anesthetist intention during performing UGFNB was to position the LA i. above to ii. below to or iii. circumferential to the femoral nerve. We also studied the characteristics of FNB in relation to different patterns of local anaesthetic injection (above, below or circumferential).

6.3 Methods

With the approval of the Clinical Research Ethics Committee of the Cork Teaching Hospitals (ECM 4 (zz) 08/12/09.) and having registered the trial at ClinicalTrials.gov (NCT01527812) a prospective, double blinded, randomized study in patients awaiting operative fixation of FNF at the Cork University Hospital was undertaken between December 2009 and November 2011. The patients were randomly allocated using a random number sequence and sealed envelopes (generated by DM). Written, informed consent was obtained from all patients.

Patients with FNF, American Society of Anesthesiologists grades I to III and aged above 50 years, were invited to participate in the study. Exclusion criteria included patient refusal, the presence of more than one fracture; Mini-Mental Score <22 (appendix 1) ; coagulation disorders; head injury; loss of consciousness; acute heart failure; allergy to lignocaine; skin lesions/infection at block site; and renal dysfunction. Patients with evidence of systemic infections (clinically defined or elevated C-reactive protein levels, leucocytosis, or body temperature higher than 37.8^{o} C) were also excluded.

In all patients an experienced anesthetist, who reformed previously more than 20 successful UGFNB, one of the authors (SS, DM or SF) performed the UGFNB. A 5 cm, 6-13 MHz linear transducer probe (Sonosite Turbo M, Bothwell WA, USA) was used to locate the nerve. For optimal visualization of the femoral nerve the transducer was applied transversely to the thigh below the inguinal crest. After examination of the anatomy of the femoral artery, the femoral nerve was identified at a level immediately above the deep femoral artery branch bifurcation. A 22 G 50 mm long Stimuplex

BBraun needle was used. After identification of the nerve and fascia around the nerve the skin was infiltrated with local anaesthetic (0.2 ml lignocaine 1%) on the lateral aspect of the thigh, 1 cm lateral from the edge of the transducer. The needle was inserted in-plane from lateral to medial orientation and advanced toward the lateral part of the femoral nerve.

For patients randomly allocated to the “above” group (Group A) the LA (15 ml 2% lidocaine) was injected below the fascia iliaca and above the femoral nerve; for patients randomly allocated to the “below” group (Group B) the LA was injected below the femoral nerve and above the fascia of the iliopsoas muscle and for those patients randomly allocated to the circumferential group (Group C) circumferential spread was achieved with multiple injections around the nerve (Figure 1.).

An independent blinded observer (not present during block placement) assessed the sensory nerve block using a modified Bromage score (cold, mildly cold and just spray) at 5 minute intervals during the first 30 minutes after block completion. Sensory perception was assessed using cold (ethyl-chloride spray) spray on the skin in the lateral, frontal, medial side of the thigh and medial side of the leg according the terminal branch of femoral nerve.

Our primary outcome was verbal rating (VRS) pain score 0-10 assessed immediately after positioning the patient (lateral decubitus with operative side independent) for performing spinal anaesthesia.

We recorded the patients pain score on passive movement of the fractured limb (elevating up to 30 degrees from the supine position or to patient tolerance from the resting position) using a VRS pain score 0-10. When the patient reported less VRS < 4 during the passive movement of the limb, the sensory block was deemed adequate and the patient was positioned on the side for spinal anaesthesia. Where cold sensory

perception was still present the patients were continually assessed up to 30 minutes (if the spinal is not injected until this time). Block failure was defined as failure to achieve a VRS score of < 4 within 30 minutes of FNB completion. In these cases, additional opioid medication and/or sedation were administered in order to optimize positioning for spinal anaesthesia and these patients were excluded from further data collection. We recorded the times at which the patients arrived in the anaesthetic induction room, UGFNB started at the skin infiltration and completion of patient positioning for spinal anaesthesia.

Spinal anaesthesia was performed under sterile circumstance, in all cases isobaric bupivacaine were used as local anaesthetic. The amount of local anaesthetic what was given was decided by the anaesthetist who was present during the surgical fixation. Patient satisfaction with analgesia during anaesthesia was measured using a 100 mm linear visual analogue scale (VAS), immediately after arriving to the recovery area. Patients were also asked if they would choose the same analgesic modality again. Adverse events were recorded by the attending anaesthetist on a dedicated data sheet, and discussed at weekly research meetings.

Statistical analysis

Sample size calculation was limited by the absence of historical data on pain on positioning for FNF. It was arbitrarily decided to proceed on the basis that at least 20 patients / group would be required to demonstrate a clinically relevant effect size. Collected data were examined for normality. Normally distributed variables were tested between groups using ANOVA and t-test, non-normal data were analyzed using the non-parametric Kruskal-Wallis and Mann-Whitney U test. Categorical variables were tested using chi-squared tests. $P<0.05$ was considered significant.

6.4 Results

Sixty patients were recruited to this study of whom 52 were managed per protocol. Seven patients were excluded because of an breaches of study protocol. One patient (Group A) developed fast atrial fibrillation after performing spinal anesthesia with haemodynamic instability resulting in cancellation of surgery. In one case (Group C) the anaesthetist who performed the UGFNB had difficulties in visualizing the femoral nerve, and a nerve stimulator was used to confirm its position.

Patient characteristics were similar in the three groups (Table 1.).

Block failure was deemed to occur in three patients out of 20 from Group A (20 %), seven out of 15 patients from Group B (46.7%) and two out of 17 from Group C (11.8%). (Figure 2. Flow diagram). The patients in whom the UGFNB block was deemed to have failed received iv. drugs: fentanyl, midazolam or propofol, as at the discretion of the anaesthetist responsible for their clinical care and excluded from further data collection.

Pain scores on positioning for spinal anaesthesia were similar in the three groups [VRS pain scores in the Group A / Group B / Group C: 2(0-9)/0(0-10)/3(0-10), median (range), Kruskal-Wallis test p:0.32)] (Figure 3). Patient satisfaction (VAS scores on arrival to the recovery room) were greater in Group C patients compared with those in Group A [Group C vs Group A: 93.8(12.3) vs 83.5(19.8), mean (SD), p: 0.01)]. Sensory distributions of nerve block achieved similar in the three groups.

Procedural pain (VRS), block procedural time, block onset time, the time to position for spinal anaesthesia and spinal block performance time were also similar in the three groups (Table 2.). Once spinal anaesthesia was converted to general anaesthesia because

the insertion of the spinal needle was impossible during seven attempts. As sedative agents during the spinal anaesthesia was administered iv. fentanyl and midazolam. In Group A one patient got 20 microgram fentanyl iv. and two patients got 2 and 5 mg midazolam iv. In Group B two patients got 20 and 25 microgram fentanyl iv. and one patient 1 mg midazolam iv. In Group C three patients got one and twice two mg midazolam iv. The number of needle passes was less in the Group A compared with the Group C (1.0 vs 2.0, Mann-Whitney U between Groups A vs. C, $p=0.009$).

6.5 Discussion

The most important finding of this study is that the attempt to place LA circumferentially around the femoral nerve offered no clinical advantage (in terms of pain on positioning for spinal anaesthesia) relative to placing the LA only above the nerve. The latter approach resulted in fewer needle passes during performance of the block and was associated with greater patient satisfaction on arrival to the postoperative recovery room.

We believe that our understanding of the determinants of spread of LA administered during Peripheral Nerve Blockade is grossly deficient. The evidence and our understanding of the equivalent determinants when LA is administered for nerve block is greater but still incomplete. Our study attempts to apply scientific rigor to a clinical (i.e. applied) question without making unsupported assumptions around this question. Previous studies have demonstrated that ultrasound is a reliable method of detecting injectate spread in a gelatin phantom model (8). It has also been shown that ultrasound-guided circumferential injection of local anaesthetic around the sciatic nerve can improve the rate of sensory block (9). It has been found that fascia iliaca block is more efficacious than i.v. alfentanil in terms of facilitating the lateral position for spinal anaesthesia (10). FNB has been shown to be superior (compared with i.v. administration of fentanyl) in facilitating the sitting position for spinal anaesthesia in patients undergoing surgery for femoral shaft fractures (11). A recent publication investigated the influence of catheter tip positioning during continuous FNB in healthy volunteers. The conclusion was that anterior placement increase cutaneous sensory block compared

with a posterior insertion, without a concurrent relative increase in motor block(12). Ours was a clinical investigation aimed at providing useful practical information to clinicians seeking to optimize conditions for positioning of patients prior to FNF surgery. Thus, in addition to the cutaneous sensory effects, we considered that articular pain may contribute to the discomfort experienced by these patients. The posterior division of the femoral nerve gives articular branches to the hip and knee (13). Therefore we believed that it was possible that deposition of LA inferior, just below the femoral nerve at level described effect greater sensory block to these articular branches. Kullenberg et al.() reported that FNB could have other beneficial outcomes in this patient group, with earlier times to postoperative mobilization and less cognitive impairment reported (14). UGFNB is feasible to perform in the emergency department and significant and sustained decreases in pain scores were achieved with this technique (15).

The relatively great incidence of block failure we report may be attributable to the well documented variation in sensory innervation of the hip joint(with differing contribution across individuals from femoral, sciatic and obturator nerves)(13) and the relatively small sample size.

To date there have been no studies identifying the optimal spread of local anaesthetic in femoral nerve block in terms of clinical effect.

Our study has certain limitations. The data set wasn't complete in every case. Certain patients received sedation after spinal anaesthesia had been performed. Certain co-morbid factors may have influenced pain perception during positioning for spinal in these cases. For example, chronic obstructive pulmonary disease result in a longer duration of positioning the patient (and presumably greater discomfort). A negative

finding of a clinical trial in which the sample size was relatively small and arbitrarily selected may be due to a Type II error. Although this is a possibility, we believe that any clinically significant difference would have been identifiable if only as a trend (without statistical significance). Another limitation of the study could be that we didn't recorded the spreading of the LA around the femoral nerve. Based on the randomization the anaesthetist who performed the femoral nerve block have the intention to deposit LA in three area around the femoral nerve. It is unclear what was the real spread of the LA around the nerve, our calculation based on the intention of the anaesthetist who performed the nerve block.

In fact, pain scores on positioning for spinal anaesthesia tended to be lower in Group B; this trend did not reach the statistical significance level (VRS pain scores in the Group A / Group B / Group C: 2(0-9)/ 0(0-10)/3(0-10), median(range), Kruskal-Wallis test p: 0.32). (Figure 3).

6.6 Conclusion

We conclude that, in this clinical setting, attempting to place LA circumferential to the femoral nerve versus simply placing it above and adjacent to the nerve confers no clinical advantage, results in a greater number of needle passes and therefore is not justified. The recruited patients number was small and our endpoint of the block was subjective leaving to the discretion of the anaesthetist the intention to deposit LA in the predefined area, this might indicate to perform further research in the area regarding the optimal positioning of the local anaesthetic during ultrasound guided femoral nerve block.

6.7 Tables

Table 1. Patients demographic characteristics

	Group A	Group B	Group C	(p-value)
Gender(Female/Male)	11/5	4/4	7/8	0.34
Age(years, mean)	80.0	73.9	81.3	0.34
ASA status I/II/III	1/11/4	1/6/1	2/8/5	0.66
Procedure (DHS, IMHS/ hemiarhtroplasty)	10/6	6/2	10/5	0.46
BMI (kg/m^2)mean	23.16	25.29	25.51	0.18
Right/Left	9/7	2/6	7/8	0.21)

ASA: American Society of Anaesthesiologist physical status, DHS: Dynamic hip screw, IMHS: Intramedullary hip screw.

Data displayed in mean and percentage

Table 2. Secondary outcomes (medians)

	Group A	Group B	Group C	(p-value)
Time till starting the USFNB after arrival to the induction room (min)	9.4	7.4	7.0	0.88
UGFNB procedure time (min)	3.3	3.4	4.6	0.49
Pain during UGFNB (VRS 0-10)	2.3	1.4	2.6	0.64
UGFNB onset time (min)	9.3	11.4	12.3	0.49
Turning time for spinal anaesthesia after arrival in induction room (min)	32.1	29.1	35.0	0.49
Spinal performing time after arrival in induction room (min)	43.8	39.3	46.1	0.62
Sedation during spinal anaesthesia number of the patients (%)	2(12.5)	2(25)	3(20)	0.73

VAS: Visual analogue scale, VRS: Verbal rating score

Data displayed in mean and percentage

6.8 Figures

Figure 1. Composite figure of femoral nerve block

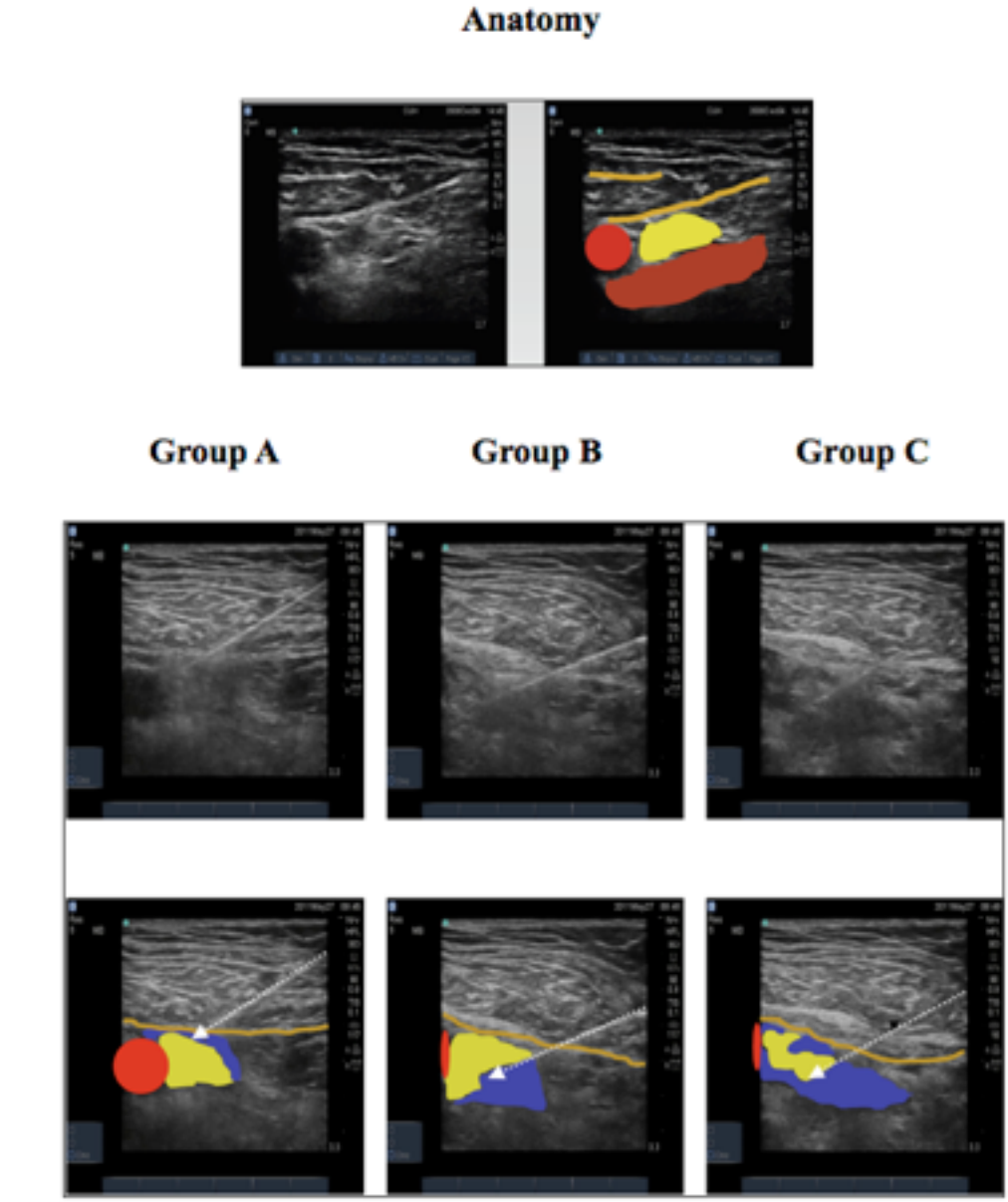


Figure 2. Flow diagram

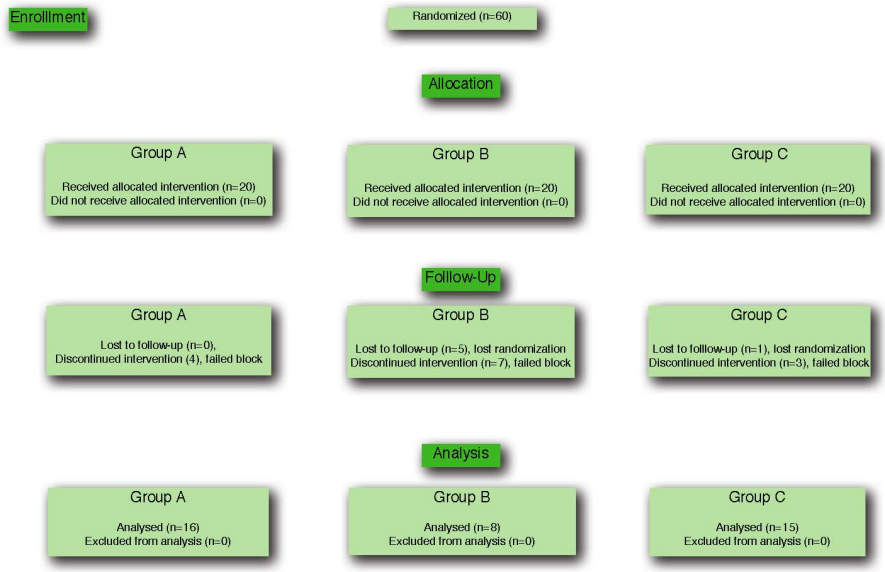
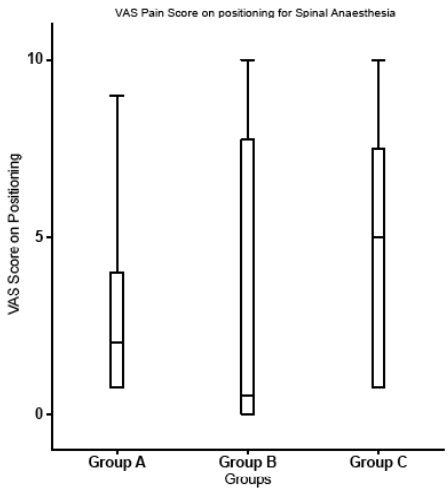


Figure 3. VRS pain scores on positioning to perform spinal anaesthesia



Data displayed as mean and IQR (25%-75%)

6.9 References to Chapter 6

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Chapter 7

Study 5

Initial minimum intrathecal local anaesthetic dose with concomitant femoral nerve block required for operative fixation of fractured neck of femur

7.1 Abstract

Background: Femoral neck fracture is a common cause of admission to hospital and requires operative fixation. Spinal anaesthesia is the preferred anaesthetic technique, although single-shot spinal anaesthesia may have severe haemodynamic side effects. Continuous spinal anaesthesia is a long established technique (2).

The "up-and-down" method described by Dixon and Massey was used to determine the initial minimum local anaesthetic dose of 0.5 % bupivacaine required to achieve surgical anaesthesia.

Methods: With institutional ethics approval and having obtained written informed consent from each, ASA I-III patients aged >60 years, scheduled for operative fixation of femoral neck fracture at Cork University Hospital were recruited. A 22G spinal catheter was inserted at the levels of L2-L4 vertebrae. An initial dose of 1 ml bupivacaine 0.5% was arbitrarily chosen as a starting point. The dose in subsequent patients was determined by the outcome of the preceding spinal block and adjusted by 0.1 ml until data on six independent pairs of patients with successful block/ failed block were acquired.

Results: Twenty three patients were recruited to the study, of whom 22 were managed per protocol. One patient was excluded due to the inability to insert the intrathecal catheter. The initial minimum local anaesthetic dose for 0.5 % bupivacaine was calculated to be 0.26 ml (95% CI 0.274-0.486).

Conclusions: Our findings may influence clinicians' initial dose selection for spinal anaesthesia when a spinal catheter is used in this or similar clinical settings. The dose may be less than previously thought.

7.2 Introduction

Femoral neck fracture (FNF) is a common cause of admission to hospital in elderly patients and requires operative fixation. Spinal anaesthesia (SA) is a technique used to facilitate operative fixation of FNF. Since 1899 when Bier described first this technique went through many changes. Spinal anaesthesia has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anaesthetic(1). However in some cases single shot SA can have severe hemodynamic side effects. Continuous spinal anaesthesia (CSA) is a technique used since the 1940's (2), was improved by catheter insertion by Touhy (3) provides fewer episodes of hypotension and severe hypotension compared with a single intrathecal injection of 7.5 mg bupivacaine (4).

The optimal initial volume of 0.5 % bupivacaine during CSA is unknown. We have evidence of minimum effective local anaesthetic dose (MLAD) in hip replacement surgery (5). It would however be beneficial for those patients who are haemodinamically unstable. The "up-and-down" method described by Dixon and Massey (6) was used successfully to estimate the minimum effective local anaesthetic volumes in ultrasound guided axillary nerve block (7) and femoral nerve block (8). Based on the modified Dixon method (9) was studied the dose of propofol (10) and fentanyl (11) for laryngeal mask insertion during induction of general anaesthesia. The aim of the this study was to determine the initial MLAD of 0.5 % bupivacaine required to achieve a successful spinal anaesthesia during CSA.

7.3 Methods

The Clinical Research Ethics Committee of the Cork Teaching Hospitals granted approval for this study (ECM 4 (ii) 10/01/12.) and it was registered at ClinicalTrials.gov (NCT01680120). Patients awaiting operative fixation of FNF at the Cork University Hospital were invited to participate in the study. Patient recruitment was undertaken between September 2012 and December 2012. Written, informed consent was obtained from all patients.

Inclusion criteria included age > 60 years and America Society of Anesthesiologists Grade I-III. Exclusion criteria included patient refusal, outside age range, coagulation disorders, head injury or other associated injuries, loss of consciousness and signs of acute coronary syndrome, Mini-Mental Score < 22, allergy to bupivacaine, lignocaine and skin lesions/infection at site of injection.

Patients received no premedication prior to their arrival to the operating room. All patients received oxygen (35% oxygen through Venturi facemask) during the procedure, including the first postoperative hours. Standard monitoring including continuous electrocardiogram, noninvasive automated arterial blood pressure and pulse oximetry were applied. Patients received ultrasound guided femoral nerve block, 15 ml of 2% lignocaine before being turned to the lateral position for lumbar puncture.

After aseptic preparation of the skin in the lumbar area, the subarachnoid puncture was performed with a 18-gauge Tuohy (B.Braun Melsungen AG, Melsungen, Germany) needle at the L4-5 or L3-4 interspace using a midline approach. The bevel of the Touhy needle at the dural puncture was held longitudinal to the dural cylinder and turned cephalad before the catheter introduction. Three cm of a 22-gauge catheter was

introduced cephalad through the needle. The lumbar punctures were performed by one of the authors, whom are experienced anaesthesiologist (S.S. or J.R.).

The initial dose was arbitrarily chosen as 1 ml of 0.5 % isobaric bupivacaine on the basis of clinical experience. After obtaining cerebrospinal fluid on aspiration, the local anaesthetic were injected through the catheter over 10-15 sec following three aspiration and injection of 1 ml of cerebrospinal fluid (barbotage). After completion of injection the patients remained in the lateral position for 5 min and were then returned to the supine position.

Successive injections of 0.2 ml of 0.5 % isobaric bupivacaine were performed every 15 min until surgical anaesthesia was achieved. Using the “up-and-down” method described by Dixon and Massey (6), the dose used for subsequent patients was determined by the outcome of the preceding spinal block. The Dixon and Massey method (6) stipulated that the difference between the doses tested should be approximately equal to the standard deviation of dose effects; we estimated that standard deviation would be approximately 0.1 ml. Therefore, in the case of failed block, the initial dose was increased by 0.1 ml. Conversely, successful block resulted in a reduction in the initial dose by 0.1 ml.

Non-invasive blood pressure and heart rate measurements was recorded before the spinal anaesthesia (baseline) and every three minutes after the end of local anaesthetic injection until the end of surgery.

Hypotension was defined as a decrease of more than 20% from the baseline systolic arterial blood pressure (SAP). Severe hypotension was defined as a decrease in SAP more than 30% of baseline value. Hypotension was treated with IV boluses of ephedrine 6 mg if the heart rate was below 60/minutes or phenylephrine 100 microgram if the heart rate was above 60/minutes.

Spinal block assessment

A blinded observer assessed the dermatome level of sensory blockade with an ice-cold test (ethyl-chloride spray) bilaterally after injection of the local anaesthetic. Block assessment was performed at 15 min intervals up to 45 min after completion of the initial intrathecal injection. Successful spinal anaesthesia was defined as absent appreciation of cold sensation in the relevant anatomical areas. The time interval at which surgical anaesthesia was achieved was noted. Total spinal anaesthesia failure was defined as absence of surgical anaesthesia at 45 min; in the event that failure occurred, the study was discontinued and the further care of the patient was at the discretion of the responsible anaesthetist. Successful spinal anaesthesia was defined as absent appreciation on cold sensation in the peripheral nerves skin innervation area, in the surgical skin incision area plus T 12 skin dermatome and the absence of pain on passive movement (up to 30 °) of the fractured limb (Table 1.).

The number of hypotensive episodes, total vasopressor administered, and the iv. fluid infused was recorded. Intrathecal catheters were removed after the surgery.

All patients received 1 g of intravenous paracetamol and 75 mg of diclofenac sodium during surgery. Postoperative analgesia consisted of 1 g of oral paracetamol every 6 hours and 75 mg of diclofenac sodium (patients >70 yrs) twice daily for 72 h after surgery. Oxycodone 5 mg was prescribed for rescue analgesia after spinal anaesthesia regression.

Statistical Analysis

The sample size was based on previous literature, which has demonstrated that a

minimum of six independent pairs of patients with successful block/failed block should provide reliable estimate of MLAD using the Dixon and Massey's "up-and-down" method (6). This method was used to calculate MLAD with a 95 % CI and the results are presented as median (range) or mean (standard deviation) as appropriate.

7.4 Results

Twenty three patients were recruited to this study of whom 22 were managed per protocol (Table 2.). One patient were excluded because the inability of insertion of the intrathecal catheter. Patients demographic characteristics are summarized in Table 3. The sequences of patients with successful/failed block are shown in Figure 1. The P 50 for initial MLAD for 0.5 % bupivacaine was calculated 0.26 ml (95% CI 0.274-0.486). Spinal anaesthesia was successful in all cases, the mean (SD) cumulative dose of 0.5% bupivacaine was 1.14 ml (0.45 ml) (Table 4). Midazolam (2.45+/-1.14 mg) was administered i.v. for 11 patients and one patient received 50 mcg fentanyl iv. beside the iv. midazolam. Eight patients became hypotensive which required 343 (SD 408) mcg phenylephrine iv. and four patients required 14.3 (SD 7.5) mg ephedrine iv. (Table 5). No patient developed severe hypotension in any of the patients.

7.5 Discussion

Continuous spinal anaesthesia enables an anaesthetist to administer additional local anaesthetic increments to optimize the quality and safety of intrathecal anaesthesia. Using this technique we were able to calculate the initial MLAD for 0.5 % bupivacaine in operative repair of FNF cases. Van Gessel and al. showed that 7.5 mg hypobaric bupivacaine through CSA is suitable for surgical repair of hip fractures in geriatric patients (13) but isobaric bupivacaine causing severe hypotension in 18 % of the cases, Biboulet and al. concluded that 5 mg bupivacaine through CSA is too great dose to consistently avoid hypotension (14), later Ben-David and al. described that a "minidose" of 4 mg bupivacaine with 20 mcg fentanyl provides spinal anaesthesia for surgical repair of hip fracture in the elderly (15). This study demonstrates that CSA in FNF cases, with initial MLAD of 0.25 ml of 0.5 % bupivacaine and 1.14 ml (0.45 ml) cumulative dose of 0.5 % bupivacaine can provide stable anaesthesia, without severe hypotension.

The reported cumulative LA dose administered through CSA has varied between 1-3.5ml of 0.5 % bupivacaine (14, 16) and 3-5 ml 0.25% bupivacaine (13). These are greater doses than the results of this study indicate to be sufficient [1.14 ml (0.45 ml) of 0.5 % bupivacaine] to provide surgical anaesthesia for operative fixation of FNF cases. Using these lesser doses, we did not observe any case of severe hypotension, which is consistent with previous retrospective, observational findings (12).

Hypotension results from decreases in systemic vascular resistance (SVR) and CVP from sympathetic block with vasodilation and redistribution of central blood volume to lower extremities and splanchnic beds (17). Our results indicate that lesser initial dose

may result in lesser likelihood of hypotension while consistently providing surgical conditions within 15 minutes.

The decision that the block was successful or not was made by one of two investigators (S.S. and J.R.) who applied clearly defined criteria strictly. All procedures were performed in similar context (same operating theatre) within a three-month period.

The statistical method employed in this study is intended to estimate P 50 MLAD based on Dixon and Massey's "up-and-down" method (6). This is not a dose recommendation and we utilized the in situ spinal catheter to administer additional doses if necessary, a technique unlikely to be justified in routine clinical practice. Statistical methods articles using stimulation methods recommend that the studies have 20 or more patients (18). Unfortunately, we were not able to assess whether the catheter tip slid cephalad or caudally. The catheter was inserted for 3 cm into the intrathecal space, this can result with a maximum difference of 6 cm in the tip of catheter position which seem to have no major effect on the anaesthesia.

The risk of postdural puncture headache with CSA technique can be relevant in young patient population, but in this age group previous studies reported incidence was 6 % (19) and our practice was to change the bevel of the needle during puncturing the dura which may cause further decrease in the risk postdural puncture headache as it was described by Flaatten and al. (20).

In summary, our study demonstrates that the initial minimum local anaesthetic dose necessary for successful continuous spinal anaesthesia for operative fixation of femoral neck fracture is 0.26 ml of 0.5 % bupivacaine. This may be less than that previously estimated by clinicians and may result in a lesser incidence of severe hypotension. The results of our study may inform clinicians' initial dose selection for CSA and could

improve safety of a high risk population of patients.

7.6 Tables

Table 1. Sensory nerve block, pain on passive movement and skin dermatoma sensation testing

	Cold Spray Test
Surgical skin incision area	1-3
Femoral nerve	1-3
Skin innervation area on the front of the thigh above the knee	
Obturator nerve	1-3
Skin innervation on the medial side of the knee	
Sciatic nerve	1-3
Skin innervation area on the posterior side of the thigh	
VRS pain on passive movement	0-10
Elevating passively the limb up to 30 °	
T 12 Skin Dermatoma block	1-3
At the inguinal ligament in the midclavicular line	

Scores: Bromage (modified) sensitivity test: 1-cold
2- mildly
3-just spray
VRS: Verbal rating scale pain scores from 1-10

Table 2. Flow diagram

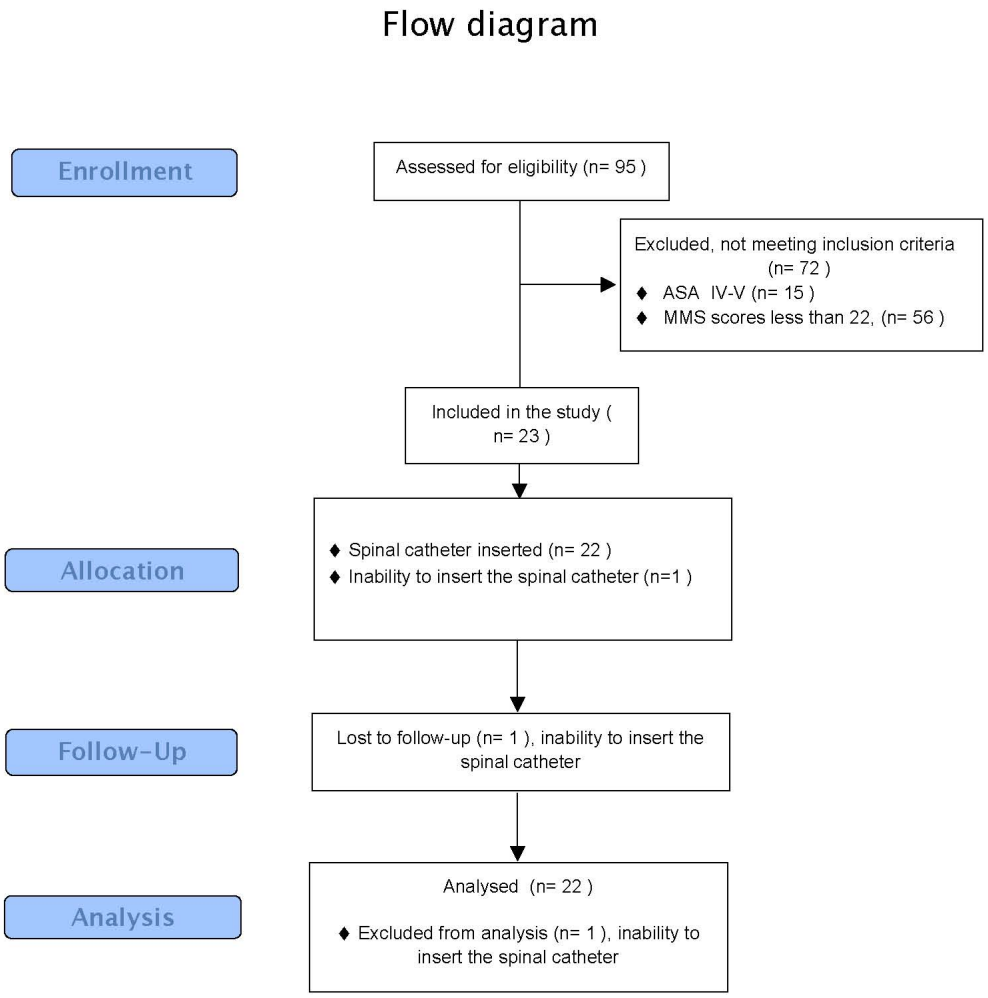


Table 3. Patients Demographic Characteristics (22)

Gender(Female/Male)	18/4
Age(years) mean(range)	81,5(60-94)
ASA status I/II/III	4/14/4
Procedure (DHS/IMHS/hemiarhtroplasty)	9/3/7
BMI (kg/m^2) mean(range)	73(45-112)
Fractured side (Right/Left)	10/12

Data displayed as number of cases.

ASA: American Society of Anesthesiologist physical status,

DHS: Dynamic hip screw, IMHS: Intramedullary hip screw,

BMI: Body Mass Index

Data are displayed in mean(range) and numbers

Table 4. Intrathecal bupivacaine doses during the surgery

Patients	First inj. /ml	Cum. dose till start / ml	Cum. dose during surgery /ml
Patient nr. 1	1	1	
Patient nr. 2	0,9	0,9	
Patient nr. 3	0,8	0,8	
Patient nr. 4	0,7	0,7	1,4
Patient nr. 5	0,6	0,6	0,6
Patient nr. 6	0,5	1,1	1,6
Patient nr. 7	0,6	0,6	1,3
Patient nr. 8	0,5	0,7	
Patient nr. 9	0,6	0,8	
Patient nr. 10	0,7	0,7	1
Patient nr. 11	0,6	0,6	1,8
Patient nr. 12	0,5	0,5	1
Patient nr. 13	0,4	0,6	0,9
Patient nr. 14	0,5	0,5	0,8
Patient nr. 15	0,4	0,4	1,5
Patient nr. 16	0,3	0,7	1,5
Patient nr. 17	0,4	0,4	1
Patient nr. 18	0,3	0,3	1,5
Patient nr. 19	0,2	0,6	1,4
Patient nr. 20	0,3	0,3	0,6
Patient nr. 21	0,2	0,6	0,8
Patient nr. 22	0,3	0,3	0,8
mean		0,62	1,14
SD		0,25	0,45

Table 5. Procedural data

USGFNB starting after arrival	13.4 min (6.5)
Spinal catheter insertion time after arrival	28.33 min (10.33)
First spinal injection time after arrival	34 min (11.45)
Cumulative LA dose till starting the surgery	0.62 ml (0.22)
0.5 % isobaric bupivacaine	
Sedation with midazolam during the case (in 11 cases)	2.45 mg(1.14)
Sedation with fentanyl (in one case)	50 microgramm
Phenylephrine (in eight cases)	343.7 microgram(408.1)
Ephedrine (in four cases)	14.25 mg(7.47)
Atropin	none

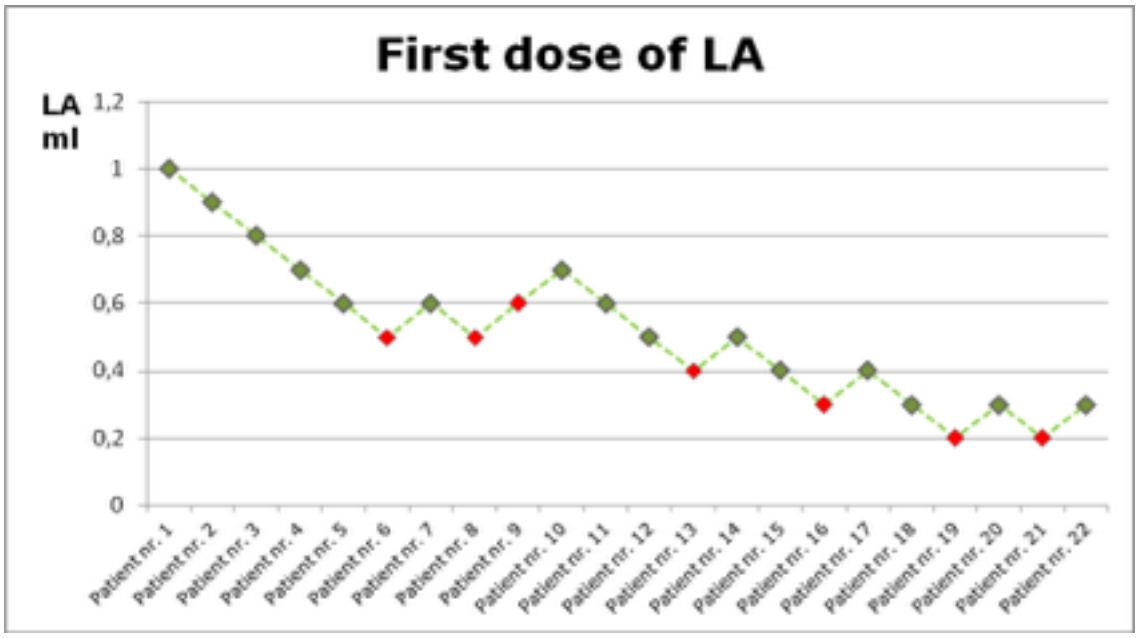
USGFNB: ultrasound guided femoral nerve block

LA: Local anaesthetic

Data are expressed as mean(SD)

7.7 Figures

Figure 1. Initial local anaesthetic dose



7.8 References for Chapter 7

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Chapter 8

Study 6

Perioperative analgesia following surgery for fractured neck of femur: a comparison of peri-surgical site infiltration of local anaesthetic with systemic postoperative analgesics, randomized, double blinded clinical trial

8.1 Abstract

Background: Fractured neck of femur is a common cause of admission to hospital for elderly patients and requires operative fixation. In our hospital, surgical fixation of fractured neck of femur is routinely performed under spinal anaesthesia with intrathecal bupivacaine. This provides excellent conditions for surgery and gives satisfactory analgesia in the early postoperative period. Wound infiltration with local anaesthetic may improve the pain control in the early postoperative period (6,8).

Our objective was to evaluate the analgesic efficacy of peri-surgical site infiltration with levobupivacaine local anaesthetic with 1:200,000 epinephrine after the surgical fixation of fractured neck of femur.

We hypothetised that the quality of analgesia at 12 hours postoperatively assessed by verbal rating score (VRS) for pain at rest with levobupivacaine infiltration will show a better result.

Methods: With institutional ethical approval and having obtained written informed consent, 37 patients were randomly allocated to one of two groups. All the patients received spinal anaesthesia (isobaric bupivacaine 0.5% 2.0 ml). The patients in the Infiltration group received peri-surgical site infiltration before wound closure with a solution of levobupivacaine 2mg/kg with epinephrine made up to a volume of 1.5ml/kg with saline.

For all the patients in both groups were prescribed regular postoperative analgesia of paracetamol 1g qds PO/PR and diclofenac 75mg bd PO. Oxycodone (‘Oxynorm’) 5-10mg PO qds/prn was also be prescribed as a rescue analgesic. Cyclizine 50 mg i.m.

prn/tds was prescribed for nausea and vomiting. If it was necessary, ondansetron 4-8mg i.v. prn/qds was administered as a rescue anti-emetic.

The patients were assessed at 2, 6, 12, 24 and 48 hours postoperatively. We assessed severity of pain, VRS pain scores was used at rest and on passive movement of the operative hip joint. Cumulative morphine consumption and adverse effects associated with opioid administration was recorded.

Results: Thirty seven patients were recruited. Demographical data did not differ significantly between the groups (Table 1). Pain scores were similar 12 hours after the surgery at rest [3.8(3.1) vs 3.1(2.9), P=0.55] and at passive movement [6.4(2.8) vs 5.5(3.1), P=0.38] in Infiltration Group compared to the Non-Infiltration group (Fig 1, 2). However two hours after the surgery at rest the pain scores were lower in the infiltration group but didn't reached the statistically significant level.

Cumulative morphine consumption was less in the Infiltration group but didn't reached the statistically significant level [39.7(36.8) vs 52.3(39.1), P=0.41]

Conclusion: Our study results suggesting that is no benefit of the levobupivacaine perisurgical site infiltration in this study circumstance. The results of the study showing that the analgesic consumption were slightly lower in the Infiltration group.

8.2 Introduction

Fractured neck of femur is a common cause of admission to hospital for elderly patients and requires operative fixation. Postoperative pain can delay mobilization and discharge from the hospital. The administration of opioid drugs in the postoperative period is associated with significant adverse effects. Postoperative pain should manage with multi-modal analgesia with additive and synergistic effects. Following total knee replacements local anaesthetic infiltration lead to a significantly decreased duration of hospital stay due to decreased postoperative pain (1). Continuous postoperative wound infiltration after shoulder surgery with ropivacaine, (2 mg/ml and 3.75 mg/ml), results in lower pain scores and opioid requirement compared with infiltration of placebo (2). Effective pain management in the postoperative period is important to aid early mobilization and decrease morbidity (3).

In our hospital, surgical fixation of fractured neck of femur is routinely performed under spinal anaesthesia with intrathecal bupivacaine. This provides excellent conditions for surgery and gives satisfactory analgesia in the early postoperative period. Wound infiltration with local anaesthetic after total hip and knee replacement has been investigated as an alternative method of postoperative analgesia (4-8). It is unclear whether including local anaesthetic peri-surgical site infiltration before wound closure after surgical fixation of fractured neck of femur provides additional pain control. Our hypothesis was that peri-surgical site infiltration, after the surgical fixation of fractured neck of femur, with levobupivacaine (in addition to standard systemic analgesics) decreases pain in the first postoperative day. This technique decreases post-operative systemic opioid requirements and the incidence of associated adverse effects.

To test these hypotheses we propose to carry out a prospective, randomized, double blinded clinical trial in patients undergoing surgical fixation of fractured neck of femur under spinal anaesthesia.

To our knowledge, a study comparing these two techniques has not been performed previously.

Our objective was to evaluate the analgesic efficacy of peri-surgical site infiltration with levobupivacaine local anaesthetic with 1:200,000 epinephrine after the surgical fixation of fractured neck of femur.

Primary outcome was quality of analgesia at 12 hours postoperatively as assessed by verbal rating score (VRS) for pain at rest and on movement.

Secondary outcome measures were i. mobilization as assessed by range of motion of joint and compliance with physiotherapy, ii. opioid consumption in the first 48 hours postoperatively, iii. incidence and severity of systemic morphine side effects (nausea and vomiting, pruritus, sedation, respiratory depression and urinary retention).

8.3 Methods

With institutional ethical approval [Clinical Research Ethics Committee of the Cork Teaching Hospitals, ECM 4(rr) 09/01/13)] a prospective, double-blinded, randomized trial was undertaken at Cork University Hospital, Cork, Ireland between January 2013 and July 2013. Patients was randomly allocated to one of two groups (Infiltration group, Non-infiltration group) using random number tables and a sealed envelope technique. The patients in the non-infiltration group received spinal anaesthesia with intrathecal bupivacaine 0.5% 2.0 ml. The patients in the infiltration group received spinal anaesthesia with intrathecal bupivacaine 0.5% 2.0ml and received peri-surgical site infiltration before wound closure with a solution of levobupivacaine 0.5% 2mg/kg body weight with epinephrine made up to a volume of 1.5ml/kg with saline. The peri-surgical site infiltration was performed by the operator who infiltrated after closure of the fascia, all surgical stratas, in equal proportions for the length of the wound. Written, informed consent was obtained from all patients.

Patients admitted on to the Emergency Department at Cork University Hospital with fractured neck of femur, American Society of Anaesthesiologists grades I -III and aged >60 years, were invited to participate in the study. Exclusion criteria were patient refusal, Mini-Mental Score <25, coagulation disorders, head injury, other associated injuries, loss of consciousness, renal dysfunction and sepsis.

For the patients in both group was prescribed regular postoperative analgesia of paracetamol 1g qds PO/PR, diclofenac 75mg bd PO(under age of 70). Oxycodone (‘Oxynorm’) 5-10mg PO qds/prn was prescribed as breakthrough analgesic. Cyclizine

50 mg i.m. prn/tds was prescribed for nausea and vomiting. If necessary, ondansetron 4-8mg i.v. prn/qds was administered as a rescue anti-emetic.

The patients was assessed at 2, 6, 12, 24 and 48 hours postoperatively. We assessed severity of pain using VRS at rest and on passive movement of the operative hip joint, cumulative morphine consumption, quality of analgesia during early mobilization, and adverse effects associated with opioid administration, [(i) sedation (1, awake; 2-drowsy; 3-asleep, easily rousable; 4-asleep, hard to rouse), (ii) incidence and severity of postoperative nausea (0 - no nausea, 1 – complaints of nausea but tolerable, 2 – needs cyclizine 50 mg i.m.), (iii) respiratory depression (ventilatory frequency less than 8 min^{-1}); (iv) pruritus (1-no itch; 2-itching but tolerable; 3-severe itch needs piriton 5 mg i.m.); (v) urinary retention (C- catheterized electively postoperatively; N-no catheter required; R-catheter sited because of urinary retention)]. Patients were asked to rate their satisfaction with perioperative pain management (on 0-10 VRS) and whether they would have the same pain therapy again.

Statistical Analysis

Collected data were examined for normality. Quantitative data e.g. analgesic consumption and visual analog pain scores were examined using the Student-t test. Categorical data were examined using the chi-squared test. Fisher's Exact test was used to compare non-parametric data (i.e. necessity of a urinary catheter). $P<0.05$ was considered significant. Sample size calculation was based on our own previous data. Power analysis showed that a decrease in the VRS for pain (in the infiltration group) of 50% would be clinically relevant. To reliably answer our question, with a power of 0.8 and a statistical significance of 0.05, we calculated that we will require a minimum of 17 patients in each group.

8.4 Results

Thirty seven patients were recruited to this study of whom 30 were managed per protocol (Table 1.). Demographical data did not differ significantly between the groups (Table 2). Pain scores were similar 12 hours after the surgery at rest [3.8(3.1) vs 3.1(2.9), P=0.55] and at passive movement [6.4(2.8) vs 5.5(3.1), P=0.38] in Infiltration Group compared to the Non-Infiltration group (Fig 1, 2). However two hours after the surgery at rest the pain scores were lower in the infiltration group but didn't reached the statistically significant level.

Cumulative morphine consumption was less in the Infiltration group but didn't reached the statistical significancy level [39.7(36.8) vs 52.3(39.1), P=0.41].

We detected no difference in terms of secondary outcomes or opioid adverse events.

8.5 Discussion

Our study results suggesting that is no benefit of the levobupivacaine peri-surgical site infiltration in this study circumstance. The results of the study showing that the analgesic consumption were slightly lower in the Infiltration group.

Intermittent local anaesthetic wound infiltration after internal fixation of femoral neck fractures through intraarticular catheters have some analgesic effect in the postoperative period (9). In shoulder surgery postoperative ropivacaine, ketorolac and morphine injected in intraarticular catheter followed by bolus of local anaeshtetic provided better analgesia in the postoperative period (10). However the results of this study wasn't able to show difference between the peri-surgical site infiltration with local anaesthetic vs. placebo after surgical fixation of hip fractures, in the studies mentioned above was used multiple postoperative injections.

In the total knee replacement cases the periarticular injection with local anaesthetic vs. femoral nerve block resulted with identical analgesic efficacy with avoiding motor block and it's negative functional impact (11,12).

In shoulder, total hip replacement and total knee replacement surgery peri- or intraarticular infiltration with local anaesthetic showed analgesic effect in the postoperative period. We weren't able to show difference in analgesic efficacy with infiltration of local anaesthetic before surgical closer of the wound vs. placebo after surgical fixation of fractured neck of femur.

Our study have some limitations. The study wasn't powered to detect a smaller

difference than 50% so with higher level of power the results might be significant. To clarify this further research would be indicated. The analgesic effect of a single postoperative local anaesthetic peri-surgical site infiltration may worn off earlier than the assessment time point came. Another limitation which might contributed to the negative result was the homogenous patients group. In our practice the patients who had a DHS procedure reporting higher pain scores in the first postoperative day. The number of DHS procedure was double in the infiltration group compared with the non-infiltration group patients.

In conclusion the result of our study suggesting that in this setting peri-surgical site infiltration after surgical fixation of fractured neck of femur have no effect on early postoperative analgesia. Further research are warranted to detect smaller difference in terms of pain or morphine consumption or with different dose or concentration of the local anaesthetic, which may have beneficial effect.

8.6 Tables

Table 1. Flow diagram

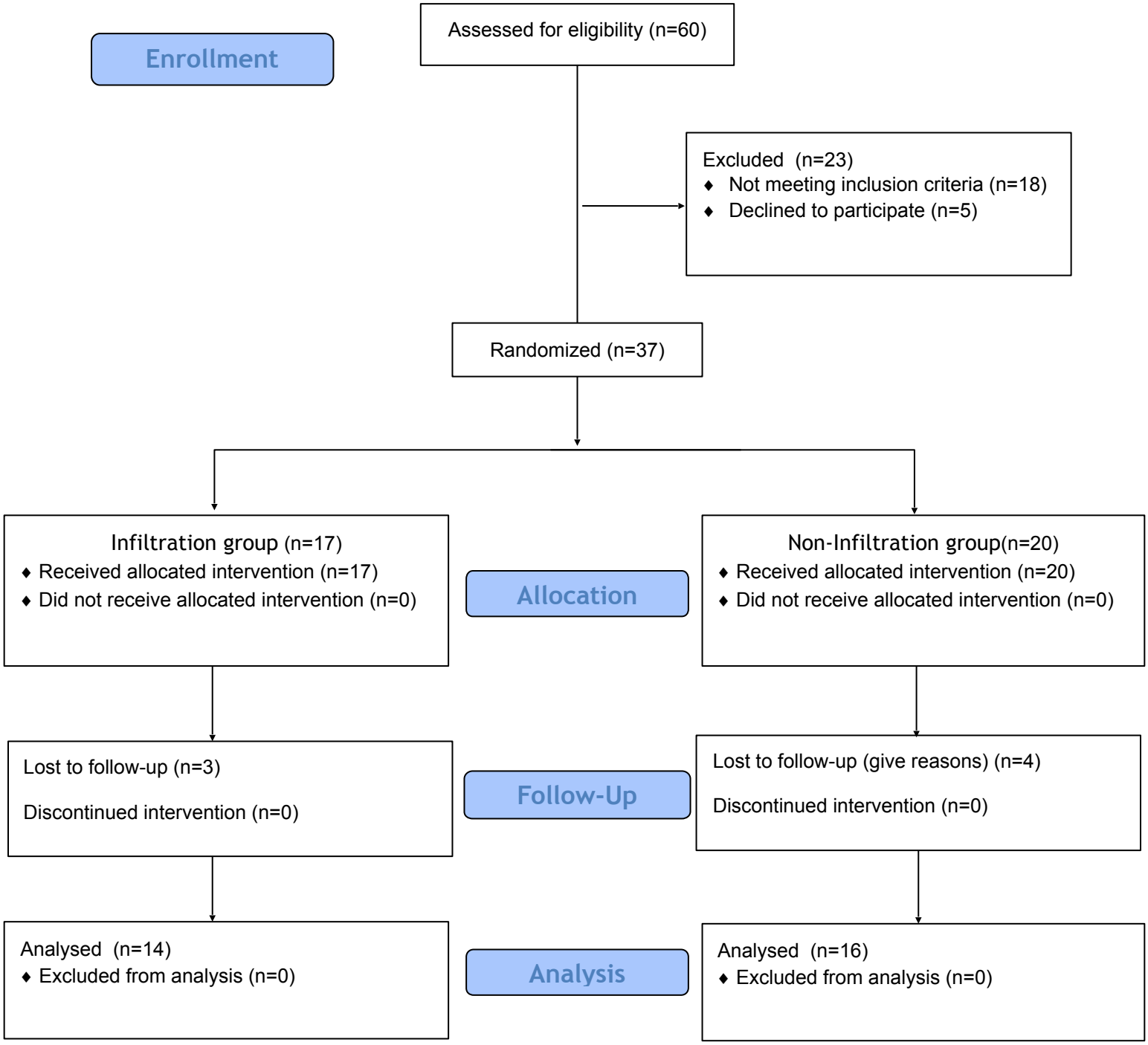


Table 2.

Patients demographic charactheristics

	Infiltration group	No Infiltration group	(p-value)
Gender(Female/Male)	12/5	12/8	
Age(years, mean(SD))	79.4(9.2)	77.5(19.0)	0.51
ASA status I/II/III	2/13/2	2/12/6	
Procedure	8/1/8	4/6/10	
(DHS/IMHS/hemiarhtroplasty)			
BMI (kg/m^2) mean(SD)	24.3(4.3)	25.3(7.6)	0.52
Right/Left	7/10	7/13	

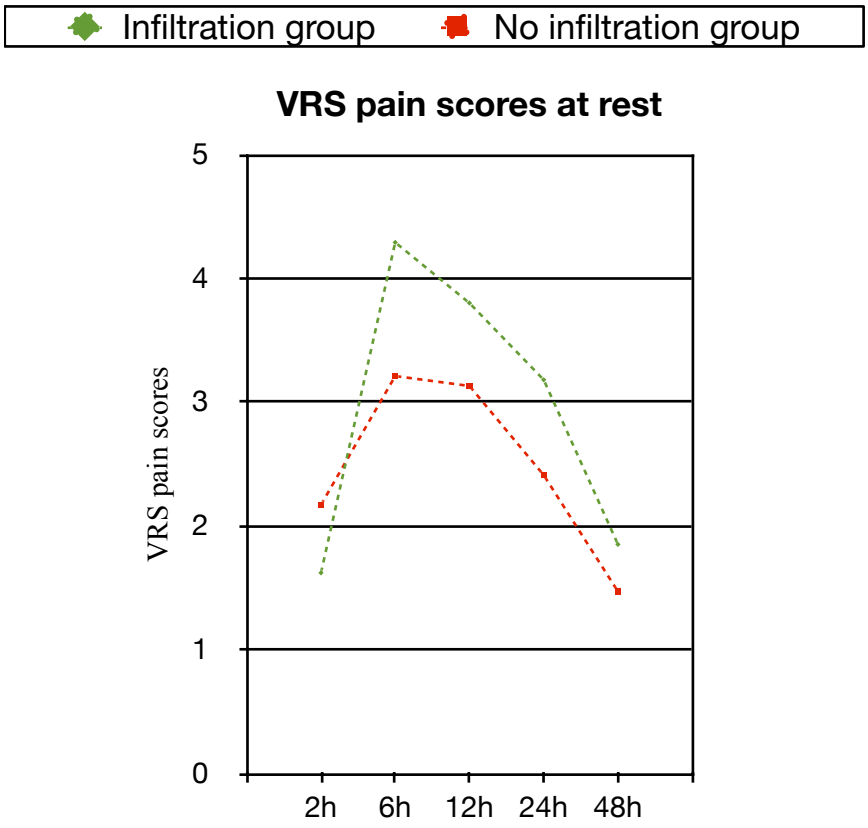
ASA: American Society of Anaesthesiologist physical status,

DHS: Dynamic hip screw,

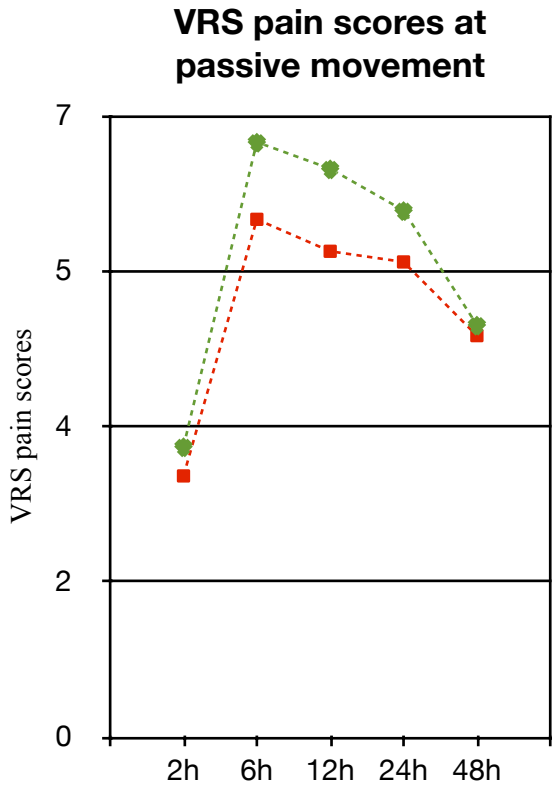
IMHS: Intramedullary hip screw.

Data displayed in mean(SD) and numbers

8.7 Figures



VRS postoperative pain scores



8.8 References to Chapter 8

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Conclusions

9.1 Summary of the main findings

We analyzed the perioperative effects of continuous femoral nerve block, single preoperative dose of i.v. dexamethasone, the intention to deposit local anaesthetic in different location around the femoral nerve during ultrasound guided femoral nerve block, continuous spinal anaesthesia and periarticular local anaesthetic infiltration after the surgical fixation in fractured neck of femur cases.

In the first study: **Analgesic efficacy of continuous femoral nerve block prior to operative fixation of fractured neck of femur** we investigated the effectiveness of continuous femoral nerve block in patients admitted to hospital awaiting operative fixation of fractured neck of femur. In the intervention group we inserted a perineural femoral nerve catheter and after a bolus of local anaesthetic we started an infusion for 72 hours. Continuous femoral nerve block provides more effective perioperative analgesia six hours after the insertion of the catheter than a standard opiate-based regimen for patients undergoing operative fixation of fractured neck of femur. It is associated with lesser opiate use and greater patient satisfaction.

In the second study: **Pain relief effect of a single dose of dexamethasone after operative fixation of fractured neck of femur: randomized, double blinded clinical trial** we studied the effect of a single dose of preoperative dexamethasone in patients undergoing operative fixation of fractured neck of femur. Single dose of preoperative 0.1 mg/kg i.v. dexamethasone in the intervention group decreased the pain scores by 75% six hours after the surgery.

In the third study: **Recovery after fractured neck of femur in elderly** patients recruited in the previous two studies was followed up. The results showed that preoperative administered continuous femoral nerve block and the single dose of preoperative i.v. dexamethasone had no major effect on the functional recovery in the first year after the surgical fixation of fractured neck of femur.

In the fourth study: **Comparing circumferential spread of local anaesthetic with deposition above or below the femoral nerve during ultrasound guided femoral nerve block prior to operative fixation of femoral neck fracture: randomized control trial** we analyzed the intention to deposit the local anaesthetic in different areas around the femoral nerve in ultrasound guided femoral nerve block prior to operative fixation of fractured neck of femur in terms of analgesic efficacy at the positioning for performing spinal anaesthesia.

The results showed no clinical advantage to intending to deposit LA circumferentially during performing femoral nerve block. The intention to deposit the LA above the femoral nerve was similarly effective and needed less needle passes.

In the fifth study: **Initial minimum intrathecal local anaesthetic dose with concomitant femoral nerve block required for operative fixation of fractured neck of femur** we determined the minimum initial local anaesthetic dose needed in the intrathecal catheter to start surgery in 15 minutes. Using the Dixon and Massey's "up-and-down" method, we demonstrated that intrathecal 0.26 ml of 0.5% bupivacaine provided adequate surgical anaesthesia in 50% of cases receiving in 15 minutes an operative fixation of femoral neck fracture. This may be less than that previously

estimated by clinicians and may result in a lesser incidence of severe hypotension. The results of our study may inform clinicians' initial dose selection for continuous spinal anaesthesia and could improve safety of a high risk population of patients.

The sixth study: **Perioperative analgesia following surgery for fractured neck of femur: a comparison of peri-surgical site infiltration of local anaesthetic with systemic postoperative analgesics, randomised, double blinded clinical trial** demonstrated that the local anaesthetic infiltration has no effect on pain scores 12 hours in the surgical fixation of fractured neck of femur.

In addition to this following original body of work a review article was published on **Femoral nerve block** highlighting the use of ultrasound guidance.

9.2 Clinical implications and future directions

Proximal femoral fractures present an unique challenge to anaesthetists, involving the peri-operative care of large numbers of older patients with significant co-morbidities. The majority (95%) of hip fractures occur in patients over the age of 60, 75% occurring in females(1). 1.66 million hip fractures were worldwide in 1990, this population is predicted to grow during the next decades. According to the epidemiological projection, this worldwide annual number will rise to 6.26 million by the year 2050 (2). Of the fractures linked with osteoporosis, hip fractures are most important in terms of death, functional dependence, and social cost (3). The 30 day mortality didn't change significantly in the last decades, it is varying between 5.6 %- 12.3% (4-7).

We don't have enough convincing evidence available from clinical trials about the benefits of regional anaesthesia. This may reduce acute postoperative confusion but no conclusions can be drawn for mortality or other outcomes(8).

Surgery is the best analgesic in hip fractures. Perioperative anaesthetic care may however have some aspects through which we can improve patient care and satisfaction. Our research results added the following to the optimization of perioperative analgesic care: i. in the preoperative period continuous femoral nerve block with low dose of local anaesthetic improved analgesia, ii. a single minor dose of preoperative i.v. dexamethasone improved early postoperative analgesia. iii. Prior to positioning for spinal anaesthesia the intention to deposit local just above the femoral nerve result in the same analgesic effect at positioning to performing spinal as circumferential deposition, with less needle passes, iiii. The use of spinal catheter and lower initial dose of local anaesthetic with the option of topping up the spinal anaesthesia provided

reliable surgical anaesthesia with improved balance between safety and efficacy. With the additional potential beneficial treatments we increased the range of the anaesthetic options for hip fracture care. As each patient is individually different, the anaesthetists should tailor the anaesthetic management of each patient. The results of the studies from this thesis is summarized to form a possible guideline for the clinicians, highlighted the main findings (Table 1.).

Although some guidelines favor the use of spinal anaesthesia for all patients undergoing hip fracture repair, unless contraindicated (9) the optimal local anaesthetic for single shot of spinal anaesthesia is still awaited. The way forward to reduce the risk of haemodynamic adverse effects of the intrathecal local anaesthetics in patient may be to lower our doses and administer additional drugs. Opioids and clonidine were used in the past for this purpose without major adverse effects(10). The optimal dose of intrathecal additional clonidine remains unknown(11). Using a spinal catheter with lower doses of local anaesthetics have the ability to combine the advantages of previously mentioned methods, namely to decrease the risk of haemodynamic adverse events and at the same time having the option to administer extra local anaesthetic during surgery if needed.

Ultrasound guided pre- or postoperative peripheral nerve blockade is already part of our armamentarium in the perioperative anaesthetic care of operative fixation of hip fracture. Our results shown that perioperative CFNB is effective and deposition of the local anesthetic above the femoral nerve during single shot UGFNB is as effective as with circumferential spread of LA around the femoral nerve. However future research on education and training for ultrasound guided peripheral nerve blockade still needed and may result in improved efficacy and widespread use of this technique.

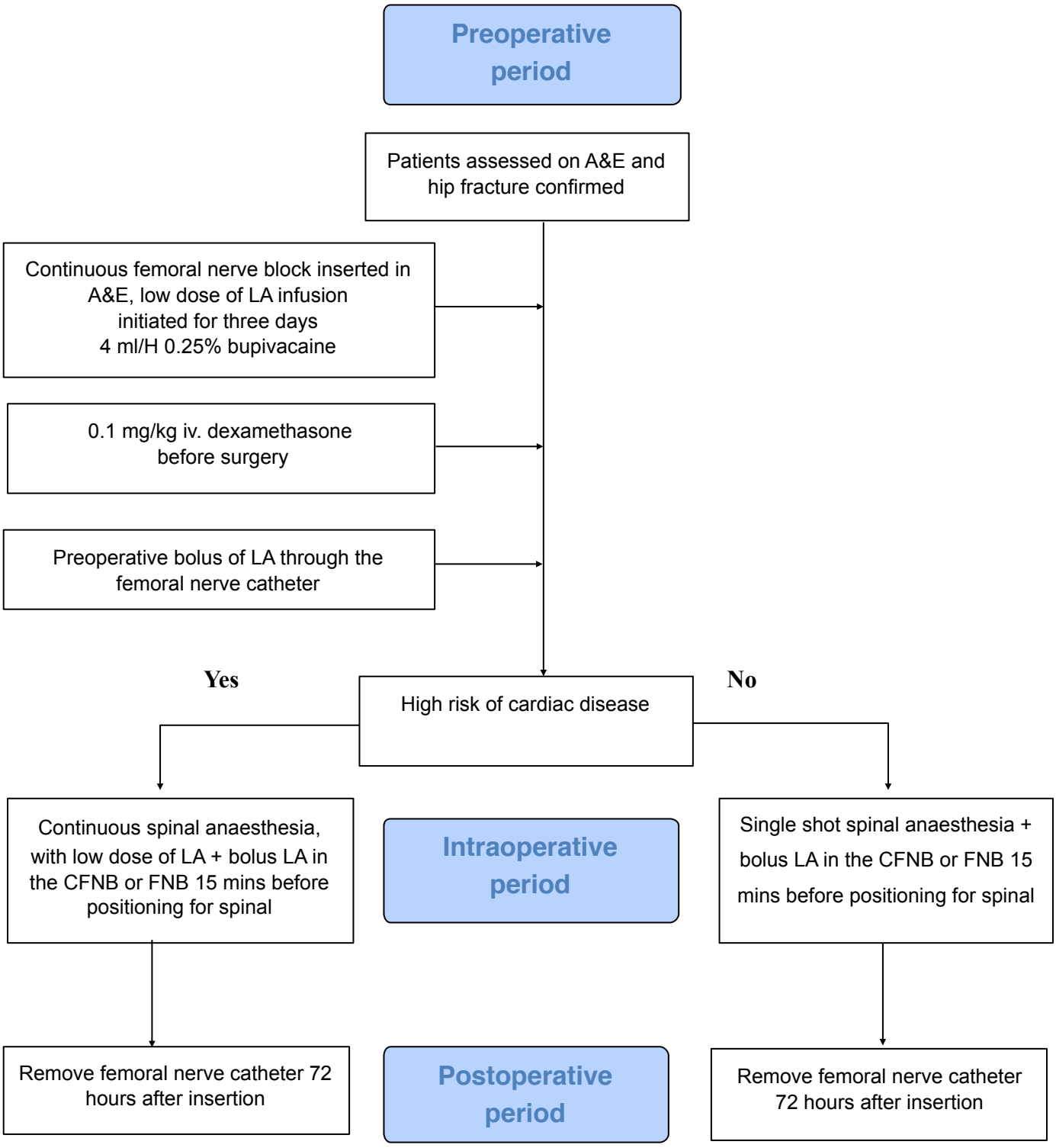
Preoperative dexamethasone has been used in dental surgery(12), laparoscopic cholecystectomy(13-16), thyroidectomy(17) and shown to be safe and effective method to reduce significantly the postoperative analgesic requirement. Our result shown that a single minor preoperative i.v. dose of dexamethasone has analgesic effect in the early postoperative period in hip fractures. The exact time of administration, the dose and dose related side effect of dexamethasone remains unclear and further research is still awaiting in this area.

Another area of potential development could be related to more accurate positioned of the tip of the peripheral nerve blockade needle beside the target nerve.

The proximal femur fracture patients' management required multidisciplinary care(1), close collaboration with general practitioners, community assessment nurses, Emergency Department staff, orthopaedic surgeons, orthopaedic nursing staff, orthogeriatricians, anaesthetists, physio and occupational therapists. Preoperative anaesthetic assessment of this patients is mandatory, this allows a careful planning for anaesthesia. Audits and research in this area may improve the multidisciplinary care and selection of the anaesthetic technique individualized to the patient.

9.3 Table for Chapter 9

Table 1. **Hip fracture guideline**



9.3 References for Chapter 9

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Appendices

10.1 Original publication of the review article

Review

Medical Ultrasonography
2010, Vol. 12, no. 2, 139-144

Femoral nerve blockade

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Abstract

Femoral nerve blockade is the most widely performed lower limb block. Methods of femoral nerve blockade are briefly reviewed with particular reference to ultrasound guidance.

Keywords: femoral nerve, anaesthetic block, ultrasonography

Rezumat

Blocajul anestezic al nervului femural este cel mai frecvent blocaj efectuat la nivelul membrului inferior. Sunt trecute în revistă metodele de blocaj anestezic ale nervului femural, cu referire în particular la ghidajul ecografic

Cuvinte cheie: nerv femural, bloc anestezic, ecografie

Introduction

Femoral nerve blockade is widely practiced by phisicians in a variety of circumstances, i.e. analgesia for femur fractures in pre-hospital medicine [1], in the accident and emergency departments and in the clinical setting of perioperative care [2]. Femoral nerve blockade is likely to be the most widely performed lower limb block.

Anatomy

The femoral nerve is a terminal branch of the lumbar plexus [3]. It arises from the ventral rami of the second, third and fourth lumbar nerves and it descends through the substance of the psoas major muscle, emerging from the muscle at the lower part of its lateral border. It runs in the gutter of the iliopsoas muscle under the fascia iliaca, it then passes behind the inguinal ligament and enters the femoral triangle. At this level the fascia along the internal aspect of the iliopsoas thickens to form the iliopectineal band that separates the femoral vessels from the nerve.

The femoral nerve divides into superficial and deep terminal branches in the femoral triangle [4]. The superficial branches include the lateral musculocutaneous nerve which innervates the sartorius muscle and the skin of the anterior thigh; and the medial musculocutaneous nerve which divides to innervate the pectineus muscle, the articular surface of the acetabulum, and skin of the medial thigh.

The deep branches comprise the saphenous nerve and the branches which innervate the quadriceps muscles - rectus femoris, vastus lateralis, vastus medialis and vastus intermedius muscles. The saphenous nerve is sensory only and supplies the skin of the medial leg as far as the medial malleolus. In the thigh it descends with the nerve to the vastus medialis muscle.

Applied anatomy

Dermatomal innervation

Femoral nerve blockade results in anaesthesia of the skin of the antero-medial thigh (femoral nerve), knee (femoral nerve) and the medial border of the leg (saphenous nerve).

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Myotomal innervation

The main muscles innervated by the femoral nerve are the sartorius, quadriceps femoris (rectus femoris, vastus lateralis, intermedius and medialis), as well as the iliopsoas and pectineus muscles.

Osteotomal innervation

The femoral nerve innervates the anterior wall of the hip joint, the anterior aspect of the femur and the anteromedial walls of the knee joint.

Indications

Analgesia in the following scenarios

Fractured neck/shaft of femur

Hip joint (following total hip replacement)

Knee joint (following anterior cruciate ligament repair, total knee replacement)

Anaesthesia. Alone: skin graft from the anterior aspect of the thigh, muscle biopsy

In combination with a popliteal block (any procedure on the foot and lower leg), with high sciatic and obturator blocks (any procedure on the lower limb)

Targeted femoral nerve block

The femoral nerve is situated most superficially at the level of inguinal crease, although its relative depth may vary [3]. Femoral nerve blockade has been attempted blindly in the past, with a sharp needle, 1-1.5 cm laterally from the femoral pulse. Paraesthesia technique followed, based on eliciting paraesthesia in the femoral innervation area. Peripheral nerve stimulation techniques have the added benefit of targeting more precisely the nerve while minimizing potential nerve injury. The classical endpoint for injection in the case nerve stimulator guided femoral block is the 'dancing patella' sign, i.e. quadriceps contraction [2].

Fascia iliaca (iliacus) compartment block – an indirect femoral nerve block

Following an injection under the fascia iliaca in the inguinal region (iliacus or fascia iliaca block), anaesthetic solution is distributed to the femoral nerve (>90%), lateral femoral cutaneous nerve (>85%) and occasionally to the genito-femoral nerve.

The fascia iliaca block is very similar to the femoral nerve block in terms of extent of blockade, although the lateral femoral cutaneous nerve (sometimes called the lateral cutaneous nerve of the thigh) is blocked more consistently with this approach compared with a femoral block [3].

The fascia iliaca block was initially described in children and then extrapolated to adults. The main landmark for its performance is the inguinal ligament outlined by a line connecting the anterior superior iliac spine and the pubic tubercle. The needle insertion point is approximately one cm below of the junction between the outer on-third and inner two-thirds of this line. Block performance is based on the highly unrelible 'two pop' feel as a result of piercing the fascia lata and the fascia iliaca [5].

Sonoanatomy

The femoral nerve block is ideally suited for ultrasound guidance with a high frequency (>10 MHz) linear probe because of the relatively superficial position of the femoral nerve [6, 7]. Distal to the inguinal ligament, the femoral nerve lies lateral to the femoral artery, deep to the fascia iliaca, on the anterior aspect of the iliopsoas muscle (fig 1). The artery is easily located due to its pulsation and/or flow identified by doppler (fig 2, fig 3). The femoral nerve is often found within a triangular hyperechoic region, lateral to the femoral artery and superficial to the iliopsoas muscle. The femoral nerve may be quite thin and flat in this region as the nerve fans out into multiple branches. The nerve may also appear as a biconvex or oval hyperechoic structure.

From superficial to deep, the fascia lata is first encountered, then the fascia iliaca (hyperechoic line). Inguinal lymph nodes also appear hyperechoic and hence may be confused with the nerve in the short axis view. A nerve is a continuous structure that can be traced (by scanning proximally and distally) while a lymph node is not and can be seen only in a discrete location.

The ultimate aim is to deposit local anaesthetic solution adjacent to the femoral nerve in order to ensure a successful block. Similarly to other ultrasound guided blocks, an aggressive and a more conservative approach may be described. The first would typically aim to surround the femoral nerve with a pool of local anaesthetic (often referred to as the 'doughnut sign'), and would correspond to the classical femoral nerve block (fig 4). Ultrasound guidance, through a more precise injection has allowed for a reduction of the effective local anaesthetic dose. The conservative approach would correspond to the classical fascia iliaca block, i.e. injecting at a distance from the nerve under the fascia iliaca and observing the spread of local anaesthetic solution towards the femoral nerve. Due to contrast enhancement, following injection of the hypoechoic local anaesthetic, often the hyperechoic femoral nerve becomes more prominent (fig 5).

Ultrasound guidance may facilitate peripheral nerve blockade in many ways, including visualization of the

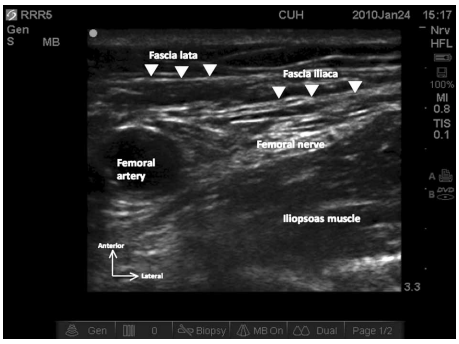


Fig 1. Scout scan of the left femoral nerve (short axis) at the level of inguinal crease (lateral to femoral artery, deep to fascia lata, superficial to iliopsoas muscle)

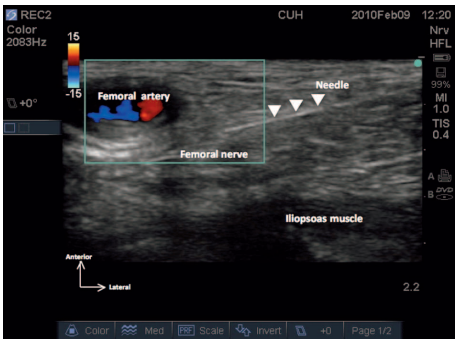


Fig 2. Doppler identification of intravascular flow; needle in plane

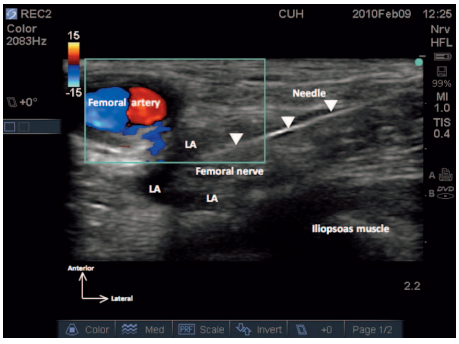


Fig 3. Circumferential spread of local anaesthetic solution following injection between femoral artery and nerve (aggressive appoach). Doppler used to avoid intravascular injection

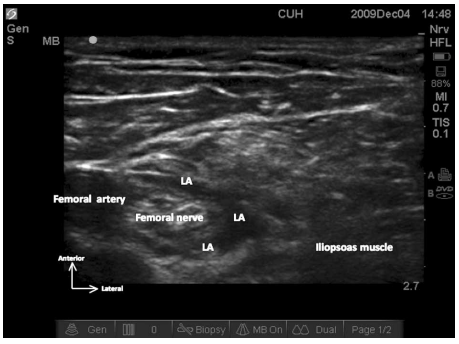


Fig 4. Femoral nerve surrounded by local anaesthetic solution following needle withdrawal. LA local anaesthetic solution

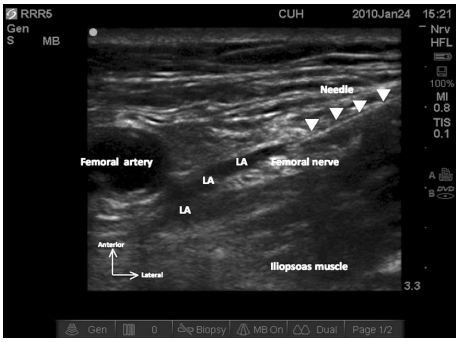


Fig 5. Left femoral nerve (short axis) more visible following injection of some local anaesthetic solution around it. The needle is approaching in plane. LA local anaesthetic solution

neural target and its surrounding structures, assessment of adequate needle-tip position, observation of local anaesthetic spread around the target nerve, identification of anomalous anatomy or pathology. Ultrasound guidance holds the potential to minimize complications associated with peripheral nerve blockade such as nerve injury or inadvertent intravascular injection of local anaesthetics. However, no clinical studies exist to confirm or refute these potential advantages of ultrasound guidance, and both nerve injury and intravascular injection has occurred despite its use. In addition the technique is highly operator dependent [8].

Visualization of nerves with ultrasound depends on the operator's ability to properly locate the nerve, handle the transducer, maximize the ultrasound machine capability (e.g., the choice of transducer frequency, proper adjustment of depth, focus and gain and the use of com-

pound imaging). Needling requires considerable hand-eye coordination [9].

Single shot

Out of plane needle insertion technique

A 5 cm 22 G insulated needle (preferably with an echogenic tip design) is inserted perpendicular to the transducer and the ultrasound beam (fig 6a). In this case, only the cross section of the needle shaft (a white dot) may be observed during needle advancement. It can be technically challenging to track the location of the needle tip during out of plane needle insertion. Gentle scanning over the needle may prove useful. Injection of a small amount of fluid e.g., glucose 5% or local anaestehtic (hydrolocalization) may expand the femoral triangle and the hypoechoic fluid collection can bring the hyperechoic nerve and the fascia iliaca into view [7]. Correct needle tip location may be confirmed by electrical stimulation aiming for patellar movement.

In plane needle insertion technique

The in plane approach is most commonly used for femoral nerve block by aligning the block needle with the ultrasound beam (fig 2, 3, 5, 7). The needle shaft and tip can be visualized distinctly but it may take a longer time to align the needle with the beam compared to the out of plane approach. Also, depending on the depth of femoral nerve, a longer needle may be required.

Fascia iliaca block

In essence this is an indirect femoral nerve block (fig 7). Traditionally, a blunt needle has been used to perform a 'two pop' technique at the junction of lateral one third and medial two thirds of the inguinal ligament. Whit ultrasound, whether using and in plane or out of plane approach at couple of centimeters laterally from the neurovascular bundle, the aim is to pierce both fascia lata and fascia iliaca and observe the spread of local anaesthetic solution medially towards the femoral nerve. Higher volumes of local anaesthetic solution may be necessary [5].

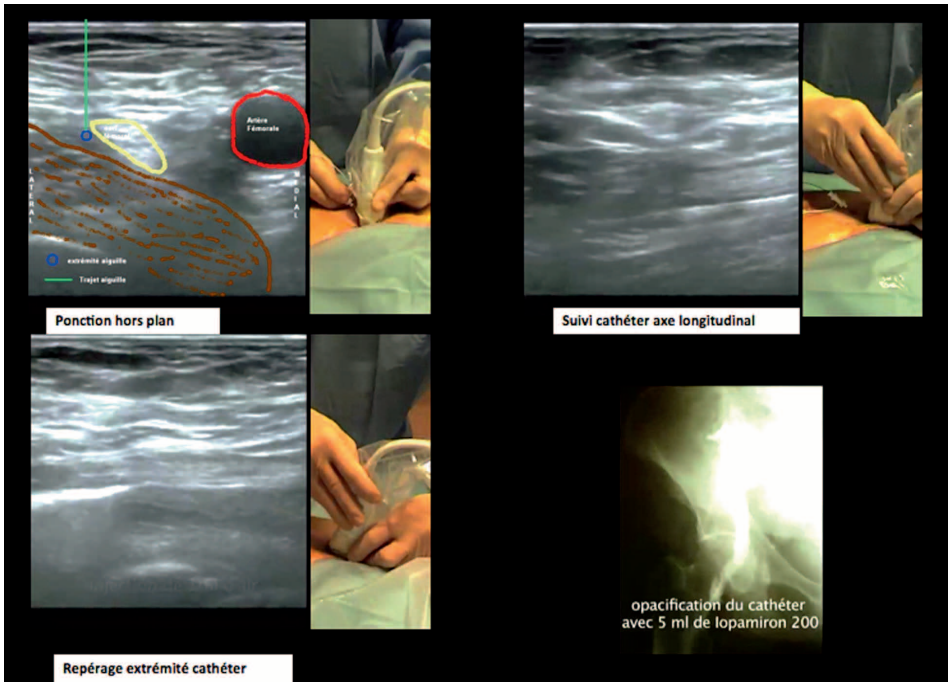


Fig 6. Sequence of catheter insertion; a) top left: out of plane puncture adjacent to femoral nerve; b) top right: probe turned to visualize nerve in long axis, catheter inserted through needle appears alongside the nerve; c) bottom left: catheter tip confirmed by injecting 1 mL of air; d) bottom right: correct position of catheter confirmed with opacification

Catheter technique

Duration of analgesia may be extended beyond the pharmacologic effect of a single shot injection using perineural indwelling catheters through which local anaesthetic solution may be administered up to 72 hours [10]. Regimens include repeted boli, continuous infusions or patient controlled boli with or without a background infusion of local anaesthetic solutions. Risk of infection may be minimized by strictly adhering to sterility guidelines (mask, sterile gown, gloves, ultrasound probe sheat and gel, antiseptic solution, etc).

Several technical issues are specific to continuous perineural catheter placement [11, 12]. The optimal method is still unknown. Herein we illustrate the technique most often used at our institution (fig 6) whereby the nerve (in short axis) is approached through an out of plane needle insertion using a catheter trough needle technique (fig 6a). Local anaesthetic solution may be injected at this point to dilate the perineural space. This will facilitate further visualization of the nerve and the actual catheter insertion and advancement. The next manouvre is to turn the ultrasound probe aiming to visualize both the nerve in long axis and the needle in plane (fig 6b, c, 8). In this view the catheter may be visualized appearing through the needle tip and positioning itself alongside the nerve (fig 9). A small volume of air may be injected to confirm the location of the catheter tip (fig 10). The ultimate confirmation, although not performed routinely, is opacification of the catheter (fig 6d). Alternatively, the catheteter may be inserted blindly through the neeedle and its position subsequently confirmed using ultrasound as described (fig 11, 12).

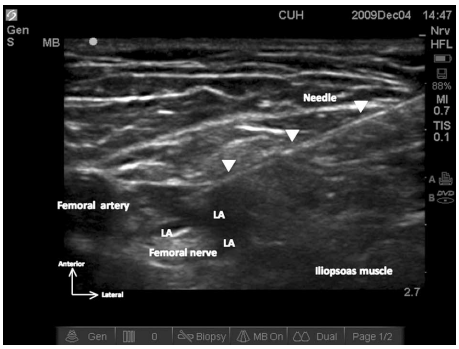


Fig 7. Needle in plane, femoral nerve in short axis, local anaesthetic being deposited around it (needle tip at distance from nerve, conservative approach). LA local anaesthetic solution

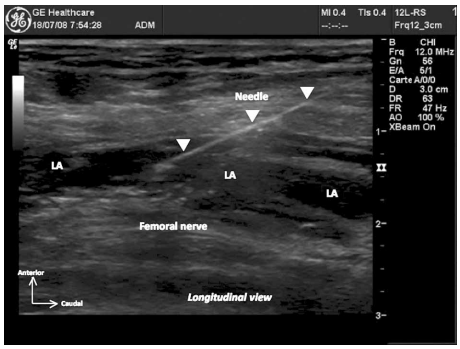


Fig 8. Needle approaching in plane, femoral nerve visualised in long axis. LA local anaesthetic solution

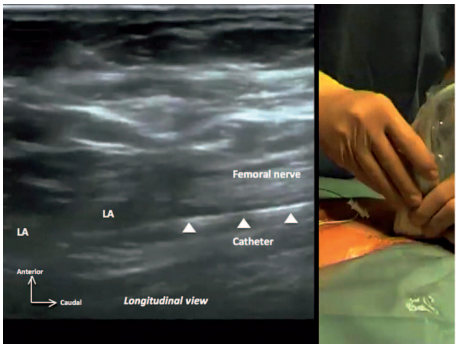


Fig 9. The echogenic catheter parallel to femoral nerve in longitudinal view

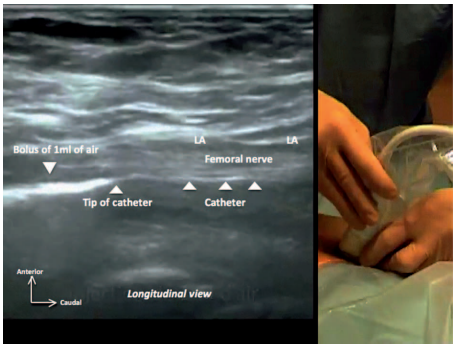


Fig 10. Correct position of catheter tip verified with injection of an air bubble

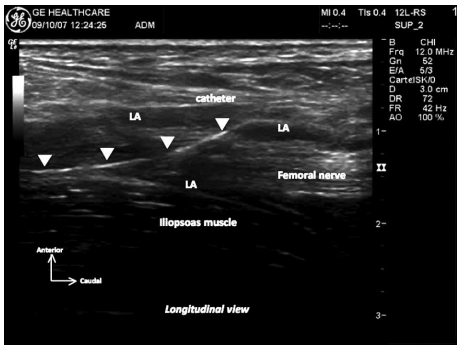


Fig 11. Catheter crossing the femoral nerve and disappearing in the pelvis alongside the nerve. LA local anaesthetic solution

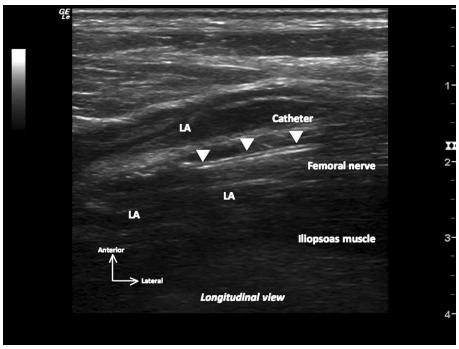


Fig 12. Catheter adjacent to femoral nerve in long axis surrounded by local anaesthetic solution (LA)

Future directions

Currently, research is ongoing with regards to minimal efficient local anaesthetic dose and volume, with regards to the effect of different distribution patterns of local aanesthetic around nerves, finding the best delivery, dosing strategy and drug combinations for perineural infusions to mention but a few. Similarly, the ideal local anaesthetic is still awaited, to provide prolonged selective sensory blockade with no motor block.

In conclusion, a simple technique is described to perform a femoral nerve block using ultrasound guidance. With increasingly available ultrasound machines it is concievable that this technique will become standard practice in the near future. However, adherence to standard monitoring, asepsis, prevention of complications and immediate availability of emergency drugs should not be underestimated.

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10.2 Original publication of Study 1.

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Perioperative Medicine

RESEARCH Open Access

Analgesic efficacy of continuous femoral nerve block commenced prior to operative fixation of fractured neck of femur

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Abstract

Background: Peripheral nerve blocks are effective in treating acute pain, thereby minimizing the requirement for opiate analgesics. Fractured neck of femur (FNF) is a common, painful injury. The provision of effective analgesia to this cohort is challenging but an important determinant of their functional outcome. We investigated the analgesic efficacy of continuous femoral nerve block (CFNB) in patients with FNF.

Methods: Following institutional ethical approval and with informed consent, patients awaiting FNF surgery were randomly allocated to receive either standard opiate-based analgesia (Group 1) or a femoral perineural catheter (Group 2). Patients in Group 1 received parenteral morphine as required. Those in Group 2 received a CFNB comprising a bolus of local anaesthetic followed by a continuous infusion of 0.25% bupivacaine. For both Groups, rescue analgesia consisted of intramuscular morphine as required and all patients received paracetamol regularly. Pain was assessed using a visual analogue scale at rest and during passive movement (dynamic pain score) at 30 min following first analgesic intervention and six hourly thereafter for 72 hours. Patient satisfaction with the analgesic regimen received was recorded using verbal rating scores (0-10). The primary outcome measured was dynamic pain score from initial analgesic intervention to 72 hours later.

Results: Of 27 recruited, 24 patients successfully completed the study protocol and underwent per protocol analysis. The intervals from recruitment to the study until surgery were similar in both groups [31.4(17.7) vs 27.5 (14.2) h, P = 0.57]. The groups were similar in terms of baseline clinical characteristics. For patients in Group 2, pain scores at rest were less than those reported by patients in Group 1 [9.5(9.4) vs 31(28), P = 0.031]. Dynamic pain scores reported by patients in Group 2 were less at each time point from 30 min up to 54 hours [e.g at 6 h 30.7 (23.4) vs 67.0(32.0), P = 0.004]. Cumulative morphine consumption over 72 h was less in Group 2. Patient satisfaction scores were greater in Group 2 [9.4(1.1) vs 7.6(1.8), P = 0.014].

Conclusions: CFNB provides more effective perioperative analgesia than a standard opiate-based regimen for patients undergoing fixation of FNF. It is associated with lesser opiate use and greater patient satisfaction.

Keywords: Perioperative pain relief, Hip fractured neck of femur, Continuous femoral nerve block

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Background

Fractured neck of femur (FNF) is a common, painful reason for hospital admission in elderly patients [1]. Pain management in the elderly can be challenging due to the presence of co-morbidities, altered pharmacokinetics and pharmacodynamics. Despite clinical guidelines favoring surgical repair of FNF within 24 hours of injury [2] patients may wait considerable periods of time for their turn in the operating room. In this context, preoperative pain is an important distressing factor.

The sensory innervation of the proximal femur and a variable portion of the intra-capsular neck of femur arise from the femoral nerve [3]. Femoral nerve block is effective in providing analgesia for femur factures, and has been previously described in FNF [4]. Perineural catheter placement permits the provision of continuous peripheral nerve block, thereby extending the duration of analgesia. Continuous femoral nerve block (CFNB) may therefore have a role in the provision of high quality analgesia in patients awaiting surgery for FNF. Such regional analgesia techniques may improve the quality of pain relief and potentially limit both opiate use and associated opiate-related side effects [5].

It is not known whether CFNB improves analgesic outcomes in elderly patients presenting acutely with FNF. We conducted a study to compare the analgesic efficacy of CFNB and conventional parenteral opiate analgesia in this patient group. Our hypothesis states that continuous femoral nerve block provides better peri-operative analgesia than standard parenteral opiate regimens in patients awaiting surgery to repair FNF.

Methods

Ethical approval was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals. Written, informed consent was obtained from all patients. Patients presenting via the emergency room of Cork University Hospital with fractured neck of femur, American Society of Anesthesiologists grades I to III and aged above 50 years, were invited to participate in the study. Exclusion criteria included patient refusal, the presence of more than one fracture; Mini-Mental Score <22 [6]; coagulation disorders; head injury; loss of consciousness; 10 mg or more morphine administration pre-hospital; acute intercurrent heart disease; allergy to bupivacaine, morphine or paracetamol; skin lesions/infection at block site; and renal dysfunction. Patients with evidence of systemic infections (clinically defined or elevated C-reactive protein levels, leucocytosis, or body temperature higher than 37.8°C) were also excluded.

On recruitment to the study, patients were randomized using a random number sequence and sealed envelopes. Those randomized to Group 1 received standard analgesia consisting of paracetamol 1 g po 6 hourly and parenteral morphine up to 0.1 mg/kg im 4 hourly as required. Patients in Group 2 received 10 ml of 2% lidocaine and 10 ml of 0.5% bupivacaine after repeated negative aspirations slowly over two to three minutes via a perineural femoral catheter followed by 0.25% bupivacaine infused at 4 ml per hour for 72 hours. They also received paracetamol 1 g po 6 hourly. Breakthrough pain in Group 2 was treated with intramuscular morphine as required.

Cyclizine 50 mg im 8 hourly as required was used to treat nausea and vomiting.

Anaesthesia for surgical repair FNF was provided using an intrathecal block. Fifteen minutes prior to positioning for spinal anaesthesia, a lidocaine bolus (10 ml 2% lidocaine) was administered through the catheter. On positioning for spinal anaesthesia (fractured limb dependent in view of using weight/height appropriate dose of hyperbaric bupivacaine), additional analgesia was provided at the discretion of the attending anaesthetist.

Continuous femoral block technique

Having attached standard monitoring (non-invasive blood pressure, oxygen saturation and electrocardiography) and inserted a peripheral intravenous cannula, the femoral catheter was placed, in the emergency department, using nerve stimulation by the primary investigator (SS). The needle insertion point was first determined using predefined landmarks. A skin mark was placed one centimeter caudal to the inguinal ligament and one centimeter lateral to the point of maximal palpable pulsation of the femoral artery.

The skin of the anterior thigh was prepared aseptically and a sterile drape was placed. The skin was anaesthetised using a 25 G hypodermic needle and 1% lidocaine. The block needle (Contiplex, BBraun, Melsungen, Germany) was attached to a nerve stimulator set at 2 mA with 2 Hz pulse cycle and pulse duration of 0.1 ms. Appropriate needle position was determined by the presence of quadriceps contractions resulting in patellar movement at a current of 0.4 mA. On attaining this endpoint the needle was immobilized, and following negative aspiration 10 ml 2% lidocaine was injected. The Contiplex cannula was then advanced over the needle, the needle withdrawn and the catheter placed through the cannula 3 cm in cephalad direction. Finally, the cannula was removed and the catheter secured to the skin using an adhesive, transparent dressing. The patient received 10 ml 0.5% bupivacaine, following which a continuous infusion of 0.25% bupivacaine was commenced at 4 ml per hour, delivered via an elastomeric pump (Acemedical, AutoFuser, Seoul, South Korea).

Primary outcome

The primary outcome measure was pain assessed using visual analogue score (VAS 0-100) on passive movement

(30 degree flexion) of the injured limb from initial analgesic intervention until 72 hours thereafter.

Secondary outcomes

Visual analogue scores for pain were measured at rest and passive movement at recruitment, 30 minutes after recruitment and 6 hourly for the next 72 hours. Passive movement was defined as 30 degree flexion of thigh. Pain on positioning for spinal anaesthesia was also recorded (Verbal Rating Score, VRS 0-10). Satisfaction with the analgesic regimen received was measured at the end of the assessment period using a VRS (0-10).

Patients were evaluated for i. Nausea/Vomiting, ii. Pruritus and iii. Excessive sedation (4 on a observational scale 1-4) immediately after initial analgesic intervention and six hourly thereafter for 72 hours.

Adverse events were recorded by the attending anaesthetist on a dedicated data sheet.

Statistical analysis

Our study was powered to detect a 50% reduction in VAS pain score six hours after recruitment. With alpha error rate of 0.05 and power of 0.80, it was estimated that 24 patients would be required. Assuming 15% exclusion rate, we planned to recruit 27 patients. Statistical analysis was performed using EpiInfo™ 2002 (Centers for Disease Control and Prevention) statistics software. Quantitative data were analyzed using ANOVA or Fisher Exact test. Categorical data were examined by Kruskal-Wallis test.

Results

With initial ethics approval and having obtained written informed consent 27 (of 57 approached) patients were recruited to the study. Three patients were subsequently excluded leaving 24 patients for final analysis (12 patients in Group 1; 12 patients in Group 2). Patients were excluded for the following reasons: (1) elastomeric pump failure resulting in the local anaesthetic administered over less than 54 hours instead of 72 hours, (2) patient confusion with subsequent pump disconnection after 12 hours, (3) late diagnosis of a complicating acetabular fracture.

The two groups were similar in terms of baseline characteristics (Table 1), time to surgery and VRS at positioning for spinal anaesthesia. Overall satisfaction recorded at the 72 hour time point was greater in group 2 (Table 2).

Table 1 Baseline characteristics

	Group 1 N=12	Group 2 N=12
Age (year), mean (SD)	**80.2(5.1)**	**76.0(13.7)**
Female/Male	**10/2**	**6/6**
FNF side left:right	**4/8**	**8/4**

Table 2 Time to surgery, pain at positioning before spinal and satisfaction scores

	Group 1 N=12	Group 2 N=12
Time to surgery, mean(SD)	**27.0(3.6)**	**31.45(17.9)**
VRS before spinal anaesthesia, mean(SD)	**6.44(2.7)**	**3.72(3.2)**
Overall satisfaction VRS, mean(SD)	**7.6(1.8)**	**9.4(1.1), P=0.01**

All femoral nerve blocks including insertion and securing the femoral nerve catheter were completed in less than 15 minutes.

Patients in Group 1 reported greater pain scores (VAS) on passive movement at 6 hours compared to Group 1 [30.7(23.4) vs 67.0(32) mm, p = 0.004]. Pain measured during passive movement was less in Group 2 at each time point up to 54 hours (Figure 1). Similarly, pain measured at rest was consistently less in Group 2 at all time points, reaching the statistical significance level 30 minutes, six and 42 hours after recruitment (Figure 2). Cumulative morphine consumption was lower in Group 2 at each time point except at 30 minutes after recruitment (Figure 3).

Hemodynamic parameters were not different between groups perioperatively up to 66 hours post recruitment. At 66 and 72 hours patients in Group 2 had higher heart rate compared to those in Group 1, i.e. 81.71(7.29) vs 74.09(6.70) bpm, P = 0.03 and 84.88(9.84) vs 73.27 (11.03) bpm, P = 0.02, respectively (Figure 4). Respiratory rate was higher in Group 1 compared to Group 2 at 12 h [(17.81 (1.40) vs 16.16 (2.16) per minute, P = 0.04] and 30 h post recruitment [18.36(1.74) vs 16.18(2.04) per minute, P = 0.01] (Figure 4).

The intervals from recruitment to the study until surgery is similar to intervals reported in a previous study [7] and were similar in both groups [27.1(13.6) h vs. 31.5 (17.9), P = 0.25]. Pharmacological agents used for sedation and analgesia for positioning of patients in Group 1 were fentanyl (1 instance), fentanyl plus midazolam (3 patients), propofol plus fentanyl (2 patients). No medication was administered for this purpose to patients in Group 2.

The incidence of nausea/vomiting [3/12 (25%) vs. 4/12 (33%) in Group 1 and 2 respectively], pruritus [2/12 (16.6%) vs. 1/12 (8.3%) in Group 1. and 2. respectively] were similar in the two groups ($P < 0.05$). The incidence of excessive sedation was also similar in the two groups [1/12 (8.3%) vs. 1/12 (8.3%) in both group].

A trend towards lesser pain sensation (VRS) was identified in Group 2 vs Group 1 at positioning for spinal anaesthesia [3.7(3.2) vs 5.4(2.7), P = 0.10], although this did not reach statistical significance.

Scores for patients satisfaction with analgesia overall were greater in Group 2 [9.4(1.1) vs 7.6(1.8), P = 0.014].

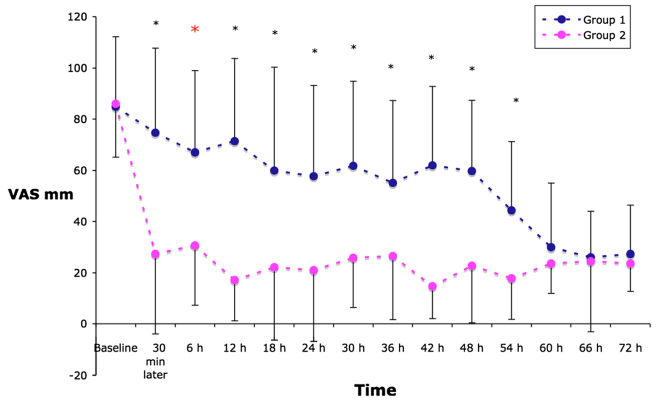


Figure 1 VAS pain scores at passive movement.

Discussion

The most important finding of our study was that continuous femoral nerve blockade offered superior analgesia compared to systemic opioids in the period around operative fixation of fractured neck of femur. In addition, CFNB it was associated with greater patient satisfaction.

Best practice review of the care of patients with fractured neck of femur included a continuous femoral nerve block as analgesia in the Emergency Department [8], however this is not common practice. When performed at all, usually a single shot femoral nerve block is administered by physicians in the emergency department [9] or in the pre-hospital setting [10].

Our study demonstrated feasibility of continuous femoral nerve block in this clinical context. The femoral perineural catheter was successfully placed in each of the 15 patients randomized to Group 2. The true economic input of the use of perineural catheters and elastomeric pumps requires further evaluation.

Opioid consumption was not eliminated by the presence of a perineural catheter. This may account for the presence of morphine associated side effects in this group. A logical explanation for this is the sciatic contribution to the innervation to the femur and that of the lateral cutaneous nerve of the thigh to the surgical incision in the postoperative period. Our chosen continuous

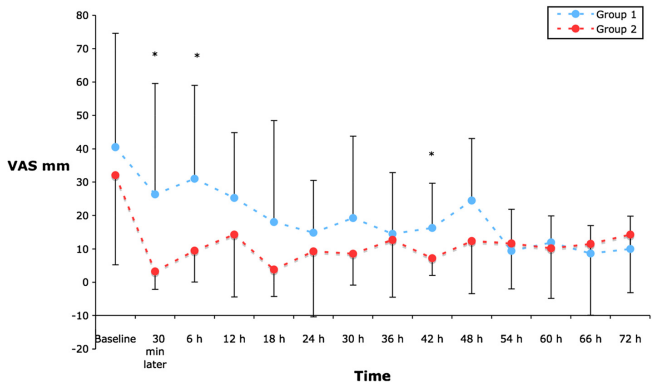


Figure 2 VAS pain scores at rest.

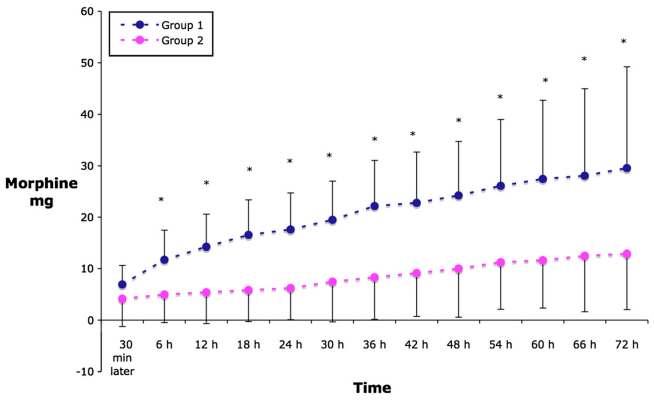


Figure 3 Cumulative morphine consumption.

infusion regime, while limiting local anaesthetic dose and potential toxicity, may have decreased the spread of local anaesthetic towards the lateral cutaneous nerve of the thigh.

In our study, the average intervals between initial analgesic intervention and surgery were 27.1 and 31.5 hours (Groups 1 and 2 respectively). Therefore the first bolus of 10 mls of bupivavacaine probably had minimal effect at the time of surgery. We believe that one of the benefits of the combined bolus + continuous infusion is that it is suitable in a setting in which the duration of the need for potent analgesia is variable and unpredictable (such as for patients with FNF). Cuvillon et al [11] have demonstrated that the duration of a single bolus of bupivacaine 0.5% 20 mL for FNB is 22 h (range 15-32). Thus the analgesic benefits (in the 72 hour study interval defined for this investigation) of the CFNB technique were of greater importance preoperatively.

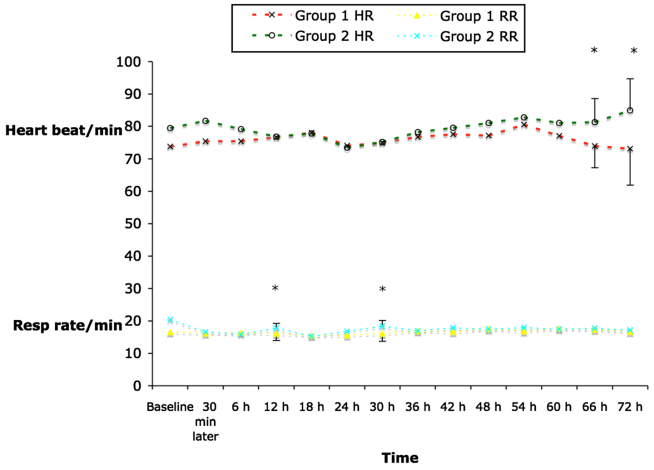


Figure 4 Haemodynamical parameters.

There are several limitations to this study. For ethical and economic reasons, it was not possible to use a double-blinded methodology. The authors considered it to be ethically unacceptable to insert a placebo femoral nerve catheter for blinding purposes only. At our institution, the standard dressing employed for securing a femoral nerve catheter comprises a transparent adhesive layer (usually Tegaderm™ Film, 3 M). This made it unfeasible to apply a "dummy" catheter to the groin. A patient controlled analgesia (PCA) pump would have allowed a more precise measurement of parenteral opioid consumption. Analgesia for positioning prior to spinal anaesthesia was not standardized, and may account for the observed results. Outcomes such as time to mobilization, postoperative respiratory or cardiovascular morbidities and time to achieve discharged criteria were not assessed. One cohort of patients, the confused elderly, which might be expected to benefit most from this intervention were not studied for ethical reasons (difficulty ensuring that consent was informed). The interval from initiating analgesic management until surgery were similar in the two Groups. As we arbitrarily selected a cut-off time of 72 hours for the continuous perineural blockade, our results contain both pre- and postoperative parameters. We did not specifically address whether any benefits associated with the catheter occurred pre- or postoperatively.

Although ultrasound guidance was not used in this study, we believe that it would enhance the benefits of the CFNB technique. Specifically it may minimize the patient discomfort associated with use of peripheral nerve stimulation during the nerve block procedure and, in expert hands, may decrease the likelihood of block failure or nerve injury.

Our study reflects other available evidence substantiating the use of continuous peripheral nerve block analgesia in FNF [12]. Whether this has an impact on early mobilization or long term rehabilitation requires further research.

Conclusions

We conclude that, compared with a systemic opiate based regimen, continuous femoral nerve blockade provides superior perioperative analgesia for patients undergoing operative fixation of fractured neck of femur.

Competing interests
The authors declare that they have no competing interests.

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Authors' contributions
GI: participated in the design of the study, coordination of data collection and in manuscript preparation. BO'D: participated in the design of the study and manuscript preparation. PS: participated in the data collection and in statistical analysis. IA: participated in the data collection. NS: participated in the data collection. GS: participated in the design of the study, coordination of data collection and manuscript preparation. All authors read and approved the final manuscript.

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RESEARCH ARTICLE Open Access

A comparison of three techniques (local anesthetic deposited circumferential to vs. above vs. below the nerve) for ultrasound guided femoral nerve block

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Abstract

Background: Fractured neck of femur generally requires operative fixation and is a common cause of admission to hospital. The combination of femoral nerve block and spinal anesthesia is a common anesthetic technique used to facilitate the surgical procedure. The optimal disposition of local anesthetic (LA) relative the femoral nerve (FN) has not been defined. Our hypothesis was: that the deposition of LA relative to the FN influences the quality of analgesia for positioning of the patient for performance of spinal anesthesia. The primary outcome was verbal rating (VRS) pain scores 0–10 assessed immediately after positioning the patient to perform spinal anesthesia.

Methods: With Institutional ethical approval and having obtained written informed consent from each, 52 patients were studied. The study was registered with ClinicalTrials.gov (NCT01527812). Patients were randomly allocated to undergo to one of three groups namely: intention to deposit lidocaine 2% (15 ml) i. above (Group A), ii. below (Group B), iii. circumferential (Group C) to the FN. A blinded observer assessed i. the sensory nerve block (cold) in the areas of the terminal branches of the FN and ii. VRS pain scores on passive movement from block completion at 5 minutes intervals for 30 minutes. Immediately after positioning the patient for spinal anesthesia, VRS pain scores were recorded.

Results: Pain VRS scores during positioning were similar in the three groups [Above group/Below group/Circumferential group: 2(0–9)/0(0–10)/3(0–10), median(range), p:0.32]. The block was deemed to have failed in 20%, 47% and 12% in the Above group, Below group and Circumferential group respectively. The median number of needle passes was greater in the Circumferential group compared with the Above group (p:0.009). Patient satisfaction was greatest in the Circumferential group [mean satisfaction scores were 83.5(19.8)/88.1(20.5)/93.8(12.3), [mean(SD), p=0.04] in the Above, Below and Circumferential groups respectively.

Conclusions: We conclude that there is no clinical advantage to attempting to deposit LA circumferential to the femoral nerve (relative to depositing LA either above or below the nerve), during femoral nerve block in this setting.

Keywords: Optimal positioning of the local anesthetic, Femoral nerve block

Background

Fractured neck of femur (FNF) often requires operative fixation and is a common cause of hospital admission for elderly patients. Spinal anesthesia is a technique which is commonly used for these cases and which is performed with the patient in the lateral decubitus position. Positioning the patient for spinal anesthesia can be very painful; avoidance of this discomfort is a common and unsolved problem for anesthetists.

Regional anesthesia is effective in alleviating pain due to trauma; it offers the advantage of producing localized and very effective pain relief [1]. Prior to positioning a patient with FNF for spinal anesthesia, femoral nerve blockade (FNB) can provide excellent pain relief and is generally well tolerated [2-5]. Ultrasound-guidance for peripheral nerve blockade is intended to improve the

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block success rate and it is increasingly used around. Casati and al. demonstrated a 42% decrease of effective dose (ED50%) by using ultrasound to localize the femoral nerve prior to FNB [6]. A recent editorial by Sites pointed out that the optimal disposition of the local anesthetic in ultrasound-guided peripheral nerve blockade has yet to be defined [7]. We currently employ different approaches in relation to injection of local anesthetic (LA) solution close to the femoral nerve. Firstly, one may attempt to position the LA circumferentially around the nerve. This technique requires several needle passes, which may cause patient additional, perhaps unnecessary discomfort. Another option is to inject the LA either above or below the nerve without changing the position of the tip of the needle, thereby minimizing the number of needle passes and, probably, the degree of patient discomfort. It is not known if this later approach (single injection above or below the nerve) results in an equivalent quality of sensory block and subsequent analgesia. The femoral nerve has separated into branches at this level and we assume that the spread of LA may influence the quality and the extent (distribution) of the block.

Our objective was to compare i. the analgesic efficacy of ultrasound-guided FNB to facilitate positioning of patients for spinal anesthesia and ii. block success when LA was positioned i. above ii. below or iii. circumferential to the femoral nerve.

Methods

With the approval of the Clinical Research Ethics Committee of the Cork Teaching Hospitals (ECM 4 (zz) 08/12/09.) and having registered the trial at ClinicalTrials.gov (NCT01527812), a prospective, double blinded, randomized study of patients undergoing operative fixation of FNF at the Cork University Hospital was undertaken between December 2009 and November 2011. The patients were randomly allocated using a random number sequence and sealed envelopes. Written, informed consent was obtained from each patient.

Patients with FNF, American Society of Anesthesiologists grades I to III and aged >50 years, were invited to participate in the study. Exclusion criteria were patient refusal, the presence of more than one fracture; Mini-Mental Score <22 (Additional file 1); coagulation disorders; head injury; history of loss of consciousness; acute heart failure; allergy to lidocaine; skin lesions/infection at block site; and renal dysfunction. Patients with evidence of systemic infections (clinically defined or elevated C-reactive protein levels, leucocytosis, or body temperature higher than 37.8°C) were also excluded.

In all patients, an experienced anesthetist performed the ultrasound guided FNB. A 5 cm, 6–13 MHz linear transducer probe (Sonosite Turbo M, Bothwell WA, USA) was used to locate the nerve. For optimal visualization of the femoral nerve the transducer was applied transversely to the thigh below the inguinal crest. After examination of the anatomy of the femoral artery, the femoral nerve was identified at a level immediately above the deep femoral artery branch bifurcation. A 22 G 50 mm Stimuplex BBraun needle was used. After identification of the nerve and fascia around the nerve, the skin was infiltrated with local anesthetic (0.2 ml lidocaine 1%) on the lateral aspect of the thigh, 1 cm lateral to the lateral edge of the transducer. The needle was inserted in-plane from lateral to medial and advanced toward the lateral aspect of the femoral nerve.

For all patients, lidocaine 2% 15 ml was administered to perform ultrasound guided FNB. We used lidocaine, because it had a short onset time and our aim it was to facilitate positioning for performing spinal anesthesia in the shortest time. For patients allocated to the "Above" group (*Group A)* the LA was injected below (i.e. deep to) the fascia iliaca and above (i.e. superficial to) the femoral nerve; for patients allocated to the "below" group (*Group B)*, the LA was injected below the femoral nerve and above the fascia of the iliopsoas muscle and for those patients allocated to the circumferential group (*Group C)*, circumferential spread was achieved with multiple injections around the nerve (Figure 1).

An independent blinded observer (not present during performance of the block) assessed the extent and degree of sensory blockade using a modified Bromage score (cold, mildly cold and just spray) at 5 minute intervals during the initial 30 minutes after block completion. Sensory perception was assessed using cold (ethyl-chloride spray) spray on the skin in the lateral, frontal, medial side of the thigh and medial side of the leg corresponding to common distributions of the terminal branches of the femoral nerve.

Our primary outcome parameter was pain, evaluated using verbal rating (VRS) pain score (0–10) immediately after positioning the patient (lateral decubitus with operative side superior/independent) for spinal anesthesia.

We recorded each patient's pain (also using a VRS pain score 0–10) on passive movement of the fractured limb (elevating up to 30 degrees from the supine position or to patient tolerance from the resting position). When the patient reported VRS < 4 during the passive movement of the limb, the sensory block was deemed adequate and the patient was positioned for spinal anesthesia. In the event that cold perception was still present, assessment was continued up to 30 minutes after block completion (if the spinal is not injected until this time). Block failure was defined as failure to achieve a VRS score of < 4 within 30 minutes of FNB completion. In these cases, additional opioid medication and/or sedation were administered in order to optimize positioning for spinal anesthesia and these patients were excluded from further data collection.

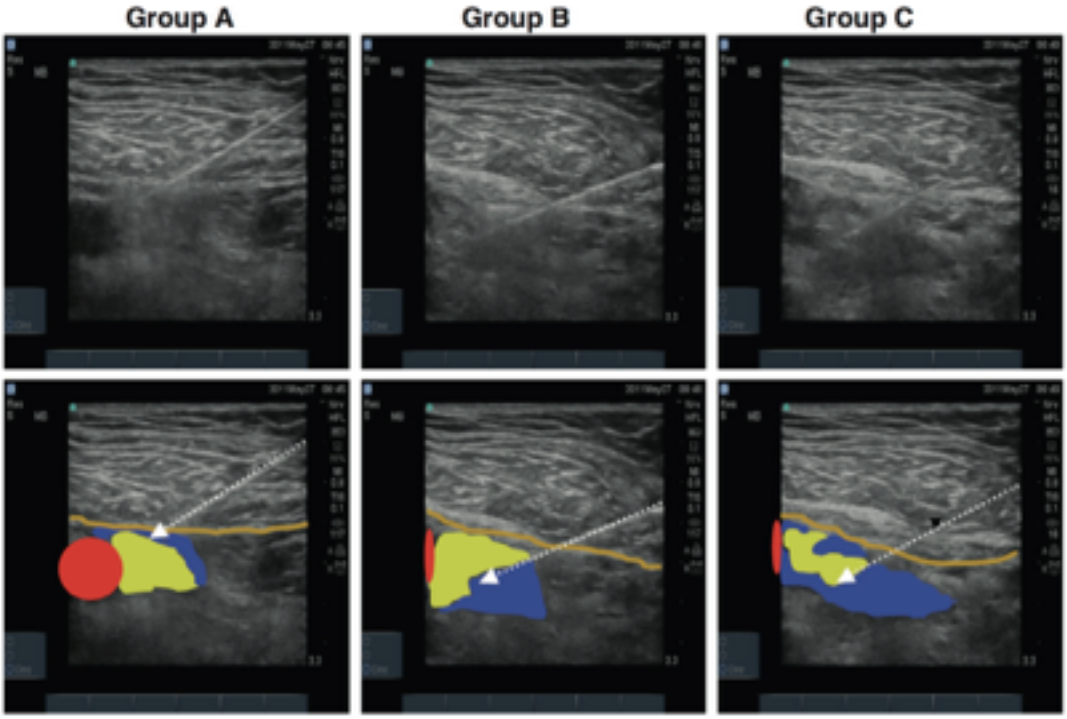


Figure 1 Composite figure of the femoral nerve block. Representative images depicting the anatomy: fascia iliaca (light brown lines), femoral artery (red), femoral nerve (yellow), needle (arrow) and local anesthetic (blue) position in Group **A**, **B** and **C**.

We recorded the times at which the patients arrived in the anesthetic induction room, ultrasound-guided FNB started (i.e. skin infiltration with LA) and completion of patient positioning for spinal anesthesia.

Spinal anesthesia was performed using standard aseptic technique; isobaric bupivacaine 0.5% were administered at a dose indicated by the responsible clinician. Patient satisfaction was assessed using a 100 mm linear visual analogue scale (VAS) during the surgical procedure and immediately after arriving to the recovery area. Patients were also asked in the recovery area if, given the option, they would choose the same analgesic modality again.

Untoward or adverse events were recorded by the responsible clinician (anesthetist) on a dedicated data sheet.

Statistical analysis

Sample size calculation was limited by the absence of historical data on the degree of pain patients with FNF experienced while being positioned for spinal anesthesia. It was arbitrarily decided to proceed on the basis that at least 20 patients/group would be required to demonstrate a clinically relevant effect size. Collected data were examined for normality. Normally distributed variables were tested between groups using ANOVA and t-test, non-normal data were analyzed using the non-parametric Kruskal-Wallis and Mann–Whitney U test. Categorical variables were tested using Chi-squared tests. $P < 0.05$ was considered significant.

Results

Sixty patients were recruited to this study of whom 52 were managed per protocol. Seven patients were excluded because of breaches of study protocol. For instance, one patient (Group A) developed fast atrial fibrillation after performing spinal anesthesia resulting in hemodynamic instability and cancellation of surgery. In one case (Group C), the anesthetist who performed the ultrasound-guided FNB had difficulties in visualizing the femoral nerve, and a nerve stimulator was used to confirm its position.

Patient characteristics were similar in the three groups (Table 1). Block failure (as defined above) occurred in four patients of 20 from Group A (20%) seven of 15 patients from Group B (46.7%) and three of 17 patients from Group C (17.6%) (Figure 2). The patients in whom

Table 1 Patients demographic characteristics

	Group A	Group B	Group C	(p-value)
Gender (female/male)	11/5	4/4	7/8	(0.346)
Age (years, mean)	80.0	73.9	81.3	(0.343)
ASA status I/II/III	1/11/4	1/6/1	2/8/5	(0.666)
Procedure	10/6	6/2	10/5	(0.464)
(DHS, IMHS/hemiarhtroplasty)				
BMI (kg/m2) mean	23.16	25.29	25.51	(0.181)
Right/left	9/7	2/6	7/8	(0.212)

ASA, American Society of Anesthesiologist physical status; *DHS* Dynamic hip screw; *IMHS* Intramedullary hip screw.

the FNB block was deemed to have failed received iv. fentanyl, midazolam or propofol, at the discretion of the anesthetist responsible for their clinical care and excluded from further data collection.

Pain scores on positioning for spinal anesthesia were similar in the three groups [VRS pain scores in the Group A/Group B/Group C: 2(0–9)/0(0–10)/3(0–10), median (range), Kruskal-Wallis test p:0.32)] (Figure 3). Patient satisfaction (VAS scores on arrival to the recovery room) was greater in Group C patients compared with those in Group A [Group C vs. Group A: 93.8(12.3) vs. 83.5(19.8), mean (SD), p: 0.01)]. The distribution of sensory block achieved was similar in the three groups.

Procedural pain (VRS), block procedural time, block onset time, the time to position for spinal anesthesia and spinal block performance time were also similar in the three groups (Table 2), during the FNB.

On one occasion, spinal anesthesia was converted to general anesthesia because the insertion of the spinal needle was impossible during multiple attempts. Fentanyl iv. and midazolam iv. were administered as clinically indicated during performance of spinal anesthesia (again at the discretion of the responsible anesthetist). In Group A, one patient received 20 microgram fentanyl iv. and two patients received 2 and 5 mg midazolam iv. In Group B, two patients received 20 and 25 microgram fentanyl iv. and one patient 1 mg midazolam iv. In Group C. one patient received fentanyl 20 mcg and two received 2 mg midazolam iv.

Discussion

The most important finding of this study is that the attempt to deposit LA circumferentially around the

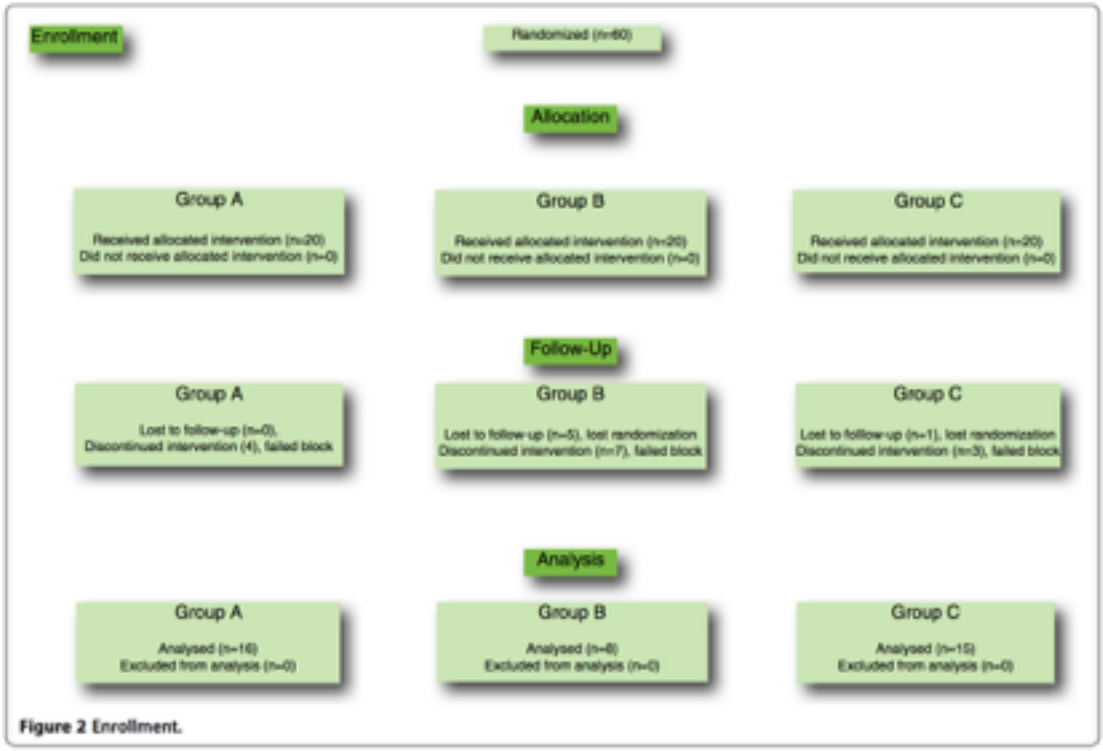


Figure 2 Enrollment.

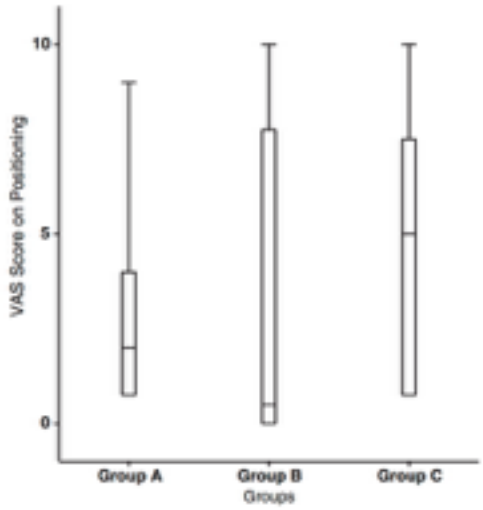


Figure 3 VAS pain scores on positioning for spinal anesthesia. VRS median pain scores at positioning to perform spinal anesthesia in Group A /Group B /Group C: 2.5(0–9)/3.2(0–10)/4.7(0–10), median (range) Kruskal-Wallis test p: 0.43) The box-and-whiskers plots show maximum and minimum values and 90th percentiles, lower and upper quartiles and the median (horizontal bar) for each group.

femoral nerve offered no clinical advantage (in terms of pain on positioning for spinal anesthesia) relative to attempting to deposit LA only above (i.e. superficial to) the nerve. The latter approach resulted in fewer needle passes during performance of the block (Figure 4) and was associated with greater patient satisfaction on arrival to the postoperative recovery room.

We believe that our understanding of the determinants of spread of LA administered during peripheral nerve blockade is grossly deficient. The evidence and our understanding of the equivalent determinants when LA is administered for neruraxial block is greater but still incomplete. Our study attempts to apply scientific rigor to a clinical (i.e. applied) question without making unsupported assumptions.

Previous studies have demonstrated that ultrasound is a reliable method of detecting injectate spread in a gelatin phantom model [8]. It has also been shown that ultrasound-guided circumferential injection of local anesthetic around the sciatic nerve can improve the rate of sensory block [9]. It has been demonstrated that fascia iliaca block is more efficacious than i.v. alfentanil in terms of facilitating the lateral position for spinal anesthesia [10]. FNB has been shown to be superior (compared with i.v. administration of fentanyl) in facilitating the sitting position for spinal anesthesia in patients undergoing surgery for femoral

Table 2 Secondary outcomes (medians)

	Group A	Group B	Group C	(p-value)
Time till starting the USFNB after arrival to the induction room (min)	9.4	7.4	7.0	(0.886)
UGFNB procedure time (min)	3.3	3.4	4.6	(0.497)
Pain during UGFNB (VRS 0-10)	2.3	1.4	2.6	(0.64)
UGFNB onset time (min)	9.3	11.4	12.3	(0.49)
Turning time for spinal anesthesia after arrival in induction room (min)	32.1	29.1	35.0	(0.49)
Spinal performing time after arrival in induction room (min)	43.8	39.3	46.1	(0.62)
Sedation during spinal anesthesia, number of the patients (%)	2(12.5)	2(25)	3(20)	(0.73)

VAS Visual analogue scale; VRS Verbal rating score.

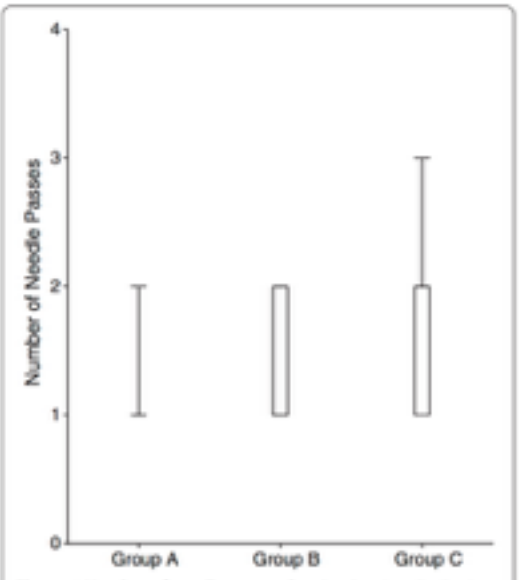


Figure 4 Number of needle passes. Boxplot showing distributions within each group of number of needle passes during ultrasound guided FNB. The median number of needle passes was statistically significantly higher in the Group C compared with the Group A (2.0 vs. 1.0, Mann–Whitney U between Groups C vs. A, p = 0.009). The Group B median was also higher than the group A median i.e. 1.5 but this was not significant.

shaft fractures [11]. A recent investigation of the influence of catheter tip positioning during continuous FNB in healthy volunteers concluded that anterior (vs. posterior) placement increased cutaneous sensory block, without a concurrent relative increase in motor block [12]. Ours was a clinical investigation aimed at providing useful practical information to clinicians seeking to optimize conditions for positioning of patients prior to FNF surgery. Thus, in addition to the cutaneous sensory effects, we considered that articular pain may contribute to the discomfort experienced by these patients. The posterior division of the femoral nerve gives articular branches to the hip and knee [13]. Therefore we believed that it was possible that deposition of LA inferior, just below the femoral nerve at the level described could effect greater sensory block via these articular branches. Kullenberg et al. reported that FNB could have other beneficial outcomes in this patient group, including earlier times to postoperative mobilization and less cognitive impairment [14]. Ultrasound-guided FNB is feasible to perform in the emergency department and significant and sustained decreases in pain scores were achieved with this technique [15].

The relatively great incidence of block failure we report may be a function of the strict definition of failure we applied. There is well documented variation in sensory innervation of the hip joint (with differing contribution across individuals from femoral, sciatic and obturator nerves) [13]. The relatively small sample size may also have contributed to this unexpected finding.

Our study has certain limitations. The data set wasn't complete in every case. Certain patients received sedation after spinal anesthesia had been performed. Certain co-morbid factors may have influenced pain perception during positioning for spinal in these cases. For example, chronic obstructive pulmonary disease result in a longer duration of positioning the patient (and presumably greater discomfort). A negative finding of a clinical trial in which the sample size was relatively small and arbitrarily selected may be due to a Type II error.

Conclusions

We believe that that is the first study which examines the association between distribution of injectate (or technique to achieve such a distribution) following FNB and defined clinical effect. We conclude that, in the clinical setting described, attempting to deposit LA circumferential to the femoral nerve (versus depositing it above/superficial to the nerve) confers no clinical advantage, results in a greater number of needle passes and therefore is not justified.

Additional file

Additional file 1: Mini Mental examination.

Abbreviations

FNF: Fractured neck of femur; FN: Femoral nerve; FNB: Femoral nerve block; LA: Local anesthetic; VRS: Verbal rating score; VAS: Visual analog scale; ANOVA: Analysis of variance; SD: Standard deviation.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SS participated in the design of the study, performed statistical analysis, carried out data collection and led preparation of the manuscript. DM participated in the design of the study, performed randomization, carried out data collection and contributed to preparation of the manuscript. SFS participated in the design of the study, carried out data collection, GI participated in the design of the study, co-ordinated data collection and contributed to the preparation of the manuscript GS conceived of the research question addressed, co-ordinated the conduct of the study and contributed to the preparation of the manuscript. All authors read and approved the final manuscript.

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