

**The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board**

PROJECT SUMMARY

Study Title: Ultrasound-guided fascia iliaca compartment block *versus* periarticular infiltration for pain management after total hip arthroplasty: a randomized controlled trial

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Sponsor/Funding Source: Department of Anesthesiology and Pain Management, UT Southwestern Medical School

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Purpose:

In this randomized, controlled, observer-blinded study we plan to evaluate ultrasound-guided fascia iliaca compartment block with ropivacaine and periarticular infiltration with ropivacaine for postoperative pain management after total hip arthroplasty (THA).

Background:

Despite substantial advances in our understanding of the pathophysiology of pain and availability of newer analgesic techniques, postoperative pain is not always effectively treated (1). Optimal pain management technique balances pain relief with concerns about safety and adverse effects associated with analgesic techniques. Currently, postoperative pain is commonly treated with systemic opioids, which are associated with numerous adverse effects including nausea and vomiting, dizziness, drowsiness, pruritus, urinary retention, and respiratory depression (2). Use of regional and local anesthesia has been shown to reduce opioid requirements and opioid-related side effects. Therefore, their use has been emphasized (3, 4, 5, 6).

Fascia Iliaca compartment block (FICB) is a field block that blocks the nerves from the lumbar plexus supplying the thigh (i.e., lateral femoral cutaneous femoral and obturator nerves). The obturator nerve is sometimes involved in the FICB but probably plays little role in postoperative pain relief for most surgeries of the hip and proximal femur. It has been traditionally used by loss of resistance using palpable anatomical landmarks to provide analgesia for procedures involving the hip joint, anterior thigh and knee surgery (7, 8, 9). The extent of nerve blockade depends on the spread of local anesthesia under the fascia, therefore, a large volume of local anesthetic up to 60 mL may be needed to ensure adequate coverage (8, 10, 11). One study compared FICB to sham block without showing significant benefit, but used significantly lower volume (30 mL) than proposed for this study (12). Another study showed use of doses of ropivacaine up to 300mg for wound infiltration is safe which is equivalent to 60 mL 0.5% ropivacaine (13). The advent of ultrasound guided regional anesthesia has brought more precision to this technique, including the ability to visualize the anatomy, perform real-time navigation, and direct observation of local anesthetic spread, as it allows a greater degree of sensory and motor blockade (4,14).

An alternative to the FICB is periarticular infiltration, which is increasingly being used, as it has also been reported to provide adequate analgesia (15). However, to date, FICB has not been compared with periarticular infiltration.

We hypothesize that a FICB would provide superior analgesia when compared to infiltration, because infiltration is surgeon and technique dependent. The primary aim of this study is to compare the pain scores and the secondary objectives are to compare opioid requirements and opioid related adverse effects such as nausea and vomiting.

Concise Summary of Project:

Patients undergoing THA (n=60) at Parkland and UT Hospitals will be randomized into one of two groups to receive either ultrasound-guided FICB with ropivacaine 300 mg and 150 mcg epinephrine diluted to 60 mL (Group 1) or periarticular infiltration ropivacaine 300 mg and 150 mcg epinephrine total volume 60 mL (Group 2) for postoperative pain management. The remaining aspect of perioperative care, including the anesthetic technique (i.e., spinal anesthetic), pre- and postoperative care will be standardized and will be similar for all patients.

The duration of the involvement in the study will be until 48 hours postoperatively. Subjects will be identified by pre-anesthesia care unit personnel during their preoperative clinic visit and Day Surgery unit. There will be no incentive or payment to the patients.

Patients in Group 1 will receive ultrasound-guided FICB after surgery. Patients in Group 2 will receive ropivacaine via periarticular infiltration prior to closing the incision. All patients in both groups will receive gabapentin 600 mg, acetaminophen 1000 mg, and oxycodone CR 10 mg po 2-3 hours preoperatively. Intraoperative all patients will receive dexamethasone 8 mg, and acetaminophen 1000mg IV at the start of surgery and ondansetron 4 mg, IV at the end of surgery. In the first 24-h postoperative period, patients in both groups will receive acetaminophen 1000 mg and gabapentin 300 mg, po every 8 h, meloxicam 15 mg, po daily, Oxycodone 10 mg, in the evening and hydromorphone 0.4 mg, IV bolus, q 3h, prn as a rescue. In the 24-48 h study period, all patients will receive meloxicam 15 mg, po daily, gabapentin 300 mg, po every 8 h , and a hydrocodone/acetaminophen 10mg/ 325 mg, po q 4 h, as needed.

The postoperative analgesia will be documented using the visual analog score (0=no pain, 10=worst pain). In addition, total opioid dose over the 48-h study period will be documented. Postoperative nausea will be measured using a categorical scoring system (none=0, mild=1, moderate=2, severe=3) and episodes of vomiting will be documented. Rescue antiemetics will be given to any patient who complains of nausea and/or vomiting. All variables will be assessed at 2, 6, 12, 24, and 48 hours, postoperatively by an investigator blinded to group allocation.

Study Procedures:

We will study 60 American Society of Anesthesiologists (ASA) physical status 1-3 subjects scheduled for total hip arthroplasty who will be identified by pre-anesthesia care unit personnel during the preoperative clinic visit or at the day of surgery at Parkland, Zale, Clements hospitals. If the subjects agree to participate in the study, the researchers will determine eligibility. If the subject meets all inclusion/exclusion criteria, the subject will be asked to sign the Consent Form and HIPAA Authorization Form prior to any study procedures in a face-to-face meeting with the researchers.

Protected patient information will include name, medical record number, date of birth, and contact information including telephone number. Height and weight will also be recorded. All patients will receive a standardized spinal anesthetic including antiemetic prophylaxis with ondansetron 4 mg IV and dexamethasone 8 mg IV. One of the investigators will randomly allocated patients using computer generated randomization schedule to one of two groups - ultrasound-guided FICB with ropivacaine or periarticular infiltration with ropivacaine.

Fascia iliaca compartment block will be performed by anesthesiologists with previous experience of the ultrasound-guided technique using the SonoSite Edge and linear 6-13 MHz transducer. With the patient placed supine position, the ultrasound transducer will be placed in a para-sagittal orientation inferior-medially to the anterior superior iliac spine, over the inguinal ligament (4). Using real-time ultrasound imaging we will identify internal oblique, sartorius and iliacus muscles, covered by the fascia iliacus. Following aseptic preparation of the injection site and the ultrasound probe, a 22-gauge 10 mm insulated needle (Stimuplex A, B-Braun Medical, Melsungen, Germany) will be introduced parallel to the ultrasound guided beam (in- plane technique) from caudad-to-cephalad direction, through the sartorius muscle, directed towards the iliacus muscle, until its tip reaches the plane between internal oblique and iliacus muscles. With the needle tip placed beneath the fascia and above the muscle), a few milliliters of

ropivacaine, injected slowly, will push the fascia off the iliacus muscle. After negative aspiration, the rest of 0.5% ropivacaine (total 60 ml) will be injected in 5 ml increments to further separate the iliaca fascia from the iliacus muscle. We will observe local anesthetic spread under real-time imaging between the internal oblique and iliacus muscles.

Periarticular wound infiltration will be performed by surgeons using a 22 gauge 1.5 inch needle. 20 ml of ropivacaine will be infiltrated deep into the posterior capsule and posterior soft tissue, 20 ml will be given in the mid layer and 20 ml will be infiltrated into the subdermal tissues and around the drain. All injections will as the needle is withdrawn.

A standard postoperative analgesic regimen for the first 24-h postoperative period patients in both groups will include acetaminophen 1000 mg and gabapentin 300 mg, po every 8 h, meloxicam 15 mg, po daily, oxycodone 10 mg, in the evening and hydromorphone 0.4 mg, IV bolus, q 3h, prn as a rescue. In the 24-48 h study period, all patients will receive, meloxicam 15 mg, po daily, gabapentin 300 mg, po every 8 h and a hydrocodone/acetaminophen 10mg/ 325 mg, po q 4 h, as needed.

The efficacy of postoperative analgesia will be documented in all patients using the visual analog score (0=no pain, 10=worst pain). In addition, total opioid dose over the 48-h study period will be documented. Postoperative nausea will be measured using a categorical scoring system (none=0, mild=1, moderate=2, severe=3) and episodes of vomiting will be documented. Rescue antiemetics will be given to any patient who complains of nausea or vomiting. All variables will be assessed at 2, 6, 12, 24, and 48 hours postoperatively by an investigator blinded to group allocation.

Sub-Study Procedures: N/A

Criteria for Inclusion of Subjects:

- Female and male ASA physical status 1-3 scheduled for total hip arthroplasty
- Age 18-80 years old
- Able to participate personally or by legal representative in informed consent in English or Spanish

Criteria for Exclusion of Subjects:

- History of relevant drug allergy
- Age less than 18 or greater than 80 years
- Chronic opioid use or drug abuse
- Significant psychiatric disturbance
- Inability to understand the study protocol
- Refusal to provide written consent

Sources of Research Material:

Patient information including name, medical record number, birth date, and contact information including phone number

Patients undergoing total hip arthroplasty

Baseline vital signs (heart rate, blood pressure)

SonoSite Edge ultrasound machine
Performance of fascia iliaca plane block for the purpose of postoperative pain relief
Evaluation of efficacy of postoperative analgesia with visual analog score
Evaluation of nausea with categorical scoring system
Total amount of opioids used

Recruitment Methods and Consenting Process:

Subjects will be identified by pre-anesthesia care unit personnel during their preoperative clinic visit and Day Surgery unit. Patients scheduled for total hip arthroplasty will be selected for this study. The researchers will then be contacted to review the patient's chart for eligibility with the use of the HIPAA waiver form. If the subject meets all inclusion/exclusion criteria, the subject will be informed about the study in a face-to-face meeting with the researchers. If the subject agrees to participate, then he or she will sign the consent form and HIPAA Authorization Form prior to any study procedures. Once patient information is obtained, it will be protected by the study team in locked cabinets.

Potential Risks:

Risk of ropivacaine:

- The incidences of adverse neurologic reactions associated with the use of local anesthetics may be related to the total dose of local anesthetic administered and are also dependent upon the particular drug used, the route of administration, and the physical status of the patient.
- There is minimal risk of local anesthetic toxicity with inadvertent injection of local anesthetic into the blood vessel while performing the block. If injected into a blood vessel, in large amounts it can cause seizures and even cardiac arrest. There are no major vessels at the site of injection with both techniques, therefore the risk is minimal. If it happens lipid emulsion will be given which is standard treatment of local anesthetic toxicity.

Risk of Injection:

There is a risk of hematoma at the site of block placement or local infiltration. Anytime a needle is used there is a risk of bleeding, infection, or damage to surrounding tissue.

Risk for epinephrine:

Epinephrine may increase heart rate and blood pressure, however the dose of epinephrine use in study is very low and investigators don't expect the increase of heart rate and blood pressure.

Risk of increased opioid use for pain relief during postoperative period:

Opioids are part of the standard treatment for pain after surgery and will be given as needed after surgery in addition to the scheduled pain control medications.

There is risk of loss of confidentiality and psychological stress with any research participation.

Subject Safety and Data Monitoring:

Independent research experts, Drs. John Pennant and Weike Tao, will review data and safety information at 5 subject recruitment intervals and report any safety concerns to PI and IRB within twenty four hours of discovery.

As with any local anesthetic products, monitoring of cardiovascular and neurological status, as well as vital signs should be performed during and after injection of ropivacaine.

Procedures to Maintain Confidentiality:

A non-identifiable code will be assigned to the data collection sheet so that there is not a direct link to specific names. Patient IDs will be standardized as Principal Investigator initials followed by the 3 digit number: IG01, IG02.....IG30.

A key to the coding system will be maintained in a locked storage cabinet with limited access until all the data is collected and analyzed. Patient identifiers will not be destroyed, as they are necessary for one of the functions of this research, however, identifiers and protected health information will not be stored together. Only the Principal Investigator will have access to the code linking patient identities to the information contained within the research database. Subject identifiers will not be reused or disclosed to any other person or entity for research unless required by law, for authorized conduct and oversight of the study, or for other IRB-approved research.

Following the completion of the analysis and the project, the key to the coding system or subject identifiers themselves will be destroyed by shredding the documents so that there is no direct or indirect link to subject identifiers and information.

All electronic data generated will be password protected with access limited to the immediate study team.

Potential Benefits:

The study is not designed for direct benefit to study subjects who participate in research. However, patients who involved in this study may have superior postoperative pain relief. However, the potential benefits to patients in the future could be substantial. We can potentially improve the course of the early postoperative period in terms of better pain control, less opioid use and less opioid-related side effects.

Statistics:

Sample size was calculated assuming a standard deviation of 2.5 and an alternative mean difference of 1.5 in favor of patients undergoing FIB procedure. With an alpha level of 0.05, the study will need a total of 52 patients to have 80% power using a repeated measures ANOVA F test. Assuming a 14% loss to follow-up, n = 60 patients will be enrolled at 1:1 ratio. Demographic data will be summarized as means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Repeated measures ANOVA analyses with one between subject (FIB vs. local infiltration) and one within subject (time) factor will be used for the primary outcome of pain scores and other continuous outcome measures. Model assumptions will be assessed using standard residual diagnostics and alternative analyses procedures will be considered in case of violations. All analyses will be done using SAS 9.3 (SAS Inc., Cary, NC) software and p-values less than 0.05 will be considered statistical significance. Bonferroni adjustments will be used for multiple comparisons where appropriate.

References:

1. Joshi JP, Schug SA, Kehlet H. Procedure-specific pain management and outcome strategies. *Best Practice & Research Clinical Anaesthesiology* 2014; 28:191-201
2. Ovendyk FJ, Carter R, Maddox RR, Callura J et al. Continuous oximetry/capnometry monitoring reveals frequent desaturation and bradypnea during patient-controlled analgesia. *Anesth. Analg* 2007; 105:412-18
3. Joshi GP, Kehlet H. Procedure-specific pain management: the road to improve postsurgical pain management? *Anesthesiology* 2013; 118:718-2
4. Hebbard P, Ivanusic J, Sha S. Ultrasound-guided supra-inguinal fascia iliaca block: a cadaveric evaluation of a novel approach. *Anaesthesia* 2011; 66:300-5
5. Gasanova I, Alexander J, Ogunnaike B, Hamid C, Rogers D, Minhajuddin A, Joshi PG. Transversus Abdominis Plane Block versus Surgical Site Infiltration for Pain Management after Open Total Abdominal Hysterectomy. *Anesth Analg* 2015; 121: 1383--8
6. Sun Y, Li T, Gan TJ. The Effect of Perioperative Regional Anesthesia and Analgesia on Cancer Recurrence and Survival after Oncology Surgery: A Systematic Review and Meta-Analysis. *Reg Anesth Pain Med* 2015; 40:589-98
7. Dalens B, Tanguy A, Vanneuville. Lumbar plexus block and lumbar plexus nerve blocks. *Anesth Analg* 1998; 69:852-4
8. Diakomi M, Papaioannou M, Mela A, Kouskouni E, Makris A. Preoperative Fascia Iliaca Compartment Block for Positioning Patients With Hip Fractures for Central Nervous Blockade. *Reg Anesth Pain Med* 2014; 39:394-8
9. Newman B, McCarthy L, Thomas PW, May P, Layzell M, Horn K. A comparison of pre-operative nerve stimulator-guided femoral nerve block and fascia iliaca compartment block in patients with femoral neck fracture. *Anaesthesia* 2013; 68:899-903
10. Stevens M, Harrison G, McGrail. A modified fascia iliaca compartment block has significant morphine-sparing effect after total hip arthroplasty. *Anaesth Intensive Care* 2007; 35:949-952
11. Vaughan B, Manley M, Stewart D. Distal Injection Site May Explain Lack of Analgesia From Fascia Iliaca Block for Total Hip. *Reg Anesth Pain Med* 2013; 38:556-7.
12. Shariat A, Hadzic A, Xu D, Shastri U, Kwofie K, Gandhi K, McGally CM, Gratenstein K, Vandepitte C, Gadsden J, Unis D. Fascia Iliaca Block for Analgesia after Hip Arthroplasty: A Randomized Double-Blind, Placebo Controlled Trial. *Reg Anesth Pain Med* 2013; 38: 201-5
13. Pettersson N, Emanuelsson BM, Reventlid H, Hahn RG. High-Dose Ropivacaine Wound Infiltration for Pain Relief after Inguinal Hernia Repair. *Reg Anesth and Pain Medicine* 1998; 23(2); 189-96
14. Dolan J, Williams A, Murney E, Smith M, Kenny G. Ultrasound Guided Fascia Iliaca Block: A Comparison with the Loss of resistant Technique. *Reg Anesth Pain Med* 2008; 33:526-31
15. Joshi JP, Cushner FD, Barrington JW, Lombardi AV, Long WJ, Springer BD, Stulberg BN. Techniques for Periarticular Infiltration With Liposomal Bupivacaine for the Management of Pain After Hip and Knee Arthroplasty: A Consensus Recommendation. *J Surg Orthopaedic Advances* 2015; 24:27-36