Trial Comparing Impact of Peri-capsular Nerve Group (PENG) Block on Quality of Recovery Compared to No-block for Primary Total Hip Arthroplasty

Study Protocol & Statistical Analysis Plan

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Study Title: A randomized-controlled, double-blind, single-center trial comparing impact of Peri-capsular Nerve group (PENG) block on quality of recovery compared to no-block for primary Total Hip Arthroplasty.

1.0 Summary of Study

Background: Total hip arthroplasty (THA) is now the second most common joint replacement surgery in the US due in part to an aging population [1]. Opioid sparing analgesic treatments such as lumbar plexus and femoral nerve blocks are effective but they carry a high risk of undesirable lower limb motor or muscle weakness. Fascia iliaca block, on the other hand, does not consistently provide adequate pain relief [2, 3]. Today, early mobilization, rehabilitation and participation in physical therapy is an integral part of enhanced functional recovery program after THA. Because innervation of the hip joint is complex and preservation of lower extremity motor function is paramount, optimal regional analgesic intervention for THA has yet to be defined [4, 5]. The pericapsular nerve group (PENG) block is a novel regional anesthesia technique for providing analgesia after hip fractures and hip arthroplasties. Quality of recovery scores are patient reported outcome measures evaluating recovery after surgery and anesthesia. The quality of recovery-15 (QoR-15) is a validated questionnaire to assess postoperative recovery (6). The aim of this single center, double blind, randomized controlled trial is to confirm the efficacy of the PENG block for postoperative recovery after primary THA.

Methods: The participants will be randomly assigned to either PENG block group or "no Block" group using a random number generator. The patient will be blinded to the group allocated. The primary outcome will be the quality of recovery 15 score (QoR-15). The secondary outcomes will be visual analog scale score of pain postoperatively, opioid

requirements in first 24 hours, ambulation distance on postoperative day1 and patient satisfaction. Statistical analysis will be performed using the student's t-test, Mann-Whitney U test, and Fisher's exact test as appropriate per sample. A p-value of less than 0.05 will be considered statistically significant.

INTRODUCTION

2.0 Background and Rationale

As the practice of anesthesiology has grown increasingly safe, the focus has shifted to improving quality, as evidenced by the robust spread of Enhanced Recovery after Surgery protocols. The implications from poor quality recovery is vast, including prolonged stay in the recovery room or hospital [7]. The Quality of Recovery (QoR-15) questionnaire is a method to measure five dimensions using 15 questions: physical independence, pain, comfort, patient support, emotional state [8]. It is an extensively validated measure of patient-assessed quality of recovery after surgery, having been demonstrated over a variety of clinical settings. QoR-15 scores range from 0 (extremely poor quality of recovery) to 150 (excellent). Mean time to complete the 15-question survey is 3 minutes, a marker of its clinical utility [9]. As we aim to improve our perioperative care and develop approaches to improve medicine in this regard, the QoR-15 provides a useful tool.

The effective postoperative analgesia is vital as acute surgical pain is a potential risk factor for future chronic pain. Persistent pain after THA (more than three months) is reported in 27% of patients and is reported to be correlated with the intensity of early postoperative pain

rather than preoperative pain levels [10,11]. Utilizing regional anesthesia helps to limit the use of opioids, however, which technique is best has yet to be determined. The lumbar plexus blocks, lumbar epidurals, and femoral nerve blocks have been associated with motor weakness. Fascia iliaca compartment block (FICB) has not been found to predictably decrease pain intensity or opioid use [12]. Quadratus lumborum (QL) block is a relatively new regional block found to provide effective analgesia after primary THA, but it can indirectly block lumbar plexus branches and may cause some motor weakness [13]. It is also a deep block and therefore contraindicated in patients on anticoagulation [14].

Recent anatomic studies by Short et al. confirmed the innervation of the anterior capsule of hip joint to be the obturator nerve, accessory obturator nerve, and femoral nerve. These studies also evaluated the relationship with these nerves and other bony or soft tissue landmarks visible by ultrasound guidance [15]. Previous studies have found histologically that the anterior capsule has predominantly nociceptive fibers, while the posterior capsule is largely made up of mechanoreceptors [16]. The pericapsular nerve group (PENG) block was introduced to target and block these articular branches providing innervation to the hip. This regional anesthetic technique was described in 2018 by Giron-Arango et al. for acute analgesia related to hip fractures [17]. Given the case reports showing the efficacy of PENG blocks for hip fracture surgeries, we sought to investigate the analgesic efficacy of PENG blocks for primary and revision THAs. The PENG block targets only the sensory branches and not the posterior mechanoreceptors; there is a potential motor-sparing effect which is desirable for early ambulation, better physical therapy, and earlier discharge. The effective analgesia and early ambulation provided by such regional anesthesia block may have positive impact on patient's mood, sleep, appetite and overall feeling of well-being. A similar postoperative recovery study

protocol has been proposed for anterior quadratus lumborum blocks for THA (18). It remains unclear whether PENG block provides sufficient analgesia and improves the quality of post-operative recovery after primary THA.

The ideal regional anesthesia technique for THA will provide adequate postoperative analgesia, reduced opioid requirements, early ambulation and physical independence. The aim of this single center, double blind RCT is to confirm the efficacy of PENG block for postoperative recovery with respect to parameters mentioned above.

3.0 OBJECTIVE(S) & HYPOTHESIS

The objectives of the study are as follows:

1. Determine the efficacy of PENG for primary THA compared to no peripheral nerve block on Quality of Recovery (QoR) after surgery.

2. Determine the efficacy of PENG for analgesia, post-operative mobilization, side effects, patient satisfaction and length of hospital stay for THA compared to no peripheral nerve block

We hypothesize that patients receiving PENG prior to primary THA will have superior quality of recovery, compared to the patients who do not receive PENG block.

Trial design: This randomized-controlled, double-blind, single-center, pragmatic, superiority trial with the two-parallel group (1:1 allocation) is designed to assess the efficacy of PENG block compared to no-block in improving the QOR for patients undergoing primary THR. The unit of randomization will be individuals (not clusters). The QOR-15 questionnaire was chosen as a measure of efficacy because it is an extensively validated measure of patient-assessed quality of recovery after surgery, having been demonstrated over a variety of clinical settings. Allocation ratio of 1:1 would allow the research question with a minimal number of subjects.

METHODS

Study setting: The study will be conducted at UAB Highlands Hospital.

4.0 INCLUSION & EXCLUSION CRITERIA

Inclusion criteria:

1. Patients undergoing primary total hip arthroplasty
2. Adults 18 years of age and older
3. Patients with an American Society of Anesthesiology (ASA) physical status classification of I, II or III
4. Primary THA

Exclusion criteria:

1. Patients with ASA physical status classification 4 or above
2. Patients with allergies/intolerances to local anesthetic
3. Patients with pre-existing neurologic or anatomic deficits in the lower extremity on the side of the surgical site
4. Patients on chronic opioid use or opioid tolerant (The FDA defines a **patient** as **opioid tolerant** if for at least 1 week he or she has been receiving oral morphine 60 mg/day; transdermal fentanyl 25 mcg/hour; oral oxycodone 30 mg/day; oral hydromorphone 8 mg/day; oral oxymorphone 25 mg/day; or an equianalgesic dose of any other **opioid**)
5. Poor understanding of English language.
6. Patients with coexisting coagulopathy
7. Patients that are pharmacologically anticoagulated will be excluded if placement of peripheral nerve block would be contraindicated according to ASRA (American Society for Regional Anesthesia) guidelines

5.0 RANDOMIZATION/RECRUITMENT DETAILS (If applicable)

- Randomization groups, how will subjects be randomized:

  Upon enrollment in the study, participants will be randomized 1:1 to either the investigational group ("PENG Block" group) or the control group ("No Block" group). Participants will be randomized using a random number generator. The randomization will be performed using computer-generated random numbers. The study will follow a 1:1 allocation ratio for the intervention (PENG) and control (No-PENG). A random permuted block will be used to reduce the predictability of allocation. The randomization sequence will be generated using computer software using a block randomization method where blocks are variable in size (minimum block size four). The study will use a sealed opaque envelope as method to comply with allocation concealment.

- Blinded ☒ Yes ☐ No (Single ☐ Double ☒ please check box).
- Participants and outcome assessors will be blinded. The anesthesiologist performing the block will not be blinded to the group allocation.

6.0 STUDY INTERVENTIONS/PROCEDURES

All patients will receive standard pre-operative dose of 1000 mg of acetaminophen, and 200 mg of celecoxib as multimodal analgesia regimen.

- Study design: Click here to enter text.
  - Participants in the study will be blinded to their treatment group. All patients will receive acetaminophen 975 mg PO and celecoxib 200 mg PO. Dose of celecoxib will be adjusted based on renal function, and no celecoxib will be given for GFR < 30 ml/min.
  - Participants in the pericapsular nerve group block (PENG) arm will receive a PENG block preoperatively in the block area placed under direct ultrasound guidance as follows:
    - Patients will be placed in the supine position resting comfortably. Standard noninvasive monitors will be applied, and oxygen will be administered via nasal cannula. Parenteral midazolam and fentanyl will be titrated to patient comfort. Standard skin sterilization, prepping and draping will be applied to the area Anatomical landmarks identified using ultrasound and skin will be numbed using 2-3 cc of 2% lidocaine. Long acting local anesthetic, a bolus of 25 cc of 0.5 % Bupivacaine will be injected lateral to iliopubic eminence (IPE). A Curvilinear low frequency (2-5 MHz) ultrasound probe will be used to identify landmarks. A 22 G, 10 cm needle will be inserted using in-plane technique and advanced to target site (17).

    - After the PENG block is placed, patients will have THA under spinal or general anesthesia. Spinal anesthesia will be provided by intrathecal injection of hyperbaric (0.75%) bupivacaine. General anesthesia will be provided by propofol induction, rocuronium for muscle relaxation and inhalation anesthetics for maintenance. Patients will receive fentanyl 25-50 mcg iv for increase in systolic blood pressure (SBP) > 25% of baseline SBP. Intraoperatively patients will also receive 4mg dexamethasone iv and 4 mg ondansetron iv.
  - Control group participants will be transferred to the block area preoperatively, and care will proceed as if they were receiving injection.
    - Patients will be placed in the supine position resting comfortably. Standard noninvasive monitors will be applied, and oxygen will be administered via nasal cannula. Parenteral midazolam and fentanyl will be titrated to patient comfort. Standard skin sterilization, prepping and draping will be applied to the area. The ultrasound probe will be used to

identify the iliopubic eminence (IPE). Only skin will be numbed using 2-3 cc of 2% lidocaine and NO bolus of bupivacaine will be injected.

- Postoperative patients in both the PENG arm and the control arm will be given scheduled PO acetaminophen 975 mg BID, and celecoxib 200mg BID (Dose of celecoxib will be adjusted based on renal function, and no celecoxib will be given for GFR < 30 ml/min) as part of multimodal pain regimen. Patients will be given a standard pain regimen of PRN Oxycodone 5 mg Q 4 hours for breakthrough pain, and hydromorphone 1mg IV every 6 hours prn as rescue analgesia for severe pain (NRS score more than 7/10). Patients will get prn ondansetron 4 mg iv every 4 hours. Naloxone iv prn will be used for any opioid related itching or respiratory depression.
- The following data will be collected
  - Quality of recovery (QoR) survey will be filled on post-operative day at 24 and 48 hours.
  - Patients will be evaluated immediately post-operatively in PACU, and 6, 12 and 24 hours post-surgery to determine VAS pain scores at rest and movement on the scale of 0-10. Also highest pain score during first 24 hours will be recorded.
  - Twenty-four hour opioid consumption will be calculated with respect to 24 hours oxycodone use and 24 hours hydromorphone use.
  - Data for postoperative use of ondansetron and naloxone will be collected. Also any postoperative episodes of nausea, vomiting, and itching will also be recorded.

  - Patient will be followed up until nerve block resolves.
  - Patients' participation in physical therapy will be recorded from physical therapy notes. Specifically, independence in mobility and transfers (independently, with minimal supervision, with moderate supervision, with maximal supervision) and ambulation distance will be recorded using standard PT protocols used at UAB Highlands.
  - The patients will be surveyed regarding their satisfaction with postoperative analgesia. Likert scale will be used to assess their satisfaction level. There will be 4 options to report: very unsatisfied, unsatisfied, satisfied, and very satisfied.
  - The hours from block placement until hospital discharge will be calculated.
- A blinded research associate will evaluate the patients postoperatively to collect data.

Procedure	Length of Time Required of Participants	Frequency of Repetition
Presurgical Evaluation on the day of surgery	30 minutes	once
Randomization on day of surgery	5 minutes	Once
Placement of block	Approximately 30 min.	Once
Post Anesthesia Care Unit (PACU) assessment	10 minutes	Once
First postoperative assessment survey (approximately 24 hours after surgery)	20 minutes	Once

Second postoperative assessment survey (approximately 48 hours after surgery)	**10 minutes**	**Once**

- Measured Outcomes:

    a. Primary outcome:
        a. Quality of Recovery after surgery assessed on postoperative day 1 (at 24 hours).
        QoR-15 scale (form attached) will be used to assess post-operative recovery based on 15 questions: scores will range from 0-150, 0 being the worst recovery and 150 being the best (excellent) recovery.

    b. Secondary outcomes:
        a. QoR-15 at 48 hours
        b. VAS scores (0-10) at immediate postoperatively, 6, 12 and 24 hours at rest and movement. VAS score 0 indicates "no pain" and 10 indicates "worst pain experienced". Highest pain score in first 24 hours will be recorded.
        c. Opioid consumption intraoperatively, as well as at 24 hours postoperatively. Oxycodone PO and Hydromorphone iv usage in first 24 hours postoperatively.
        d. Incidence of nausea, vomiting and itching in first 24 hours postoperatively.
        e. Physical therapist assessment of independence in mobility and transfers (independent, with minimal supervision, with moderate supervision, with maximal supervision)
        f. Physical therapist documentation of ambulation distance
        - Patient satisfaction on Likert scale will be used to assess their satisfaction level. There will be 4 options to report: very unsatisfied, unsatisfied, satisfied, and very satisfied.
        g. Hours to hospital discharge (Surgery finish time to discharge time).

List of variables/data points you will be collecting (e.g. – age, gender, date of surgery, etc.):

We will collect the following data:

1. patient age
2. patient gender

3. Weight
4. Height
5. BMI
6. Surgical approach
7. ASA physical status
8. Average amount of opioids consumed daily in the week prior to surgery
9. VAS scores immediately postoperatively in the recovery room, 24 hours postoperatively
10. Opioid consumption intraoperatively and postoperatively
11. Physical therapy assessments
    1. Degree of independence in mobility and transfers at 24 hours
    2. Ambulation distance at 24 hours
12. Time to discharge from the hospital

Projected Overall Study Timeline

Date	Study Start-Up	Enrollment	Data Entry and Analysis	Study Write-Up
12 2020	X			
01 2021		x		
04 2021			x	
05 2021				x

7.0 **PLAN FOR STUDY:** Click here to enter text.

a. What is the potential impact of your study findings (e.g., how will findings impact clinical outcomes)? This study will compare the quality of recovery after total hip arthroplasty with PENG block for postoperative pain control versus no PENG block. The PENG block targets only the sensory branches and not the posterior mechanoreceptors; there is a potential motor-sparing effect which is desirable for early ambulation, better physical therapy, and earlier discharge. The effective analgesia and early ambulation provided by such regional anesthesia block may have positive impact on patient's mood, sleep, appetite and overall feeling of well-being. It remains unclear whether PENG block

provides sufficient analgesia and improves the quality of post-operative recovery after primary THA. .

b. Do you plan to submit an abstract based on this project? ☒ Yes ☐ No (If yes, to which meeting venue? American Society of Regional Anesthesia
c. Do you intend to publish the finding from this research project: ☒ Yes ☐ No

8.0 **DRUG INFORMATION** (if applicable)

Drug Name: 0.75% Bupivacaine

Other Names: Marcaine

Classification: Amino-amide local anesthetic

Mode of Action: Blocks both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions, which results in inhibition of depolarization with resultant blockade of conduction

Storage and Stability: store at 20-22 degree centigrade (Room Temperature)

Metabolism: Hepatic metabolism via CYP1A2 (minor), CYP2C19 (minor), CYP2D6 (minor), CYP3A4 (minor). Local anesthetics and their metabolites are excreted by the kidney. Urinary excretion is affected by urinary perfusion and factors affecting urinary pH. Only 6% of bupivacaine is excreted unchanged in the urine.

Preparation: Bupivacaine Hydrochloride is a sterile isotonic solution containing 2.5 mg/ml bupivacaine, 5 mcg/ml epinephrine and 8.5 mg/ml sodium chloride

Administration: Local infiltration, peripheral nerve block, retrobulbar block, sympathetic block, lumbar epidural, caudal

Incompatibilities: Bupivacaine with epinephrine should not be used concomitantly with ergot-type oxytocic drugs, because a severe persistent hypertension may occur. Likewise, solutions of bupivacaine hydrochloride containing a vasopressor such as epinephrine should be used with extreme caution in patients receiving monoamineoxidase iiinhhhibitors (MAOI) or antidepressants of the triptyline or imipramine types, because severe prolonged hypertension may result.

- *Contraindications: Hypersensitivity to bupivacaine, amide-type local anesthetics, or any component of the formulation; obstetrical paracervical block anesthesia. Until further experience is gained in pediatric patients younger than 12 years, administration of bupivacaine in this age group is not recommended. There have been reports of cardiac arrest and death during the use of bupivacaine hydrochloride for intravenous regional anesthesia (Bier block). Information on safe dosages and techniques of administration of bupivacaine hydrochloride in this procedure is lacking. Therefore, bupivacaine hydrochloride is not recommended for use in this technique.*
- *Precautions: The lowest dosage of local anesthetic that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. The rapid*

injection of a large volume of local anesthetic solution should be avoided and fractional [incremental] doses should be used when feasible. Local anesthetic solutions containing a vasoconstrictor should be used cautiously and in carefully restricted quantities in areas of the body supplied by end arteries or having otherwise compromised blood supply such as digits, nose, external, ear, or penis. Patients with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result. Because amide-local anesthetics are metabolized by the liver, these drugs, especially repeat doses, should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally , are at a greater risk of developing toxic plasma concentrations. Local anesthetis should also be used with caution in patients with impaired cardiovascular function because they may be less able ot compensate for functional changes associated with the prolongation of AV conduction produced by these drugs.

Click here to enter text.

Side Effects: Adverse effects indicated in *italics* are the most frequent adverse effects. Adverse events in bold are severe/life-threatening, otherwise they are mild to moderate in reaction.

CNS: ***Seizures**: convulsions due to systemic toxicity leading to cardiac arrest have also been reported, presumably following unintentional intravascular injection or administration near the head or neck.*

CV: **arrhythmias, cardiac arrest, death**

EENT: ***Respiratory arrest**, especially when administered near the head or neck*

ENDO: Click here to enter text.

GI: Click here to enter text.

GU: Click here to enter text.

INTEG: Click here to enter text.

MS: *Intra-articular infusion related chondrolysis: Continuous intra-articular infusion of local anesthetics after arthroscopic or other surgical procedures is not an approved use; chondrolysis (primarily shoulder joint) has occurred following infusion, with some patients requiring arthroplasty or shoulder replacement.*

Investigational New Drug (IND) Application required (check yes or no): ☐Yes ☒No

Will the research Pharmacy be involved in the ordering, storage, dispensing and blind of the study drug? ☐ Yes ☒ No

8.0 **DRUG INFORMATION** (if applicable)

Drug Name: 2% Lidocaine

Other Names: Click here to enter text.

Classification: Amide-type local anesthetic

Mode of Action: Cardiac antiarrhythmic effect is exerted by increasing the electrical stimulation threshold of the ventricle during diastole

Storage and Stability: Room temperature (25°C); brief exposure up to 40°C does not adversely affect the product

Metabolism: 90% hepatic metabolism; 10% renally excreted, unchanged

Preparation: Lidocaine hydrochloride and 5% dextrose injection is a sterile, nonpyrogenic solution prepared from lidocaine hydrochloride and dextrose in water for injection.

Administration: Intravenous, local infiltration

Incompatibilities: Lidocaine should be used with caution in patients with digitalis toxicity accompanied by atrioventricular block. Coadministration of propranolol or cimetidine with lidocaine has been reported to reduce the clearance of lidocaine from the plasma nad may result in toxic accumulation of the drug. When lidocaine is administered with other antiarrhythmic drugs such as amiodadrone, phenytoin, procainamide, propranolol or quinidine, the cardiac effects may be additive or antagonistic and toxic effects may be additive. Phenytoini may stimulate the hepatic metabolism of lidocaine, but the clinical significance of this effect is not known.

- *Contraindications: Lidocaine hydrochloride is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type. Lidocaine should not be used in patients with Stokes-Adams syndrome, Wolff-Parkinson-White syndrome, or with severe degrees of sinoatrial, atrioventricular or intraventricular block. Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products.*
- *Precautions: Caution should be employed in the repeated use of lidocaine hydrochloride in patients with severe liver or renal disease because accumulation may occur and lead to toxic phenomena, since lidocainie hydrochloride is metabolized mainly in the liver and excreted by the kidneys. The drug should also be used with caution in patients with hypovolemia and shock and in all forms of heart block. In patients with sinus bradycardia or incomplete heart block, the administration lidocaine hydrochloride intravenously for the elimination of ventricular ectopic beats without prior acceleration in heart rate (by isoproterenol or electric pacing) may promote more frequent and serious ventricular arrhythmias or complete heart block. Most potent anesthetic agents, local anesthetics of the amide type, which includes lidocaine, and muscle relaxants of both depolarizing and non-depolarizing types, have been associated with malignant hyperthermia.*

Click here to enter text.

Side Effects: Adverse effects indicated in *italics* are the most frequent adverse effects. Adverse events in bold are severe/life-threatening, otherwise they are mild to moderate in reaction.

CNS: **respiratory depression and arrest; unconsciousness; convulsions; tremors; twitching; vomiting; blurred or double vision; drowsiness; dizziness; light-headedness; tinnitus; sensation of heat, cold or numbness; euphoria, apprehension**

CV: **Prolongation of PR interval, widening of the QRS interval and appearance or aggravation of arrhythmias**

EENT: Click here to enter text.

ENDO: **Methemoglobinemia**

GI: Click here to enter text.

GU: Click here to enter text.

INTEG: Click here to enter text.

MS: Click here to enter text.

Investigational New Drug (IND) Application required (check yes or no): ☐Yes ☒No

Will the research Pharmacy be involved in the ordering, storage, dispensing and blind of the study drug? ☐ Yes ☒ No

DEVICE INFORMATION (if applicable)

Device Name: Click here to enter text. Other Names: Click here to enter text.

Classification: Click here to enter text.

Mechanism of Action: Click here to enter text.

Medication(s) Delivered: Click here to enter text.

Incompatibilities: Click here to enter text.

Contraindications: Click here to enter text.

Precautions: Click here to enter text.

SIDE EFFECTS: Adverse effects indicated in *italics* are the most frequent adverse effects. Adverse events in **bold** are severe/life-threatening, otherwise they are mild to moderate in reaction.

CNS: Click here to enter text.

CV: Click here to enter text.

EENT: Click here to enter text.

ENDO: Click here to enter text.

GI: Click here to enter text.

GU: Click here to enter text.

INTEG: Click here to enter text.

MS: Click here to enter text.

Investigational Device Exemption (IDE) required check yes or no): ☐Yes ☐No (If yes, provide details. Click here to enter text.

9.0 STATISTICAL CONSIDERATIONS

General Data Analysis Plan:

The distribution of the continuous factors will be examined using data visualization techniques such as q-q plots and the Shapiro-Wilk test. All normally distributed demographic and continuous variables will be expressed as means and standard deviations; categorical factors will be expressed as proportions. For non-normal data, the medians and inter quartile ranges will be displayed. For data that are normally distributed, Student's t-test will be used to compare the groups. For data that are not normally distributed, a Mann-Whitney tests will be used for comparisons. Chi-square or Fisher's exact tests will be used to analyze categorical data. Time to event data such as distance of first ambulation will be analyzed using Kaplan-Meier curves. The planned sub-group analysis will be conducted for GA vs. Spinal using a 2x2 ANOVA test. For all comparisons, a value of $p < 0.05$ will be considered statistically significant. Statistical analyses will be performed using SAS for Windows, version 9.2.

Statistical Power and Sample Size Estimates: Fifty-six patients in each group are required to detect a Minimal Clinically Important Difference (MCID) of 8 points for QoR-15 score assuming a standard deviation of 15 points using data from previous studies (19, 20) for 5% significance level and 80% power.

10.0 PATIENT SAFETY AND DATA SECURITY MONITORING

- Does this research involve children (i.e. <18 years of age)? no
- Assessment of Level of Risk: ☐High ☐Medium ☒ Low ☐ Not applicable

  Click here to enter text.
- Reporting adverse events:

  A data and safety monitoring plan will be implemented by Drs. Kukreja and MacBeth to ensure that there are no changes in the risk/benefit ratio during the course of the study and that confidentiality of research data is maintained. This will be achieved by close following of study participants to screen for adverse events during data collection phase. Investigators and study

personnel will meet either electronically or in person, monthly (more often if needed) during active participant enrollment to discuss the study (e.g., study goals and modifications of those goals; subject recruitment and completion; progress in data coding and analysis; documentation, identification of adverse events or research subject complaints; violations of confidentiality) and address any issues or concerns at that time.

The mechanisms for HIPAA compliance [including a detailed electronic personal health information (PHI) data path]:

Mechanisms for HIPAA compliance: The de-identified study data will first be entered onto standardized, preprinted data collection sheets that will have no patient identifiers on them such as name, medical record number and date of surgery. The study data will be collected and stored on a secure research server maintained by the Department of Anesthesiology. The research server is HIPAA compliant, has researcher specific restricted access, and is password protected. This research server is backed up to another secure research server at a different location. The list of patients participating in the study with their medical record numbers and dates of surgery will be kept separately and securely in a locked filing cabinet in the locked office of Dr. Kukreja and will be destroyed, after final data analysis, using the UAB contracted confidential shredding service. The original paper data collection forms will be disposed of using the UAB contracted confidential shredding service after the de-identified data have been transferred to the password-protected, computer database. From that point in time onward, all study participants will be identified only by their individual study specific number, both on the above server and the backup server. All personnel who are involved in the design or conduct of this research study will have successfully completed

required IRB training which includes the importance of measures to protect patient confidentiality.

References:

1. Wolford ML, Palso K, Bercovitz A. Hospitalization for total hip replacement among inpatients aged 45 and over: United States, 2000-2010. NCHS data brief 2015(186): 1-8.
2. Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France: The SOS Regional Anesthesia Hotline Service. Anesthesiology 2002;97(5):1274-1280.
3. Shariat AN, Hadzic A, Xu D, et al. Fascia iliaca block for analgesia after hip arthroplasty: a randomized double blind, placebo-controlled trial. Reg Anesth Pain Med 2013;38(3): 201-205.
4. Bugada D Bellini V, Lorini LF, Mariano ER. Update on selective regional analgesia for hip surgery patients. Anesthesiology Clinics 2018;36(3): 403-415.
5. Guay J, Parker MJ, Griffiths R, Kopp SL. Peripheral nerve blocks for hip fractures: A Cochrane Review. Anesth Analg 2018;126(5): 1695-1704.
6. Chazapis M, Walker EMK, Rooms MA, et al. Measuring quality of recovery-15 after day case surgery. Br Journal of Anaesthesia 2016, 116(2): 241-248.
7. Myles P, Weitkamp B, Jones K, Melick J, Hensen S. Validity and reliability of a postoperative quality of recovery score: the QoR-40. Br J Anaesth 2000;84:11-15.
8. Pauls RN, Crisp CC, Oakley SH, et al. Effects of dexamethasone on quality of recovery following vaginal surgery: a randomized trial. Am J Obstet Gynecol 2015;213:718.e1-7.
9. Gornall BF, Myles PS, Smith CL, Burke JA, Leslie K et al. Measurement of quality of recovery using the QoR-40: a quantitative systematic review. Br J Anaesth 2013; 111: 161-169.
10. Wylde V, Hewlett S, Learmonth ID, et al. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. Pain 2011;152: 566-572. doi: 10.1016/j.pain.2010.11.023
11. Nikolajsen I, Brandsborg B, Lucht U, et al. Chronic pain following total hip arthroplasty: A nationwide questionnaire study. Acta Anesthesiol Scand 2006; 50:495-500. doi: 10.1111/j.1399-6576.2006.00976
12. Shariat AN, Hadzic A, Xu D, et al. Fascia Iliaca Block for Analgesia after Hip Arthroplasty: A Randomized Double-blind, Placebo-controlled Trial. Reg Anesth Pain Med. 2013, 38:201-205. 10.1097/AAP.0b013e31828a3c7c
13. Kukreja P, MacBeth L, Sturdivant A, et al. Anterior quadratus lumborum block analgesia for total hip arthroplasty: a randomized, controlled study. Reg Anesth Pain Med. 2019, 44:1075-1079. 10.1136/ramp-2019-100804
14. Gupta A, Sondekoppam R, Kalagara H. Quadratus Lumborum Block: a Technical Review. Curr Anesthesiol Rep. 2019, 9:257-262. 10.1007/s40140-019-00338-9
15. Short AJ, Barnett JJG, Gofeld M, et al. Anatomic Study of Innervation of the Anterior Hip Capsule: Implication for Image Guided Intervention. Reg Anesth Pain Med. 2018, 43:186-192. 10.1097/AAP.0000000000000701
16. Bugada D, Bellini V, Lorini L, Mariano ER. Update on Selective Regional Analgesia for Hip Surgery Patients. Anesthesiology Clin. 2018, 36:403-415. 10.1016/j.anclin.2018.04.001
17. Giron-Arango L, Peng PWH, Chin KJ, Brull R, Perlas A. Pericapsular Nerve Group (PENG) Block for Hip Fracture. Reg Anesth Pain Med. 2018, 43:859-863. 10.1097/AAP.0000000000000847

18. Kikuchi M, Mihara T, Mizuno Y, et al. Anterior quadratus lumborum block for postoperative recovery after total hip arthroplasty: a study protocol for a single center, double blind, randomized controlled trial. Trials 2020, 21: 142.
19. Myles PS, Myles DB, Galagher W, et al. Minimal clinically important difference for three quality of recovery scales. Anesthesiology 2016, 125(1): 39-45.
20. Tan NL, Gotmaker R, Barrington MJ. Impact of local infiltration analgesia on quality of recovery after anterior total hip arthroplasty: A randomized controlled, triple blind placebo controlled trial. Anesth Analg 2019, 129(6): 1715-1722.

Appendix:

QOR-15 FORM

QoR-15 Patient Survey

Date: __/__/__ Study #: _____

Preoperative ☐ Postoperative ☐

PART A

How have you been feeling in the last 24 hours?

(0 to 10, where: 0 = none of the time [poor] and 10 = all of the time [excellent])

1. Able to breathe easily	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
2. Been able to enjoy food	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
3. Feeling rested	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
4. Have had a good sleep	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
5. Able to look after personal toilet and hygiene unaided	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
6. Able to communicate with family or friends	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
7. Getting support from hospital doctors and nurses	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
8. Able to return to work or usual home activities	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
9. Feeling comfortable and in control	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time
10. Having a feeling of general well-being	None of the time	0	1	2	3	4	5	6	7	8	9	10 All of the time

PART B

Have you had any of the following in the last 24 hours?

(10 to 0, where: 10 = none of the time [excellent] and 0 = all of the time [poor])

11. Moderate pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
12. Severe pain	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
13. Nausea or vomiting	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
14. Feeling worried or anxious	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time
15. Feeling sad or depressed	None of the time	10	9	8	7	6	5	4	3	2	1	0 All of the time

Fig. 2. The quality of recovery score (QoR)-15 questionnaire.

Statistical analysis

Data were summarised using means and standard errors (SE) for continuous outcomes or counts and percentages for categorical outcomes. Two-sample t-tests and chi-square tests were used to compare the two groups. Normality for continuous outcomes was assessed using probability plots and the Shapiro-Wilk test for normality. For any outcomes where normality could not be reasonably assumed, medians and interquartile ranges were reported instead of medians and standard errors, respectively, and the Wilcoxon rank sum test was used in place of the t-test. A 95% confidence interval for differences in means (for continuous outcomes) or relative risks (for categorical outcomes) were calculated. For any non-normally distributed continuous outcomes, asymptotic Hodges-Lehmann confidence limits were calculated.[16] A p-value < 0.05 was considered statistically significant. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used to conduct all statistical analyses.

Sample size calculation

A difference of 8 points is widely accepted as a minimal clinically important difference (MCID) for QoR-15 scores for perioperative interventions.[17] A previous study showed a median QoR-15 score of 115 in the control group for the THA population.[18] Assuming an increase to 123 in the QoR-15 score would be clinically relevant and a standard deviation of 15 points, we estimated that fifty-six patients were needed in each group for 80% power at a 5% significance level.