Short Title
PENG Block versus LP Block for Postoperative Analgesia after Anterior Total Hip Arthroplasty

Full Title
Peri-capsular Nerve Group Block versus Lumbar Plexus Block for Postoperative Analgesia after Primary Anterior Approach Total Hip Arthroplasty

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Summary/Purpose/Rationale
Regional anesthesia procedures represent a common modality for postoperative analgesia after total hip arthroplasty surgeries (THA). The standard practice at our institution for many years has been the Lumbar Plexus block (LPB), which anesthetizes the L1-L5 lumbar nerve roots[1]. While the LPB offers analgesia from the associated sensory block, it also blocks motor fibers, leading to lower extremity weakness that could potentially delay the patient's ability to participate in early physical therapy and may thereby delay discharge. In the past several years, newer regional anesthesia block approaches have been described and investigated in an attempt to provide patients with postoperative analgesia while avoiding associated muscle weakness, facilitating earlier physical therapy participation and discharge. One such nerve block is the peri-capsular nerve group (PENG) block, which anesthetizes the articular branches of the femoral, obturator, and accessory obturator nerves providing sensory innervation to the hip joint capsule without consistently causing lower extremity weakness[2]. While we continue to perform LPB for postoperative analgesia after THA at our institution, some institutions are utilizing the PENG block to provide postoperative analgesia and facilitate early mobilization. There are currently no prospective studies that directly compare the efficacy of LPB to PENG block for providing postoperative analgesia after THA.

Objectives
The purpose of this randomized, double blinded, prospective study is to compare the postoperative analgesia provided by the PENG block to that provided by the LPB for patients undergoing primary anterior approach THA. We hypothesize that the PENG block will provide equivalent analgesia to LPB after THA. The primary outcome will be a comparison of patient-reported numeric rating scale (NRS) pain scores with movement at six hours following block placement. Equivalency will be defined as a difference of less than one point in either direction on the eleven-point NRS pain scale (0-10). Secondary outcomes will include NRS pain scores with movement at 12, 18, and 24 hours, NRS pain scores at rest at 6, 12, 18, and 24 hours, time to first opioid administration, cumulative dose of postoperative opioid administration within the first 24 hours, motor strength at six hours after block placement as assessed by straight leg raise on a six-point scale (0-5)[3], and distance walked at first postoperative physical therapy session. The 18 hour assessment for pain at rest and with movement is allowed to be done retrospectively at the time of the 24 hour assessment, as this time point would end up interrupting the sleep of the study subject as would be occurring in the early morning hours. If the subject reports asleep

at the 18 hour scheduled time point, the no pain score will be obtained. This will be considered a missing data point and not a deviation. If the subject reports they were awake at the 18 hour time point, then a pain score at rest will be obtained but if the subject reports no movement, this score will be a missing data point and not a deviation.

Methods/Measurements

Design

This will be a randomized, double blinded, equivalency trial that will take place after approval from our Institutional Review Board. Written informed consent will be obtained from all study participants prior to randomization. The trial will be registered on clinicaltrials.gov before any enrollment begins.

Selection Criteria

Inclusion: Adults between 18 and 90 years of age undergoing elective primary total hip arthroplasty surgery by an anterior approach at Atrium Health Wake Forest Baptist Davie Medical Center, and who have consented to and lack any contraindications to either LPB or PENG block for postoperative analgesia will be recruited for participation in the study.

Exclusion: Patients with any contraindications to regional anesthesia, such as history of allergy to amide local anesthetics, pre-existing coagulopathy or thrombocytopenia (less than 100,000 per microliter), refusal to either analgesic block, presence of a progressive lower extremity neurological deficit, localized or systemic infection, chronic use of high dose opioid analgesics (defined at daily use greater than 60mg oxycodone equivalents), as well as those who are pregnant, will be excluded from participation. A diagnosis of multiple sclerosis and Parkinson's disease will also exclude potential study subjects. Any patients who refuse enrollment or withdraw their consent will be excluded and any of their information already collected will be destroyed.

Setting

Patients between 18 and 90 years of age, scheduled to undergo elective, primary total hip arthroplasty surgery at Davie Medical Center performed by the two orthopedic surgeons who perform THA by an anterior approach at our institution, will be identified for eligibility. These patients will be seen in the preoperative assessment clinic per our standard protocol prior to their surgery date, at which time the study will be discussed with all eligible patients, and they will be offered the ability to enroll in the study. Written informed consent will either be obtained during this visit, or the patient will be allowed to take the consent form home with them to discuss with their family and consider participation, and written informed consent can be finalized on the day of surgery.

Study Protocol

Baseline data collection

Upon arrival and check-in to the regional anesthesia area of surgical services at Davie Medical Center on the day of surgery, enrolled patients will be asked to rate their baseline verbal pain score both at rest and with movement on the eleven-point NRS pain scale (0-10, where 0 represents no pain and 10 represents the worst imaginable pain). Patient characteristics will be recorded, including age, gender, height, weight, BMI, surgeon, and operative side, as well as preoperative opioid use and doses. Baseline motor function will be assessed by straight leg raise on the surgical side to resistance and measured on the six-point Medical Research Council (MRC) scale (0-5, where 0 represents no voluntary contraction possible, 1 represents muscle flicker without movement of limb, 2 represents active movement only with gravity eliminated, 3 represents movement against gravity but without resistance, 4 represents movement possible against some resistance, and 5 represents normal motor strength against resistance)[3].

Two phone numbers will be obtained from the patient, if the patient consents, for contact after discharge. Each patient will also be provided with a pain journal with which to document pain scores for any remaining time points after discharge, in case they are not available by phone at the time points of interest. All patients will still be admitted at the six hour mark, for collection of the primary endpoint of NRS pain with movement, as well as motor strength at six hours after block placement.

Randomization

Prior to beginning any regional anesthesia procedures, each patient will be randomized to one of the aforementioned treatment arms consisting of LPB or PENG block by research personnel and/or the attending anesthesiologist in charge of the patient's care. Randomization will occur in blocks of sequentially numbered opaque envelopes. Patients will be blinded to their treatment arm assignment, as will all research personnel who collect outcome data. Patient blinding will occur through the use of a sham block procedure as detailed below.

Interventions

Once randomization occurs, standard American Society of Anesthesiology (ASA) monitors and supplemental oxygen will be applied to the patient, and a timeout procedure will be conducted to verify all patient data and paperwork are correct. Unless the patient has a contraindication, each patient will also receive a weight-appropriate dose of acetaminophen and celecoxib, or meloxicam (if the patient has an allergy to sulfonamide medications or to celecoxib) at this time.

All blocks will be performed by an experienced faculty anesthesiologist well versed in the performance of LPB and PENG blocks, or by a regional anesthesia fellow directly supervised by a regional anesthesia specialized faculty anesthesiologist. Sedation for block placement will be administered using midazolam and fentanyl titrated to patient comfort, at the discretion of the attending anesthesiologist performing or supervising the regional anesthesia procedures. All subjects will start in the supine position, and their relevant anatomy for PENG block will be imaged using an ultrasound as described previously[2], after skin preparation with chlorhexidine solution. All subjects will then receive a skin wheal using 1mL of 1% lidocaine at the skin entry site for a typical PENG block. Those subjects assigned to the PENG treatment arm will subsequently receive a PENG block using 20mL of 0.2% ropivacaine with 1:400,000 epinephrine dosed in 5mL increments with negative aspiration beforehand and between each aliquot. All subjects will then be transitioned to lateral decubitus positioning with the surgical

side up (standard at our institution, as we use an isobaric spinal solution). Using a skin marker, midline will be marked on their lumbar spine at the level of the iliac crests, and a point two thirds the distance between midline and the posterior superior iliac spine on the surgical side will be marked[1]. Following this, their lower back areas will be prepared with antiseptic solution and draped in sterile fashion. All subjects will then receive a skin wheal with 1cc of 1% lidocaine at the standard LPB block site just marked as described above. Those subjects assigned to the LPB treatment arm will subsequently receive a stimulation-based LPB dosed with 20cc of 0.2% ropivacaine with 1:400,000 dilution epinephrine dosed in 5mL increments with negative aspiration beforehand and between each aliquot. The PENG block site skin wheal will behave as a sham block for subjects enrolled in the LPB arm, and the LPB block site skin wheal will behave as a sham block for those enrolled in the PENG arm.

All patients will then receive a spinal block as the primary anesthetic using 3.5mL of 0.5% ropivacaine with 10mcg fentanyl. Following placement of the spinal block, the patients will be brought to the operating room and receive our standard intraoperative protocol of propofol infusion for sedation, along with dexamethasone 10mg IV, ondansetron 4mg IV, surgical antibiotic prophylaxis as appropriate, and IV tranexamic acid 1g at both capsule opening and capsule closure. Any patients whose spinal block are determined to have failed, as checked prior to initiation of propofol sedation and surgical skin preparation with a pinch test on the surgical lower extremity, will be induced under general anesthesia using propofol with placement of a laryngeal mask airway or endotracheal tube at the discretion of the attending anesthesiologist.

Materials

Ultrasound guidance for imaging the relevant anatomy for the PENG block will be obtained using curvilinear probe and a sterile probe cover. An insulated, stimulating block needle be used to perform the PENG blocks for subjects enrolled in the PENG treatment arm, as well as for the LPB for subjects enrolled in the LPB treatment arm. The entire lower back area will be prepped in sterile fashion prior to LPB and spinal block placement. All products and medications used are FDA approved for the abovementioned procedures.

Measurements

Following the completion of surgery, all subjects will be brought to the post-anesthesia care unit (PACU) for recovery, where they will recover until satisfactory resolution of spinal block as judged by an attending anesthesiologist is shown. Subjects will then be transported to an inpatient room, where nurses will monitor their vital signs and pain scores regularly. Subjects will receive standard of care pain medications for postoperative pain management as indicated. Subjects will continue to receive scheduled acetaminophen 1000mg every six hours (or 15mg/kg if their weight is below 65kg), and the NSAID administered preoperatively (either celecoxib 200mg twice daily or meloxicam 15mg once daily) barring any contraindication such as renal impairment or vascular disease. Oxycodone every four hours may also be administered as needed with dose ranges determined by the Davie Medical Center perioperative surgical home anesthesiologist consulted for postoperative care, or another narcotic at equipotent dosages if they have a contraindication to oxycodone. Alternatively, they may receive combination products such as Percocet (oxycodone/acetaminophen) or Vicodin/Norco (hydrocodone/acetaminophen) instead, with the acetaminophen dosage adjusted accordingly. All

opioids will be converted to oxycodone equivalents to allow for appropriate comparison using a widely available dose conversion table[4].

Nurses will chart vital signs and medication administration in the electronic medical record (EMR) as per our standard protocol. Research personnel will measure patient-reported NRS pain scores at rest and with movement for each time by patient interaction, either face to face, or by calling the patient's room or phone numbers. This will include the primary outcome of patient-rated pain with movement of the surgical extremity on the NRS pain scale at six hours after block placement (roughly correlating to two hours after arrival to their room) as well as secondary outcomes that include but are not limited to pain at rest and with movement at 12, 18, and 24 hours following block placement, and strength to straight leg raise at six hours post-block placement. The cumulative 24 hour opioid consumption will be abstracted from the EMR for doses received while admitted, and documented by the patient in their pain journal and abstracted via phone call after their discharge, if this occurs prior to 24 hours after the block. Physical therapists will also document their encounters in the EMR, including but not limited to the secondary outcome of distance ambulated during their first session in feet. These metrics will be accessed, abstracted, de-identified, and analyzed by research personnel who are blinded to group allocation.

Statistical Analysis

Power Analysis

We define an equivalent mean pain score to be a margin of one point in either direction on the eleven-point NRS scale. Based on retrospective quality improvement data at our institution, the patient-reported surgical site pain on the eleven point NRS scale following THA in patients who received a preoperative LPB at Davie Medical Center had a mean of 4.8 and standard deviation of 2.0. Using these values, and setting the significance level to 0.05 with a power of 80%, we calculated the minimum required sample size to be n=69 in the LPB group and n=69 in the PENG group to conclude equivalence of movement pain at six hours between the two groups. Power was calculated using the R package 'TOSTER'[5]. We intend to recruit n=80 patients per arm to allow for attrition and dropout.

Data Analysis

Demographic information will be collected and compared between the groups to verify that randomization balanced out important baseline variables between LPB and PENG. For the primary outcome of patient-reported pain with movement at six hours after block placement, the equivalence hypothesis test of LPB versus PENG groups will be performed using two one-sided t-tests. We will also calculate a point and confidence interval estimate of the difference between LPB and PENG groups. Secondary outcomes will also be compared using t-tests and confidence intervals.

Missing Data Points

If we find that study participants are missing substantial parts of their sequence of longitudinal measurements (6, 12, 18, and 24 hours), we will employ a mixed effects modeling framework that allows us to use all available data to test hypotheses about differences between PENG and

LRB at each time point. Models will be implemented using the 'lme4' package[6] in R statistical software[7].

Human Subjects Protection

Subject Recruitment Methods

Potential candidates for the study will be identified based on the posting for the surgical procedure of elective primary anterior approach total hip arthroplasty. Patients will be approached during their preoperative assessment clinic visit for eligibility and told about the study in detail, including any known or possible risks, benefits, and alternatives. They will be advised there will be no financial incentive to participate Potential subjects will also be recruited over the phone if they are not scheduled for a preoperative evaluation by anesthesia. They will be identified by the surgery schedule. Upon phone discussion they demonstrate interest a copy of the IRB approved informed consent form will be mailed to them to allow for adequate review of the study prior to the morning of surgery. . Written informed consent will be obtained and scanned into the EMR during that visit, if they consent, or on the day of surgery, if they need more time to deliberate on enrolling. Ample opportunity to ask questions will be given both during this preoperative visit and on day of surgery. All patients meeting the aforementioned eligibility criteria, regardless of gender, age, race, and ASA physical status, will be offered to participate.

Informed Consent

Written informed consent will be obtained from each subject who agrees to enroll, scanned, and uploaded into the patient's EMR for permanent storage. Each patient will have the opportunity at any time to decline enrollment, withdraw informed consent, and have their data removed from the dataset and destroyed at any point in time.

Confidentiality and Privacy

Confidentiality will be protected by collecting only the requisite information required to assess the study outcomes, minimizing the collection of any information that could directly identify subjects. Each patient will be assigned a unique study identifier that will appear on the data collection form, and any protected health information that may directly identify the patient corresponding to the unique study identifier will be kept secure with access limited to designated study personnel. Following collection of all data, subject identifying information will be destroyed at the earliest opportunity, consistent with data validation and study design, producing an anonymous data set for analysis. All patient information collected will be kept confidential during recruitment as well as the remainder of the study. All identifying protected health information will be de-identified in the electronic database during data collection, which will be encrypted and secured in the Atrium Health Wake Forest Baptist private servers and only accessible by two-factor authenticated, password-protected computers. Only selected research personnel will have access to the dataset. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigators will be responsible for overall monitoring of the data and safety of study participants and will be assisted by other members of the research personnel in the identification of any safety concerns.

Reporting of Unanticipated Problems, Adverse Events, or Deviations
Each participating attending anesthesiologist will report to the principal investigators about any protocol violations, unanticipated problems with the protocol, or adverse events, which will promptly be reported to the IRB and corresponding government agency, if appropriate.

Resources/Citations

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3: Compston A. Aids to the investigation of peripheral nerve injuries. Medical Research Council: Nerve Injuries Research Committee. His Majesty's Stationery Office: 1942; pp. 48 (iii) and 74 figures and 7 diagrams; with aids to the examination of the peripheral nervous system. By Michael O'Brien for the Guarantors of Brain. Saunders Elsevier: 2010; pp. [8] 64 and 94 Figures. Brain. 2010 Oct;133(10):2838-44.

4: McPherson, ML. Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing. American Society of Health-Systems Pharmacists, Bethesda, MD (2010).

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6: Douglas Bates, Martin Maechler, Ben Bolker, Steve Walker. Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*. 2015;67(1),1-48. doi:10.18637/jss.v067.i01.

7: R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing.Vienna, Austria. URL https://www.R-project.org/