Functional and Analgesic Effects of The Addition of iPACK Blocks to Continuous Adductor Canal Blocks Following ACL Reconstruction with Quadriceps Tendon Autograft: A Randomized Controlled Trial

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PROTOCOL TITLE:

Studying the effects of iPACK blocks with adductor canal blocks for postoperative analgesia following ACL reconstruction

PRINCIPAL INVESTIGATOR:

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1.0 Objectives / Specific Aims

We hypothesize that participants receiving the ACB-iPACK intervention will have lower subjective pain scores and lower total opioid consumption in the initial 72-hours of the postoperative window and increased range of motion at subsequent follow up visits with their surgeon.

2.0 Background

Adequate analgesia with maintained functionality is crucial to recovery for patients undergoing outpatient anterior cruciate ligament (ACL) reconstruction. Perioperative peripheral nerve blocks have been utilized in these procedures to maximize postoperative pain control, minimize side effects from IV analgesics, and facilitate discharge from PACU. Past research has pointed to adductor canal blocks (ACBs) being superior to femoral nerve blocks (FNBs) for preserving motor strength during postoperative analgesia following knee arthroplasty [1]. Similar studies specifically looking at ACL reconstruction have shown similar analgesic effects between both blocks, with ACBs having a much higher maximal voluntary contraction of the quadriceps while in the PACU [2]. Further studies have found that for patients who underwent TKAs, ACBs were insufficient in reliving posterior knee pain due to the saphenous nerve innervating only the anterior and medial knee [3] [4]. This study looks to determine whether an increasingly used technique called iPACK block can be used to augment postoperative analgesia when used in conjunction with an ACB for ACL reconstruction. iPACK (infiltration between the popliteal artery and the capsule of the posterior knee) is thought to work by blocking branches of the popliteal plexus and genicular nerves, providing analgesia for the posterior knee that ACBs do not cover [5]. Previous studies have shown positive outcomes for TKA patients using an ACB-iPACK combination with regards to subjective pain measures and opioid consumption, however this relationship has not been confirmed for ACL reconstruction [6].

3.0 Intervention to be studied (if applicable)

This study will consist of participants 12 years and older undergoing ACL reconstruction using a quadriceps or bone-patella tendon bone (BTB) graft. The primary goal will be to determine the differences in postoperative pain during the first 72 hours when comparing an ACB + iPACK block to an ACB alone. Secondary outcomes will include opioid utilization during the first 72 hours postoperatively and range of motion including terminal knee extension at postoperative follow-up visits.

4.0 Study Endpoints (if applicable)

- The primary endpoint will measure subjective pain scores as 12-hour intervals during the first 72 hours of the postoperative window as collected by a study team member.
- The secondary endpoints will measure total postoperative opioid consumption through postoperative day 2, as well as measure the range of motion and terminal knee extension of participants at postoperative follow-up visits.

5.0 Inclusion and Exclusion Criteria/ Study Population

Participants being scheduled for an ACL reconstruction procedure who meet inclusion criteria will be approached and offered enrollment upon arriving to the pre-operative area before the procedure.

Inclusion Criteria

- Age 12 years and older
- Patients who are scheduled to undergo an ACL reconstruction with quadriceps or BTB graft.

Exclusion Criteria

- Any contraindication to receiving regional anesthesia. This may include infection at the site of injection, allergy to local anesthetic, or pre-existing nerve injury.
- Patients undergoing hamstring graft or allograft for ACL
- Pre-existing infection at the site of injury
- Patients on chronic opioid treatments
- Pre-existing sensory or motor deficit in operative extremity
- Patients having a revision of previous ACL reconstruction
- Pregnant and/or lactating women
- Weighs less than 40kg

6.0 Number of Subjects

We will enroll and randomize 82 subjects.

7.0 Setting

Participants will be approached about the study during their pre-surgical consultation with their surgeon and formal consent will be obtained while they are in pre-op/holding prior to the procedure, both of which will take place at MUSC's Charleston West campus, or MUSC's Rutledge Tower. The study procedure will also take place at either of these locations.

8.0 Recruitment Methods

The study team will refer to the OR and clinic schedules available on EPIC to see which patients qualify. If time allows, the surgeon will introduce the study during the surgical consultation in clinic and provide an informational brochure about the study. If not, the study will be introduced to the patient in the pre-operative holding area prior to the procedure.

9.0 Consent Process

Consent will be obtained by IRB approved study team members who have a medical degree and are qualified to discuss the clinical nature of the options being offered.

- Potential study participants will be invited to participate in the study. Initial contact will be made with the patient on the day of the scheduled procedure by an IRB

approved study team member. The study will be explained, and the patient will be given time to read the consent thoroughly and ask any questions. This will happen in the private pre-op area.

- Written informed consent will be obtained if the participant agrees to participate after the study is thoroughly explained. For participants under 18 years of age, informed consent will be obtained by their parent or legal guardian and assent will be obtained from the participants themselves. A copy of the signed informed consent will be provided to the participant.

10.0 Study Design / Methods

This study will be a prospective, single-center, single-blind randomized controlled trial. Participants will be randomized by using a stratified randomization technique, stratified by sex into two groups:
1) continuous adductor canal block alone (ACB Only) ***or***
2) continuous adductor canal block with iPACK block (ACB + iPACK).

Preoperative: Adult participants and pediatric patients >70kg will receive 1g Tylenol and 1-2mg midazolam and up to 20mcg of dexmedetomidine for pre-procedure anxiolysis. Patients between 12 and 18 years old will receive Tylenol with a dose based on weight (Table 1), and 1-2mg midazolam and up to 20mcg of dexmedetomidine.

Table 1. Tylenol Dosage Based on Weight for Pediatrics

Weight	**Dosage**
≥70kg	1,000mg
45-70kg	650mg
<45kg	500mg

All participants will receive the continuous adductor canal block which consists of 20cc of 0.25% plain ropivacaine and will be given followed by placement of an OnQ pump infusing 0.2% ropivacaine at 6cc/hr. (4cc/hr. for participants less than 60Kg).

Those who are randomized to the ABC + iPACK group will receive an additional block consisting of 20cc of 0.25% Ropivacaine placed in the popliteal fossa between the popliteal artery and the posterior aspect of the capsule of the knee joint.

Participants randomized to the ACB-only group will receive a skin wheal at the same site where the iPACK block would have been placed in an effort to maintain the blind.

Perioperative: Participants will be appropriately sedated as per clinical care.

Postoperative: Participants will be given 0.2mg hydromorphone every 8 minutes as needed for pain, and 5mg of oxycodone may be administered adjunctively as needed if pan scores remain elevated after intravenous hydromorphone

Post-discharge: Participants will be instructed to schedule two post-operative follow up appointments with their surgeon as well as physical therapy. They will also be prescribed the following medication regimen after discharge:

Ages 12-18 and <70kg

- Tylenol 650mg q8h
- Naproxen 250mg q8h
- Oxycodone 5mg q4h PRN pain
- Aspirin 81mg daily for DVT prophylaxis

All patients ≥ 18 years of age and pediatric patients ≥70kg

- Tylenol 1,000mg q8h
- Naproxen 500mg twice daily
- Oxycodone 5-10mg q4h PRN pain
- Aspirin 325mg daily for DVT prophylaxis

Additionally, participants will be instructed to follow the following bracing and weight bearing instructions:

- Weight bearing as tolerated and no brace for isolated ACL reconstruction, small 2 or less sutures and all inside repair
- Brace for bucketed meniscus with inside out repair, and associated mcl, OR large repaid (more than 3 sutures) 0-90, and weight bearing as tolerated in extension
- Non-weight bearing with brace for meniscus roots, and lateral meniscus tears.

Currently, there is no consensus guidelines for venous thromboembolism prophylaxis in the setting of anterior cruciate ligament reconstruction surgery. Moreover, there is no universally agreed-upon dose for use of aspirin in the postoperative state for VTE prophylaxis. There is current evidence which would suggest aspirin is an effective and safe medication for DVT prophylaxis and other major lower extremity orthopedic surgical procedures. Additionally, current practice patterns would suggest that aspirin is the most commonly utilized VTE prophylaxis following anterior cruciate ligament reconstruction. [8]

Baseline and Randomization

After consenting and confirmation of meeting eligibility criteria, the participant will undergo the procedure as scheduled and as standard of care. The participant will be

randomized before they are anesthetized, as the block will be prepared and placed prior to the start of surgery.

If randomized to ACB-Only (Group A) the participant will receive the ACB block first. The injection site is prepared with a sterile solution, an injection of lidocaine is given to numb the area, then using ultrasound guidance a needle is inserted into the adductor canal at the mid-thigh where a catheter is placed to administer the long-acting anesthetic. Next, to maintain the blind, the participant will receive a skin wheal with lidocaine at the same location as Group B has the iPACK block placed.

Table 5. Post-Op Follow Up Assessments		
Outcome Measure	**Instrument**	**Collected**
Pain Rating	Average pain, most pain, least pain from 0-10	POD Days 0-3
Opioid Consumption	Number of pills taken in time period	POD Days 0-3
Physical Therapy	Range of Motion and terminal knee extension	Postoperative Visit 1 and 2
Adverse Events	Adverse Events	Throughout enrollment

If randomized to ACB + iPACK (Group B) the participant will be administered the ACB first as stated above and the iPACK block second. The iPACK block will be placed at the posterior part of the knee. The area will be numbed first using lidocaine, then using ultrasound guidance, a needle will be inserted in the popliteal fossa between the popliteal artery and the capsule of the knee.

Table 4. Baseline and Intraoperative Assessments
Demographics
Baseline
Pre-op meds including opioids in past 24 hours
Randomization
Anesthesia intra-op data
Surgical techniques
Adverse Events

Follow-Up

The participant will be asked to provide their average pain score, worst pain score, and lowest pain score using a visual analog scale from 0-100 with 100 being the worst at various time points during the postoperative period. The first pain scores will be recorded before they leave the PACU on the day of the procedure. Beginning the following morning, the participant will receive a text message link sent by Twilio's secure server that opens a survey housed in RedCap. The first text message will arrive at 9:00 AM and will follow the schedule in Table 6.

They will receive a text message from a secure server asking the average pain questions as well as what medications they took for pain (including medication name, dosage, and frequency). The set of questions will state what time window (example:

12:00 AM midnight the night prior to 12:00 PM noon the same day) to consider when answering the questions. If the participant has been discharged from the hospital, they will answer these questions in the text message each day. If they are admitted to the hospital at this point in time, the information will be gathered from their chart for medications and asked verbally for pain scores. Range of motion and terminal knee extension will also be recorded at the in-person postoperative follow up visits.

If the participant is unable or unwilling to receive text messages, they will be provided a document to record their pain and medications for the pre-determined intervals so when a study member contacts them, they are able to relay their answers back accurately.

Table 6. Post-Op Follow Up Assessment Schedule

Post-Op Day	Time of Text Message	Data Collection Time Period
POD 0	Right before discharge	Waking up from surgery to discharge
POD 1-AM	9:00 AM	Discharge to 11:59 midnight prior
POD 1-PM	3:00 PM	12:00 AM midnight night prior to 12:00 PM noon same day
POD 2-AM	9:00 AM	12:01 PM noon day prior to 11:59 AM midnight night prior
POD 2-PM	3:00 PM	12:00 AM midnight prior to 12:00 PM noon same day
POD 3-AM	9:00 AM	12:01 PM noon day prior to 11:59 AM midnight night prior
POD 3-PM	3:00 PM	12:00 AM midnight prior to 12:00 PM noon same day

11.0 Data Management

- The study will be a double-blinded randomized controlled trial of participants undergoing ACL reconstruction at one academic medical center. Although the anesthesiologist administering the block will not be blinded, the surgeons, participants, and study statistician will be blinded to treatment assignment. Participants will be randomized to receive either ACB or ACB + iPACK block. We will use stratified randomization, stratifying on biologic sex, to ensure similar distributions of male/female participants in each treatment arm the same.
- The primary outcomes of interest are participant reported postoperative pain over time and quadricep strength based on the leg raise and knee extension test. Post-operative VAS pain score reported as average, worst, and least pain will be collected on post-op day 0 (after 12pm), 1 (prior to 12 pm and after 12 pm), and 2 (before 12 pm). The association between postoperative pain with block type will be evaluated using a series of linear mixed models evaluating average pain, worst pain, and least pain as dependent variables. Models will include fixed effects for preoperative pain score, block type, postoperative time, and the interaction between block type and post-operative time and a random subject effect to account for correlation between pain scores collected on the same subject over time. Model assumptions will be checked graphically, and transformations will be considered as needed. The difference in patient reported pain between block type by post-operative time and pain score type will be evaluated using a series of linear contrasts. A similar study

by Amer (2018)[1] comparing combined Adductor Canal and iPACK Blocks versus combined Adductor Canal and Periarticular Injection blocks for pain management in ACL Reconstruction Surgery found a difference in VAS pain scores of 1.5 between 0 to 8 hours post-op and standard deviation in VAS pain of 2.5 units. A sample size of n = 35 participants per treatment arm (70 total) with at least 3 measures of pain provides 80% power to detect a difference in pain score of 2 units at significance level $\alpha = 0.004$ (Bonferroni corrected for 4 comparisons) and assuming a compound symmetric covariance structure with a conservative standard deviation = 3.0 and correlation within subject is $\rho = 0.33$. We will enroll 41 participants (82 total) in each arm to allow for up to 20% attrition.

- Secondary outcomes include cumulative post-operative opiate consumption over time (POD 0 pm, 1 am/pm, and 2 am), and difference in range of motion between surgical and non-surgical leg at first clinic visit (7-21 days post-op) and 6 weeks PO. Associations between these secondary outcomes with block type will be evaluated using a linear mixed approach. Similar to the primary outcome, models will include fixed effects for type, time, and the interaction between block type and time. The model for cumulative opiate consumption will also include a fixed effect for intra-operative opiates received and the model for range of motion will include a fixed effect for pre-operative difference in range of motion between surgical and non-surgical leg.
- All data will be kept on a password protected MUSC server and in a REDCap database. All paper data sheets will be kept in a locked cabinet, in a locked office that only IRB approved study team members have access to. Participants will be given a study ID number that will be used to identify them throughout the study.

12.0 Data Safety Monitoring

- The study will be reviewed annually by the Department of Anesthesia's DSMB. Minutes and outcomes from these meetings will be reported to the IRB as required.

- Information regarding Adverse Events is to be obtained and documented by the surgery center anesthesia attending and/or the study team member performing the data collection by questioning or examining the subject. All new complaints and symptoms (i.e., those not existing prior to signing of informed consent) will be recorded on the AE CRF. All AEs will be characterized in terms of their start and stop dates, start and stop times, intensity, action taken, relationship to research study, subject outcome and whether or not the AE led to an SAE.

- Adverse events will be recorded and reported to the Department of Anesthesia's Data Safety Monitoring Board and the IRB per policy.

- PHI will be managed in a manner that complies with institutional rules and regulations. There will be an enrollment log that links the study ID number to the participant. This log will be kept on a MUSC password protected server that can only be accessed by IRB approved study personnel.

13.0 Withdrawal of Subjects

- The participant has the right to voluntarily withdraw consent from the study at any time for any reason without prejudice to his/her future medical care by the physician or at the institution. For the occasional participant who withdraws consent, the date and reason for consent withdrawal should be documented. Participant data will be included in the analysis up to the date of the consent withdrawal.
- Investigators may stop a subject's participation in the study at any time if they decide it is in the subject's best interest. They may also do this if the subject does not follow the investigator's instructions.

14.0 Risks to Subjects

- If a subject chooses not to participate the risk is the same since the interventions used are both standard of care at MUSC and will be offered regardless of study population.
- The interventions for both blocks include risks such as bleeding, infection, nerve damage, local anesthetic toxicity, allergic reaction, and/or damage to surrounding structures. These risks are rare.
- Subjects will be randomly assigned to receive either the adductor canal block, or adductor canal block with iPACK block. One group may prove to be less beneficial than the other.
- There is a risk of loss of confidentiality.

15.0 Potential Benefits to Subjects or Others

There is a potential benefit that the subject's participation in the study may contribute to knowledge in this area of practice and may impact subject care in the future. The subject could also experience less post-operative pain.

16.0 Sharing of Results with Subjects

- Results will not be shared with participants or their families.

17.0 Drugs or Devices (if applicable)

- The drugs (all FDA approved for ACB blocks and iPACK blocks) used for both blocks will be prepared by the OR pharmacy under a sterile hood.
- The contents of the injectate will be based off of the participant's randomly assigned group.
- The pharmacist will not be blinded to the randomization.
- All drugs are FDA approved for use in adults and standard of care off label in children according to ASRA/ESRA guidelines[7].

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