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PROTOCOL TITLE**:**

# INJECTION PRESSURE AND ADDUCTOR CANAL BLOCK

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## 1) **Protocol Title**

Impact of Injection Pressure on the Spread of Local Anesthetic During Adductor Canal Nerve Block

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**Brief description:** This is a prospective, randomized, single-blinded human clinical trial that will examine how injection pressure influences the spread of a given volume of injectate in the adductor canal, during adductor canal nerve block. Our study population will be patients undergoing elective anterior cruciate ligament repair in the distal lower extremity and receiving preoperative adductor canal nerve blocks for postoperative analgesia. They will be randomized into two groups of 25 patients each. We speculate that high injection pressures (>20 psi) will lead to greater spread of local anesthetic than low injection pressures (<15 psi) during mid-thigh adductor canal nerve blocks. Our primary endpoint is the spread of injectate, defined as the distance between the uppermost and lowermost limits of spread of local anesthetic as assessed by ultrasound. Our secondary endpoints are the incidence of femoral and sciatic nerve blocks 30 minutes after block placement, amount of IV opioid administered intraoperatively and postoperatively, postoperative pain (Numeric Rating Scale, 0-10), and postoperative physical therapy milestone achievement.

## 2) **Objectives***

The purpose of this study is to evaluate the impact of injection pressure on the spread of local anesthetic in the adductor canal during an adductor canal nerve block. Our primary endpoint is the spread of injectate, defined as the distance between the uppermost and lowermost limits of spread of local anesthetic as assessed by ultrasound. Our secondary endpoints are the incidence of femoral and sciatic nerve blocks 30 minutes after block placement, amount of IV opioid administered intraoperatively and postoperatively, preoperative and postoperative pain (Numeric Rating Scale, 0-10), and postoperative physical therapy milestone achievement, namely Lower Extremity Function Scale (LEFS) scores.

## 3) **Background***

The adductor canal block of the saphenous nerve is a well-established regional anesthetic technique for knee surgery, and it is recognized for its excellent analgesia with a notable absence of motor involvement, even with continuous perineural local anesthetic infusions. The adductor canal block is known for a high success rate because the adductor canal can be easily visualized with ultrasound at the mid-thigh. While the anatomy of the adductor canal has been elucidated by several imaging and cadaveric studies, factors influencing the spread of local anesthetic during adductor canal nerve block are less well understood. Different volumes of local anesthetic injected

through myriad anatomic approaches produce variable spread. Injectate spread has been shown to span from the femoral triangle to the popliteal fossa with only 15 mL of aqueous volume. One case report notes the apparent partial blockade of the sciatic nerve as a result of a common transsartorial approach to the adductor canal block. Another case report notes motor block of the quadriceps muscle with a midthigh approach to the adductor canal block. Furthermore, one study reports a staggering 67% incidence of motor weakness associated with a bolus of 15 mL of local anesthetic through an adductor canal catheter placed in the midthigh. Additionally, injection pressure has been shown to dramatically influence the spread of lumbar plexus block. Sustained injection pressures > 20 psi during intermittent injection of local anesthetic into the lumbar plexus have been associated with a 60% incidence of bilateral femoral nerve block and a 50% incidence of neuraxial block to the level of T11 or above, compared to no spread in the low injection pressure group (< 15 psi). Injection pressure has not been studied in adductor canal nerve blocks in human clinical trials. We hypothesize that, for a given injectate volume, the pressure during injection will affect local anesthetic spread towards the femoral triangle (cranially) and the popliteal fossa

(caudally). We speculate that high injection pressures will lead to greater spread of local anesthetic during mid-thigh adductor canal nerve blocks.

## 4) **Inclusion and Exclusion Criteria***

Inclusion criteria:
1. Planned general anesthetic.
2. ASA classes I, II, or III.
3. Patients aged 18-65.
4. English-speaking patients.

Exclusion criteria:
1. ASA classes IV and V.
2. Patients younger than 18 or older than 65.
3. Contraindication to regional anesthesia (coagulopathy, patient refusal).
4. Allergy to local anesthetic or other study medications.
5. BMI > 35 $kg/m^2$.
6. Chronic opioid use (daily or almost daily use for > 3 months).
7. Active illicit drug use.
8. Additional surgical site other than the limb for adductor canal block.
9. Pregnancy.
10. Preexisting neuropathy in the operative limb.
11. Inability to communicate to investigators or hospital staff.
12. Inability to speak or understand English.

## 5) **Number of Subjects***

50 subjects will be recruited into this study—25 in each group.

## 6) **Study-Wide Recruitment Methods***

Potential research subjects will be recruited for the research study on the day of surgery at the University of Miami ambulatory surgery suite. The study team will have access to the operating room surgical schedule and will identify any patients scheduled for an elective anterior cruciate ligament repair in the distal lower extremity. These patients will be evaluated on the day of surgery in the preoperative holding area and the preoperative history and physical will be reviewed. If all inclusion criteria are fulfilled and all exclusion criteria absent, the informed consent process will begin. The risks and benefits of participating in the research study will be discussed at length with the potential subject and a comprehensive informed consent form will be reviewed. Potential subjects will be advised that they may refuse to take part in the study at any time without any

adverse consequences on their medical care. They will be informed that they will not receive any direct benefit from the study, nor will they receive any compensation for participation.

## 7) **Study Endpoints***

Our primary endpoint is the spread of injectate, defined as the distance between the uppermost and lowermost limits of spread of local anesthetic as assessed by ultrasound. Our secondary endpoints are the incidence of femoral and sciatic nerve blocks 30 minutes after block placement, amount of IV opioid administered intraoperatively and postoperatively, preoperative and postoperative pain scores (Numeric Rating Scale, 0-10), and postoperative physical therapy milestone achievement.

## 8) **Procedures Involved***

This will be a randomized, single-blinded controlled trial in patients undergoing elective, anterior cruciate ligament repair in the distal lower extremity at the ambulatory surgery suite at the University of Miami Hospital. Cohort-matched (ASA status, BMI range, age, height, weight) patients will be randomly assigned via a method of predetermined randomization via assigned numbers to a low injection pressure group (injection pressure < 15 psi) and a high injection pressure group (injection pressure > 20 psi). Patients will receive preoperative adductor canal blocks for postoperative analgesia, and will undergo general anesthesia intraoperatively.

Patients will be assessed preoperatively in a designated presurgical area at UMH and the Lennar Foundation Medical Center After undergoing an initial history and physical, the patient will rate his or her pain in the operative extremity on the Numeric Rating Scale. The patient will subsequently undergo sensory and motor testing of both lower extremities. Sensory testing will use a pinprick method in the femoral (anterior thigh), saphenous (medial calf proximal to the medial malleolus, top of the patella) and sciatic (posterolateral calf, plantar surface of the foot) nerve distributions, with a score of 2 indicating "sharp", 1 indicating "dull", and 0 indicating "unable to feel the stimulus". The control limb for pinprick testing will be the contralateral lower extremity. Motor testing will evaluate the femoral and sciatic nerves of each lower extremity by assessing strength of knee extension, and plantarflexion and dorsiflexion of the ankle, respectively, against resistance. The patient will be assessed for motor function in the seated position on an examination table with both legs dangling passively. A score of 3 will indicate full power, 2 mild weakness, 1 moderate weakness, and 0 a complete absence of power. After testing is completed, a subsequent NRS pain rating will be recorded.

Blocks will be performed preoperatively, with standard ASA monitors (electrocardiography, noninvasive blood pressure at least every 5 minutes, pulse oximetry, and qualitative capnography). Blocks will be performed under conscious sedation (midazolam 0.05-0.08 mcg/kg IV and fentanyl 0.5-2 mcg/kg IV) if necessary, but the ability to interact with the anesthesiology team will be preserved.

The patient will be positioned supine, with the ipsilateral thigh and knee prepped in sterile fashion using chlorhexidine/alcohol. A high-frequency ultrasound probe will be covered in a sterile transparent dressing. First a survey scan will be performed at the anteromedial aspect of the mid-thigh, defined as the middle one-third of the distance between the base of the patella and the lower border of the greater trochanter. The probe will be oriented transversely to identify the femoral artery and saphenous nerve in short-axis cross-section, and an image will be recorded. The adductor canal will be scanned in its entirety, with special consideration paid to the femoral triangle just caudad to the inguinal ligament and the popliteal fossa; images will be recorded at both locations. An in-line injection pressure manometer, the Compass CT (Centurion Medical Products, Williamston, MI), will be used to measure injection pressure during adductor canal nerve blocks. A 4 inch, blunt, short beveled needle will be introduced in-plane, in an anterolateral to posteromedial direction, close to the fascial plane between the sartorius and vastus medialis muscles. After negative aspiration, the needle tip location will be confirmed by injection of 0.5 mL of air. Subsequently, an initial bolus of 1 mL of local anesthetic will be administered at < 15 psi in order to decrease risk of intraneural injection and nerve injury. The remaining 14 mL of ropivacaine 0.5% will thereafter be injected in 5 mL aliquots, maintaining either > 20 psi or < 15 psi based on patient randomization. Injectate spread will be assessed by ultrasound survey after completion of the adductor canal nerve block, where injectate spread is defined as the distance between the uppermost and lowermost limits of spread of local anesthetic as assessed by ultrasound.

Block evaluation will occur 30 minutes after block placement, with motor and sensory testing of both lower extremities as previously mentioned. Additionally, NRS pain ratings will be recorded pre- and post-evaluation. Block success will be determined by testing for pinprick sensation in the saphenous nerve distribution in the ipsilateral lower leg as compared with the contralateral lower leg. Patients who fail to demonstrate block success will be withdrawn from further study.

Intraoperatively, patients will undergo general anesthesia. General anesthesia will be induced with IV propofol and maintained with sevoflurane or desflurane. Intraoperative fentanyl will be titrated in as needed intraoperatively, and the doses will be recorded.

The regimen for postoperative analgesia will consist of oxycodone/acetaminophen 5/325 mg by mouth every 4 hours as needed and hydromorphone 0.5 mg intravenously every hour as needed for breakthrough pain. Doses will be recorded. Postoperative antiemetics will include ondansetron 4 mg intravenously every 8 hours as needed for nausea and/or vomiting, and a single dose of promethazine 12.5 mg intramuscularly if intractable to ondansetron.

Postoperative evaluation will be performed by a research team blinded to injection pressure randomization information. The patient will be assessed in person immediately postoperatively, 30 minutes postoperatively, 1 hour postoperatively, and at the time of discharge. Both sensory and motor testing will be repeated in both lower extremities as previously described, and NRS pain scores will be recorded.

The patient will be evaluated by physical therapy postoperatively using the Lower Extremity Function Scale (LEFS). The LEFS is a self-reporting measure which will be administered during

the initial physical therapy assessment, and will then be administered at weekly intervals for 4 weeks.

Of note, all operative and post-operative procedures are standard of care for subjects undergoing elective anterior cruciate ligament repair in the distal lower extremity, except for the purposeful application of an injection pressure > 20 psi during an adductor canal block. The standard of care for adductor canal block is the injection of local anesthetic easily, without having to overcome high resistance. The reason for this is to avoid intrafascicular injection, which is thought to be associated with nerve injury. Usually, this translates to injection at a low pressure. However, if the injection can be proved not to be against high resistance, then a high injection pressure would be no different from a low injection pressure with regards to the risk of intrafascicular injection and nerve injury. Both injection pressure groups in this study include the provision of an initial 1 mL bolus of injection to rule out intrafascicular injection, and therefore to minimize the risk of nerve injury. Thus, despite the deviation from the standard of care in the high injection pressure group, there is no additional risk for any complications related to the high injection pressure.

## 9) **Data Management***

Power analysis using a 2-sided type I error protection of .05 and a power of 80% yields a minimum of 20 patients in each group to detect a reduction in incidence of motor weakness of 30% with normal pressure (<15 psi) vs. high pressure (>20 psi). We plan to enroll 25 patients in each group to account for possible unanticipated patient dropout.

Study data will be stored in the UMH office of Anesthesiology, Perioperative Medicine & Pain Management, located at 1400 NW 12$^{th}$ Avenue, Suite 3028, Miami, FL 33136. Study files will be locked and accessible only to the study team, in order to prevent any breach of confidentiality.

The study investigators and their staff will have access the research subjects' medical records and associated information as may be necessary for purposes of this study. These records and results will not be identified as pertaining to the research subject in any publication without subjects' expressed permission. The Investigator, collaborators and staff will consider these records confidential to the extent permitted by law. The Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) and the patients' health care providers, including authorized University or Hospital staff not involved in the study may review these research records. The records may also be reviewed for audit purposes by authorized University of Miami employees or other agents who will be bound by the same provisions of confidentiality.

## 10) **Provisions to Monitor the Data to Ensure the Safety of Subjects***

During the procedure, the patients will be monitored in accordance with the standard of care. Should research subjects exhibit any signs of toxicity or other complication from the procedure,

they will be cared for in the standard manner as they would be if not enrolled in the study—cessation of the procedure and a systematic evaluation for any possible treatment.

An extra precautionary step during the procedure will be taken to minimize any risk of nerve injury associated with high pressure injection. This is the injection of 1 mL of local anesthetic at a low pressure to rule out intrafascicular injection, which is thought to cause nerve injury. This precautionary step will be taken in both the low injection pressure and high injection pressure groups, such that the risk of nerve injury as a result of procedure is both minimized and equalized between both groups.

Outside of standard monitoring and the extra precautionary step, patients will not receive any further monitoring for safety concerns. There are no other study-related safety concerns.

## 11) **Withdrawal of Subjects***

Research subjects will be counseled that their participation in the study is voluntary, and that they may refuse to participate or withdraw from the study at any time without penalty or loss of benefits to which the patients are otherwise entitled. Withdrawal from the study will not affect their medical care they receive from the study doctor or from the University of Miami Hospital. The patient will be counseled that they must tell their study doctor if they wish to stop taking part in the study.

Furthermore, the research subjects' participation in the study may be discontinued without their consent at any time by the study doctor, for instance if the patient has a medical condition which is a contraindication for the procedure, or if a serious, potentially life-threatening complication develops as a result of the procedure. The IRB or regulatory authorities may also discontinue research subjects' participation in the study.

In the case that research subjects are withdrawn from the study, the study staff and the investigator will stop collecting health information; however, they will continue to use the information already collected to evaluate the study results.

Finally, if research subjects start the study and then decide to withdraw, they cannot later continue to participate in the study.

## 12) **Risks to Subjects***

There are risks normally associated with adductor canal nerve block. These risks are listed below:

| UNCOMMON | RARE |
|---|---|
| Failure of the nerve block to work properly. | Injury to the blocked nerve. |
| | Excessive bleeding at the site of injection. |
| | Infection at the site of injection. |

| | |
|---|---|
| | Inadvertent injection of local anesthetics into the bloodstream, causing seizures and/or heart rhythm problems. |

In patients receiving an injection pressure > 20 psi, there is an increased risk of injury to the blocked nerve, such as with intrafascicular injection. To minimize this risk, all injections will be preceded by injection of 1 mL of local anesthetic at an injection pressure < 15 psi, to rule out intrafascicular injection.

## 13) **Potential Benefits to Subjects***

There is no direct benefit to the subjects.

## 14) **Sharing of Results with Subjects***

Results will not be shared with research subjects or their physicians.

## 15) **Setting**

Our research team will conduct our procedures and evaluation in the University of Miami ambulatory surgery suite. We will follow-up with patient postoperative progress telephonically on a weekly basis with the use of a self-reporting physical therapy questionnaire known as the Lower Extremity Function Scale (LEFS).

## 16) **Resources Available**

The facilities at the ambulatory surgery suite at the University of Miami Hospital and The lennar Foundation Medical center are sufficient for adequate assessment, monitoring, and execution of study-related procedures. There is a designated pre-surgical holding area with blood pressure, ECG, and pulse oximetry monitoring as well as a continuous source of oxygen in order to conduct the procedure according to the standard of care. There is adequate nursing and ancillary staff to facilitate all study-related perioperative procedures. An ultrasound adequate for conducting the procedure is available at all times, as well as an emergency cart containing emergency drugs and equipment in the case of a serious, possibly life-threatening emergency.

All research staff conducting procedures will be licensed physicians clinically trained in anesthesiology and procedure technique will be standardized. Clinical evaluation will be

performed by licensed physicians or nurse practitioners. Physical therapy will be conducted by licensed physical therapists and physical therapy milestones will be standardized.

Recruitment of potential research subjects will be straightforward. The volume of anterior cruciate ligament surgeries is sufficient to expect a recruitment period of 3-6 months, even if as few as 25% of potential research subjects actually agree to participate in the study.

The amount of time we intend to devote to conducting and completing the research is 6-12 months.

## 17) Recruitment Methods

Potential research subjects will be recruited for the research study on the day of surgery at the UMH and The Lennar Foundation Medical Center ambulatory surgery suite They will be evaluated prior to surgery in the preoperative holding area and if all inclusion criteria are fulfilled and all exclusion criteria absent, the informed consent process will begin. The risks and benefits of participating in the research study will be discussed at length with the potential subject and a comprehensive informed consent form will be reviewed. Potential subjects will be advised that they may refuse to take part in the study at any time without any adverse consequences on their medical care. They will be informed that they will not receive any direct benefit from the study, nor will they receive any compensation for participation.

## 18) Local Number of Subjects

50 subjects will be recruited into this study—25 in each group.

## 19) Provisions to Protect the Privacy Interests of Subjects

The study investigators and their staff will have access the research subjects' medical records and associated information as may be necessary for purposes of this study. These records and results will not be identified as pertaining to the research subject in any publication without subjects' expressed permission. The Investigator, collaborators and staff will consider these records confidential to the extent permitted by law. The Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) and the patients' health care providers, including authorized University or Hospital staff not involved in the study may review these research records. The records may also be reviewed for audit purposes by authorized University of Miami employees or other agents who will be bound by the same provisions of confidentiality.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify the research subjects. At most, the Web site will include a summary of the results.

## 20) Compensation for Research-Related Injury

The research subjects will undergo a procedure which is already considered a standard of care for the surgery at hand, with regards to pain control. The only modification to this is that one group will receive a high pressure injection which may be associated with an increased risk for nerve injury.

Although risks are unlikely, if injury should occur, treatment will in most cases be available, depending on the insurance coverage policy of the patient, or the financial resources of the patient. In other words, if the patient has insurance, then the insurance company may (or may not) pay for the costs of treatment; if the patient does not have insurance, then the patient will be expected to pay for the treatment. The University of Miami will not be held responsible for any injury and funds to compensate for pain, expenses, lost wages and other damages caused by injury will not available.

All medications can have side effects or other reactions. While you are taking part in this clinical study, your doctor will check your health very carefully.

## 21) Consent Process

Potential research subjects will be evaluated prior to surgery in the preoperative holding area and if all inclusion criteria are fulfilled and all exclusion criteria absent, the informed consent process will begin. The risks and benefits of participating in the research study will be discussed at length with the potential subject and a comprehensive informed consent form will be reviewed. Potential subjects will be advised that they may refuse to take part in the study at any time without any adverse consequences on their medical care. They will be informed that they will not receive any direct benefit from the study, nor will they receive any compensation for participation.

For Spanish-speaking only potential research subjects, the entire informed consent process take place in Spanish. A Spanish consent form will be reviewed with the subject.

## 22) Process to Document Consent in Writing

We will document consent in writing. The consent document will be attached.

## 23) Drugs or Devices

The study-related device to be used is called a Compass CT, which is an in-line pressure manometer which can record and display the pressure during a hand-bolus of medication injection. All investigators will be trained in the use of this device during the study procedure. It

will be locked securely along with equipment and drugs, and be accessible only to the investigational team conducting the study.