ACL Repair and Multimodal Analgesia

NCT01868425

Version 8/16/2017

ACL Repair and Multimodal Analgesia

Patients and surgeons have many choices to make about the type of graft to use for anterior cruciate ligament (ACL) repair. One of the decisions they need to make is whether or not to use the patient's native hamstring tendon graft for the ACL repair. When the decision is made to use this type of graft, there are implications to the anesthetic the patient receives.

It is standard-of-care at this institution, and at many others, for patients to receive a femoral nerve block (FNB) for this type of surgery. A FNB, because it numbs the nerves located on the anterior (front) surface of the thigh and knee, is quite effective at treating the intraoperative and postoperative pain response when ACL repairs are performed anteriorly using allografts or native patellar tendons. When FNB is performed on patients having their own hamstring graft used for the repair, a significant portion of the surgical work is not covered by the block because the graft is harvested from behind the knee (posteriorly). This surgical activity not covered by the block may lead to a pain in the back of the leg post-operatively.

There are many different ways to treat the post-operative posterior leg pain in patients having a hamstring graft for their ACL repair. Some institutions perform an additional nerve block during the surgical procedure, such as a sciatic nerve block to numb the back of the leg, to treat this pain. We tend to avoid that approach at UWHC because it leaves the patient with an entirely numb leg which can make ambulating, even with crutches, difficult. Without thorough instructions and very good help at home, that situation could lead to falls at home, until the block wears off.

Other ways to treat the post-operative pain would be with standard intravenous narcotics. This is a perfectly acceptable way to approach this patient population, but narcotics do have a side effect profile which includes nausea, vomiting, urinary retention, pruritus, and over sedation. When patients experience these side effects they are more likely to experience prolonged stays which is in direct opposition to the goals of an outpatient surgical anesthetic. In the outpatient setting, an emphasis is not only placed on administration of a safe anesthetic, but also one that facilitates a more rapid discharge and emphasizes the importance of improved postoperative pain control with minimal side effects. In the ambulatory setting, the use of multimodal analgesics for this type of ACL repair makes sense in order to minimize narcotic use and optimize pain control.

Multimodal analgesia is defined as the use of more than one modality of pain control to obtain additive beneficial analgesic effects while minimizing opioid-related side effects[1]. Studies have been performed that describe improved recovery and patient outcomes after ambulatory procedures while using multimodal analgesia[1,2,3,4,5]. Drugs commonly used with this type of analgesic plan include a combination of nonsteroidal anti-inflammatory drugs (NSAIDS), acetaminophen (or paracetamol), low dose ketamine, perioperative administration of local anesthetics by the surgeon, regional anesthesia procedures, and gabapentin. Both gabapentin and ketamine have been studied extensively for use as an analgesic, within multimodal regimens and independently, in an effort to reduce opioid consumption

and therefore opioid related side effects [2,3]. Two metaanalyses of perioperative gabapentin use showed benefits from single doses of 300-1200 mg of gabapentin claim 20-60% reduced narcotic usage equivalent to 25-35 mg of morphine in the first 24 hours[2,4]. These doses in the same study also showed significantly reduced nausea, vomiting & urinary retention[4] all of which are significant risk factors causing unplanned hospital admission in ambulatory surgery. Literature reviews of ketamine support its use perioperatively to improve pain control and reduce narcotic side effects[3]. These studies show that loading doses followed by low dose continuous infusion are the most effective at achieving these goals. Low dose infusions (<=20ug/kg/min) offer narcotic reduction without the psychotropic effects seen in higher doses. [3]

At UWHC anesthesiologists use a variety of approaches to achieve good pain control with minimum side effects. My own practice exactly mimics the protocol outlined here. I use gabapentin, ketamine, and acetaminophen quite frequently for painful procedures in an outpatient setting. In fact, in some ambulatory centers multimodal analgesia, excluding narcotics, is the standard regimen for all surgeries (personal communication, Michelle Parra, Dartmouth-Hitchcock Medical Center). At this point I have seen good pain control in patients I have used multimodal analgesia, along with no noted side effects that could be attributable to the drugs used for the case.

In support of the surgical infiltration of the non-blocked portion of this surgery, there has been one small study (n=27) which examined the effect of adding local anesthetic infiltration (injecting an anesthetic agent directly into the surgical area) to a femoral nerve block in ACL repairs using hamstring grafts[6]. This study, published in 2010 in the Journal of Arthroscopic and Related Surgery, found that this additional anesthetic injection, administered by the surgeon into the hamstring donor graft site, resulted in an improvement of pain scores for up to 2 hours postoperatively. Initial pain score in the recovery room was 6 in the standard treatment group compared to 3 in the treatment group. At the 2 hour mark, average pain score was 5 in the standard group compared to 3 in the treatment group. It did not appear that opioid use was standardized intra-operatively (except for the use of a pre-operative femoral nerve block), and post-operative opioid consumption was also not examined in this study. With the exception of the pain score, no other post-operative variables were examined and there was no follow-up beyond 2 hours post-operatively. Despite the limitations of this study, this type of local infiltration injection does appear promising and could be used as part of a multimodal analgesic regimen to assist with pain control and recovery of patients having this type of surgery.

We propose the evaluation of a multimodal pain control regimen in patients having ACL surgery using hamstring grafts. This evaluation will be conducted in patients scheduled to undergo an ACL repair procedure (using hamstring graft), performed by an orthopedic surgeon on the study team. Two treatment groups will be evaluated in this study: control (or standard of care) treatment and multimodal treatment. Post-operative variables will then be compared across groups.

- The control group will receive standard of care clinical treatment throughout their participation. Standard of care anesthetic treatment for this surgery includes pre-operative femoral nerve block placement and general anesthesia during the surgical procedure. Standard of care

anesthetic treatment for this surgery also includes IV administration of dexamethasone 4 mg (for anti-nausea prophylaxis) at induction, ketorolac 15 mg after the hamstring graft has been harvested, and odansetron 4 mg prior to the end of the case (to reduce potential risk for post-operative nausea/vomiting). Standard of care treatment for surgery performed by study surgeons also includes an injection of an intra-articular narcotic in the knee joint space during the surgical procedure.

- In addition to the standard of care treatment outlined above, the multimodal group will receive additional analgesics both pre-operatively and intra-operatively. Pre-operatively, the multimodal (treatment) group will receive gabapentin and acetaminophen. Intra-operatively, this group will receive IV bolus (50 mg) and infusion (15 ml/hr) of ketamine. This group will also intra-operatively receive a local anesthetic infiltration of bupivacaine (0.125%, 20 ml) by the surgeon along the route of hamstring graft harvest.

The primary outcome will be narcotic use in the immediate post-operative period (from time of arrival in recovery area through discharge from the outpatient surgery center). The hypothesis would be that there will be a 50% reduction of opioid use during this immediate recovery time period in the group receiving multimodal analgesia.

Primary outcome

Opioid use in the immediate post-operative recovery period. This period is defined as the time from post-operative arrival in recovery to discharge from the outpatient surgery center.

Secondary outcomes

1. Pain scores during recovery period through the first 24 hours of recovery and medication usage.
2. Nausea in recovery and the first 24 hours.
3. Pruritus in recovery and the first 24 hours.
4. Sedation scale measured in recovery and in the first 24 hours.
5. Impact of block characteristics on pain control.
6. Intraoperative medication use in patients.
7. Complications and side effects in both groups related to procedures (such as block) and medications.
8. Time to discharge from the recovery room (Phase I recovery) and the outpatient surgery center (Phase II recovery).

Patients of orthopedic surgeons on the study team scheduled for ACL repair using hamstring graft from the same leg will be considered for inclusion in this study. Other inclusion criteria are as follows:

1. American Society of Anesthesiologists (ASA) physical status 1-3
2. 18-55 years of age, inclusive
3. BMI of < 40 kg/m2.
4. Consents to general anesthesia and pre-operative femoral nerve block for case.
5. No contraindication to a femoral nerve block present.
6. No allergies to medications used in study or as part of standard clinical care outlined in protocol.

Exclusion criteria include:

1. Peripheral or central nervous system disease
2. Renal or hepatic impairment
3. History of opioid dependence or current regular narcotic use (as determined by anesthesiology staff)
4. Significant psychiatric disease
5. Pregnancy or lactation (by verbal report)
6. Seizure Disorder
7. History of post- operative nausea and vomiting (as determined by anesthesiology staff)
8. Latex allergy
9. Clinically significant cardiac or pulmonary disease
10. History of chronic pain syndrome.
11. Have previously been enrolled in this study protocol.

Patients who appear eligible by review of the medical record and the clinical anesthesia evaluation will be approached on the day of surgery by a study investigator about study participation. Subjects are

given up to 15 minutes to consider participation. Potential subjects who are interested will sign consent in person on the day of surgery. Patients will need to be agreeable to receiving a general anesthetic and femoral nerve block. Patients will be asked to arrive prior to their scheduled operative time to the ambulatory surgery center. There, they will be assessed by their anesthesiologist to determine fitness for surgery and discuss their anesthetic. If the patients' anesthetic plan includes general anesthesia and a pre-operative femoral nerve block then they will be considered potentially eligible for the study. The regional anesthesiologist on the study team will verify that no contraindications to enrollment in the study are present and approach the patient about the study. If the subject is interested the anesthesiologist will conduct the consent process with the subject. The study will be explained and all questions will be answered. If the patient decides to participate, s/he will then sign the consent form. Randomization will be performed by the pharmacy. Study subjects and all members of the study team and clinical care team (including the study coordinators, study anesthesiologists, clinical surgeon, clinical anesthesia team, and clinical recovery care team) will be blinded to subject treatment assignment. In the event of an emergency, however, this information can be obtained from the pharmacy.

Pre-Operative Procedures

For all subjects (both treatment groups), the ambulatory surgery nurses will perform their usual duties in checking the patient in, and a peripheral intravenous line (IV) will be started per standard care. Once each patient has all their paperwork in order and has an IV placed, they will be brought to the block room per standard care. The "time-out" procedure will be performed in the block room, prior to the block, which verifies the patient name, a unique identifier, the surgery to be performed, and the block to be performed.

Pharmacy will provide the study team with the blinded oral pre-operative medications that the subject has been assigned to receive by randomization:

- The multimodal group will receive 300 mg gabapentin and 1000 mg acetaminophen;

- The control (standard of care) group will receive placebo pills instead of active drug. The control group will be provided with the same number of pills as the treatment group to maintain the blind.

Oral pre-operative study drugs may be given to subjects at any time during the pre-operative period after consent and the investigator has verified the subject's eligibility but prior to the onset of surgery.

Pre-Operative Procedures, continued: Block Placement

All subjects, regardless of treatment assignment will receive a femoral nerve block as is currently the standard of care. Monitoring will be standard (EKG, pulse oximetry, and a blood pressure monitor) for all subjects. They will receive continuous oxygen enrichment of their inspired air via nasal cannula at a rate of 4 L/min, and positioned for the block. All subjects will receive sedation while blocks are being placed. Midazolam and fentanyl will be titrated to patient comfort.

Per standard of care, all subjects will be supine for block placement. The inguinal crease on the same side as surgery will be prepped with chlorhexidine and the procedure performed with sterile gloves. The block will be placed with the assistance of ultrasound and/or nerve stimulation. The local anesthetic that will be used is 20-30 ml of 0.5% bupivacaine with 2.5ug/ml epinephrine. All blocks will be placed by a practitioner experienced in placing femoral nerve blocks. As this is standard of care treatment, block placement will not necessarily be performed by someone on the study team. Also, per standard UWHC procedure, the block anesthesiologist may or may not move with the patient into the operating room, allowing for more than one anesthesiologist to provide care during a single surgical case.

Intraoperative Procedures

Once in the operating room, all subjects (regardless of treatment assignment) will undergo standard of care general anesthesia for the case as described here. All subjects will have standard monitors placed, and will be induced using propofol and lidocaine, with or without the addition of fentanyl. Sevoflurane will be used as the inhalational agent for the case. An endotracheal tube or laryngeal mask airway may be used to control the airway. Relaxant may be used if deemed necessary. Subjects will also receive any antibiotic clinically ordered for administration for the case. Dexamethasone, 4mg, will be administered to all subjects at induction as well for anti-nausea prophylaxis. During the case inhaled agent and fentanyl in boluses will be used to maintain the subjects' heart rate and blood pressure to within a goal range of plus or minus 20% of pre-operative values. When appropriate, respiratory rate may also be used to titrate use of narcotic to a goal respiratory rate of between 8-20 breaths per minute. Other vasoactive agents and anesthetics will be used as deemed necessary by the team managing the subject.

To avoid potential influence on study outcomes, however, this treatment may not include additional ketorolac, ketamine, intravenous lidocaine outside of induction bolus, narcotics besides fentanyl or additional steroid boluses. If clinical treatment with these exclusionary medications is required, the subject's data will be excluded from analysis. Furthermore, if a subject does not receive one or more of the study medications as required per protocol, the subject will be excluded from analysis.

Pharmacy will provide a blinded bolus syringe and blinded infusion bag for the anesthesiologist, as well as a blinded syringe of fluid for the surgeon to be used during the case.

- The blinded bolus syringe will be administered prior to incision by the case (in O.R) anesthesiologist. The syringe will contain 0.5mg/kg of ketamine (up to 50mg) bolus for the multimodal group or normal saline for the control group.

- The blinded infusion will then be started (before or during incision) through IV administration at 15ml/hr by the case anesthesiologist. The multimodal group will receive 15mg/hr of ketamine and the control group will receive 15ml/hr of saline.

- The surgeon will use the final blinded syringe to inject fluid along the hamstring graft harvest after the hamstring tendon is harvested. For the multimodal group the syringe will contain 20 ml of 0.125% bupivacaine. If the control group, the syringe will contain 20ml of preservative free normal saline.

The remainder of the intra-operative procedures will be performed per standard of care and will be administered to all subjects, regardless of treatment group. This standard of care treatment includes an intra-articular injection of narcotic administered by the surgeon, as well as IV administration of ketorolac(15mg) administered by the anesthesiologist after the hamstring graft has been harvested, per standard of care.

Prior to the end of the case all subjects will receive 4mg of ondansetron (via IV) to reduce potential risk for nausea and/or vomiting post-surgically per standard of care. They will also receive reversal of their relaxant if the anesthesia team feels it is necessary. They will be extubated and taken to the recovery room (PACU).

For all standard care drugs, if a drug shortage occurs, a similar drug will be used in lieu of the protocol described drug. This would reflect a required clinical modification to standard of care therapy and not to study therapy, and will not impact the conduct of the trial.

Once subjects enter the recovery room they will receive intravenous hydromorphone and fentanyl as needed for pain. Per standard of care treatment, pain medicines are dispensed in Phase I recovery approximately every 6-10 minutes as needed for pain control; however the specific amount of drug administered is not always standardized for specific reported pain levels. For purposes of this study, a standardized titration scale based on reported pain scores was developed in order to allow unbiased analysis of opioid use in recovery (primary study outcome). The recovery orders will include IV hydromorphone titrated as follows: for pain score less than 5, 0.1-0.3mg hydromorphone every 6 minutes prn for pain control; for pain score greater than 5, 0.2-0.5mg hydromorphone q 6minutes prn for pain control. Fentanyl will also be prescribed at doses of 25-50ug q5 minutes prn for pain scores greater than 7. All narcotics will be administered with a parameter to keep the respiratory rate greater than 10. They may also receive any other medications necessary for their recovery, including anti-emetics or meperidine for shivering.

Pain scores will be recorded upon arrival into the recovery room by the recovery room nurse and as per normal routine during their recovery room stay. These will be recorded in the medical record. Once the patient reaches the second phase of recovery they will receive mainly oral pain medications as necessary for pain control. They will be offered oxycodone in 5mg increments for pain control for pain scores of greater than 3. . If their pain score is 7 or greater they may receive 10 mg instead of 5mg

and/or intravenous pain medications. Similar to the Phase I recovery titration scale, this was standardized to allow for unbiased analysis of the primary outcome.

Subjects will also be visited by a member of the research team (usually a study coordinator) 1 hour post-operatively. This will allow data collection of pain scores, nausea, sedation and side effects at a singular time point in all patients in a standardized way. The research team will interview the subject for current pain score at the front and back of the knee, as well as for the combined surgical site, worst and least pain score since leaving the operating room, worst nausea and itchiness since leaving the operating room, and sleepiness or sedation level at the one-hour time point. If the subject is too sedated to answer questions appropriately, study staff will return at a later time when the subject can appropriately answer study questions.

The research team will collect demographic information, block details, pain scores, pain medication usage, nausea medication usage, medications administered during the case, the duration spent in first phase of recovery, the duration from end of surgery through outpatient surgery discharge, and additional information on complications or side effects from the chart. For the majority of subjects (expected to be discharged on the same day of their surgery), study data will be collected from the time of subject randomization through the post-operative Day 1 standard of care clinic visit or the 24 hour follow-up study phone call (whichever occurs later). If the subject has been admitted for additional inpatient care following the surgery, data collection will continue through subject discharge from inpatient care.

Subjects will be contacted by phone the following day by the research team to determine 24-hour pain score as well as peak/low/average pain scores through the first 24 hour period, nausea during the first 24 hour period, medications used for nausea and/or pain, complications during the first 24 hour period, and if the subject contacted medical staff about complications since their discharge from the hospital. The subjects will be asked when they noticed pain return in the front of their leg and the back of their leg as well. Prior to discharge, subjects will be given an information sheet detailing what questions will be asked in the 24 hour follow-up.

All patients in this study will receive our current standard of care which is anti-nausea prophylaxis (dexamethasone pre-operatively; odansetron at the end of the case), and a pre-operative femoral nerve block, general anesthesia, and intra-operative ketorolac for pain control. Patients randomized to receive multimodal analgesia will have the standard care plus gabapentin and acetaminophen preoperatively, ketamine intraoperatively, and a local anesthetic injection along the hamstring graft harvest site intraoperatively.

The side effect profile for any of these medications is minimal. A single 1000 mg dose of acetaminophen is not expected to have any significant side effects. In fact, there are no available reports of adverse effects from a single adult dose. Although nausea and vomiting are the most commonly reported side effects of acetaminophen use, subjects will be provided with antiemetic prophylaxis as part of the standard of care regimen. Similarly, adverse effect reports from a single 300 mg dose of gabapentin are

also not available. In studies of subjects treated with gabapentin for the treatment of postherpetic neuralgia, the most common side effects included dizziness and drowsiness. These studies included up to 8 weeks of treatment and up to doses of 3600 mg/day. With a half-life of approximately 5 – 7 hours, it is unlikely that subjects will experience significant side effects from a single 300 mg dose. Ketamine can commonly result in nightmares and hallucinations, but typically not at such low doses and co-administered with a general anesthetic. The local anesthetic (bupivacaine) injection has minimal risk associated with it as well. The most common side effects include hypotension and nausea, which will be monitored for per clinical anesthetic monitoring of the subject. Per standard care, the anesthesia team will use appropriate methods to maintain subjects' heart rate and blood pressure to within 20% of pre-operative values, as described in intraoperative procedures section. The track to harvest the hamstring tendon will already be made and the local anesthetic will just be placed along that pre-made track. The previous study performed using this technique reported no complications associated with its use.

Sample Size Justification

The primary outcome for this study is patient total opioid usage as defined by morphine equivalents, including hydromorphone and dilaudid, during the first 24 hours of recovery in which patients with standard care are compared to patients with multimodal analgesia. Based on preliminary data, we estimate the mean opioid for standard care will be 6.6 with a standard deviation of 6.2. We expect patients with multimodal analgesia will exhibit a similar standard deviation. We will test for the ability of multimodal analgesia to reduce opioid usage by at least 50%. A minimal sample size of 45 subjects per group is based on a one-tailed t-test using a power of 0.80 and a type I error of 0.05.

In order to account for potential block failure up to 20%, we will recruit 56 subjects to each group, for a total of 112 patients. Subjects will be randomized into each arm of the study to minimize the effects of confounders. Two surgeons will be used in this trial that utilize different surgical methods that are suspected to lead to different opioid usage during the first 24 hours of recovery. Therefore, stratified randomization based on surgeon will be used to assign patients to standard care and multimodal analgesia groups. Although each surgeon may treat a different number of total patients, the patients each surgeon treats will be an equal number of standard care and multimodal analgesia. Beyond this stratification requirement, all patients will be randomized and assigned to standard care or multimodal analgesia using standard procedures. This will account for potential differences in the primary outcome due to different surgeons. For the analysis of the resulting data, a t-test will be performed to determine if multimodal analgesia reduces opioid usage by 50% or more.

Potential confounding variables include age, gender, and BMI. In addition, the use of fentanyl and sevoflurane administered intraopertively to each patient may also affect the primary outcome. Finally, even though stratified randomization is designed to correct for differences in the primary outcome due to surgical technique in the two surgeons, the operating surgeon will also be considered a potential confounder for additional assurance that the effect of surgical procedure on the primary outcome is fully addressed. Therefore, the data will be stratified by each confounder to ensure the validity of all inferences. If stratification indicates that any of these potential confounders modulates the effect of

multimodal analgesia on opioid usage, regression analysis will be used. The dependent variable will be total post-operative opioid usage and the independent variables will be the use of multimodal analgesia and confounders that modify the effect of multimodal analgesia on the primary outcome as determined by stratification analysis.

Data and Safety Monitoring

Adverse events will be collected for each patient pre-operatively from the time of study enrollment, during surgery, and through the first 24 hours of recovery. These adverse events will be categorized as either minor or severe. Minor adverse events are temporary without any significant impact to the patient's overall health. Based on the components of multimodal analgesia treatment, such as ketamine, there are some expected minor adverse events including, but not limited to:

- Nausea
- Nightmares
- Skin irritation
- Readily treated infection

There are, however, no suspected or documented severe adverse events for multimodal analgesia. Severe adverse events include events that are life-threatening or have a long-term impact on the patient. These events include, but are not limited to:

- Death
- Stroke
- Heart Attack
- Extended hospitalization
- Extended incapacitation of the leg

Per standard of care, anesthesiology staff is notified by the patient's clinical team of any possible adverse events. In addition, the clinical care team will follow standardized orders which instruct them to contact a study investigator immediately if a serious complication occurs during recovery. 24 hours post-operatively, study personnel will also contact the subject by telephone to gather the remaining secondary outcome data including any additional complications which may have occurred since outpatient surgery center discharge. All complications will be recorded on the study's data collection sheets.

In order to establish that there are no clinically unacceptable differences in safety or tolerability of multimodal analgesia compared with standard care, an interim analysis of adverse events will be conducted. This will be a single analysis conducted at the halfway point of the trial, after data has been

collected for 56 subjects. As this analysis compares severe adverse events between treatment groups, the data will be temporarily unblinded by a staff nurse anesthesiologist not involved in the study. Only the staff nurse anesthesiologist will have access to the full unblinded data at the interim point and will submit a portion of the data to directly to the biostatistician. The data submitted to the biostatistician will consist solely of the treatment group and presence of a severe adverse event for each individual. The variable "severe adverse event" is a single binary measurement categorized for each patient as present or not present.

Although both minor and severe adverse events will be tracked in this trial, only severe adverse events will be considered in this interim analysis since minor adverse events are considered insufficient grounds for stopping the trial. However, severe adverse events can be life-threatening and therefore need to be carefully monitored. As this is a single point interim analysis, a one-sided Fisher's exact test using an alpha of 0.05 will be performed on the patient count data to determine if there are significantly more severe adverse events in the multimodal analgesia group as compared to the standard care group. No adjustment in alpha will be used in this secondary safety analysis since this would result in a reduction in alpha, making it less likely to identify difference in adverse events between treatment groups. If there is a statistically significant difference in adverse events between treatment groups, the trial will be stopped.

An independent reviewer will assess whether any potential severe adverse event should be categorized as severe and whether it is associated with the treatment. If the severe adverse event is not determined to be associated with the treatment, it will not be included in the interim safety analysis. A prolonged minor adverse event could become severe and, in such situations, will also be referred to the independent reviewer for classification as minor or severe. Any events which meet institutional reporting criteria will be reported to the IRB per reporting guidelines.

Prevalence of minor adverse events between multimodal analgesia and standard care will be evaluated at the end of the study.

References

1. Elvir-Lazo O, White P: The role of multimodal analgesia in pain management after ambulatory surgery. Current Opinion in Anesthesiology 2010; 23:697-703.

2. Ho K, Gan TJ, Habib AS. Gabapentin and postoperative pain-a systematic review of randomized controlled trials. Pain 2006;126:91-101.

3. Schmid RL, Sandler AN, Katz J. Use and efficacy of low dose ketamine in the management of acute postoperative pain: a review of current techniques and outcomes. Pain 1999;82:111-125.

4. Tiipana EM, Hamunen K, Kontinen VK, KAlso, E: Do surgical patients benefit from perioperative gabapentin/pregabalin? A systematic review of efficacy and safety. Anesthesia and Analgesia 2007: 104:1545-56.

5. Williams BA, Kentor ML, Vogt MT, Irrgang JJ, Bottegal MT, West RV, Harner CF, Fu FH, Williams JP: Reduction of verbal pain scores after anterior cruciate ligament reconstruction with 2-day continuous femoral nerve block. Anesthesiology 2006; 104:315-327.

6. Bushnell BD, Sakryd G, Noonan TJ: Hamstring donor site block: Evaluation of pain control after anterior cruciate ligament reconstruction. Arthroscopy: The Journal of Arthroscopic and Related Surgery 2010; 26:894-900.