

**LOYOLA UNIVERSITY CHICAGO  
HEALTH SCIENCES DIVISION  
MAYWOOD, ILLINOIS**

**ORTHOPAEDIC SURGERY & REHABILITATION**

**Project Title:** The effect of intra-articular local anesthetic injection and hematoma aspiration on pain and narcotic/opioid analgesia use following tibial plateau fractures

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**Background**

The tibial plateau is one of the most complex load-bearing surfaces in the body, helping to account for alignment of the knee, knee mechanics, load sharing, and stability. Fractures of the tibial plateau can have devastating consequences, as they are often a result of high-energy falls or motor vehicle accidents with concomitant trauma to other areas of the body. Patients with osteoporotic bone or multiple severe medical co-morbidities are also at risk for fracture of the tibial plateau in low energy situations. Most often, fractures occur as a result of combined axial loading with varus or valgus stress applied at the level of the tibial plateau.<sup>1-2</sup>

Tibial plateau fractures are painful injuries, often requiring prolonged high doses of opioid/narcotic analgesia both pre-operatively and post-operatively. With the ever increasing attention being paid to the amount of narcotics prescribed to patients and the potential serious side effects associated with these medications, it is crucial to identify ways in our orthopaedic trauma population to decrease the use of narcotic pain medications while simultaneously improving patient outcomes and satisfaction.<sup>2</sup>

There have been several studies examining the concept of injecting local anesthetics into joints that have dislocated, have associated intra-articular fractures, or have recently undergone operation. We are unaware of any studies regarding the use of local anesthetics in the initial management of tibial plateau fractures, though there is extensive research regarding the use of local anesthetics or multimodal analgesia (MMA) in the knee joint following both total knee arthroplasty and arthroscopic knee surgery. Stein, et al examined the analgesic effect of intra-articular morphine after arthroscopic knee surgery in a double-blinded study with 52 patients receiving one of four potential injections: 1mg morphine in knee and saline in iv, Saline in the knee and morphine in the IV, 0.5mg morphine in knee and 0.5mg morphine IV, 1mg morphine and 0.1mg naloxone intra-knee and IV. The pain scores were tested at 1,2,3,4,6,24hrs post-operatively. It was determined that 1mg of morphine in the knee and saline in the IV had significantly lower pain scores at 2,3,4,6 hours and also had lower mean consumptions of supplemental analgesia than the other groups.<sup>3</sup> This study shows that there may be options other than simply locally active anesthetics in managing the pain associated with tibial plateau fractures acutely. Busch et al took this study a step further, exploring the efficacy of periarticular multimodal drug injection in total knee arthroplasty. The researchers used a mixture of ropivacaine (400mg), ketorolac (30mg), epimorphine (5mg) and epinephrine (0.6mL of 1:1000) and compared it to no injection in terms of Visual Analogue Pain Score (VAS) scoring at rest and with activity, in addition to PCA use post-operatively. They showed that the injection arm had significantly less PCA use at 6 hrs, 12hrs, and 24 hrs; higher VAS for patient satisfaction and lower VAS for pain during activity in PACU and at 4 hours post-op.<sup>4</sup> The importance of such a study is to illustrate that patient satisfaction was improved with MMA injection, in addition to decreased need for opioid analgesia post-operatively. It is the goal of this research team to not only achieve anatomic reduction of a fractured tibial plateau but also to decrease post-operative opioid/narcotic analgesia and increase patient satisfaction.

In choosing whether to use MMA, opioids or local anesthetic for injection into the knee following tibial plateau fractures, several studies have compared these in terms of pain reduction. Francheschi et al compared morphine and ropivacaine intra-articular injections following knee arthroscopy in terms of post-operative pain control. 90 patients were included in the study with procedures ranging from diagnostic scopes, lateral and medial meniscectomies, meniscal repairs, removal of loose bodies; all were performed under general anesthesia by the same surgeon. 3 groups were randomized into injections of either 75 mg ropivacaine in 20mL solution, 2mg morphine in 20mL solution, or 20mL isotonic saline. A blind observer assessed post-operative pain using 10 cm VAS at 0,2,4,6,12,24 hours. The study showed that VAS in the first 4 hours showed better efficacy in ropivacaine versus the morphine arm, but no difference in VAS existed at 24 hours.<sup>5</sup> Jauareguido et al compared morphine and bupivacaine intra-articularly for pain control after outpatient knee arthroscopy. Patients were given one of the following injections: 4 mg morphine, 0.25% bupivacaine, or 0.9% saline. VAS scores and supplemental analgesia was recorded at 0,0.5, 2,4,6,8,12,24 hours post-operatively. The researchers found that the cumulative amount of pain medication used was significantly lower in the morphine and bupivacaine groups at 2 to 6 hours after surgery than in the saline control group, and the morphine group used the least supplemental pain medication during the 12 to 24 hour interval.<sup>6</sup> Ropivacaine and Bupivacaine are both local anesthetics but are not identical.

White et al studied the use of intra-articular lidocaine vs. conscious sedation for the reduction and splinting of closed ankle fracture-dislocations demonstrating a similar degree of analgesia, which was significant enough to achieve adequate reduction without having to sedate a patient.<sup>7</sup> This study demonstrates the adequacy of local anesthetics in terms of usefulness in peri or intra-articular fracture management. The use of intra-articular lidocaine conveys less cardiopulmonary risks to the patient than conscious sedation.

Other studies have used multimodal analgesia cocktails for injection into joints following operative management of a variety of pathologies. Perdreau et al used a combination of morphine, ropivacaine and methylprednisolone as an intra-articular injection following arthroscopic rotator cuff repair, with injection of isotonic saline as a control arm and measured pain intensity and post-operative morphine use at various post-operative time points. It was found that postoperative pain was significantly less intense in the MMA group than in controls at 30 min, H1, H4, H6, H12, H18 and H24 ( $P < 0.05$ ). A rebound at D10 occurred in both groups. Additionally, during the first 24 hours, MMA significantly reduced cumulative resort to morphine ( $P < 0.05$  at H1/2,  $P < 0.001$  at H1–24). The mean time to first bolus of morphine post-operatively was significantly longer in the MMA group (71.6 vs. 33 min;  $P < 0.05$ ).<sup>8</sup>

One study conducted by Chalidis et al compared aspiration of the elbow joint versus aspiration with bupivacaine injection in the initial management of closed, non-displaced radial head fractures and failed to demonstrate a difference in terms of range of motion, pain and elbow function between the 2 groups in all the examined time points.<sup>9</sup> This study, as it relates to our proposed research, aims to show that not all fractures are amenable to intra-articular anesthetic injections in terms of functional outcomes or reduction in narcotic analgesia use. However, Ditsios et al studied the effect of hematoma aspiration of intra-articular pressure and pain relief following Mason I radial head fractures in 16 patients and demonstrated that there was a statistically significant decrease for both pressure in the elbow joint and pain (by VAS scoring) in patient's who underwent aspiration compared to no aspiration.<sup>10</sup> This study shows the potential for alleviation of pain and pressure in tibial plateau fractures as the knee is capable of holding much larger volumes of blood than the elbow after a traumatic injury; the intra-articular pressure after a tibial plateau fracture may be one of the reasons the injury is so painful in the acute injury period.

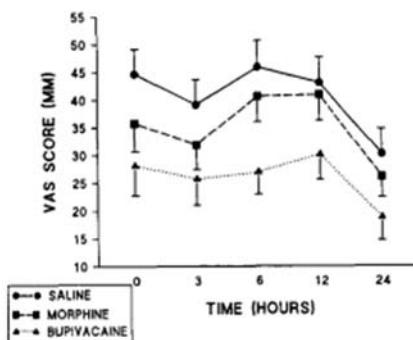
## Rationale and Specific Aims

The primary objective of this study is to determine whether a patient with a tibial plateau fracture (non-displaced, displaced, depression type) will have decreased pain and narcotic analgesia requirements following an intra-articular injection of local anesthetic and aspiration of the knee. In order to determine whether this institution has an appropriate volume of tibial plateau fractures to adequately perform such a trial, we have reviewed our volume of tibial plateau fractures and have determined we have an adequate volume to conduct such a study. The primary outcome of the study could potentially guide future management of tibial plateau fractures at this institution and potentially systemically.

- a) Specific Aim 1: Examine the effect of hemarthrosis aspiration and intra-articular bupivacaine injection on recorded Numerical Rating Scale (NRS) pain scores for patients with tibial plateau fractures in the first 24 hours following injury.**
- Working Hypothesis: Hemarthrosis aspiration and intra-articular bupivacaine injection will significantly decrease subjective pain scores in the early post-injury period.*
  - As stated previously, there has been substantial research to support the aspiration of fracture hematoma with intra-capsular injuries as it has been shown to decrease pain in the immediate presentation. There has been no research regarding intra-articular injection of local anesthetics in the acute setting of tibial plateau fractures, though there are several studies showing the efficacy of intra-articular anesthetics following total knee arthroplasty and various knee arthroscopic procedures involving the knee. There exist several methods for collecting subjective pain scores. One of the most common pain assessment tools, and the tool documented most in our institution is the VAS. To truly collect VAS data, one must use a 10cm or 100mm rule and have the patient point or state the area on the ruler than most appropriately depicts their current level of pain. The left most position represented by zero is “no pain” whereas the right most position, represented by 10cm or 100mm, is “maximal pain.” However, this method is infrequently carried out in clinical practice and as such we have chosen to use a validated Numerical Rating Scale (NRS) for pain. NRSs range from 0 to 10 and were validated for emergency department patients.<sup>11</sup> One validation study demonstrated that the verbally administered NRS (0 representing “no pain” and 10 representing “maximal, excruciating pain”) had a strong correlation with the VAS. This suggests that for patients who are asked to quantify their pain on a scale of 0-10 after tibial plateau fractures, the NRS is equivalent to using VAS pain scales but with easier reproducibility among varying clinical team members.

**b) Preliminary studies 1.1: Analgesic Effect of Intraarticular Bupivacaine or Morphine After Arthroscopic Knee Surgery: A Randomized, Prospective, Double-Blind Study.**

- This study randomized patients undergoing arthroscopy of the knee into 3 arms: injection of normal saline (n=49), 0.25% bupivacaine (n=44), or 0.03% morphine (N=46) at the end of the procedure and VAS scores were recorded at times 3, 6, 12, and 24 hours post-operatively. The VAS data were analyzed using analysis of covariance (ANCOVA). VAS was analyzed only for treatment effect in this study. Bupivacaine provided significant postoperative analgesia compared to morphine or saline (where no statistically significant difference was demonstrated). Figure 1 demonstrates the VAS scores for the 3 arms of the study showing that the effect of Intra-articular bupivacaine was noted for all 24 hours of data collection. Additionally, the study found that the time to first supplemental



**Figure 1.** Visual analogue scale (VAS) scores for the three groups who received general anesthesia. The time  $\times$  treatment effect was not statistically significant ( $F = 0.31, P = 0.96$ ) but the treatment effect was significant ( $F = 5.49, P = 0.006$ ). Post-hoc analysis using the Newman-Keuls test showed the bupivacaine group ( $n = 28$ ) to have significantly lower VAS scores than either of the other two groups ( $P < 0.05$ ). There was no difference between the morphine ( $n = 36$ ) and placebo ( $n = 27$ ) groups ( $P = 0.32$ ).

analgesia was increased in both the morphine and bupivacaine arms compared to the placebo.<sup>12</sup>

**c) Specific Aim 2: Determine if patients who undergo hemarthrosis aspiration and intra-articular bupivacaine injection use less supplemental opioid analgesia.**

a. *Working Hypothesis: Intra-articular aspiration and bupivacaine injection will significantly decrease the patients' use of supplemental opioid analgesia in the early post-injury period.*

**Preliminary Studies 2.1: Intra-Articular Injection of Bupivacaine in Knee-Replacement Operations: Results of Use for Analgesia and for Preemptive Blockade.**

This study starts with a review of animal model research, stating that trauma to tissue and bone can lead to long-lasting alterations with regard to pain perception by the central nervous system. Local anesthetics inhibit neural input to the CNS, which may inhibit or lessen the perception changes. The study had 3 arms: Group 1 received 30 ml 0.5% bupivacaine with 1:200,000 epinephrine prior to incision and 30ml saline after closure. Group 2 received 30ml of plain saline solution before the incision and 30mL of 0.5% bupivacaine and 1:200,000 epinephrine in saline solution after closure. The patients in Group 3 received 30mL of plain saline solution (a placebo) for both injections. The syringes were all prepared by the pharmacy in a double-blinded fashion. Pain scores were recorded at 1, 2, 4, 24 hours post-operative using the VAS scale. Each patient was placed on a patient-controlled analgesia (PCA) pump with morphine as the analgesic, and dosing was recorded for 24 hours. *RESULTS:* The study found that the patient who received bupivacaine after closure of the wound had lower mean VAS scores during the 24 hour study period, though it was not statistically significant. However the need for supplemental analgesia (morphine via PCA) in the post wound closure bupivacaine group was significantly lower than the placebo or preemptive blockade. The finding that post-trauma (post-operative) bupivacaine was more beneficial than preemptive analgesia or placebo actually bolsters our study hypothesis, that post-traumatic intra-articular bupivacaine will result in decreased need for supplemental narcotic medication.<sup>13</sup>

### **Inclusion/Exclusion Criteria**

We will enroll patients based on eligibility for the study.

#### **Inclusion Criteria:**

- Patients with isolated tibial plateau fractures aged 18 years and older.
- Patients with tibial plateau fractures and associated soft tissue complaints about the knee, not associated with a fracture outside of the tibial plateau
- Patients with bilateral tibial plateau fractures and no other noted fractures

#### **Exclusion Criteria:**

- Any Patient that does not wish to participate in the study or is unable to give consent at the initial encounter will be excluded.
- Patients under 18 years old
- Pregnant patients
- Mentally handicapped patients who are unable to give consent

- Incarcerated patients
- Inability or unwillingness to consent for participation
- History of allergic reaction to local anesthetics
- Emergent conditions requiring operations or airway protection
- Polytrauma patients
- Patients presenting for care > 24 hours following their injury.

## **Enrollment/Randomization**

Sample sizes of 22, 22, and 22 will be allocated to 3 groups (control, aspiration, and aspiration plus injection) using an equal 1:1:1 block randomized allocation.

## **Study Procedures**

We propose to study all tibial plateau fractures treated at LUHS for which we have fracture data, treated with ORIF or treated non-operatively. Patients will be identified based on the classification of their injury, that being tibial plateau fracture; we will seek to sub-classify each patient based on the Shatzker classification of tibial plateau fractures and using OA classification as our prospective study will be based on both tibial plateau fractures as a whole and their sub-classification: lateral tibial plateau fracture without depression (I), lateral tibial plateau fracture with depression (II), compression fracture of the lateral (IIIA) or central (IIIB) tibial plateau, medial tibial plateau fracture (IV), bicondylar tibial plateau fracture (V), and tibial plateau fracture with diaphyseal discontinuity (VI).<sup>2</sup> It is important for our prospective study to classify each fracture pattern as they generally differ in energy of injury and thus may affect pain management or need for narcotic pain medications and also potentially affect functional outcomes. Patient inclusion will be based on agreement to participate using informed consent. Additionally, patients may be excluded from the study if they choose not to consent, are incapacitated on initial presentation, have an emergent condition necessitating either operative management or airway protection or have a history of allergic reaction to local anesthetic injection.

Following consent for participation in the study, patients will be blinded to initial management of the tibial plateau fracture with either: Aspiration of the joint alone, aspiration of the knee joint and injection of 20cc bupivacaine 0.5% with 1:200,000 epinephrine or no injection or aspiration therapy for a control arm. Using the block randomization list, the patient will be randomized at the time of consent for participation. For the sake of consistency, all participating treating physicians (orthopaedic on-call residents) will be trained on Sawbones™ Fully Encased Knee Joint with Patella and Ligaments for a standardized aspiration and injection technique.

For the patients randomized into the treatment arms, the knee will be held in 15-30\* short of full extension and fully prepped using chlorhexidine wipes in a centrifugal manner. An 18 gauge spinal needle will be introduced into the superolateral aspect of the knee (if the knee is too edematous, an inferolateral or inferomedial approach is appropriate, but requires documentation). Aspirate the knee with 60cc syringe until unable to draw out more fluid and record volume on

given study form. Remove the syringe from the needle connection, leaving the 18 gauge needle in place. Draw up 30cc of 0.5% bupivacaine with 1:200,000 epinephrine (Marcaine) with .18-gauge needle into 2nd 60cc syringe. Place the filled syringe on the 18 gauge needle already in the knee and INJECT. Remove needle-syringe construct and place bandage over injection site.

The patient's initial NRS score will be recorded immediately. Subsequent VAS scores will be recorded at time points 0 (5 minutes after intervention), 2, 4, 6, 8, 12, 24 hours after initial work-up of the patient. Patients treated as an outpatient will record these values themselves (copy of recording form submitted with this application). Patients will be directed to bring the completed form with them to their regular clinic follow-up visit. Additionally, supplemental analgesia requirements will be recorded upon administration and will be converted to morphine equivalent units for analysis (copy of recording form submitted with this application). All patients admitted to the orthopedic service will be placed on morphine PCA (determined dosing by weight of patient). All other patients (those admitted to other services) will have analgesia converted to Opioid Morphine Equivalents (OMEs).

Prospectively: Patients will be blinded to initial management of the tibial plateau fracture with either: Aspiration of the knee joint alone, aspiration of the joint and injection of bupivacaine 0.5% with epinephrine or no injection or aspiration therapy for a control arm. Using the block randomization list, the patient will be randomization at the time of consent for participation. The patient's initial VAS score will be recorded at the time of initial work-up. Subsequent VAS scores will be recorded at time points 2, 4, 6, 8, 12, 24 hours after initial work-up of the patient. Additionally, supplemental analgesia requirements will be recorded upon administration and will be converted to morphine equivalent units for analysis.

Demographic information to be collected includes Age, BMI, Problem list: Medications, Allergies, Smoker, Alcohol and Drug use.

## Risks

Risks associated with aspiration of the knee joint include:

- Pain
- Infection
- Inability to remove any fluid or blood from the joint
- The need to attempt another needle stick to place the needle in the correct position

Risks associated with injection of a local anesthetic in the joint include:

- Pain
- Infection
- Chondrolysis reported in vitro with bovine cartilage; no human studies support this finding.
- There have been no reported incidences of systemic issues associated with a single intra-articular knee injection of any local anesthetic

## **Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others**

Adverse event identification will be the responsibility of each member of the research team and to report same to one of the trauma surgeons, William Lack, MD; Hobie Summers, MD; and Mitchell Bernstein, MD. Specifically, Dr. William Lack will be responsible for reporting promptly to the IRB office.

### **Study Withdrawal/Discontinuation**

If at any time during the course of the patient's treatment or data collection, the patient decides to withdraw from the study they may do so without any consequence. If the patient decides to withdraw after consent is given they may do so and will not be included in the study.

### **Statistical Considerations**

Sample sizes of 22, 22, and 22 will be allocated to 3 groups (control, aspiration, and aspiration plus injection) using an equal 1:1:1 block randomized allocation. The null hypothesis is that at 24 hours the mean VAS score for these three groups will be equivalent. Power is computed to reject this null hypothesis. A total sample of 66 subjects achieves 84% power to detect at least one pairwise minimal difference score of 1.60mm using the Tukey-Kramer (Pairwise) multiple comparison test at a 0.05 significance level. An assumption was made to set the common standard deviation of the VAS score within any one group to 1.00mm.

### **Privacy/Confidentiality Issues**

The principal investigator and research team members listed on the protocol will have access to protected health information.

All patient health information (PHI), demographics and sensitive data will be kept on the Loyola provided secure server in an assigned password protected folder located on the R: drive and/or in a REDCap database. All paper records, if any, will be kept in a locked cabinet in the offices of the principal investigator.

### **Follow-up and Record Retention**

All records will be removed from secure server upon completion of the study. All paper records, if any, will be disposed of using Loyola approved system and receptacles.

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