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Ultrasound Guided Motor Sparing Knee Blocks for Postoperative Analgesia Following Total Knee Arthroplasty

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Kinesiology

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ULTRASOUND GUIDED MOTOR SPARING KNEE BLOCKS FOR
POSTOPERATIVE ANALGESIA FOLLOWING TOTAL KNEE ARTHROPLASTY: A
RANDOMIZED BLINDED STUDY

(Thesis format: Monograph)

by

Olawale Sogbein

Graduate Program in Kinesiology

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Sport's Medicine

The School of Graduate and Postdoctoral Studies
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Abstract

Postoperative total knee arthroplasty (TKA) pain is severe and can inhibit patients' rehabilitation. We devised a single injection motor sparing knee block (MSB) by targeting the adductor canal and lateral femoral cutaneous nerve with a posterior knee infiltration under ultrasound. Our primary objective was to evaluate the duration of the MSB compared to a standard periarticular infiltration (PAI) using time to first rescue analgesia as the end point. We randomized 82 patients undergoing TKA to receive either preoperative MSB or intraoperative periarticular infiltration. Duration of analgesia was significantly longer in the MSB group with a mean difference of 8.8 hours. No significant differences were found in quadriceps strength, functional outcomes, side effects, satisfaction, or length of stay between groups. The MSB provided longer analgesia than the PAI while not negatively affecting quadriceps strength, length of stay, or functional rehabilitation.

Keywords

Total knee arthroplasty, motor sparing, nerve block, adductor canal block, periarticular infiltration

Co-Authorship Statement

This randomized clinical trial was designed in collaboration with Drs. Sondekoppam Vijayashankar, Howard, Bryant, and Ganapathy. I was responsible for conducting the study including: patient identification, patient recruitment, data collection, and data analysis. I wrote the original draft of this thesis document. Drs. Bryant and Howard made comments and suggestions towards the final submission.

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Table of Contents

Abstract	ii
Co-Authorship Statement.....	iii
Acknowledgments.....	iv
Table of Contents	v
List of Tables	ix
List of Figures	x
List of Appendices	xii
Acronyms.....	xiii
Chapter 1	1
1 Introduction	1
Chapter 2	3
2 Literature Review.....	3
2.1 Anatomy of The Knee Joint.....	3
2.1.1 Bony Structures.....	3
2.1.2 Muscles	4
2.1.3 Menisci.....	5
2.1.4 Ligaments.....	5
2.1.5 Innervation	6
2.1.6 Blood Supply	8
2.2 Osteoarthritis.....	9
2.3 Non-Operative Treatment	9
2.4 Total Knee Arthroplasty	10
2.4.1 Epidemiology	10
2.4.2 Postoperative Pain.....	11

2.5 Analgesic Drugs.....	11
2.5.1 Opioid and Nociceptors	12
2.5.2 Ketorolac.....	13
2.6 Analgesic Techniques	13
2.6.1 Patient-Controlled Analgesia	13
2.6.2 Continuous Epidural Analgesia	14
2.6.3 Lumbar Plexus Blocks	14
2.6.4 Femoral Nerve Blocks	17
2.6.5 Adductor Canal Blocks	20
2.6.6 Periarticular Injections	28
2.7 Summary	38
Chapter 3	40
3 Objectives.....	40
Chapter 4.....	41
4 Materials and Methods.....	41
4.1 Study Design.....	41
4.2 Eligibility Requirements	41
4.3 Subject Recruitment.....	41
4.4 Randomization	41
4.5 Interventions	42
4.5.1 Motor Sparing Block (experimental group).....	42
4.5.2 Periarticular Infiltration (control group)	43
4.5.3 Standardization of Potential Co-interventions	44
4.6 Blinding	44
4.7 Outcome Measures.....	45
4.7.1 Primary Outcome Measure	45

4.7.2	Secondary Outcome Measures.....	46
4.8	Sample Size.....	50
4.9	Data Analysis.....	50
Chapter 5		52
5	Results.....	52
5.1	Participant Flow.....	52
5.2	Primary Outcome Measure.....	55
5.2.1	Total Duration of Analgesia.....	55
5.3	Secondary Outcome Measures.....	57
5.3.1	Overall Pain.....	57
5.3.2	Quadriceps Muscle Strength.....	58
5.3.3	Western Ontario McMaster Osteoarthritis Index.....	59
5.3.4	SF-12 Health Survey (SF-12) – version 2.....	60
5.3.5	Physiotherapy and Mobilization.....	61
5.3.6	Total Opiate Consumption.....	62
5.3.7	Timed Up and Go Test.....	64
5.3.8	Site of Predominant Pain.....	64
5.3.9	Side Effects.....	65
5.3.10	Length of Hospital Stay.....	66
5.3.11	Satisfaction.....	66
5.4	Adverse Events.....	66
Chapter 6		67
6	Discussion.....	67
6.1	Study Limitations.....	72
Chapter 7		74
7	Conclusion.....	74

7.1 Clinical Relevance	74
7.2 Future Direction	74
Bibliography	75
Curriculum Vitae	98

List of Tables

Table 1: Baseline Demographics for patients undergoing total knee arthroplasty with either the motor sparing block or periarticular infiltration techniques	54
Table 2: Block characteristics for patients undergoing total knee arthroplasty with either the motor sparing block or periarticular infiltration techniques	54
Table 3: Western Ontario McMaster Osteoarthritis Index scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)	60
Table 4: SF-12 Health Survey scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means).....	60
Table 5: Time to Complete the Timed Up and Go in seconds following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)	64
Table 6: Knee Society Score Satisfaction following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)	66

List of Figures

Figure 1: Structures of the knee joint.....	4
Figure 2: Nerves and Muscles of the Upper Leg	7
Figure 3: Cross-sectional MR scan of the adductor canal.	21
Figure 4: Ultrasonography image of the adductor canal.....	23
Figure 5: Participant flow through study	53
Figure 6: Total duration of analgesia following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques	56
Figure 7: Numerical rating pain scores at rest following TKA with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)	57
Figure 8: Numerical rating pain scores during activity following TKA with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals).....	58
Figure 9: Quadriceps muscle strength in pounds following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals).....	59
Figure 10: Pain following postoperative physiotherapy appointments following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals).....	62
Figure 11: Oxycodone consumption following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals).....	63

Figure 12: Hydromorphone consumption following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals) 63

Figure 13: Nausea scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals) 65

List of Appendices

Appendix A: Ethics Approval.....	87
Appendix B: Letter of Information and Consent	89
Appendix C: Image Permissions.....	96

Acronyms

ACB – adductor canal block

FNB – femoral nerve block

PAI – periarticular infiltration

MSB – motor sparing block

PCA – patient controlled analgesia

TKA – total knee arthroplasty

LPB – lumbar plexus block

CEA – continuous epidural analgesia

PNB – peripheral nerve block

Chapter 1

1 Introduction

The total knee arthroplasty (TKA) is a highly successful procedure for treating patients with advanced osteoarthritis (OA)¹. The number of knee replacement surgeries has risen over the past decade and is projected to increase 6-fold from 2005 to 2030 because of the aging population². Severe acute postoperative pain may interfere with patients' ability to sleep, walk, and participate in rehabilitation activities³.

Traditionally, analgesia techniques such as patient-controlled analgesia (PCA), continuous epidural analgesia (CEA), lumbar plexus block (LPB), and femoral nerve blocks (FNB) have been performed to reduce pain during the immediate postoperative period. PCA using intravenous opioids and continuous epidurals pose the risk of side effects such as; nausea, pruritus, vomiting, dizziness, urinary retention, sedation, poor muscle control, and constipation⁴⁻⁷. LPBs require advanced skills and FNBs cause quadriceps weakness that increase the risk of inpatient falls⁸⁻¹⁰.

It is important to preserve quadriceps strength in the immediate postoperative period, leading to early mobilization after surgery and enhancing functional recovery. Recently, adductor canal blocks (ACB) and periarticular infiltrations (PAI) have become popular because they are able to preserve quadriceps strength while providing similar postoperative analgesia to the traditional FNB^{3,11-15}. One drawback to ACBs is that they do not provide analgesia to the posterior knee. Single injection PAIs performed at the end of surgery can have a shorter duration of analgesia¹⁵. Although continuous infusions prolong postoperative pain relief, the potential risk of joint infections caused by the catheter used to administer the infusion is an impediment to its popularity^{5,16}.

We have developed a motor sparing knee block (MSB) for providing regional analgesia that minimally interferes with quadriceps innervation following TKA. Further, the MSB involves a combination of the single injection ACB with the addition of posterior knee infiltration and blockage of the lateral cutaneous nerve. Our clinical trial is the first to investigate whether there are any differences in duration of analgesia, quadriceps strength, function,

pain, satisfaction, side effects, and length of stay between the MSB and PAI techniques following TKA. We believe the MSB can serve as an attractive alternative regional block technique for patients undergoing TKA.

Chapter 2

2 Literature Review

2.1 Anatomy of The Knee Joint

2.1.1 Bony Structures

The knee is one of the largest and most complex joints in the body consisting of three bones; the femur, tibia, fibula, and patella¹⁷. The distal femur is asymmetrical allowing for attachment of various ligaments and tendons. The convex eminence of the medial epicondyle serves as the attachment point for the medial collateral ligament. The lateral epicondyle of the femur serves as the femoral attachment for the lateral collateral ligament. The epicondylar axis in normal knees is defined as the line that passes from the sulcus of the medial epicondyle to the prominence of the lateral epicondyle¹⁸.

The tibia also consists of medial and lateral condyles and articulates with the distal femur. The prominent aspect of the tibia has a spine, which has an anterior depression that serves as attachments for the anterior horns of the medial and lateral menisci and anterior cruciate ligament (ACL)¹⁷. Anteriorly, the tibia has a tubercle that functions as the insertion point for the patella tendon. The Gerdy's tubercle is located three centimeters laterally from this and is the insertion site for the iliotibial band (ITB)¹⁸. The fibula is a leg bone located laterally to the tibia. The head of the fibula forms the proximal tibiofibular joint with the lateral edge of the tibia. At its distal end, the fibula forms a lateral malleolus. At the medial malleolus of the tibia, the fibula forms the distal tibiofibular joint. Finally, the patella articulates with the trochlea of the distal femur¹⁷. The patella functions to protect the front of the knee and increase leverage through the range of knee extension¹⁹.

Figure 1: Structures of the knee joint

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2.1.2 Muscles

The anterior aspect of the upper leg consists of four muscles collectively called the quadriceps that function to extend the knee joint¹⁸. The rectus femoris muscle originates proximally from the ilium forming a muscle belly in the anterior thigh. It then narrows into a tendon above the patella. The largest muscle of the quadriceps group, the vastus lateralis originates from the proximal intertrochanteric line of the femur extending halfway down the linea aspera¹⁷. The vastus lateralis ultimately inserts into the tibia. The vastus medialis, which is sometimes divided into the vastus medialis obliquus (VMO) and the vastus medialis longus (VML) originates from the intertrochanteric line and inserts with the other muscles of the quadriceps in the quadriceps tendon¹⁸. Lastly, the vastus intermedius originates at the lateral and anterior aspect of the femur. Its fibers also end in the quadriceps tendon. Overall, the rectus femoris forms the most superficial layer of the quadriceps tendon. The vastus medialis and vastus lateralis contribute to the middle layer, and the insertion of the intermedius forms the deepest layer¹⁷. After forming

the quadriceps tendon, these four insertions become the patellar tendon, which inserts at the tibial tubercle¹⁸.

The sartorius, gracilis, semitendinosus, semimembranosus, and medial head of the gastrocnemius are all located at the medial side of the knee¹⁷. Collectively the semimembranosus, semitendinosus, and bicep femoris make up the posterior hamstring thigh muscles that function in knee flexion. Known as the pes anserinus muscles, the sartorius, gracilis, and semimembranosus muscles flex and internally rotate the knee¹⁸. The lateral side of the knee contains the iliotibial band (ITB), biceps femoris, popliteus, and lateral gastrocnemius muscles¹⁹.

2.1.3 Menisci

The menisci are two crescent-shaped fibro-cartilaginous structures functioning to deepen the tibial surface for the articulation of the distal femur¹⁹. Their circumferential pattern aids in absorbing the compressive load on the knee. Each meniscus covers approximately two-thirds of the matching articular surface of the tibia¹⁸. The medial meniscus is semicircular shaped and is broader posteriorly. The lateral meniscus is almost completely circular allowing it to cover a larger surface area. The menisci serve many functions such as aiding in load transmission by increasing the contact area, distribution of synovial fluid, enhancement of articular conformity, and prevention of soft tissue impingement during motion¹⁷.

2.1.4 Ligaments

The knee joint consists of four ligaments that provide stability to the knee. The anterior cruciate ligament (ACL) is the primary static stabilizer of the knee and prevents the tibia from shifting anteriorly to the femur. The ACL originates from the medial aspect of the femoral condyle at the posterior aspect of the intercondylar notch and travels in an anterior, distal, and medial direction toward the tibia¹⁸. The posterior cruciate ligament (PCL) functions to prevent the tibia from shifting posteriorly relative to the femur. It provides approximately 95% of the total restraint to posterior translation of the tibia on the femur¹⁷. The PCL originates posteriorly in the intercondylar notch of the medial

femoral condyle and attaches to the posterior intercondyloid fossa of the tibia¹⁸. The medial collateral ligament (MCL) is a broad flat membranous band originating from the medial epicondyle of the femur and runs to the medial condyle of the tibia. It functions to resist forces that would push the knee medially preventing valgus deformity. More narrow than the MCL, the lateral collateral ligament (LCL) originates from the lateral epicondyle of the femur above and travels to the head of the fibula below¹⁷. It also functions in maintaining knee stability as it moves through its full arc of motion¹⁹.

2.1.5 Nerve anatomy of the lower limb

The nerves of the leg and foot arise from the lumbar and sacral roots arising from the spinal cord in the lower back and pelvis. These roots form two networks of crossed nerves called the lumbar plexus and sacral plexus¹⁸. The femoral, saphenous, obturator, and lateral femoral cutaneous nerves all extend from the lumbar plexus into the muscles and skin of the lower limb¹⁷. Innervation of the knee joint can be divided by location. The femoral nerve provides anterior and medial innervation to the knee¹⁸. Branches of the femoral nerve innervate the quadriceps muscles and skin of the anterior and medial thigh. Its largest branch the saphenous nerve, extends this innervation to the skin of the medial lower leg and foot^{17,20}. The lateral femoral cutaneous nerve supplies the skin on the lateral region of the thigh.

The saphenous nerve is the largest cutaneous branch of the femoral nerve and begins from the distal division of the femoral nerve^{8,11,17}. At the distal end of the adductor canal it penetrates the deep fascia on the medial area of the knee situated between the sartorius and gracilis tendons. The saphenous nerve divides into two branches; the infrapatellar branch of the saphenous nerve follows the sartorius muscle and innervates the anteromedial capsule, skin of the knee, and the patellar tendon¹⁸. The sartorial branch travels further distally and innervates the medial area of the lower leg and ankle¹¹.

The tibial nerve and obturator nerve function in posterior knee and medial thigh innervation respectively¹⁸. Branching from the long sciatic nerve originating from the sacral plexus, the tibial nerve begins in the distal posterior aspect of the thigh¹⁷. Running distally through the popliteal fossa, the tibial nerve continues between the two heads of the

gastrocnemius. The medial sural cutaneous nerve is a branch of the tibial nerve that travels on the surface of the gastrocnemius¹⁷. The largest articular branch of the tibial nerve, the posterior articular nerve arises within the popliteal fossa and then joins the popliteal plexus laterally.

Finally, the common peroneal (or fibular nerve) enters the popliteal fossa lateral to the tibial nerve and continues distally along the medial side of the biceps femoris tendon. It branches into the lateral sural cutaneous nerve. It continues between the biceps femoris tendon and the lateral head of the gastrocnemius. Distally it travels superficially across the lateral aspect of the fibular neck before dividing into the superficial and deep peroneal nerves¹⁸.

Figure 2: Nerves and Muscles of the Upper Leg

Reprinted with permission from

http://www.daviddarling.info/encyclopedia/F/femoral_nerve.html

2.1.6 Blood Supply

The adductor canal also known as the Hunter's canal or sub-sartorial canal, is an aponeurotic tunnel in the medial aspect of the upper leg^{8,11,17,21}. This canal extends from the beginning of the femoral triangle to the adductor hiatus and contains the femoral artery, femoral vein, and branches of the femoral nerve. Coursing between the anterior and medial component of the thigh, the adductor canal is bounded anteriorly by the sartorius, posteromedially by the adductor longus and magnus, and laterally by the vastus medialis muscle^{17,18}. The femoral artery is the primary arterial supply to the lower limb. It descends from the femoral triangle and through the adductor canal. Before passing through the adductor hiatus the femoral artery becomes the descending genicular artery, which splits into two branches¹⁷. The first branch is the saphenous branch, which accompanies the saphenous nerve to the medial side of the knee. The saphenous branch travels between the sartorius and the gracilis muscles before combining into the medial inferior genicular artery^{17,18}. Secondly, the articular branch of the descending genicular artery passes through the vastus medialis and then forms an anastomosis with the medial superior genicular artery and anterior recurrent tibial artery¹⁷.

The popliteal artery is a continuation of the femoral artery after it exits the adductor canal and before it enters the popliteal fossa¹⁸. It descends superficially to the popliteus fascia and then separates at the lower border of the popliteus into the anterior and posterior tibial arteries. Around the knee the popliteal artery divides into many muscular branches and specifically five genicular branches; the medial superior, lateral superior, middle, medial inferior, and lateral inferior¹⁷. All of these genicular branches supply blood to the peripheral third of the menisci, however a majority of the blood comes from the superior and inferior lateral geniculates¹⁸. Finally, the middle genicular artery forms branches that enter the synovium and form a plexus that covers the ACL and PCL. These branches anastomose with vessels that run parallel to the collagen fibers.

The anterior anastomosis of the knee joint connects the circulation of femoral artery with popliteal and anterior tibial arteries¹⁷. It is formed by the two medial genicular branches, the two lateral genicular branches, the descending genicular branch, the descending

branch of the lateral femoral circumflex, and the anterior recurrent tibial artery^{17,18}.

Collectively, these vessels surround the patella and then split into nutrient vessels at the inferior pole of the patella that ascend proximally on the anterior surface of the bone.

The skin of the anterior knee receives blood from both the medial and lateral side, however the primary vascular supply comes from the medial side¹⁸.

2.2 Osteoarthritis

Arthritis is an umbrella term used to describe more than 100 diseases and conditions that affect the joints causing pain, swelling, and stiffness which often lead to disability¹⁹. It is one of the most prevalent chronic health conditions in Canada and is the second and third most common chronic conditions reported by women and men respectively²². As the most common form of arthritis, osteoarthritis (OA) also known as degenerative arthritis or degenerative joint disease, is caused by a group of mechanisms that result in the deterioration of joint cartilage and thickening of the bones underneath in one or more joints^{23,24}. According to the World Health Organization (WHO), 9.6% of men and 18% of women older than 60 years of age worldwide have symptomatic OA, making this condition one of the most prevalent chronic conditions²⁵. In Canada, one in ten adults are affected with OA²⁶. As the disease progresses, joint damage, pain, and stiffness manifest with the knee being the most common joint involved²⁷. Exact causes of OA can be difficult to determine however the condition has been divided into two types. Primary OA is when there is no identifiable initiating event, though risk factors may be present. Secondary arthritis occurs when there is a likely cause for the onset of OA. The most common cause of secondary OA is prior injury to the joint. However risk factors such as age, family history, excess weight, and overuse can contribute to OA development²⁶.

2.3 Non-Operative Treatment

There are a number of conservative options to decrease pain and improve function for patients with mild and moderate OA. These options include: weight reduction, switching from high impact to low impact exercises (i.e. swimming, biking, elliptical trainer); using over the counter anti-inflammatory medications, physical therapy, and cortisone injections²⁸. How long an individual should try conservative treatment is dependent upon

the recommendations from their physician. Once a patient's OA becomes severe and conservative medical therapies are ineffective, surgery can be considered.

2.4 Total Knee Arthroplasty

The TKA has been established as a successful procedure for treating patients with advanced OA and functions to establish a functional less painful knee with improved longevity^{28,29,30}. This procedure replaces the surfaces of the damaged knee joint bones through four basic steps^{19,28}. First, the damaged cartilage surfaces and a small amount of underlying bone at the end of the femur and tibia are removed in order to prepare for the installation of components. These implants can be press-fit or cemented into the ends of the femur and tibia to recreate the surface of the knee joint^{22,28}. The undersurface of the patella can be cut and resurfaced with an implant depending upon the patient and surgeon preference. Patellar resurfacing can be performed when patients have a loss of cartilage, exposed bone, gross surface irregularities, and or anterior knee pain. Finally, a plastic spacer is secured to the tibial component, with the goal of creating a smooth gliding femoro-tibial surface¹⁹.

2.4.1 Epidemiology

Total knee arthroplasty (TKA) is the most common elective orthopaedic procedure. It is performed for severe end-stage osteoarthritis and is associated with significant improvement in pain, function, and daily activities in patients²⁹. This procedure is reserved for patients with intractable pain and functional limitations whom have failed conservative treatment and are not candidates for other procedures such as arthroscopy³⁰.

In 2004 Kurtz *et al.* developed a predictive model and concluded that because of an aging population, the number of knee replacement surgeries have drastically risen over the years and are projected to increase 6-fold from 2005 to 2030 in the United States².

Furthermore, according to the 2014 Annual Report by the Canadian Joint Replacement Registry (CJRR) between 2012-2013, approximately 57, 718 knee replacements were performed in Canada, which is a 21.5% increase from 2008-2009. More specifically there was a 5% increase in knee replacements from 2011 to 2013³¹. As Ethgen *et al.* concluded,

patients with end-stage joint deterioration because of osteoarthritis or rheumatoid arthritis constitute the largest group of patients who require total knee replacements³⁰.

The demand for lower-limb arthroplasty is expected to increase, as indications for replacement surgeries extend as a consequence of advancements in prosthetic materials and expected clinical benefits. The etiology of knee pain that requires treatment with a TKA is often attributed to osteoarthritis, inflammatory arthritis, and post-traumatic arthritis²⁸.

2.4.2 Postoperative Pain

Since the TKA procedure is invasive, it is often associated with intense postoperative pain and therefore a comprehensive multimodal analgesic regimen^{4,11,32,33}. Pain management after a TKA is of great importance because of the high incidence for severe acute postoperative pain which can interfere with patients' ability to sleep, walk, and participate in rehabilitation activities required for hospital discharge^{3,34}. Results from studies conducted by Chavis and Hawker *et al.* indicate a fear of poorly controlled pain or unrelieved pain during hospitalization may result in failure to achieve functional outcomes. In turn, this may contribute to increased risk for postoperative complications such as pneumonia, deep vein thrombosis, or pulmonary embolus^{35,36}. Therefore adequate postoperative pain control is crucial in the immediate and early postoperative period when pain levels are typically the highest. Earlier discharge, which primarily involves early rehabilitation, is only possible if pain control is effective and muscle function is conserved³⁷.

2.5 Analgesic Drugs

Analgesics are any member of a drug class used to achieve a relief from pain. Since a substantial number of patients experience severe pain after TKA, healthcare professionals prescribe multiple drugs that work via different mechanisms to promote healing and recovery, faster patient mobilization, shortened hospital stays, and reduced healthcare costs³⁸. Major targets for analgesia following TKA are the opioid receptors, nociceptors, and local inflammatory mediators³⁹.

2.5.1 Opioid and Nociceptors

Immediately following surgical trauma, peripheral receptors are among the first expressed, subsequently relaying signals to central receptors⁴⁰. When peripheral tissue is damaged, sensory neurons transduce noxious mechanical stimuli into action potentials. The cell bodies of these neurons are found in the dorsal root ganglia (DRG) and give rise to A-delta and C nerve fibers¹⁸. After synaptic transmission and modulation within the afferent neurons and spinal cord, nociceptive signals reach the brain where they are registered as pain. Opioids such as morphine and its derivatives; codeine, oxycodone, and hydrocodone can produce analgesia by activating opioid receptors on peripheral sensory neurons. Specifically morphine acts on three peripheral nerve opioid receptors (mu, delta, kappa) to exert an analgesic effect at the wound site^{18,40}. As indicated by Stein and Lang, opioids are still the most powerful drugs for severe pain. However, their use is hampered by side effects such as respiratory depression, nausea, constipation, addiction and tolerance^{40-43,44}. As opioids bind to opioid receptors they cause a decrease in the excitability of the nociceptive neurons producing analgesia. Inhibition of nociceptors is increased by the use of local anesthetics such as ropivacaine¹⁵.

2.5.1.1 Ropivacaine

Ropivacaine is a local anesthetic drug belonging to the amino-amide group developed for the purpose of reducing potential toxicity and improving relative sensory and motor block performance⁴⁵. This drug is indicated for local anaesthesia often used in TKA operations such as local infiltration, peripheral nerve blocks, epidurals, and intrathecal anesthesia. Ropivacaine is related structurally to bupivacaine, with similar pharmacokinetic disposition but is less lipid soluble. Ropivacaine use has been popularized since bupivacaine was correlated with higher CNS and cardiac toxicity⁴⁶.

Ropivacaine's mechanism of action is by reversible inhibition of sodium ion influx causing impulse blockage in nerve fibres. It has selective action on the pain-transmitting A delta and C fibres over the A beta fibres that are also involved in motor function⁴⁵. This selective action is because of its less lipophilic nature than bupivacaine and its stereoselective properties. Ropivacaine has been shown to provide equal analgesia, allow

for greater mobility, and reduce opioid consumption in patients following TKA in comparison to opioid based analgesia⁴⁷. Ropivacaine can also be administered as a cocktail containing epinephrine and Ketorolac⁴⁷. Epinephrine functions to cause localized vasoconstriction to maintain optimal concentration of ropivacaine at the wound site⁴⁸.

2.5.2 Ketorolac

Ketorolac is a non-steroidal anti-inflammatory drug (NSAID). It functions by inhibiting the production of prostaglandin inflammatory mediators by the eicosanoid pathway, exerting anti-inflammatory, antipyretic and analgesic effects³⁹. This serves to blunt the initial pain response. Andersen *et al.* found that local infiltration containing ketorolac in combination with ropivacaine and epinephrine resulted in patients consuming less postoperative morphine for pain in comparison to patients receiving no ketorolac in their analgesic cocktail⁴⁹.

2.6 Analgesic Techniques

Adequate pain relief is extremely important in postoperative knee rehabilitation. Many modes of perioperative analgesia have been reported for patients undergoing TKA. Patient-controlled analgesia (PCA), continuous epidural analgesia (CEA), peripheral nerve blocks (PNB), and periarticular infiltration (PAI) are traditional and current pain management regimens.

2.6.1 Patient-Controlled Analgesia

Patient-controlled analgesia is a method that allows patients to administer their own pain relief through the use of a computerized intravenous infusion pump. Healthcare providers ensure the pump is programmed specifically for the patient's pain relief and to prevent drug overdose. Traditionally, postoperative protocols for TKA were based on a general anesthetic and opioid intravenous PCA³⁹. Although opioids provide effective analgesia, they are associated with side effects such as nausea, pruritus, vomiting, dizziness, urinary retention, sedation, and constipation⁴⁻⁶.

2.6.2 Continuous Epidural Analgesia

Epidural analgesia involves the administration of drugs through a catheter placed in the epidural space. The epidural space is the outermost part of the spinal canal, specifically lying just outside the dura mater¹⁸. Within this epidural space, the spinal nerve roots and small arteries are found. Epidural analgesia involving the combination of a local anesthetic agent and an opioid has traditionally played a major role in orthopaedic anaesthesia since its analgesic efficacy is very high³³. Studies have indicated that the benefit of epidural analgesia must be weighed against the risks of its adverse outcomes such as nausea, pruritus, hypotension, urinary retention, poor muscle control, and delayed mobilization⁷.

2.6.3 Lumbar Plexus Blocks

The inhibition of afferent pain fibers is the primary goal of peripheral nerve blocks. The optimal nerve block, combination of blocks and/or combination of catheter and single-injection techniques is still a matter of debate³³. Winnie *et al.* introduced an approach to blocking the lumbar plexus in the early 1970s^{8,50}. The three nerves to the lower limb arising from the lumbar plexus: the obturator nerve, lateral femoral cutaneous nerve, and femoral nerve can be blocked by single injection. Also called the '3 in 1 block', the placement of an indwelling catheter can allow continuous block of the lumbar plexus⁴⁴. Winnie *et al.* indicated that the fascial envelope is identified by the production of a paresthesia of the femoral nerve. If a sufficient volume of anesthetic solution is injected to reach the lumbar plexus, a blockade of these nerves results⁵⁰. Winnie described an anterior inguinal paravascular approach. In this technique a needle is inserted into the sheath that surrounds the femoral nerve. The injection is made just below the inguinal ligament, with the solution being forced cephalad to block the nerves at the level where they lie closer together in the lumbar plexus. A more common approach is the posterior lumbar paravertebral approach. The patient is placed on their side and a needle is inserted into the interfascial space between the quadratus lumborum and psoas major muscles. This allows the anesthesia to be placed where the roots form the plexus. The main risk of the advanced lumbar plexus block is the close proximity of the epidural space and retroperitoneum of the kidney. Mislead catheters, kidney injuries, and local anesthetic

toxicity have been reported^{8,54}. However, studies have shown that continuous lumbar plexus blocks (CLPB) have provided adequate analgesia for TKA patients⁵¹.

A prospective cohort study conducted by Luber *et al.*⁵² enrolled 87 patients with similar characteristics (age, sex, height, and weight) to receive a combined lumbar plexus and sciatic nerve block. Their results indicated that 78% of their patients had successful pain relief using the block alone for an average of 13 hours post operation (range, 4.25-22)⁵². Of the 87 patients, 86 completed a satisfaction survey that contained questions never used in literature previously. They found that the overall satisfaction rate was 92%, and 95% agreed to consider lumbar plexus blocks if future surgery was necessary. No control groups were used in this study.

In 1991 Serpell *et al.*⁴⁴ published a randomized clinic trial comparing the analgesic efficacy of CLPB to a control group for the first 48 hours following TKA. A total of 30 patients were randomly assigned to receive the lumbar plexus block (n=13), or no block (n=16). The control group did not have a placebo injection at the femoral site. Both groups were attached to an on-demand analgesic computer (ODAC) set to deliver morphine upon return to the ward following surgery. The ODAC delivered morphine in 2 mg intravenous boluses to a maximum of 12 mg/hour with a lockout interval of nine minutes. If further pain control was required, intramuscular morphine 10 mg or paracetamol 1g orally was administered. Outcome measures included pain numerical rating scales (NRS), morphine consumption, and any adverse effects in the 48-hour postoperative period. Patients in the lumbar plexus group required a third less morphine than the control group in the total 40 hour postoperative period (mean(SEM), 60mg(8.7) vs 91mg(9.8) p<0.05). There were no significant differences in pain scores between the two groups at 24 and 48 hours and the incidence of nausea and vomiting was not significantly different between groups. Though this randomized control trial had a smaller sample size and functional outcomes were not assessed, Serpell *et al.* concluded that lumbar plexus blocks offer similar analgesia to continuous morphine, but with significantly reduced opioid requirements.

Watson *et al.*⁵³ assessed functional outcomes in their randomized clinical trial comparing CLPBs to single injection lumbar plexus blocks (SLPB). They wanted to determine whether a block infusion is required or whether single-injection nerve blocks alone would be as effective. A total of 32 patients were randomly allocated to the continuous block group (n=16), or the single block group (n=16). Both groups received PCA morphine, using a 1 mg bolus and a 5-minute lockout period with no background infusion. Outcomes measured were pain, morphine consumption, motor power, ambulation, and nausea. Results indicate that total morphine consumption over the 48-hour postoperative period was significantly reduced by 41% in the CLPB group compared to the SLPB group (19mg vs 32mg, $p < 0.05$). Days to first mobilization after surgery were significantly reduced in the CLPB group: 5 patients in this group mobilized in the first operative day and the remaining 11 on the second day. In the SLPB group no patients mobilized on the first day, 10 on the second day, and the remaining 6 on the third day ($p < 0.01$). No significant differences in pain, nausea, motor block, or time to meet discharge criteria were found between groups.

. Kaloul *et al.*⁵⁵ conducted a randomized trial comparing CLPB to continuous femoral nerve blocks (CFNB) in 60 patients undergoing primary TKA. Their aim was to evaluate the efficacy of CLPB and CFNBs for postoperative analgesia following TKA. Patients were randomly allocated to receive PCA with morphine (n=20), PCA plus CLPB (n=20), or PCA plus CFNB (n=20). Both continuous blocks were set to deliver an infusion of 0.2% ropivacaine at 12 mL/hour for 48 hours following surgery. All patients received intravenous PCA with one milligram of morphine infused over two minutes with a five-minute lockout period. Outcomes measured were morphine consumption, pain using a visual analogue scale, motor blockade (weakness in knee flexion against resistance), and satisfaction. CFNB and CLPB reduced morphine consumption during the 48-hour study period by 48% ($p = 0.0002$) and 50% ($p < 0.0001$) respectively compared to PCA. There was no statistical or clinical difference in morphine consumption between the CFNB and CLPB groups. Pain scores at rest were significantly reduced in the CLPB and CFNB groups compared to patients who received PCA ($p < 0.0001$). Pain scores during physiotherapy did not differ between the three study groups. Patient satisfaction with the overall pain management was high with no significant differences between the groups

(PCA 86.5 ± 10.3 ; CFNB 94.8 ± 8.2 ; CLPB 93.0 ± 7.8). However, motor blockade was achieved more frequently in the CLPB group than in the CFNB group ($p < 0.0001$). Motor blockades can be linked to patient falls inhibiting adequate postoperative rehabilitation. Lumbar plexus blocks can be used as regional anesthesia for patients undergoing TKA; however because of the potential for complications and advanced skills to perform the block, it is currently not widely used⁸.

2.6.4 Femoral Nerve Blocks

The femoral nerve block (FNB) was first described in the 1920's by Labat⁵⁶. In contrast to the lumbar plexus block, femoral blocks have a well-defined insertion site that is based on three land marks; the inguinal ligament, inguinal crease, and femoral artery⁸. FNBs are common methods for postoperative pain control after TKA that are easy to administer and are associated with low risks of complications⁵⁷. The femoral nerve alone only provides sensation to the anteromedial aspect of the knee. Therefore, the femoral nerve block can be performed in combination with a sciatic nerve block, which innervates the posterior aspect of the knee. Studies indicate that FNB's offer improved or equivalent patient pain scores, length of stay, and morphine consumption compared to more traditional techniques⁵⁷⁻⁵⁹.

In 2010, Paul *et al.*⁵⁷ performed a meta-analysis of randomized trials that compared PCA opioids alone or epidural analgesia versus patients receiving FNB (single shot or continuous) for up to 72 hours following TKA. Studies included addressed at least opioid consumption and pain scores. Additional outcomes such as opioid side effects, knee range of motion, length of stay, early ambulation, and patient satisfaction were extracted if available. Following article screening, 23 RCT's were extracted and assessed for quality. Of the selected studies included, 14 compared FNB with PCA, four compared FNB with epidural, three compared different types of FNB (single shot FNB, continuous FNB, sciatic combined with continuous or single shot FNB), and two compared FNB with both epidural and PCA. Overall 665 patients received FNB, 161 received epidural, and 190 received PCA. Regarding opioid consumption, patients receiving single shot FNB, sciatic combined with single shot FNB, and continuous FNB had significantly less morphine consumption at 24 hours (compared with PCA alone) with differences of -20, -

31, and, -15 mg respectively. There were no significant differences in pain, motor block, patient satisfaction, and length of stay between comparison groups up to 48 hours following TKA. A small number of studies in this meta-analysis reported side effects; therefore all types of FNBs were grouped together in comparison with PCA. Results showed that FNB groups had significantly less nausea (0.31 odds) compared with PCA patients.

Min Lee *et al.*⁵⁹ conducted a retrospective study comparing PCA versus continuous FNB in 1582 post-TKA patients. Intravenous PCA was not used in patients who received FNB. Outcomes included the incidence of severe pain (visual analogue scale (VAS)>6), and incidence of adverse reactions. One thousand and three patients received PCA and 579 patients received FNB. The incidence of severe pain (VAS>6) from postoperative day (POD) 1-3 was higher in the PCA patients (69.1%) compared to the FNB group (32.3%) ($p=0.003$). There was one incident of hypotension and one incident of respiratory depression in the PCA group but no documented adverse events in the FNB group.

Evidence published by Chan *et al.*⁶⁰ in 2013 suggests that whether the FNB was performed as a single injection or a continuous FNB block, pain scores and functional outcomes were superior to PCA in the postoperative period. However, whether the FNB should be performed as a single shot block or as a continuous block was up for debate. In their randomized trial 200 TKA patients were allocated to one of three regimens; single FNB ($n=69$), continuous FNB ($n=65$), or intravenous PCA ($n=66$). All patients had similar characteristics. In the FNBs the local anesthetic used was 20 mL of 0.25% bupivacaine with 1:400,000 adrenaline (2.5 mcg/mL). For the continuous FNB the catheter was connected to a pump to deliver bupivacaine 0.125% 4 mL/h, which is the standard at this study's center. PCA was initiated immediately after surgery via a pump set to deliver bolus doses of morphine 1mg with 5-minute lockout (maximum 10 mg/h). The primary outcome was significant pain on movement (VAS>4) at postoperative 24 hours. Secondary outcomes were knee pain at rest or movement, cumulative opioid consumption, side effects, and days to achieve 90-degree active knee flexion. The proportion of patients with significant knee pain on movement at 24h after TKA was significantly lower in the single injection (OR 0.36; 95% CI 0.15 to 0.86; $p=0.022$) and

continuous FNB groups (OR 0.25; 95% CI 0.11 to 0.60; $p=0.002$), compared to patients receiving PCA (OR 1). Knee pain at rest was significantly lower in the continuous FNB group at 6 hours (mean difference -1.19, 95% CI -2.18 to -0.21, $p=0.018$) and at 24h (mean difference -0.67, 95% CI -1.18 to -0.17, $p=0.010$) compared to the PCA group. Knee pain during movement was significantly lower in both the continuous (mean difference -1.15, 95% CI -1.72 to -0.58, $p<0.0001$) and single-injection (mean difference -0.58, 95% CI -1.14 to -0.01, $p=0.045$) FNB groups at 24h compared to the PCA group. The continuous FNB group reported significantly less pain on movement at 24h (mean difference -0.57; 95% CI -1.14 to -0.01; $p=0.045$), when compared to the single-injection FNB group. Prior to 24 hours there was no significant difference in pain between the single and continuous techniques. This result is most likely because of the duration of analgesia of the single-injection FNB block not lasting 24 hours. Opioid consumption for both FNB groups was significantly lower compared to the PCA group. The opioid consumption for the continuous FNB group was also significantly less compared to the single-injection FNB (mean difference at Day 1 morning: -18.5; 95% CI -25.6 to -11.4; $p<0.001$; and mean difference at Day 2 morning: -24.4; 95% CI -34.9 to -13.9; $p<0.001$).

The single-injection (SI) and continuous (C) FNB groups reached ROM of 90 degrees earlier than the PCA group (SI: 2.3 days (1.4) $p=0.014$, C: 2.4 days (1.4) $p=0.024$, PCA: 3 days (1.6)). Recorded side effects were lower in the FNB groups compared to PCA. No adverse events such as falls were recorded. Length of stay was comparable regardless of allocation. Chan *et al.*⁶⁰ concluded that both single-injection and continuous FNBs were generally more effective than PCA, with continuous FNBs providing additional clinical benefits compared to single-injection FNBs. However, placement and management of catheters can be time consuming and require additional resources in terms of skill and cost which should be considered⁵. They recognized that their study was not designed to have sufficient statistical power to detect all small differences in treatment benefits between the two FNB groups. Furthermore, patients and clinicians were not blinded to treatment allocation and intraoperative parameters (spinal/general, PCA opioids) were not standardized since they followed their center's protocols and clinician's preferences.

One major reported drawback with FNBs is quadriceps weakness leading to inpatient falls in fast track arthroplasty regimens^{10,61}. A reduction in quadriceps strength of up to 80% can be observed^{8,62}. This occurs when efferent motor nerves are interrupted predisposing a patient to falls during the early postoperative period when rehabilitation practices are important^{1,63}. Pelt *et al.*, evaluated the rate of falls in 707 primary TKA's performed at their center and found a 2.7% incidence rate⁶⁴. They reported this incidence rate as unacceptably high. Ilfeld *et al.* also reported seven falls in 171 TKA patients receiving a femoral nerve block⁹. Each fall occurred in the experimental femoral nerve block group in this clinical trial. Catheter dislodgement and nerve injury can also occur during the patients' recovery. Memtsoudis *et al.* did not find an increase in the odds for inpatient falls when peripheral nerve blocks were used in a population based analysis of 190,000 patients². Therefore a careful choice of block technique and anesthetic volume is necessary after carefully weighing the benefits and possible limitations of each technique.

2.6.5 Adductor Canal Blocks

The adductor canal block (ACB) or saphenous block is a modification of the FNB and has been gaining popularity in the anesthesia community over the last few years³³. Initially described by Lund *et al.*, the ACB block involves injection of local anesthetic into the adductor canal deep to the sartorius muscle resulting in an almost purely sensory blockade⁶⁵. This block technique is a technically easy and reliable method for blocking the saphenous nerve⁶⁶.

Figure 3: Cross-sectional MRI scan of the adductor canal.

The scan shows the position of the saphenous nerve lateral to the artery and anterior to the vein. Arrow points to the saphenous nerve. A, femoral artery; V, femoral vein; LA, local analgesic; SM, sartorius muscle; RFM, rectus femoris muscle; VMM, vastus medialis muscle; ALM, adductor longus muscle; AMM, adductor magnus muscle; GM, gracilis muscle.

Reproduced with permission from Lund *et al.* Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: Preliminary results. *Acta Anaesthesiol Scand.* 2011;55(3):14-19⁵⁹.

2.6.5.1 Adductor Canal Block vs Placebo

Jenstrup *et al.*⁶² conducted the first blinded randomized clinical trial comparing the analgesic efficacy of a continuous adductor canal block to a placebo. Overall 75 patients were randomly allocated to receive an ACB with 0.75% ropivacaine (n=37) or a placebo infusion with isotonic saline (n=38). A continuous infusion of ropivacaine or saline was administered postoperatively as per allocation. All patients received intravenous PCA.

Postoperative outcomes assessed were cumulative morphine consumption, VAS pain scores, knee ambulation assessed by timed up and go (TUG) test, and nausea. Total morphine consumption from 0 to 24 hours postoperatively was significantly reduced in the ropivacaine group compared with the saline group (40 ± 21 mg vs 56 ± 26 mg; respectively, 95% CI -27 to -5 mg; $p=0.006$). Pain scores during activity from 2 to 24 hours was significantly lower in ropivacaine group ($p=0.01$). This same result did not reach significance at rest. They concluded that administration of high-volume local anesthetic into the adductor canal is a useful option for postoperative analgesia after TKA. Patients in the ropivacaine group performed the TUG test at 24 hours postoperatively faster than patients in the placebo group (36 ± 17 s vs 50 ± 29 s, respectively $p=0.03$). There was no significant difference in this functional test at 26 hours between groups. Regarding side effects, no significant differences in nausea or vomiting were found.

By targeting the adductor canal, the largest sensory branch of the femoral nerve; the saphenous nerve, the medial femoral cutaneous nerve, and the articular branches of the obturator nerve are blocked. The nerve to the vastus medialis, a motor nerve is also blocked¹¹. As a result, the ACB leaves three out of the four components of the quadriceps muscle unblocked. Numerous studies have shown less reduction of quadriceps muscle strength, less reported falls, and improved functional outcomes in comparison to patients receiving the FNB^{11-14,62}.

Figure 4: Ultrasonography image of the adductor canal.

Mid thigh level at a distance approximately halfway between the iliac spine and the patella. SM, sartorius muscle; A, femoral artery; V, femoral vein and branch. Arrow points to the saphenous nerve.

Reproduced with permission from Lund *et al.* Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: Preliminary results. *Acta Anaesthesiol Scand.* 2011;55(3):14-19⁵⁹.

2.6.5.2 Adductor Canal Block vs Femoral Nerve Block

In 2015, Grevstad *et al.*¹¹ performed a randomized clinical trial hypothesizing that pain relief provided by the single injection ACB could improve functional quadriceps muscle strength in comparison to single injection FNB after TKA. In this single-center, randomized and blinded trial, 50 patients were randomized to receive either; 3x10 mL containers with 0.2% ropivacaine for the ACB and 3x10 mL containers with isotonic saline for the FNB (ACB group) or 3x10 mL containers with isotonic saline for the ACB and 3x10 mL containers with 0.2% ropivacaine for the FNB (FNB group). Patients with severe pain (VAS >60/100) were approached and assessed for study inclusion on post

surgical day one or two. All patients received a standardized multimodal analgesic regimen including local infiltration and slow-release opioids. The primary outcome was the difference of maximum voluntary isometric contraction (MVIC) of the quadriceps femoris muscle between groups at two hours after block performance. This result was expressed as a percentage of the baseline MVIC taken before block performance. TUG tests, ability to ambulate, pain scores at rest, activity, and during TUG test were assessed as secondary outcomes at two hours after block performance. Muscle strength was assessed with a handheld dynamometer. During the performance of TUG tests, all patients used a 4-wheel walker. Quadriceps MVIC was significantly higher in the ACB group, with a median change from baseline of 193% (95% CI, 143%-288%) vs 16% (95% CI, 3-33%) in the FNB group. At two hours after block performance all patients in the ACB group were able to perform the TUG test in comparison to 28%, (7/25) of the FNB group patients who could not. Of this seven, six were could not stand up because of muscle weakness and one because of dizziness. Patients in the ACB group performed the TUG test significantly faster (32 seconds, 95% CI 27-37s) compared to the FNB group (52 seconds, 95% CI, 41-62s), with a mean difference of 20 seconds (95% CI, 9-30s, $p=0.001$). No significant differences for pain at activity or rest were found between the groups from zero to two hours. Though this study demonstrated that ACB increased quadriceps muscle strength and functional outcomes compared to FNB, this study only looked at the immediate effects after block performance (2 hours) and did not investigate longer term (24-48 hours) functional or pain outcomes, which may be more clinically relevant.

Patterson *et al.*¹² conducted a retrospective chart review of TKA procedures performed at their center in order to determine if single injection ACB provided adequate analgesia and improved physical therapy performance in comparison in patients who received FNB. Patients in the ACB group (n=39) received single shot ACB with 15 to 30 cc of 0.5% bupivacaine. Patients in the FNB group (n=41) received a catheter bolused with 30 to 40 cc of 0.25% ropivacaine followed by a continuous postoperative infusion of 0.2% ropivacaine at 6 to 8 cc/h. In addition to the block, all patients received hydromorphone PCA as well as multimodal analgesia. Cumulative opioid consumption and pain scores (VAS) were assessed at discharge from the postanesthesia care unit (PACU), 8 ± 3 , $16 \pm$

3, and 24 ± 3 hours. Functional outcomes measured were gait distance during physiotherapy at postoperative day one. Results indicated that there were no significant differences between groups in opioid consumption or pain scores at any of the time points assessed. However, the median gait distance was significantly greater in the ACB group compared to the FNB group (median, 25ft (4-60) vs. 6ft (4-60); $p=.0009$). Therefore, Patterson *et al.* concluded that single-shot ACB provides equivalent analgesia to a continuous FNB within the first 24 hours after TKA and improves gait distance during physiotherapy. Since every participant in this study received local infiltration it is not clear if the analgesic benefits were a result of the ACB or the local infiltration. Furthermore, all patients received postoperative hydromorphone analgesia, which could have further lowered pain scores. Adverse events and side effects were not reported and since data was collected retrospectively and without randomization, the study could have been biased.

Kim *et al.*¹³ conducted a blinded randomized trial comparing ACB to FNB in patients undergoing TKA. They hypothesized that ACB would cause less quadriceps motor weakness than FNB and provide non-inferior analgesia determined by pain scores and opioid use. Overall 94 patients were randomly allocated to receive FNB ($n=47$) or ACB ($n=47$). Patients in the ACB group received ultrasound-guided single injection ACB with 15 cc of 0.5% of bupivacaine with 5 ug/mL epinephrine. Study patients in the FNB group received ultrasound-guided single injection FNB with 30 cc of 0.25% of bupivacaine with 5 ug/mL epinephrine. All patients received a standardized epidural PCA regimen, which was discontinued on postoperative day two. The primary outcomes measured were quadriceps muscle strength (via dynamometer) and pain scores (NRS) at baseline, six to 8, 24, and 48 hours postanesthesia. Opioid consumption was measured from surgery to postoperative day two. Secondary outcomes included side effects, length of stay, and patient satisfaction. A joint hypothesis test was performed on all three primary outcomes previously mentioned at 6 and 8 hours postanesthesia administration. Results indicated that ACB was found to be non-inferior to FNB in motor score readings (mean difference 5.2kgf; 95% confidence limit (3.1, 7.2); delta -3, $p<0.0001$). For pain scores at rest and opioid consumption non-inferiority was also found. Next, a superiority test was conducted and found only the muscle strength readings for the ACB to be superior to the

FNB readings (difference ACB-FNB kgf (98.3% CI), 5.2 (2.7-7.7); $p < 0.0001$). Muscle strength readings were further compared and interestingly at 24 and 48 hours, the ACB and FNB groups were not statistically different ($p < 0.9999$). For pain and opioid consumption at 24 and 48 hours, the ACB group was found to be no worse than the FNB group. No significant differences were found in secondary outcomes such as nausea, length of stay, and patient satisfaction. However, this study was underpowered to detect differences in nausea. In this study muscle strength was found to be reduced compared to baseline. They found that this could be because of nerve blockage to the vastus medialis, pain limiting painful extension, and the effects of surgery and tourniquet use on quadriceps strength. Successful pain relief in this study could have also been attributed to the postoperative use of an epidural PCA.

Though numerous studies suggest that ACBs spare motor function to a higher degree than FNBs, practitioners still question the analgesic equivalence of these two approaches. The issue in this comparison is that pain perception is highly dependent on the individual causing inter-patient variability⁶⁷.

Memtsoudis *et al.*¹ conducted a novel clinical trial to address this issue by randomizing 60 patients undergoing bilateral TKA to receive ultrasound-guided FNB on one leg and ACB on the other. The primary outcome assessed was postoperative pain in either extremity at six to eight, 24, and 48 hours postoperatively. Secondary outcomes included motor strength and patient satisfaction. Patients, surgeons, physical therapists, and the research assistant performing follow-ups were blinded to the allocations. ACBs were performed by injecting 15 mL of 0.25% bupivacaine and FNBs with 30 mL of 0.25% bupivacaine. All patients received an epidural catheter to assist in postoperative pain control. Group one ($n=30$) had a left leg saphenous block and a right leg femoral block. Group two ($n=29$) had a right leg saphenous block and a left leg femoral block. Average pain levels at rest and with exercise were lowest at six to eight hours postoperatively and increased thereafter ($p < 0.001$), but no significant differences were seen between extremities at any time point ($p=0.4154$). In a direct extremity comparison, 25.4% (15/60) of patients reported that the leg which received FNB was more painful, 50.9% (30/60) expressed that the side receiving the ACB had more pain and 23.7% (14/60) reported

both being equally as painful ($p=0.0168$). No significant differences in muscle strength were found between extremities at any time point or as an average in the postoperative period ($p=0.7548$). Patient satisfaction was also similar for both nerve blocks. Since all patients received epidural analgesia this can interfere with the independent impact of the nerve block outcome but each block should have been equally affected. Furthermore, bilateral TKAs could also be associated with more profound physiological changes and should be interpreted differently than unilateral TKAs¹. They concluded that the use of ACBs vs. FNBs in knee arthroplasty patients yielded clinically similar results in pain scores, motor strength, and patient satisfaction.

2.6.5.3 Continuous Adductor Canal Block vs. Continuous Femoral Nerve Block

A randomized trial conducted by Shah *et al.*¹⁴ assessed 98 patients comparing continuous ACB ($n=48$) to continuous FNB ($n=50$) after total knee arthroplasty. They aimed to investigate the efficacy of these two approaches with respect to: ambulation ability, pain control, opioid consumption, treatment related side effects, and length of stay. In both groups, the patients were given an initial dose of 30 mL of 0.75% ropivacaine, followed by repeated boluses of 0.25% ropivacaine every four hours until the second day after surgery. Patients also received intravenous PCA. Patients were assessed for pain at four, eight, 12, and 24 hours postoperatively using a VAS scale with 0= no pain and 100= worst imaginable pain. TUG tests and ten meter walk tests were performed at 24 hours post block performance to assess ambulation ability. Tug test results showed significantly better results in the ACB group as compared to the FNB group (95% CI -147 to -108.5; $p<0.001$). In the 10-m walk test assessments, the ACB group again performed significantly better than the FNB group (95% CI -236.33 to -177.06; $p<0.0001$). Patients in the ACB had a significantly shorter length of stay than the FNB group (3.08 vs 3.92; p value <0.001). Postoperative pain scores were lower in the ACB group than in the CFNB group at 4, 8, 12, and 24 hours postoperatively but without any significant intergroup differences (p value > 0.001). Finally, one patient in each of both groups had nausea and a single episode vomiting. In the study population, 71 out of 98 were females and both groups received intravenous PCA combined with oral analgesics which could influence

pain perception¹⁴. Blocks were also administered to patients immediate postoperatively. Shah *et al.* concluded that though continuous ACBs showed no significant difference from continuous FNBs in analgesic effect, ACB provided better ambulation ability and faster recovery post TKA.

Overall, in the early postoperative period (24 hours post-op) ACBs seem to offer an improved retention in muscle quadriceps muscle strength in comparison to FNBs leading to an improved performance in rehabilitation activities. Though ACBs have this advantage, studies indicate FNBs and ACBs are equivalent in outcomes such as pain, opioid consumption, and nausea in the early postoperative period^{11–14,20,62}. Therefore ACBs can be a reasonable alternative and provide adequate analgesia and significant spared motor strength in comparison with the FNB.

2.6.6 Periarticular Injections

Periarticular injections (PAI) or local infiltration is an analgesic technique which involves the injection of analgesic drugs into injured tissue such as the synovium, joint capsule, and subcutaneous tissues during TKA^{68,69}. It was designed to specifically avoid sedation, facilitate rapid physiological recovery, and to enable early mobilization and discharge by not compromising muscle tone^{5,70,71}. These injections often use medications to target opioid receptors, nociceptors, and local inflammatory mediators³⁹. First described by Kerr and Kohan, local infiltrations contain a mixture of ropivacaine (2mg/mL), ketorolac (30mg), and adrenaline (10ug/mL) in volumes of 150-170mL for TKA^{5,71}. Injections are usually administered in three stages during a TKA. The first injection is done after bone surfaces have been prepared before components are inserted to ensure access to the posterior joint capsule. Approximately 30-35 mL, is injected to the tissues around the posterior joint capsule, using a systematic sequence from one side to the other to ensure uniform delivery⁷¹. The second injection (35-50 mL) is done after component insertion but before wound closure and tourniquet release. This injection is into the deep tissues around the medial and lateral collateral ligaments and wound edges. The third injection (25-50 mL) is made into the subcutaneous tissue, carefully avoiding subdermal injection. Multiple injections are made in a systematic sequence. Each time the needle is inserted perpendicular to the wound edge to a depth of about 25mm, an injection is done as the

needle is withdrawn⁷¹. An intra-articular catheter for continuous infusions may be inserted preferably near the posterior aspect of the joint. Lastly, a compression bandage is applied to reduce degradation and slow the diffusion of local anaesthetic into the bloodstream^{42,72}.

A meta-analysis conducted by Xu *et al.* (2014)⁶⁹ assessed the effectiveness and safety of single injection PIA in comparison to patients who received a placebo or no intervention after TKA. Studies included were RCTs that reported one or more of the following outcome measures: VAS, postoperative morphine consumption, length of stay, early functional recovery, and side effects. Following study screening and selection, 18 RCTs were extracted and included in their meta-analysis. Heterogeneity across studies was tested using the I^2 statistic. If a moderate to high degree of heterogeneity existed, they estimated the influence of each individual study on the summary result. This post-hoc test consisted of repeating the random-effects meta-analysis after omitting each study one at a time. A total of 1858 study patients were involved in this analysis. Of the 18 studies analyzed, 16 reported VAS pain values in study patients. Analysis of these 16 RCTs indicated that patients receiving single injection PAI had significantly lower pain values at two, four, six, 12, 24, and 48 hours postoperative compared to control patients receiving saline injections or nothing ($p < 0.05$). There was some heterogeneity amongst these sixteen studies and so they omitted one study at a time and calculated the pooled weight mean differences for the remaining studies. This post hoc analysis showed no changes in the direction of effect for pain when any one study was excluded.

Only eight RCTs from the extracted studies reported postoperative morphine consumption. Analysis of these eight RCTs indicated that single-dose PAI was associated with decreased postoperative morphine consumption (WMD -5.21, 95% CI -9.89 to -0.52; $p = 0.03$; heterogeneity $p < 0.01$, $I^2 = 79.1\%$). They decided to repeat the random-effects meta-analysis after omitting one out of the eight studies at a time since there was significant heterogeneity. When one study was excluded during this post-hoc exploration, the direction of effect changed indicating no significant difference between groups in postoperative morphine consumption. This was a separate result and the authors did not indicate which was correct. The time to short leg raise (4 studies) was significantly

shorter in the PAI group than the control groups (WMD, -2.75 days; 95% CI, -3.61 to -1.90; $p < 0.01$; heterogeneity $p < 0.01$, $I^2 = 85.4\%$). After the same post-hoc single exclusion of studies because of heterogeneity, there were no changes in these results. No significant differences were found between PAI and control groups regarding postoperative nausea and vomiting, pruritus, and DVT. This meta-analysis demonstrated considerable heterogeneity across the trials, which could have resulted from non-standardized PAI (medication ingredients, dosages). A major limitation in this meta-analysis was the post-hoc exclusion of studies to explore if there was a change in the direction of effect. If one study was excluded and the direction of effect changed they would not report which was the correct result. Furthermore, different patients might have had varying responses to analgesia because of the type of anesthetic used during surgery and postoperative multimodal regimens. Overall, this study concluded that that single injection PAI is significantly better than placebos at relieving pain, and might accelerate early functional recovery of the knee while not increasing the prevalence of side effects during postoperative observations.

2.6.6.1 Periarticular Infiltration vs. Placebo or Traditional Analgesia

Compared to more traditional analgesic methods (PCA, intrathecal narcotics, or epidurals) in placebo controlled studies, patients receiving single injection or continuous PAI had equivalent or lower pain scores in the postoperative period^{39,47,73,74}, lower consumption of morphine^{4,39,47,73,74}, better functional outcomes^{39,47,75}, and less complications^{4,43,47}. Evidence has led to peripheral nerve blocks and PAI largely replacing epidural analgesia for postoperative pain management following TKA⁷⁶.

In 2014, Niemelainen *et al.*⁷³ randomized 56 patients undergoing TKA to receive either single injection PAI or placebo in this study. In the PAI group, a cocktail mixture of levobupivacaine (150 mg), ketorolac (30 mg), and adrenaline (0.5 mg) for a total volume of 150 mL was infiltrated. In the placebo group saline was infiltrated for a total volume of 150 mL. Only an independent nurse who prepared the study solutions was unblinded to group allocations. In addition, all patients were given PCA with oxycodone to ensure pain relief. The primary outcome assessed was oxycodone consumption over 48 hours postoperatively. Secondary outcomes included pain and range of motion (ROM). Overall

27 patients in the PAI group and 29 patients in the placebo group completed the study. Results showed that cumulative consumption of oxycodone was smaller in the PAI group to that in the placebo group at all measured time points up to 48 hours. However, in comparison of the different time intervals, the PAI group used significantly less oxycodone than the placebo group during the first six hours (mean: 14 (2-34)mg vs 30 (6-57)mg ; $p<0.001$). The rest of the time points did not reach statistical significance. Both groups achieved a median level of pain (VAS <3) until 48 hours. The difference in mean ROM at 6 hours between the PAI group and the placebo group was -26 degrees (95% CI: -39 to -12). Niemelainen *et al.* showed that a single intraoperative PAI containing levobupivacaine, ketorolac, and adrenaline reduced the total consumption of oxycodone during the first 48 hours postoperatively. The beneficial effect of single injection PAI was most pronounced during the first six hours as seen by the increased ROM and equal pain scores were recorded between both groups. This study however did not measure length of stay between groups. Levobupivacaine was also used in the PAI cocktail, which according to Niemelainen *et al.* has a longer effect time than ropivacaine. In theory this should prolong postoperative analgesia.

Lamplot *et al.*³⁹ performed a randomized controlled trial of patients undergoing a primary TKA. Patients were either randomized to receive either intraoperative single injection PAI and inpatient multimodal analgesics (PAI group) or to hydromorphone PCA (PCA group). During surgery patients in the PAI group received single injection PAI consisting of 30 cc 0.5% bupivacaine, 10 mg MSO_4 , and 15mg ketorolac. Postoperative multimodal pain management was given to these patients. During surgery, patients in the PCA group received no injections. For postoperative pain management these patients received hydromorphone PCA. Recorded measures in this study consisted of; VAS pain scores, narcotic consumption, medication-related adverse effects, length of stay, satisfaction, and time to physical therapy milestones. Overall, 36 patients of an eligible 55 were randomized to the two groups; PAI (n=19) and PCA (n=17). Daily narcotic consumption was significantly lower in the PAI group compared to the PCA group, with $17.0\text{mg}\pm 3.85$ versus 40.5 ± 12.7 at the end of postoperative day 0, 30.8 ± 5.5 versus 71.8 ± 15.5 during day 1 and 18.4 ± 5.5 versus 38.1 ± 11.5 during day 2, respectively ($p<0.007$). During the hospital stay, fewer patients in the PAI group (3/19) experienced narcotic-related adverse

effects in comparison to the PCA group (16/17), including nausea, vomiting, constipation, insomnia, pruritus, and mood irritability ($p < 0.01$). The VAS pain scores for postoperative pain at rest ($p < 0.0004$) and activity ($p < 0.001$) were significantly lower in the PAI group during each day of hospitalization. The ability to walk assisted > 50 ft was a physical therapy milestone recorded in this study. For this milestone 7/17 patients in the PAI group were able to perform this compared to 0/16 in the PCA group. Furthermore, on day one after surgery 19/19 patients in the PAI group were able to achieve this milestone compared to 6/17 in the PCA group. There was a trend toward decreased length of stay in the PAI group, with a mean of 1.9 days compared to 2.3 days in the PCA group. Patients in the PCA group also reported significantly higher satisfaction scores compared to the PCA group during each postoperative day ($p < 0.05$). Lamplot *et al.* found the patients receiving intraoperative single injection PAI had significantly improved patient pain control, medication-related adverse effects, functional outcomes, and patient satisfaction. Though this study seemed to have a small sample size, it was unanimously decided at their center that patients in the PAI group were having markedly better outcomes. Therefore, they stopped short of reaching their goal of enrolling 30 subjects in each group.

2.6.6.2 Single vs. Continuous Periarticular Injections

In subsequent years, different cocktail mixtures of opioids and steroids have been administered to patients with no agreed upon gold standard mixture^{4,33}. This discrepancy is because of considerable variability in factors affecting drug therapy outcomes in available clinical studies. PAIs can either be performed as single or intermittent injections, continuous infusions with the use of an intra-articular catheter, or a combination of methods, and with varying compositions of the drug solution⁷⁷. Controversy exists over which model of delivery is most effective. Continuous infusions often involve catheter placement by the surgeon at the end of surgery under aseptic conditions while requiring the use of bacterial filters and closed infusion systems. Catheters are difficult to manage with the potential for problems while troubleshooting them⁵. However, the placement of a catheter in continuous infusions allows for prolonged site-specific regional analgesia which may be beneficial¹⁶. By contrast, single injection

PAI is common in clinical practice and reported to be inexpensive and relatively easy to perform and have fewer side effects⁶⁹.

Zhang *et al.*¹⁶ conducted a randomized blinded and placebo-controlled trial with the aim of evaluating whether continuous PAI provided prolonged and superior analgesia and reduced morphine consumption in comparison to single PAI. A total of 80 study patients completed the study and were randomly allocated into three groups; continuous PAI (n=27), single injection PAI (n=27), or a control group (n=26). Patients in the continuous PAI group received ropivacaine (190mL, containing 2mg/mL) via continuous infusion (flow rate 4 mL/h for 48 hours) plus 2 mL ketorolac (30mg/mL) at 1.25 mg/h. Patients in the single injection PAI and control group received a continuous infusion of saline through the catheter. Study patients in the continuous and single PAI groups at the end of surgery received periarticular infiltration of a mixture of ropivacaine 150mL (2mg/mL), ketorolac 1mL (30mg/mL), and adrenaline 0.5mL (1mg/mL). For rescue analgesia, all patients received intravenous PCA consisting of morphine for the first 48 hours post surgery. Knee pain was evaluated after surgery at two, four, eight, 12, 16, 20, 24, 30, 36, and 48 hours and the amount of morphine delivered via the PCA pump was also recorded. Patient satisfaction and complications during the follow-up period of three months were recorded. The resulting VAS pain scores at rest and during activity were significantly higher in the control group than in the continuous PAI group ($p<0.05$) through the 48 hour postoperative period. In contrast, no significant differences in the VAS pain scores at rest between the control group and single injection PAI group at 20-48 hours postoperatively were found. VAS pain scores in the continuous PAI group were significantly lower than the single injection PAI group ($p<0.05$) from eight to 48 hours postoperatively at rest and from 16 to 48 hours postoperatively during activity ($p<0.05$). Morphine consumption was only significantly higher in the control group compared to the single injection PAI group during 0-12 hours and 12-24 hours postoperatively ($p<0.05$). In comparison to the continuous PAI group morphine consumption was significantly higher in the control group throughout the entire 48-hour postoperative period ($p<0.05$). In addition, morphine consumption from 24-48 hours was significantly reduced in the continuous PAI group compared to the single injection group ($p<0.05$). The incidence of nausea and vomiting was higher in the control group than the two PAI

groups however this difference was not statistically significant. There were no significant differences in satisfaction between the two PAI groups, and no complications, infections, or reparations occurred during the follow-up period. This studies sample size was too small to evaluate the risks of infection in the different techniques. Zhang *et al.*¹⁶ concluded that continuous PAI is associated with prolonged, superior analgesia and reduces morphine consumption compared to single injection PAI over the 48-hour postoperative period. They also recorded a higher incidence of patient satisfaction in the continuous PAI group but still state that it is important to consider the risk of infection with different PAI techniques.

2.6.6.3 Periarticular Infiltration vs. Femoral Nerve Blocks

Recently, Wang *et al.*⁷⁸ conducted a systematic review and meta-analysis comparing PAIs and FNBs for postoperative pain management in TKAs. Randomized control trials were identified that compared patients receiving PAI or FNB whether they were single or continuous techniques. Outcome assessed were; pain scores, opioid consumption, functional outcomes, length of stay, and side effects. Following study exclusions, ten RCTs were identified with a total of 744 TKAs performed in 728 patients. In this analysis, four studies used PAI with a catheter and six as a single injection. Six studies performed a continuous FNB while the other three used a single injection FNB. One study looked at bilateral TKAs. Results of nine RCTs that were analyzed indicated that there were no significant differences in VAS pain scores at rest between the PAI and FNB group at 24 hours postoperative (95% CI -0.62 to 0.37; $p=0.62$). A subgroup analysis was performed on the different analgesic techniques (single or continuous). A meta-analysis of two of their studies showed that single injection FNBs had lower VAS at rest pain scores at 12 hours than single injection PAI (95% CI 0.18 to 0.79, $p=0.002$). However, the results of four combined studies indicated single injection PAI significantly reduced VAS pain at rest at 24 hours compared to single injection FNBs (95% CI -1.44 to -0.09; $p=0.03$). No significant differences were found between the two groups regarding pain at activity. A total of seven studies in this meta-analysis were analyzed for total opioid consumption and no significant differences were found between PAI and FNB at 24 hours ($p=0.64$) or at 48 hours ($p=0.99$) postoperatively. Three studies indicated that

the number of patients able to do active straight leg raises at 24 hours following TKA was significantly larger in the PAI group (OR=11.09; 95% CI=6.24 to 19.69; $p<0.001$). Meta-analysis results from six studies of 390 TKAs showed that patients receiving PAI had significantly shorter length of hospital stay than FNB patients (95% CI -0.52 to -0.02; $p=0.04$). No significant differences were found in complications such as nausea, vomiting, and wound complications between the two groups. It appears that continuous PAIs are an efficient and safe alternative to continuous FNBs for postoperative pain management following a TKA. However, in this meta-analysis there was a lack of uniform technique of PAI and FNB. Furthermore, single injection FNBs may provide better pain relief in the early postoperative period compared to single injection PAIs.

2.6.6.4 Single Injection Periarticular Injections vs. Single Injection Femoral Nerve Blocks

In a large randomized blinded trial by Uesugi *et al.*¹⁵, 210 patients undergoing a TKA were randomized to receive either single injection PAI (PAI group) or a single injection FNB with a combined sciatic block (FNB group). Patients in the PAI group ($n=100$) received intraoperative periarticular injections containing 20mL of 0.75% ropivacaine and 0.3mg of adrenaline. Patients in the FNB group ($n=100$) received a total 30mL of 0.75% ropivacaine for peripheral nerve blockade as per the standard of their center. If patients were in postoperative pain they were given diclofenac sodium suppositories (25mg) as required. Primary outcomes measured were postoperative pain, total rescue medication consumption, motor paralysis, satisfaction, and complications. Results indicated that from three to six hours following surgery pain scores were significantly lower in the FNB group ($p<0.01$, $p<0.01$). No significant differences were found between the groups from 12 to 18 hours postoperatively. Pain scores were significantly lower in the PAI group at 24 hours ($p<0.01$) and 30 hours ($p<0.01$). From 30 hours on there were no significant differences between the two patient groups. During the zero to 12 hour postoperative period, patients in the FNB group used significantly fewer rescue pain medications than patients in the PAI group (6h $p<0.01$, 12h $p<0.01$). However from 12-24 hours after TKA, the PAI group used significantly fewer rescue pain medications than patients who received FNB (12h $p=0.03$, 18h $p<0.01$). When the total number of rescue

analgesia was analyzed throughout the entire 48-hour period after surgery there were no significant differences between groups. The duration of analgesia was shorter in patients who received PAI ($p<0.01$) but motor paralysis of the ankle was significantly longer in the FNB group ($p<0.01$). Investigators found no significant differences between the groups in complications and patient satisfaction. In this study, patients in the FNB group received their FNBs in combination with sciatic nerve block injections, which may explain why pain scores favoured the FNB group in the early postoperative period up to six hours. Furthermore, the number of functional measures reported in the early postoperative period was limited and since this is the timeframe where PAI is expected to be most effective, the study may have been unable to detect important differences. Uesugi *et al.*¹⁵ concluded that single injection PAI provided a similar analgesic effect to the combined use of sciatic and FNBs and since both techniques were administered as single injections, continuous managements was not required. Furthermore, motor paralysis in the PAI group was shorter which can lead to improved rehabilitation.

In 2013, Ashraf *et al.*¹⁰ conducted a similar randomized trial comparing single injection PAI to single injection FNB. Overall 42 patients were randomized, 22 patients in the FNB group (30mL 0.2% ropivacaine) and 20 patients in the PAI group (150mL 0.2% ropivacaine/1 mL 1:1000 adrenaline/30 mg ketolorac). The primary outcome measure was postoperative pain assessed by VAS at four hours postoperatively. Secondary outcomes assessed were pain at two hours, pain at rest and after physiotherapy on postoperative day one (POD1), total opiate use, length of stay, and functional outcomes. All patients received PCA to assist in pain management. Results showed that at four hours postoperatively patients in the PIA group (2.1 ± 2.6) had significantly lower pain scores than patients in the FNB group (6.8 ± 3.2). This difference of 4.7 points was statistically significant ($p<0.01$, 95% CI 2.8 to 7.5). There were no significant differences in pain scores between the two groups at two hours post TKA. Pain at rest and after physiotherapy on POD1 showed no significant differences between the two study groups. However, patients in the PAI group consumed significantly less opiate analgesia during their stay at the hospital compared to patients in the FNB group ($p=0.01$). There were no significant differences between the two groups in functional outcomes and length of stay. This study demonstrated that single injection PAIs provide better pain relief in the early

postoperative period and overall lower use of opiate analgesia in comparison to single injection FNBs. However, this study had a small sample size, surgeons were unblinded, and less ropivacaine was used in the FNB group (30mL) as compared to the PAI group (150mL). Furthermore, this study was underpowered in their assessments of functional outcomes.

PAIs can be seen as advantageous to FNBs since special skills are not required to administer the injection into the periarticular tissues. As Uesegi *et al.* described, the analgesic effect is simply achieved by injecting the solution around the joint while being careful to ensure that it does not enter a blood vessel¹⁵.

2.6.6.5 Single Injection Periarticular Injections vs. Continuous Femoral Nerve Blocks

Various studies indicate that single injection PAIs offer equivalent analgesia to continuous FNBs in the 48 hour postoperative period and similar side effects, while providing better functional outcomes because of its absence of motor block^{41,79–81}. In a randomized trial conducted by Chaumeron *et al.*³, 60 TKA patients were randomized to receive a single injection PAI (n=30) or continuous FNB (n=30). One patient in the PAI group was excluded prior to surgery because of the inability to receive a spinal. More patients in the FNB group experienced motor block, were unable to perform a straight leg raises, and one patient experienced a fall requiring corrective surgery³. During this study PCA was available for additional analgesia during the first 48 hours. In the PAI group, the infiltration mixture consisted of 30mg ketorolac, 0.5mL adrenaline (1/1000), and 275 mg ropivacaine for a total mixture of 108mL and a simulated FNB to ensure blinding. Patients randomized to the FNB group received an injection of 20mL ropivacaine and a 0.25% continuous infusion at 8-10mL/hour through a femoral catheter. The primary outcome was morphine consumption with PCA during the first 48 hours after surgery. Secondary measures assessed were daily pain scores (at rest and activity), length of stay, motor blockage, and functional outcomes. Significantly higher morphine consumption was observed from zero to eight hours after surgery in patients who received the FNB (p=0.04). However, there was no significant difference between the two groups in morphine consumption over the rest of the 48-hour postoperative period. No significant

differences in postoperative pain were found between the two groups, however more patients who received the continuous FNB group experienced motor block (11/30) compared to patients in the PAI group (0/30) ($p < 0.001$). On POD1, more patients in the FNB group (6/27) compared to zero in the PAI group were unable to stand ($p = 0.018$). The proportion of patients unable to perform a straight leg raise on postoperative days one to three was greater in the FNB group ($p < 0.001-0.002$). Furthermore, patients in the PAI group walked longer distances on POD zero, two, and three ($p = 0.004-0.031$). A similar number of complications were reported in each group. This study concluded that a single injection PAI showed pain control similar to a continuous FNB while avoiding motor block with its functional impact. This could be beneficial during the rehabilitation period. Study patients in this trial did receive PCA over 48 hours, which could have influenced pain score results. Furthermore, slightly more females were in the FNB group. The sample size in this study was not large enough to accurately assess complication rates. It also appears that not all patients completed postoperative functional outcomes but this was not addressed in the discussion of the paper.

A small but potentially important increase in the rates of serious infection in patients receiving continuous local infiltration through catheterization, was found in a meta-analysis conducted by Marques *et al.* within TKA patients^{73,80}. Therefore, though FNBs may negatively affect quadriceps function, are time-consuming, and are associated with complications, it still remains the most commonly used peripheral nerve block method. However, the potential and functional benefits of PAI versus FNB remain controversial and are still being investigated³.

2.7 Summary

The TKA is a surgical procedure that results in the best outcomes for osteoarthritis of the knee. Postoperative TKA pain is severe and can negatively affect patient satisfaction, functional outcomes, and the duration of hospitalization. Therefore, aggressive and effective pain control during the early postoperative period is essential. Traditional analgesic techniques such as PCA, epidurals, LPBs, and FNBs have been performed to improve postoperative recovery. Though PCA using intravenous opioids and continuous epidurals provide effective analgesia, they can be associated with side effects such as

nausea, pruritus, vomiting, dizziness, urinary retention, sedation, poor muscle control, and constipation. LPBs require advanced skills to perform and FNBs can negatively affect quadriceps function increasing risks for inpatient falls.

Recently, studies that investigated adductor canal blocks have shown them to be effective nerve blocks, providing adequate analgesia and sparing quadriceps strength in the early postoperative period. More specifically, single injection adductor canal blocks do not carry the risks associated with catheter use. Furthermore, using single injection periarticular infiltrations as a regional block technique is simple to administer, spares quadriceps strength, and provides adequate analgesia. FNBs are the most commonly used blocks and studies consistently compare them to adductor canal blocks or periarticular infiltration techniques. However, currently no clinical trial has directly compared adductor canal blocks to periarticular infiltrations. Therefore, a randomized clinical trial is needed to directly compare functional outcomes, pain, length of stay, and narcotic consumption directly following a TKA between these two interventions.

Chapter 3

3 Objectives

Our primary objective was to compare the duration of analgesia following total knee arthroplasty in patients who received periarticular infiltration to those who received a motor sparing knee block. Our secondary objectives were to compare the two analgesic techniques for the following outcomes: function using the Western Ontario McMaster Osteoarthritis Index, Timed Up and Go, eligibility to perform physiotherapy, quadriceps muscle power, length of hospital stay, and time to and length of first mobilization; pain using a Numerical Rating Scale, time to rescue analgesia, total opioid consumption, and site of predominant pain; quality of life using the Short Form 12; satisfaction, and side effects.

We hypothesized that the motor sparing knee block would provide no difference in analgesia duration compared to patients who receive periarticular local infiltration analgesia following total knee arthroplasty. We also hypothesized that function, pain, quality of life, satisfaction, side effects, and length of stay would be similar between the two groups.

Chapter 4

4 Materials and Methods

4.1 Study Design

This was a single-centre randomized clinical trial that took place in London, Ontario at the London Health Sciences Centre (LHSC), University Hospital between July 2014 and June 2015. The study involved patients undergoing a primary total knee arthroplasty (TKA). The study was approved by the University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (Appendix A).

4.2 Eligibility Requirements

Eligible patients were those between the ages of 18 and 85 years scheduled to undergo elective primary TKA at the LHSC University Hospital, with good contralateral leg strength and an ASA class between one and three. Patients were ineligible if they were being hospitalized for reasons other than the planned surgery; had a psychiatric illness or cognitive impairment that precluded them from giving informed consent or rendered the patient unable to complete questionnaires; narcotic dependency; extraneous sources of chronic pain; an allergy to any of the study drugs; any contraindications to blocks or multimodal analgesia; patients who were wheelchair bound; patients with a language barrier; or those unwilling to provide informed consent.

4.3 Subject Recruitment

Patients were recruited from the practices of four orthopaedic surgeons who specialize in joint arthroplasty at the LHSC in London, Ontario.

4.4 Randomization

Eligible patients were randomized via web-based software (www.empowerhealthresearch.ca) prior to their TKA by one of two graduate students not involved in the assessment of outcomes. The randomization contained mixed block sizes of two and four and a one-to-one allocation ratio into either (1) motor sparing block

(experimental) or (2) periarticular infiltration (control). Randomization was stratified by gender and by surgeon.

4.5 Interventions

4.5.1 Motor Sparing Block (experimental group)

A pre-procedural scan performed by the anesthesiologist identified suitable locations to perform the three major block injections. MSB blocks were performed in the PACU block room using standard preoperative monitors including electrocardiogram (ECG), pulse oximeter, and noninvasive blood pressure monitoring. Following sterile precautions, the skin was anesthetized with 1% lidocaine. Patients were sedated during the administration of the block with midazolam and fentanyl at the discretion of the anesthesiologist performing the block. The MSB was performed under ultrasound guidance in the supine position with the leg in external rotation. The MSB included 0.5% ropivacaine, 2.5 ug/mL of epinephrine, 10 mg of morphine, and 30 mg of ketorolac giving a total anesthetic volume of 60 mL. The motor sparing block consisted of three stages; the posterior peri capsular injection, adductor canal blockage, and lateral femoral cutaneous injection to provide full knee analgesia.

4.5.1.1 Posterior Peri Capsular Injection

An eight-centimeter block needle was inserted near the medial femoral epicondyle (10 centimeters from the joint line) under ultrasound guidance. At this site, 20 mL of the study drug was injected between the bone and popliteal artery. This constituted the posterior peri capsular injection.

4.5.1.2 Adductor Canal Blockage

The femoral artery was traced from the groin region under the sartorius muscle until the superior geniculate artery was seen to take off from the femoral artery. The probe was rotated 90⁰ and moved superior tracing the sartorius and the femoral artery eight to ten centimeters proximally in the long axis. This was marked as the second needle entry point for injection of the intermediate cutaneous nerve. The intermediate cutaneous nerve of thigh usually travels as a dual nerve between the sartorius and rectus femoris above the

fascia lata, which was identified at this point. An eight-centimeter block needle was inserted out of plane with the artery in short axis under the sartorius at the pre-marked site. Between the sartorius and rectus femoris muscles, 5 mL of study drug was injected to target the intermediate cutaneous nerve of the thigh. For this injection the needle was inserted from a lateral to medial direction with the needle tip lying superficial to the fascia lata. The needle was redirected to enter the fascia of the sartorius to deliver an additional 5 mL of the study drug. The needle was then advanced until the needle tip was seen to lie adjacent to the femoral artery under the sartorius within the adductor canal. Following this, 20 mL of the study drug was injected, while watching for confirmation of the study drug deposition around the femoral artery. A block catheter was inserted three centimeters beyond the tip of the needle under ultrasound guidance. Colour Doppler was used to confirm that the catheter tip was in the proper location (close to the femoral artery). Therefore, a total of 30 mL of the study drug solution was used in the adductor canal blockage.

4.5.1.3 Lateral Femoral Cutaneous Injection

Following the adductor canal block, the sartorius was traced to its origin at the anterior superior iliac spine. The lateral cutaneous nerve of thigh was blocked in the lacuna musculorum between the origin of sartorius and tensor fascia lata muscle with the final 10 mL of the study drug. Therefore, a total study drug volume of 60 mL was used. Sham periarticular injections of isotonic saline (100 mL) were administered intraoperatively to blind both the surgeon and anesthesiologist.

4.5.2 Periarticular Infiltration (control group)

Patients randomized to the control group had isotonic saline (60 mL) injected during the preoperative performance of the MSBs to ensure blinding. These patients received periarticular infiltration of local anesthetics. This 100 mL mixture consisted of 0.3% ropivacaine, 2.5 µg/mL of epinephrine, 10 mg of morphine, and 30 mg of ketorolac administered by the surgeon at the end of surgery as per usual practice at LHSC. The first 20 mL aliquot of the mixture was injected into the posterior aspect of the capsule and the medial and lateral collateral ligaments just prior to implantation of the component. Care

was taken around the area of the common peroneal nerve during this process. The quadriceps mechanism and retinacular tissues were then infiltrated with an additional 20 mL of the study drug. Finally, the remaining 60 mL was used to infiltrate the fat and subcuticular tissues.

4.5.3 Standardization of Potential Co-interventions

All study patients received preoperative multimodal analgesia of Tylenol (975mg), Naproxen (500mg), Gabapentin (600mg), and Granisetron (2mg). All TKA's were posterior stabilized using one of the following implants; Attune, Triathlon, or Genesis II. Patellar resurfacing was performed at the discretion of the surgeon. Surgery was performed in a bloodless field using a femoral tourniquet. At the end of surgery, the surgeon applied compression bandages covering the entire knee. All patients received spinal anesthesia with 15 mg of hyperbaric bupivacaine with titrated sedation intraoperatively at the discretion of the anaesthesiologist.

Following surgery the inpatient drug regimen was standardized. Infusion of local anesthetics into the catheter was initiated once patients reported pain of 6/10 or higher on the VAS pain scale. This started with a 10 mL bolus of 0.2% ropivacaine and subsequent infusion at a basal rate of 6 mL/hour with patient controlled boluses (PCRA) of 4 mL every 30 minutes as need. This ensured prolonged analgesia once the single injection MSB or PAI interventions stopped providing adequate pain relief. Secondary rescue analgesia consisted of five to ten milligrams of oxycodone as needed if pain was still poorly controlled. All patients were seen twice a day by ward physiotherapists as per standard protocol.

4.6 Blinding

An independent anesthesiologist (SG) who was not involved in administering the study interventions or conducting outcomes assessments prepared and concealed the study drugs from the outcome assessors and the anesthesiologists responsible for performing the motor sparing blocks, and the orthopaedic surgeons performing the infiltrations. An independent nurse not involved in the study measured the block characteristics. Therefore

the patient, surgeon, block anesthesiologist, and outcome assessor all remained blinded. Block mixtures and isotonic saline are visually indistinguishable. Furthermore, the containers were identical in appearance. Patients who were randomized to receive preoperative motor sparing blocks (MSB) received intraoperative periarticular infiltrations (PAI) with isotonic saline. Patients who were randomized to receive PAIs received preoperative MSBs with isotonic saline.

4.7 Outcome Measures

All patients were measured preoperatively, every day during their inpatient stay until discharge, and at three months postoperatively.

4.7.1 Primary Outcome Measure

The primary outcome in this study was duration of analgesia. This was measured using a numeric pain rating scale (NPRS). The NPRS is an 11-point interval scale from zero (no pain) to ten (worst pain imaginable). A review paper by Williamson *et al.*⁸² indicated that the 11-point interval scaled NRPS has a high sensitivity to change; is reliable, valid, and easy to administer. Time zero was defined as the end of the administration of the MSB by the anaesthetist or completion of PAI by the surgeon. Patients were assessed for pain during rest and activity (45 degrees of flexion) at baseline, upon arrival in PACU, and then at two, four, six, 12, 18, 24, 30, 36, and 48 hours. If patients were not discharged at or before 48 hours, pain was assessed at 72 hours. If patients were discharged before 48 hours, the research assistant telephoned the patient and asked them to verbally report their pain scores at 48 hours.

The end of analgesia was defined as patient reported pain equal to or more than 6/10 on the NRPS. Additional studies have used pain equal to or more than 6/10 on the NRPS as an indicator for severe pain as well^{11,59}. The first rescue analgesia was the initiation of the continuous ACB (10 mL bolus of 0.2% ropivacaine and subsequent infusion at a basal rate of 6 mL/hour with patient controlled boluses of 4 mL every 30 minutes as needed) by the bedside nurse for the purpose of controlling pain. We reported the proportion of patients who were discharged prior to starting the first rescue analgesia.

4.7.2 Secondary Outcome Measures

4.7.2.1 Quadriceps Muscle Strength

We measured maximum voluntary isometric contraction (MVIC) with a hand held dynamometer (JTECH Medical; Commander Echo Muscle Testing Dynamometer) before and 20 minutes after the administration of the blocks. Hand held dynamometers are considered reliable and valid instruments⁸³. After surgery, we repeated this measurement at six hours after the initial block, and 0800 hours and 1600 hours daily until the resolution of the initial block evidenced by NPRS pain equal to six or higher.

We evaluated quadriceps muscle strength with the patient in a seated position on the edge of the bed. The knee was flexed approximately 60 degrees with both feet hanging. The hand held dynamometer was placed perpendicular to the tibial crest five centimeters proximal to the medial malleolus as described by Grevstad *et al.*¹¹. For each assessment, three measurements were done with a five second pause between measurements. We recorded the maximum value out of the three.

4.7.2.2 WOMAC

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a widely used measure of symptoms and physical disability which was originally developed for patients with OA of the hip or knee⁸⁴. It evaluates clinically important and patient-relevant changes in health status as a result of treatment interventions. The WOMAC evaluates three dimensions: pain, stiffness, and physical function with five, two, and seventeen questions, respectively⁸⁵. For our study we used the Likert version of the WOMAC. Each question is rated on an ordinal scale of zero to five and is associated with descriptors; zero (none), one (mild), two (moderate), three (severe), and four (extreme). All three sections of WOMAC are summed together and the total score indicates the severity of the patients' pain (0-20), stiffness (0-8), and physical disability (0-68). A higher WOMAC score indicates worse pain, stiffness, and physical functionality in the individual.

McConnell *et al.*⁸⁴ conducted a literature review to assess the reliability, validity, and responsiveness of the WOMAC using 43 extracted articles. While assessing the reliability in a drug trial using the Likert WOMAC they found an internal consistency of the pain subscale to be 0.86, 0.90 for stiffness, and 0.95 for physical function. Consistent responsiveness was found for all subscales. They concluded that the WOMAC is valid, reliable, and sensitive for use in TKA trials. Marsh *et al.*⁸⁶ found excellent agreement between the paper and electronic versions of the WOMAC (WOMAC ICC= 0.96, 95% CI 0.94 to 0.98) concluding that online data collection may be substituted for the traditional paper method with no significant effect on the validity of the questionnaires. In our study, patients completed the WOMAC questionnaire at baseline and again at three months postoperatively. For our results, higher WOMAC scores indicate improved pain, stiffness, and physical functionality.

4.7.2.3 SF-12 Health Survey (SF-12) – version 2

A shortened version of the SF-36, the SF-12 health survey, is a patient reported survey that assesses general health. The SF-12 consists of two questions concerning physical function, two questions on role limitations because of physical health problems, one question on bodily pain, one question on general health perceptions, one question on vitality (energy/fatigue), one question on social functioning, two questions on role limitations because of emotional problems, and two questions on general mental health⁸⁷. These eight weighted sections are each transformed onto a scale of zero to 100 where zero indicates the worst disability. The SF-12 health survey has been proven to be a valid, reliable, and responsive outcome measure.⁸⁸ Study patients completed the SF-12 questionnaire at baseline and again at three months postoperatively.

4.7.2.4 Physiotherapy and Mobilization

We recorded when patients reached eligibility to perform their first inpatient physiotherapy appointment following TKA. Furthermore, time to first mobilization and pain on the NPRS following every physiotherapy appointment was recorded. For our study, only a walking distance greater than five meters was considered patient

mobilization. We recorded length of the first mobilization and if a study patient was unable to perform physiotherapy.

4.7.2.5 Total Opiate Consumption

We recorded the time each rescue medication was received, dose, and frequency. If poor pain control persisted after the first two rescues (ACB and oxycodone), the ward nurse administered Hydromorph Contin; the same data was recorded (time, dose and frequency) by accessing the patients' medication administration record.

4.7.2.6 Timed Up and Go Test

The timed up and go (TUG) test is a valid and reliable test (ICC=0.80, 95% CI: 0.70, 0.94) to evaluate patients on an orthopaedic rehabilitation ward on skills in functional mobility^{89,90}. The TUG test consists of recording the time it takes for an individual to get up from a chair, walk at a comfortable pace to a three-metre mark, turn around, come back, and sit back down⁹¹. The chair used in all tests was standardized and the assistive device used by the study patient during the test was recorded. All patients attempted to perform the TUG test during the first physiotherapy appointment on postoperative day one (POD1) and again at discharge. If a patient was unable to perform the test it was recorded and the reason documented.

According to Podsiadlo *et al.*⁹¹ TUG tests indicate the patients' level of physical mobility. Specifically, independent individuals can perform the test in less than ten seconds. Individuals who perform the test in ten to 20 seconds are within normal limits for frail elderly patients. Finally, patients who take 30 seconds or more to complete the test, require assistance from others for many mobility tasks.

4.7.2.7 Site of Predominant Pain

During each pain assessment (two, four, six, 12, 18, 24, 30, 36, 48, and 72 hours if needed) patients were asked to indicate where on their knee they felt the most intense pain.

4.7.2.8 Side Effects

During each assessment until discharge (two, four, six, 12, 18, 24, 30, 36, 48, and 72 hours if needed) we recorded intensity of nausea and incidence of pruritus. Patients used a four-point scale to evaluate nausea at each time point (0= no nausea or vomiting, 1=nausea no vomiting, 2=vomiting, 3=persistent vomiting)^{53,13,62,92} and pruritus (yes or no).

4.7.2.9 Length of Hospital Stay

We recorded the number of days until patients reached discharge eligibility. Patients were discharged by their attending surgeon and physiotherapist when pain and nausea were controlled, there was an absence of medical or surgical complications, and if they were mobile and able to manage stairs.

4.7.2.10 Patient Satisfaction

Study patients were given a satisfaction form to complete when discharge eligibility was achieved and again at three months postoperative. This form included the patient satisfaction section from the post-operative Knee Society Score (KSS) questionnaire and an additional question that recorded the patients' overall satisfaction with their postoperative pain control using a NRS from zero (very poor) to ten (very good)^{13,93}. The KSS is a validated and reliable questionnaire that combines an objective physician-derived component with a subjective patient-derived component that evaluates pain relief, functional abilities, satisfaction, and fulfillment of expectations^{94,95}. The patient satisfaction section contains five questions on a forty-point scale.

4.7.2.11 Patient Characteristics and PACU/Block Room Details

Preoperatively, we collected demographic information including birthdate, operative knee, gender, height, weight, BMI, comorbidities, and usual pain medications. While the patients were in the PACU and block room, the research team collected details including date of surgery, ASA score, block sedation requirement, pre-op pain score (rest/activity),

pre-op multimodal drugs given, block performance time, number of injection attempts, block failure, colour doppler, time of intraoperative infiltration, block sensation testing, patient proprioception, time of spinal recession, and intra-operative analgesics.

4.8 Sample Size

According to Zhang *et al.*¹⁶ the duration of analgesic effect from single injection PAI (control group) can range from eight to 24 hours. In an unpublished pilot study, clinicians at LHSC claimed experiencing a mean duration ($\pm$ SD) of single injection PAI analgesia to be approximately 16 ($\pm$ 5.5) hours. They also defined the minimally important difference between groups in analgesic duration to be four hours. Clinicians at LHSC chose this number based on their experiences since it was not available in the literature.

We conducted a formal equality sample size calculation using a two-sided alpha error rate of 0.05 with a statistical power of 80% to detect a minimally important difference between groups of four hours. We used the pre-determined standard deviation of $\pm$ 5.5 hours in this calculation. This required approximately 30 patients to each group. We expected a 20% dropout rate. Therefore, we chose to recruit 80 patients for the trial, 40 to each group.

4.9 Data Analysis

We analyzed all patients according to the treatment arm they were assigned to (intention-to-treat). We used SPSS version 23.0 to perform the analysis of the data. We used descriptive statistics to present the demographic characteristics of each group using means and standard deviations for continuous variables (age, height, weight, and BMI) and proportions for nominal variables (sex, operative knee, ASA score, tourniquet time, and medications).

We used an analysis of covariance (ANCOVA) to statistically compare the two groups for total duration of analgesia, quadriceps strength, WOMAC, time to eligibility for physiotherapy, time to and length of first mobilization, time to complete the TUG tests, SF-12, length of stay, satisfaction, opiate consumption, and physiotherapy pain. The

outcome served as the dependent variable, group allocation served as the independent variable and pain and tourniquet time as the covariate. Baseline scores were used as covariates for WOMAC and SF-12. If the data was not normally distributed we used the Mann-Whitney U test to statistically compare the groups. A Bonferroni correction was used to correct for multiple comparisons.

We reported the unadjusted mean with 95% confidence intervals in figures and the adjusted mean with standard error and the adjusted mean difference between groups with 95% confidence intervals in tables and text. We used the last outcome carried forward (LOCF) method in patients whose final pain score was missing (n=3).

Chapter 5

5 Results

5.1 Participant Flow

The flow of patients through each stage of the study is outlined in Figure 5. From July 2014 to March 2015, we screened 334 patients for this study. Of these, 138 patients were ineligible, 16 were missed, 22 declined to participate, and 59 were enrolled in other studies. Several patients were excluded for more than one reason.

Eighty-eight eligible patients gave their consent to participate in the study. Five patients were withdrawn prior to being randomized for surgery; four patients decided not have to surgery during the study time and one patient was rescheduled without study assessors being notified. Twelve patients were withdrawn after being randomized. Of these, five withdrew consent because they no longer wanted to undergo a spinal anesthetic, three patients withdrew because they felt the risks associated with undergoing a block were too high, one patient rescheduled their surgery outside of the study period, there was insufficient time to perform the intervention for one patient, and for two patients first rescue was erroneously initiated immediately post surgery. At the time of this analysis, 54 patients had reached the three-month study end point. Patient demographics and comorbidities were similar between groups (Table 1).

Figure 5: Participant flow through study

Some patients ineligible for more than one reason.

Table 1: Baseline Demographics for patients undergoing total knee arthroplasty with either the motor sparing block or periarticular infiltration techniques

Characteristic	Motor Sparing Knee Block (n=41)	Periarticular Infiltration (n=41)
Male, n (%)	13 (31.7)	15 (36.6)
Mean Age $\pm$ SD, y	68 $\pm$ 8	63 $\pm$ 9
Mean Height $\pm$ SD, cm	165 $\pm$ 10	167 $\pm$ 10
Mean Weight $\pm$ SD, kg	95 $\pm$ 22	91 $\pm$ 21
Mean BMI $\pm$ SD, kg/m ²	34.6 $\pm$ 7.7	32.4 $\pm$ 7.1
Operative Knee, Right n (%)	25 (61)	25 (61)
ASA Status, n (%)		
One	2 (4.9)	0 (0)
Two	23 (56.1)	26 (63.4)
Three	16 (39.0)	15 (36.6)
Tourniquet Time $\pm$ SD, min	70.2 $\pm$ 14.5	64.6 $\pm$ 10.5
Pre-Surgical Pain Medications, n (%)		
NSAIDS	22 (53.7)	20 (48.8)
Pain Killers	23 (56.1)	18 (43.9)
Narcotics	10 (13.7)	8 (19.5)

Abbreviations. SD = standard deviation, BMI = body mass index, ASA = American Society of Anesthesiologists physical status classification system, MSB=motor sparing block, PAI=periarticular infiltration

The time to perform the block and method of sedation were similar between groups as were other means of intraoperative pain management (Table 2).

Table 2: Block characteristics for patients undergoing total knee arthroplasty with either the motor sparing block or periarticular infiltration techniques

Block Characteristics	MSB (n=35)	PAI (n=35)
MSB Performance Time $\pm$ SD, min	10.09 $\pm$ 3.76	10.74 $\pm$ 4.64
Block Sedation		
Fentanyl $\pm$ SD, ug	85.0 $\pm$ 41.2	88.2 $\pm$ 35.2
Midazolam $\pm$ SD, mg	1.75 $\pm$ 0.38	1.53 $\pm$ 0.38
Intraoperative Propofol $\pm$ SD, mg	196.6 $\pm$ 113.4	197.1 $\pm$ 99.5
Postoperative Spinal Length $\pm$ SD, hrs	1.33 $\pm$ 1.03	1.06 $\pm$ 0.82
Spinal Failure, n (%)	1 (3)	1 (3)

Abbreviations. SD = standard deviation, MSB=motor sparing block, PAI= periarticular infiltration

5.2 Primary Outcome Measure

5.2.1 Total Duration of Analgesia

There was a statistically significant difference between groups in the total duration of analgesia during hospitalization (8.8 hours (95% CI 3.98 to 13.62), $p < 0.01$) in favour of the MSB with a mean duration of 18.06 ± 1.68 hours compared to the PAI group with a mean duration of 9.25 ± 1.68 hours. The distribution of the PAI group was more skewed towards lower duration hours in comparison to the MSB group with lines representing mean values (Figure 6).

Figure 6: Total duration of analgesia following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (dark line: medians)

5.3 Secondary Outcome Measures

5.3.1 Overall Pain

5.3.1.1 Pain at Rest

There was a statistically significant difference in mean pain scores at rest at two hours postoperative. There were no significant differences at any other time points (Figure 7). Eighteen patients remained in the hospital at the 72 hour time point (MSB n=9, PAI n=9).

Figure 7: Numerical rating pain scores at rest following TKA with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.1.2 Overall Pain During Activity

There was a statistically significant difference in pain scores during activity at two and four hours postoperative. There were no significant differences at any other time points (Figure

8). Eighteen patients remained in the hospital at the 72 hour time point (MSB n=9, PAI n=9).

Figure 8: Numerical rating pain scores during activity following TKA with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.2 Quadriceps Muscle Strength

Because quadriceps strength was measured at baseline, 20 minutes and six hours after the administration of blocks, and at 0800 hours and 1600 hours daily until the first rescue analgesic was received, some patients completed a greater number of muscle tests than others because of different rescue times. During the study period no patient required muscle testing after 0800 hours on postoperative day two because they had been discharged from hospital.

There were also no statistically significant differences for quadriceps muscle strength in pounds of force between groups preoperatively (adjusted mean difference -1.23 (95%CI -9.14 to 6.61), $p=0.75$) or at 20 minutes (adjusted mean difference -0.41 (95%CI -7.60 to 6.78), $p=0.91$) and 6 hours postoperatively (adjusted mean difference -1.23 (95%CI -6.8 to 4.3), $p=0.66$) (Figure 9). No significant differences were found at further time points.

Figure 9: Quadriceps muscle strength in pounds of force following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.3 Western Ontario McMaster Osteoarthritis Index

There were no statistically significant differences between the groups at baseline or three months for the pain, stiffness, and function domains. Furthermore, no significant differences were found between the groups at baseline or three months for the total WOMAC score (Table 3). Both groups improved from baseline to three months postoperative.

Table 3: Western Ontario McMaster Osteoarthritis Index scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)

Time	Domain	MSB (mean $\pm$ SE)	PAI (mean $\pm$ SE)	Adjusted Mean Difference (95% CI)	p-Value
Preop	Pain	54.2 $\pm$ 3.09	48.5 $\pm$ 2.64		
	Stiffness	42.2 $\pm$ 4.11	39.2 $\pm$ 2.86		
	Function	51.2 $\pm$ 3.58	50.1 $\pm$ 2.68		
	Total	50.5 $\pm$ 3.07	47.1 $\pm$ 2.38		
3m	Pain	77.8 $\pm$ 3.23	72.7 $\pm$ 2.88	-5.08 (-13.8 to 3.7)	0.25
	Stiffness	62.7 $\pm$ 3.99	57.3 $\pm$ 3.57	-5.41 (-16.2 to 5.4)	0.32
	Function	75.0 $\pm$ 3.14	72.1 $\pm$ 2.81	-2.87 (-11.4 to 5.6)	0.49
	Total	73.3 $\pm$ 2.75	69.5 $\pm$ 2.46	-3.80 (-11.2 to 3.6)	0.31

Abbreviations. SE = standard error, CI = confidence interval, MSB=motor sparing block, PAI= periarticular infiltration

5.3.4 SF-12 Health Survey (SF-12) – version 2

There were no statistically significant differences found between the groups at baseline or three months for the physical or mental components (Table 4). Both groups improved from baseline to three months for the physical component.

Table 4: SF-12 Health Survey scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)

Time	Domain	MSB (mean $\pm$ SE)	PAI (mean $\pm$ SE)	Adjusted Mean Difference (95% CI)	p-Value
Preop	Mental	57.9 $\pm$ 2.02	54.0 $\pm$ 1.96		
	Physical	31.5 $\pm$ 1.56	32.2 $\pm$ 1.71		
3m	Mental	51.9 $\pm$ 1.67	55.1 $\pm$ 1.48	3.16 (-1.24 to 7.65)	0.17
	Physical	43.5 $\pm$ 1.53	39.8 $\pm$ 1.37	-3.75 (-7.87 to 0.37)	0.07

Abbreviations. SE = standard error, CI = confidence interval, MSB=motor sparing block, PAI= periarticular infiltration

5.3.5 Physiotherapy and Mobilization

5.3.5.1 Time to Eligibility for Physiotherapy

The time it took patients to reach eligibility to perform their first inpatient physiotherapy following TKA was not significantly different between the groups (0.34 hours (95% CI -1.37 to 2.05), $p=0.69$). It took patients in the MSB group a mean of 20.7 ± 0.59 hours and patients in the PAI group a mean of 20.4 ± 0.59 hours.

5.3.5.2 Time to First Mobilization

The length of time it took patients to mobilize for the first time following TKA was not significantly different between groups (2.2 hours (95% CI -4.2 to 8.6), $p=0.49$). It took patients in the MSB group a mean of 27.3 ± 2.23 hours and patients in the PAI group a mean of 25.0 ± 2.23 hours.

5.3.5.3 Length of First Mobilization

The length of first mobilization following TKA was not significantly different between groups (0.5 meters (95% CI -0.69 to 1.71), $p=0.40$). Patients in the MSB group mobilized for a mean of 8.23 ± 0.42 meters compared to patients in the PAI group who mobilized for a mean of 8.74 ± 0.42 meters.

5.3.5.4 Physiotherapy Pain

The number of patients remaining in hospital decreased over time. Thus, the number of patients participating in inpatient physiotherapy also decreased. Other than being discharged, two patients in the PAI group did not undergo physiotherapy on the morning of postoperative day one (too nauseous); three patients did not participate in physiotherapy on the afternoon of postoperative day one (significant pain ($n=2$) and no physiotherapist available ($n=1$)); one did not perform physiotherapy on the morning of day two (too nauseous). There was no difference between groups for the amount of pain immediately following each physiotherapy appointment (Figure 10).

Figure 10: Pain following postoperative physiotherapy appointments following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.6 Total Opiate Consumption

There were no differences in total oxycodone consumption (Figure 11) or total hydromorphone consumption (Figure 12) between the two groups at any time point. Eighteen patients remained in the hospital at the 72 hour time point (MSB n=9, PAI n=9).

Figure 11: Oxycodone consumption following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

Figure 12: Hydromorphone consumption following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.7 Timed Up and Go Test

A total of 18 study patients could not perform the TUG test on postoperative day one. Eight of these patients were in the MSB group and ten were in the PAI group. One patient in the PAI group used crutches to complete the test while all patients in the MSB group used a walker. No statistically significant differences were found between groups for time to complete the TUG on postoperative day one (Table 5).

One patient in the MSB group refused to perform the TUG test at discharge because of muscle weakness and a fear of falling. Four patients in the PAI group used crutches to complete the test while all patients in the MSB group used a walker. No statistically significant difference was found between groups for time to complete the TUG at discharge (Table 5).

Table 5: Time to Complete the Timed Up and Go in seconds following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)

Time	MSB (mean $\pm$ SE)	PAI (mean $\pm$ SE)	Adjusted Mean Difference (95% CI)	p-Value
Day 1 $n_{\text{MSB}}=27, n_{\text{PAI}}=25$	66.16 $\pm$ 3.52	58.48 $\pm$ 3.66	-7.69 (-17.92 to 2.54)	0.14
Discharge $n_{\text{MSB}}=34, n_{\text{PAI}}=35$	50.21 $\pm$ 3.68	47.51 $\pm$ 3.62	-2.69 (-13.02 to 7.63)	0.60

Abbreviations. SE = standard error, CI = confidence interval, MSB=motor sparing block, PAI= periarticular infiltration

5.3.8 Site of Predominant Pain

There was no statistically significant relationship between group allocation and site of predominant pain at any of the time points. Nine patients in the MSB group and nine patients in the PAI group remained in the hospital at 72 hours. From arrival in PACU to two hours postoperative most patients did not report pain in their knee. At four hours postoperative, approximately half of the MSB group reported pain at the front of their knee whereas the other half still reported no pain. At this same time, about a quarter of the PAI patients reported pain at the front of their knee, another quarter reported pain at the back of

the knee whereas about half still reported no pain. From six hours postoperative until discharge the most common site of predominant pain for each group was at the front of the knee.

5.3.9 Side Effects

5.3.9.1 Nausea

There were no differences in nausea scores between treatment groups from zero to 72 hours (Figure 13).

Figure 13: Nausea scores following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (unadjusted means, 95% confidence intervals)

5.3.9.2 Pruritus

There was no difference between groups for pruritus at any of the time points. At majority of time points, no patients reported pruritus.

5.3.10 Length of Hospital Stay

The length of hospital stay following TKA was not significantly different between groups (0.23 days (95% CI -0.19 to 0.66), $p=0.29$). Patients in the MSB group had a mean hospital stay of 2.39 ± 0.15 days compared to patients in the PAI group who had a mean hospital stay of 2.17 ± 0.15 days.

5.3.11 Satisfaction

Overall NRS satisfaction with overall pain control from surgery until discharge was not significantly different between groups at discharge (adjusted mean difference -0.20 (95%CI -1.62 to 1.22), $p=0.77$). KSS satisfaction scores were also not significantly different between groups at discharge or three months (Table 6).

Table 6: Knee Society Score Satisfaction following total knee arthroplasty with either the motor sparing block or periarticular infiltration block techniques (adjusted means)

Time	MSB (mean $\pm$ SE)	PAI (mean $\pm$ SE)	Adjusted Mean Difference (95% CI)	p-Value
Discharge	21.2 $\pm$ 0.92	20.2 $\pm$ 0.86	0.23 (-371 to 4.17)	0.91
3m	28.4 $\pm$ 1.43	28.6 $\pm$ 1.33	0.05 (-0.95 to 1.05)	0.93

5.4 Adverse Events

Three adverse events occurred during this study; two in the MSB group and one in the PAI group. One patient in the MSB group suffered a deep vein thrombosis (DVT) that delayed their discharge from the hospital. A second patient in the MSB group was admitted to emergency for shortness of breath within the three-month study period after their initial discharge following TKA. They were discharged from the emergency room with suspected interstitial lung disease. One patient in the PAI group fell on the day after surgery attempting to get out of bed without assistance. This event did not affect the patients' rehabilitation and they were discharged without delay on day two from the hospital.

Chapter 6

6 Discussion

We aimed to compare the duration of analgesia following total knee arthroplasty in patients who were randomized to receive either periarticular infiltration (control group) or a motor sparing knee block (experimental group). We also assessed postoperative function, pain, satisfaction, opiate consumption, and side effects. We found a statistically significant difference in favour of the motor sparing block (MSB) group for total duration of analgesia and early pain scores during rest and activity (2 to 4 hours) were significantly lower in the MSB group. No significant differences were found between treatment groups for any other outcome.

Currently, femoral nerve blocks (FNB) are the gold standard peripheral nerve block for TKA at most centers around the world³³. At our center however, PAI is the standard postoperative analgesia because it spares quadriceps function thereby facilitating rehabilitation and a shorter length of stay. PAI does not however, offer the duration of analgesia offered by a FNB¹⁵. On the other hand adductor canal blocks (ACB) minimally affect quadriceps function but are technologically more challenging than the PAI and require ultrasound guidance like the FNB. To date there is one study showing greater early postoperative pain relief in favour of FNB¹ and six studies showing no difference^{11-14,20,96}. There are no studies that demonstrate greater pain relief for the ACB over the FNB.

For our study, we created the MSB that is essentially an ACB with the addition of injected analgesia at the posterior and lateral knee joint (posterior periscapular and lateral femoral cutaneous nerve injection) with the goal of providing pain relief for more regions around the knee joint. Since no study has ever reported duration of ACB, we were uncertain whether our MSB would provide a greater duration of pain relief compared to a PAI. We did not expect to find differences in quadriceps strength or function between MSB and PAI since both techniques retain quadriceps function. Our longer term goals are to enhance the MSB by adding a sedative as an adjuvant to prolong the duration of analgesia and avoid the use of the catheter required for continuous infusion blocks.

There are no published studies comparing single injection ACBs, which are most similar to our MSB technique, to single injection PAI. However, numerous trials have compared either single or continuous PAI to FNBs^{3,10,41,79–81}. For example, Uesugi *et al.*¹⁵ randomized 210 patients to either single injection PAI or FNB with an additional sciatic block (FNB group). The drug mixture used in their PAI group was similar in class and dose to the mixture used in our study. This study was unique in that they also measured the duration of analgesia for their treatment groups as we did. They reported that the onset of pain in patients who received the PAI was 8.4 ± 9.2 hours post block which is similar to our patients who received PAI whose onset of pain was 9.25 ± 10.3 hours post block. They demonstrated that the duration of analgesia for patients who received a femoral nerve block (FNB) was longer than those who received a PAI (15.3 ± 8.4 hours). Given this finding and the similarity between FNB and MSB (both peripheral nerve blocks), we expected the patients who received the MSB to experience a greater duration of pain relief than patients who receive a PAI. In fact, our MSB patients did not require their first rescue medication for an average of 18.1 ± 10.1 hours post block. Both groups in our study reported a longer duration of analgesia than the patients in the Uesugi study, which may be partially explained by the difference in method to measure time to first rescue. Whereas in the Uesugi *et al* study patients were instructed to press a call button when they felt postoperative pain, in our study patients were required to indicate a pain score equal to or greater than six on a pain NRS, which may have meant that our patients experienced a greater level of pain before being provided with rescue medication.

In our study, once patients reached NRS pain greater than or equal to six, the continuous infusion (first rescue) was started to reduce pain scores. Since this was standardized amongst all study patients, we were uncertain whether there would be a difference in NRS pain scores at rest or activity from arrival in PACU until discharge because no study has ever reported duration of pain relief for an ACB. What we were able to show, however, was that there was a statistically significant difference for postoperative pain scores at two and four hours during activity and at two hours during rest in favour of the MSB group with no significant differences at any other time points. This finding is likely explained by the shorter duration of pain relief (wearing off for most patients by the first

eight hours) for the PAI with increasing pain in these patients until first rescue compared to maintained pain relief in patients who received the MSB.

Studies have shown that ACBs retain quadriceps strength to a greater extent than FNBs because of the minimal blocking of motor nerves in the ACB procedure. Only the nerve to vastus medialis is blocked in the ACB. For example, Kim *et al.*¹³ hypothesized that a single injection ACB would be superior in quadriceps strength to the FNB in their randomized trial. Strength was assessed with a hand held dynamometer at six to eight hours, 24, and 48 hours postoperative. They reported superior quadriceps strength in the ACB group at six to eight hours postoperative and no significant differences at 24 or 48 hours. Similarly, Grevstad *et al.*¹¹ randomized 50 patients to receive either a single injection ACB or single injection FNB. Quadriceps strength was assessed at two hours post block. They reported 20% greater quadriceps strength in the ACB group compared to the FNB group. Finally, Jaeger *et al.*⁹² randomized 54 patients comparing continuous ACB to continuous FNB. They assessed quadriceps strength preoperatively and at 24 hours postoperatively. Their results indicated significantly greater quadriceps strength in the ACB group compared to the FNB group. On the other hand, Wang *et al.*⁷⁸ conducted a meta-analysis on 10 RCTs comparing PAIs and FNBs. Three studies indicated that the number of patients able to do active straight leg raises at 24 hours following TKA was significantly larger in the PAI group. Since the two additional injections used in our MSB do not target any additional motor nerves, we did not expect to see any differences between the MSB and PAI for quadriceps strength in our study.

In our study, muscle strength was only assessed until the first rescue analgesia was received (pain ≥ 6). This gave us the ability to directly attribute the quadriceps strength results to either the MSB or PAI instead of MSB or PAI in combination with any rescue medication. As expected, no statistically significant differences were found between groups at any time for quadriceps strength. The number of individuals at each time point who had not received the first rescue decreased faster in the PAI group than the MSB group. Only two patients in the MSB group and one patient in the PAI group never required rescue medication prior to discharge.

In addition to investigating postoperative quadriceps strength in nerve block studies, physiotherapy milestones should also be assessed to give a more accurate representation of a patient's overall functional recovery prior to discharge¹³. In our sample, we did not observe differences between groups in time to be eligible to begin physiotherapy (i.e. pain control, no nausea) or time to and length of first mobilization. This strengthens our conclusion that there was no difference in postoperative functional recovery following TKA for the MSB or PAI groups. Similar to our study, Moghtadeai *et al.*⁷⁹ randomized 40 patients to receive single injection FNB or PAI after TKA. They measured the time to first mobilization of greater than or equal to three meters following TKA and found no significant differences between groups.

We did not expect to see a significant difference in TUG test results between the MSB and PAI since both interventions are quadriceps sparing techniques. Further, if any differences did exist, we would have had to complete the TUG at an earlier time point prior to first rescue. To do this we would have needed a physiotherapist present to safely conduct the TUG test prior to first rescue, which was not feasible. Not surprisingly, there were no significant differences in the time to complete the TUG test in either group at postoperative day one or discharge. Several studies have reported similar findings^{14,62,92}. None were able to conduct the TUG earlier than 24 hours postoperative.

There were no statistically significant differences in total opiate consumption of oxycodone or hydromorphone at any time points up to 72 hours between groups. This was not an unexpected finding for our study because we used it as a second rescue, which means it is unrelated to the interventions. However, the amount of opiates consumed in our study was lower (0-11 mg) than generally reported (8-30mg)^{3,41,79} because we used it as a second rescue whereas other studies use it as their first rescue.

There was no statistically significant difference in overall nausea or pruritus between groups. We did not expect to see any differences in postoperative side effects since the techniques used in both interventions were essentially opiate sparing in turn reducing side effects such as postoperative nausea, vomiting, and pruritus^{4-6,33}. In addition, the number

of opiates used by study patients was low since the first rescue received was a non-narcotic (ropivacaine).

The MSB was designed to provide pain relief for the medial side of the lower leg, the posterior, medial anterior, and lateral areas of the knee joint, and lateral thigh. The PAI is a local infiltration of the deep tissues of the knee and is not as site specific. Therefore, we assumed most patients would complain of pain around the front and slightly above of the knee joint prior to first rescue. After their first rescue we expected study patients to also complain of pain at the back of the knee since the continuous ACB (first rescue) does not provide analgesia for that region. We did think that if there were any differences between groups and the location of pain, that these differences would be observed while the PAI was wearing off but prior to first rescue. From immediate postoperative up to 6 hours postoperative, there was no site of predominant pain; patients reported very little pain. As expected, from six hours postoperative until discharge patients indicated that the front of the knee was the most painful. This observation was the same for both groups even over time, which is most likely related to the placement of the tourniquet and surgical area not to the intervention. No other studies evaluating ACBs or PAI as interventions have reported the site of predominant pain in patients during the postoperative period.

As expected, we did not find any statistically significant differences between groups for the WOMAC or SF-12 questionnaires since the interventions used in our study exhibit their greatest influence on pain and function in the immediate postoperative period following TKA up to discharge. We were able to show that patients who received the MSB or PAI improved their scores over the duration of the study for pain, stiffness, general health, and functionality with no differences between groups. This finding was similar to other studies (Bush et al)

At our institution, it is standard for patients to be discharged on the morning of postoperative day two unless pain, muscle weakness, or extensive side effects are negatively affecting the patient. Our results showed no statistically significant difference between groups in length of stay(LOS) which was expected since both interventions have their greatest influence on pain during the early postoperative period. This finding is

consistent with other studies^{3,13,14}. Overall NRS satisfaction with pain control at discharge was not significantly different between groups. We also recorded satisfaction using the satisfaction section on the KSS questionnaire. There were no significant differences between groups at discharge or three months. This is consistent with the literature^{1,13,79}.

Strengths of our study include the randomization of patients to intervention reducing the chance of selection bias. We were also able to blind the patient, clinicians and outcome assessor reducing expectation and performance biases. Our study is also the first to assess the MSB (a modified ACB) for postoperative analgesia following TKA. It is the first study to measure duration of analgesia for ACBs and it is the first study to compare ACBs to PAIs.

6.1 Study Limitations

Limitations existed in this study including the small sample size, the start and stop time points of the duration assessment, and the timing of the TUG test assessment.

This was a preliminary analysis since some study patients had not reached the three month outcome assessments. When total study follow-up is complete, this will provide us with further certainty for these results. Furthermore, a number of outcomes were continually assessed as patients were discharged or up until first rescue. This caused smaller sample sizes for certain outcome time points, and therefore a larger sample size would improve precision.

By using pain greater than or equal to six as the end time for the duration assessment, we could of prolonged the duration calculation of both interventions. Patients could of have been in postoperative pain but had not received the rescue because their pain had not reached six, a level that patients can interpret differently. Instead, the end time could have been whenever a patient first felt they needed a rescue. Furthermore, we could of started timing the duration of analgesia in both interventions immediately after surgery instead of at two different times. This could eliminate the possible advantage of two to three hours in duration that the MSB group might have experienced since this intervention was completed prior to surgery.

Lastly, patients performed the TUG test on the morning of postoperative day one during their first physiotherapy appointment. By this time, majority of study patients had already received the continuous ACB because of severe pain. Therefore, our TUG test results are not indicative of the mobility ability of patients who exclusively received the PAI or MSB. Assessing the TUG test time earlier around six to eight hours postoperative would have been more effective.

Chapter 7

7 Conclusion

The motor sparing block provides significantly longer duration of analgesia than the periarticular infiltration while preserving muscle function and not negatively affecting length of stay, satisfaction, side effects, or functional rehabilitation.

7.1 Clinical Relevance

Our overall goal is to develop a catheter-free intervention to manage postoperative pain that will reduce adverse events like infections, reduce institutional costs, improve ease of mobility, and offer a less technologically demanding option for pain management. This study is the first step toward achieving this goal by demonstrating that the MSB offers similar pain control to a PAI, which has been shown to be similar to the FNB. We were also able to confidently demonstrate that the MSB preserves muscle function similar to the PAI and better than the FNB. And finally, we were able to show that the MSB lasts longer than the PAI. Our next step will be to add an adjuvant medication to the MSB to prolong the analgesic effects long enough to avoid the catheter required for the usual first rescue.

7.2 Future Direction

We will complete data collection for the three month outcomes of our remaining patients. This will improve the precision of our results for these outcomes. We will also evaluate whether there are significant differences in institutional costs between treatment groups.

Future directions should assess whether the addition of Dexmedetomidine as an adjuvant to the anaesthetic mixture of the motor sparing knee block can prolong the duration of analgesia and reduce the need for a catheter dependent continuous block as the first rescue. Furthermore, future studies should assess mobilization with the TUG test at earlier time points. This would provide an accurate assessment of the postoperative mobilization ability of the MSB in comparison to the PAI.

References

1. Memtsoudis SG, Yoo D, Stundner O, et al. Subsartorial adductor canal vs femoral nerve block for analgesia after total knee replacement. *Int Orthop*. 2014. doi:10.1007/s00264-014-2527-3.
2. Memtsoudis SG, Sun X, Chiu Y-L, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology*. 2013;118(5):1046-1058. doi:10.1097/ALN.0b013e318286061d.
3. Chaumeron A, Audy D, Drolet P, Lavigne M, Vendittoli PA. Periarticular injection in knee arthroplasty improves quadriceps function knee. *Clin Orthop Relat Res*. 2013;471:2284-2295. doi:10.1007/s11999-013-2928-4.
4. Jiang J, Teng Y, Fan Z, Khan MS, Cui Z, Xia Y. The efficacy of periarticular multimodal drug injection for postoperative pain management in total knee or hip arthroplasty. *J Arthroplasty*. 2013;28(10):1882-1887. doi:10.1016/j.arth.2013.06.031.
5. Ganapathy S. Wound/intra-articular infiltration or peripheral nerve blocks for orthopedic joint surgery. *Curr Opin Anaesthesiol*. 2012;25:615-620. doi:10.1097/ACO.0b013e328357bfc5.
6. R.Sinatra, G.Silverman, S.J.Brull, J.Chung, D.M. Harrison DD. Sinatra Drug Article.pdf. *Anesthesiology*. 1989;71:502-507.
7. Maheshwari A V., Blum YC, Shekhar L, Ranawat AS, Ranawat CS. Multimodal pain management after total hip and knee arthroplasty at the ranawat orthopaedic center. *Clin Orthop Relat Res*. 2009;467:1418-1423. doi:10.1007/s11999-009-0728-7.
8. Danninger T, Opperer M, Memtsoudis SG. Perioperative pain control after total knee arthroplasty : An evidence based review of the role of peripheral nerve blocks. 2014;5(3):225-232. doi:10.5312/wjo.v5.i3.225.

9. Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. *Anesth Analg*. 2010;111(6):1552-1554.
doi:10.1213/ANE.0b013e3181fb9507.
10. Ashraf A, Raut V V., Canty SJ, McLauchlan GJ. Pain control after primary total knee replacement. A prospective randomised controlled trial of local infiltration versus single shot femoral nerve block. *Knee*. 2013;20(5):324-327.
doi:10.1016/j.knee.2013.04.009.
11. Grevstad U, Mathiesen O, Valentiner LS, Jaeger P, Hilsted KL, Dahl JB. Effect of Adductor Canal Block Versus Femoral Nerve Block on Quadriceps Strength, Mobilization, and Pain After Total Knee Arthroplasty. *Reg Anesth Pain Med*. 2015;40(1):3-10. doi:10.1097/AAP.0000000000000169.
12. Patterson ME, Bland K, Elliot C, et al. The adductor canal block provides analgesia similar to a femoral nerve block in patients undergoing total knee arthroplasty-a retrospective study. *Reg Anesth Pain Med*. 2013;38 (4):1-6.
doi:10.1016/j.jclinane.2014.08.005.
13. Kim DH, Lin Y, Ph D, et al. Adductor Canal Block versus Femoral Nerve Block for Total Knee Arthroplasty. *Anesthesiology*. 2014;120(3):540-550.
doi:10.1097/ALN.0000000000000119.
14. Shah N a., Jain NP. Is Continuous Adductor Canal Block Better Than Continuous Femoral Nerve Block After Total Knee Arthroplasty? Effect on Ambulation Ability, Early Functional Recovery and Pain Control: A Randomized Controlled Trial. *J Arthroplasty*. 2014;29(11):2224-2229. doi:10.1016/j.arth.2014.06.010.
15. Uesugi K, Kitano N, Kikuchi T, Sekiguchi M, Konno SI. Comparison of peripheral nerve block with periarticular injection analgesia after total knee arthroplasty: A randomized, controlled study. *Knee*. 2014;21(4):848-852.
doi:10.1016/j.knee.2014.04.008.

16. Zhang S, Wang F, Lu ZD, Li YP, Zhang L, Jin QH. Effect of single-injection versus continuous local infiltration analgesia after total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *J Int Med Res.* 2011;39:1369-1380. doi:10.1177/147323001103900423.
17. G.Scuderi AT. *The Knee: A Comprehensive Review.*; 2010.
18. Elaine N. Marieb KH. *Human Anatomy & Physiology.*; 2012.
19. Total Knee Arthroplasty: American Academy of Orthopaedic Surgeons. <http://orthoinfo.aaos.org/topic.cfm?topic=a00389>.
20. Henningsen MH, Jaeger P, Hilsted KL, Dahl JB. Prevalence of saphenous nerve injury after adductor-canal-blockade in patients receiving total knee arthroplasty. *Acta Anaesthesiol Scand.* 2013;57(September 2011):112-117. doi:10.1111/j.1399-6576.2012.02792.x.
21. C. Egeler AJ and SF. Motor-sparing knee block – description of a new technique. *Anaesthesia.* 2013;68:541-542. doi:10.1111/anae.12246.
22. Editorial Board. *Life with Arthritis in Canada: A Personal and Public Health Challenge.*; 2010.
23. Stafinski T, Menon D. THE BURDEN OF OSTEOARTHRITIS IN CANADA : Working Paper 01-03. 2003;(June):1-20. <http://www.ihe.ca/documents/2001-03paper.pdf>.
24. Kean WF, Kean R, Buchanan WW. Osteoarthritis: symptoms, signs and source of pain. *Inflammopharmacology.* 2004;12(1):3-31. doi:10.1163/156856004773121347.
25. Tarride JE, Haq M, O'Reilly DJ, et al. The excess burden of osteoarthritis in the province of Ontario, Canada. *Arthritis Rheum.* 2012;64(4):1153-1161. doi:10.1002/art.33467.

26. The Arthritis Society. 2015. <http://www.arthritis.ca/page.aspx?pid=941>.
27. Macdonald K V, Sanmartin C, Langlois K, Marshall DA. *Symptom Onset , Diagnosis and Management of Osteoarthritis.*; 2014.
28. Lanting BA, Liberman JR, Callaghan JJ, Berend ME MS. Ensuring a Winner: The ABCs of Primary Total Knee Arthroplasty. 2015;64:369-379.
29. Chang CB, Yoo JH, Koh IJ, Kang YG, Seong SC, Kim TK. Key factors in determining surgical timing of total knee arthroplasty in osteoarthritic patients: Age, radiographic severity, and symptomatic severity. *J Orthop Traumatol*. 2010;11:21-27. doi:10.1007/s10195-010-0086-y.
30. Ethgen O, Bruyère O, Richy F, Dardennes C, Reginster J-Y. Health-related quality of life in total hip and total knee arthroplasty. *J Bone Jt Surg*. 2004;86-A(May):963-974.
31. Canadian Institute for Health Information. Hip and Knee Replacements in Canada: Canadian Joint Replacement Registry 2014 Annual Report. 2014;(June).
32. Krych APM. Review : femoral nerve block may be the most effective option for pain relief following total knee replacement. *BMJ*. 2014;10(0):101918. doi:10.1055/s-0034-1371769.
33. Bauer MCR, Pogatzki-Zahn EM, Zahn PK. Regional analgesia techniques for total knee replacement. *Curr Opin Anaesthesiol*. 2014:1-6. doi:10.1097/ACO.0000000000000115.
34. Horlocker TT, Hebl JR, Kinney M a O, Cabanela ME. Opioid-free analgesia following total knee arthroplasty - A multimodal approach using continuous lumbar plexus (psoas compartment) block, acetaminophen, and ketorolac. *Reg Anesth Pain Med*. 2002;27(1):105-108. doi:10.1053/rapm.2002.27177.

35. Chavis SW, Duncan LH. Pain management--continuum of care for surgical patients. *AORN J*. 2003;78:382-386, 389-399; quiz 400-401, 403-404. doi:10.1016/S0001-2092(06)60750-3.
36. Hawker G, Wright J, Coyte P, et al. Health-related quality of life after knee replacement. *J Bone Joint Surg Am*. 1998;80:163-173.
37. Antoni M, Jenny JY, Noll E. Postoperative pain control by intra-articular local anesthesia versus femoral nerve block following total knee arthroplasty: Impact on discharge. *Orthop Traumatol Surg Res*. 2014;100(3):313-316. doi:10.1016/j.otsr.2013.12.022.
38. Bagsby DT, Ireland PH, Meneghini RM. Liposomal Bupivacaine Versus Traditional Periarticular Injection for Pain Control After Total Knee Arthroplasty. *J Arthroplasty*. 2014;29(8):1687-1690. doi:10.1016/j.arth.2014.03.034.
39. Lamplot JD, Wagner ER, Manning DW. Multimodal pain management in total knee arthroplasty. a prospective randomized controlled trial. *J Arthroplasty*. 2014;29(2):329-334. doi:10.1016/j.arth.2013.06.005.
40. Stein C, Lang LJ. Peripheral mechanisms of opioid analgesia. *Curr Opin Pharmacol*. 2009;9(Figure 1):3-8. doi:10.1016/j.coph.2008.12.009.
41. Affas F, Nygåards E-B, Stiller C-O, Wretenberg P, Olofsson C. Pain control after total knee arthroplasty: a randomized trial comparing local infiltration anesthesia and continuous femoral block. *Acta Orthop*. 2011;82(3):441-447. doi:10.3109/17453674.2011.581264.
42. Rawal N. Epidural technique for postoperative pain: gold standard no more? *Reg Anesth Pain Med*. 2012;37(3):310-317. doi:10.1097/AAP.0b013e31825735c6.
43. Tammachote N, Kanitnate S, Manuwong S, Yakumpor T, Panichkul P. Is pain after TKA better with periarticular injection or intrathecal morphine? *Clin Orthop Relat Res*. 2013;471:1992-1999. doi:10.1007/s11999-013-2826-9.

44. Serpell MG, Millar F a, Thomson MF. Comparison of lumbar plexus block versus conventional opioid analgesia after total knee replacement. *Anaesthesia*. 1991;46(July 1990):275-277.
45. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. *Indian J Anaesth*. 2011;55(2):104-110. doi:10.4103/0019-5049.79875.
46. Knudsen K, Beckman Suurküla M, Blomberg S, Sjövall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. *Br J Anaesth*. 1997;78:507-514. doi:10.1093/bja/78.5.507.
47. Banerjee P. The efficacy of multimodal high-volume wound infiltration in primary total knee replacement in facilitating immediate post-operative pain relief and attainment of early rehabilitation milestones. *Eur J Orthop Surg Traumatol*. 2014;24:571-577. doi:10.1007/s00590-013-1231-0.
48. Busch C a, Shore BJ, Bhandari R, et al. Efficacy of periarticular multimodal drug injection in total knee arthroplasty. A randomized trial. *J Bone Joint Surg Am*. 2006;88:959-963. doi:10.2106/JBJS.E.00344.
49. Andersen K V., Nikolajsen L, Haraldsted V, Odgaard a., Søballe K. Local infiltration analgesia for total knee arthroplasty: Should ketorolac be added? *Br J Anaesth*. 2013;111(March):242-248. doi:10.1093/bja/aet030.
50. Winnie a P, Ramamurthy S, Durrani Z. The inguinal paravascular technic of lumbar plexus anesthesia: the "3-in-1 block". *Anesth Analg*. 1973;52:989-996. doi:10.1213/00000539-197311000-00036.
51. Faust AM, Fournier R, Gamulin Z. Perioperative Analgesia With Posterior Continuous Lumbar Plexus Block for Simultaneous Ipsilateral Total Hip and Knee Arthroplasty. *Reg Anesth Pain Med*. 2006;31:591. doi:10.1016/j.rapm.2006.08.007.

52. Luber MJ, Greengrass R, Vail TP. Patient satisfaction and effectiveness of lumbar plexus and sciatic nerve block for total knee arthroplasty. *J Arthroplasty*. 2001;16(1):17-21. doi:10.1054/arth.2001.16488.
53. Watson MW, Mitra D, McLintock TC, Grant S a. Continuous versus single-injection lumbar plexus blocks: Comparison of the effects on morphine use and early recovery after total knee arthroplasty. *Reg Anesth Pain Med*. 2005;30(6):541-547. doi:10.1016/j.rapm.2005.06.006.
54. Touray ST, De Leeuw M a., Zuurmond WW a, Perez RSGM. Psoas compartment block for lower extremity surgery: A meta-analysis. *Br J Anaesth*. 2008;101(December 2007):750-760. doi:10.1093/bja/aen298.
55. Kaloul I, Guay J, Côté C, Fallaha M. The posterior lumbar plexus (psoas compartment) block and the three-in-one femoral nerve block provide similar postoperative analgesia after total knee replacement. *Can J Anaesth*. 2004;51(October 2002):45-51. doi:10.1007/BF03018546.
56. Labat G. *Regional Anesthesia Its Technical and Clinical Application.*; 1924.
57. Paul, James E. Arya, Aman. Hurlburt, Lindsay. Cheng, Ji. Thabane L. Femoral Nerve Block Improves Analgesia Outcomes after Total Knee Arthroplasty. *J Am Socety Anesthesiol*. 2010;113(5):1144-1162.
58. Sakai N, Inoue T, Kunugiza Y, Tomita T, Mashimo T. Continuous femoral versus epidural block for attainment of 120° knee flexion after total knee arthroplasty: A randomized controlled trial. *J Arthroplasty*. 2013;28(5):807-814. doi:10.1016/j.arth.2012.09.013.
59. Min Lee R, Lim Tey JB, Liang Chua NH. Postoperative Pain Control for Total Knee Arthroplasty: Continuous Femoral Nerve Block Versus Intravenous Patient Controlled Analgesia. *Anesthesiol Pain Med*. 2012;1(4):239-242. doi:10.5812/aapm.3404.

60. Chan EY, Fransen M, Sathappan S, Chua NHL, Chan YH, Chua N. Comparing the Analgesia Effects of Single-injection and Continuous Femoral Nerve Blocks with Patient Controlled Analgesia after Total Knee Arthroplasty. *J Arthroplasty*. 2013;28(4):608-613. doi:10.1016/j.arth.2012.06.039.
61. Ilfeld BM. The Association Between Lower Extremity Continuous Peripheral Nerve Blocks and Patient Falls After Knee and Hip Arthroplasty. *Changes*. 2012;29(6):997-1003. doi:10.1016/j.biotechadv.2011.08.021.Secreted.
62. Jenstrup MT, Jæger P, Lund J, et al. Effects of Adductor-Canal-Blockade on pain and ambulation after total knee arthroplasty: A randomized study. *Acta Anaesthesiol Scand*. 2012;56:357-364. doi:10.1111/j.1399-6576.2011.02621.x.
63. LaReau JM, Robbins CE, Talmo CT, Mehio AK, Puri L, Bono J V. Complications of Femoral Nerve Blockade in Total Knee Arthroplasty and Strategies to Reduce Patient Risk. *J Arthroplasty*. 2012;27(4):564-568. doi:10.1016/j.arth.2011.06.028.
64. Pelt CE, Anderson AW, Anderson MB, Dine C Van, Peters CL. Postoperative Falls After Total Knee Arthroplasty in Patients With a Femoral Nerve Catheter : Can We Reduce the Incidence ? *J Arthroplasty*. 2014;29(6):1154-1157. doi:10.1016/j.arth.2014.01.006.
65. Lund J, Jenstrup MT, Jæger P, Sørensen a. M, Dahl JB. Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: Preliminary results. *Acta Anaesthesiol Scand*. 2011;55(3):14-19. doi:10.1111/j.1399-6576.2010.02333.x.
66. Quemby D. Ultrasound Guided Adductor Canal Block (Saphenous Nerve Block). *Atotw*. 2014;(January):1-11.
67. DeLoach LJ, Higgins MS, Caplan a B, Stiff JL. The visual analog scale in the immediate postoperative period: intrasubject variability and correlation with a numeric scale. *Anesth Analg*. 1998;86(1):102-106. doi:10.1097/00000539-199801000-00020.

68. Kim TW, Park SJ, Lim SH, Seong SC, Lee S, Lee MC. Which analgesic mixture is appropriate for periarticular injection after total knee arthroplasty? Prospective, randomized, double-blind study. *Knee Surgery, Sport Traumatol Arthrosc.* 2014;23:838-845. doi:10.1007/s00167-014-3366-x.
69. Xu CP, Li X, Wang ZZ, Song JQ, Yu B. Efficacy and safety of single-dose local infiltration of analgesia in total knee arthroplasty: A meta-analysis of randomized controlled trials. *Knee.* 2014;21(3):636-646. doi:10.1016/j.knee.2014.02.024.
70. Quinn M, Deakin a. H, McDonald D a., Cunningham IKT, Payne a. P, Picard F. An anatomic study of local infiltration analgesia in total knee arthroplasty. *Knee.* 2013;20(5):319-323. doi:10.1016/j.knee.2013.06.008.
71. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop.* 2008;79(2):174-183. doi:10.1080/17453670710014950.
72. Ramamoorthy K. Local Infiltratoin Analgesia Following Total Knee Arthroplasty. *Indian J Anaesth.* 2012;56(2):208-209. doi:10.4103/0019-5049.68372.
73. Niemeläinen M, Kalliovalkama J, Aho AJ, Moilanen T, Eskelinen A. Single periarticular local infiltration analgesia reduces opiate consumption until 48 hours after total knee arthroplasty. *Acta Orthop.* 2014;85(6):614-619. doi:10.3109/17453674.2014.961399.
74. Essving P, Axelsson K, Åberg E, Spännar H, Gupta A, Lundin A. Local infiltration analgesia versus intrathecal morphine for postoperative pain management after total knee arthroplasty: A randomized controlled trial. *Anesth Analg.* 2011;113(4):926-933. doi:10.1213/ANE.0b013e3182288deb.
75. Thorsell M, Holst P, Hyldahl HC, Weidenhielm L. Pain control after total knee arthroplasty: a prospective study comparing local infiltration anesthesia and epidural anesthesia. *Orthopedics.* 2010;33(2):75-80. doi:10.3928/01477447-20100104-13.

76. Fowler SJ, Christelis N. High volume local infiltration analgesia compared to peripheral nerve block for hip and knee arthroplasty - What is the evidence? *Anaesth Intensive Care*. 2013;41(4):458-462.
77. Tietje T, Davis a. B, Rivey MP. Comparison of 2 Methods of Local Anesthetic-Based Injection as Part of a Multimodal Approach to Pain Management After Total Knee Arthroplasty. *J Pharm Pract*. 2014. doi:10.1177/0897190014544815.
78. Wang C, Cai X-Z, Yan S-G. Comparison of Periarticular Multimodal Drug Injection and Femoral Nerve Block for Postoperative Pain Management in Total Knee Arthroplasty: A Systematic Review and Meta-Analysis. *J Arthroplasty*. 2015;(October 2014). doi:10.1016/j.arth.2015.02.005.
79. Moghtadaei M, Farahini H, Faiz SH-R, Mokarami F, Safari S. Pain Management for Total Knee Arthroplasty: Single-Injection Femoral Nerve Block versus Local Infiltration Analgesia. *Iran Red Crescent Med J*. 2014;16(1):e13247. doi:10.5812/ircmj.13247.
80. Marques EM, Jones HE, Elvers KT, Pyke M, Blom AW, Beswick AD. Local anaesthetic infiltration for peri-operative pain control in total hip and knee replacement: systematic review and meta-analyses of short- and long-term effectiveness. *BMC Musculoskelet Disord*. 2014;15(1):220. doi:10.1186/1471-2474-15-220.
81. Perlas A, Kirkham KR, Billing R, et al. The impact of analgesic modality on early ambulation following total knee arthroplasty. *Reg Anesth Pain Med*. 2013;38(4):334-339. doi:10.1097/AAP.0b013e318296b6a0.
82. Williamson A, Hoggart B. Pain: A review of three commonly used pain rating scales. *J Clin Nurs*. 2005;14(7):798-804. doi:10.1111/j.1365-2702.2005.01121.x.
83. Stark T, Walker B, Phillips JK, Fejer R, Beck R. Hand-held dynamometry correlation with the gold standard isokinetic dynamometry: A systematic review. *PM R*. 2011;3(5):472-479. doi:10.1016/j.pmrj.2010.10.025.

84. McConnell S, Kolopack P, Davis a M. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis Rheum.* 2001;45(5):453-461. doi:10.1002/1529-0131(200110)45:5<453::AID-ART365>3.0.CO;2-W.
85. Liebs TR, Gluth J, Rther W, Haasters J, Russlies M, Hassenpflug J. Using the patient ’ s perspective to develop function short forms specific to total hip and knee replacement based on WOMAC function items. *J Bone Jt Surg.* 2013;95(2):239-243. doi:10.1302/0301-620X.95B2.28383.
86. Marsh JD, Bryant DM, MacDonald SJ, Naudie DDR. Patients Respond Similarly to Paper and Electronic Versions of the WOMAC and SF-12 Following Total Joint Arthroplasty. *J Arthroplasty.* 2014;29(4):670-673. doi:10.1016/j.arth.2013.07.008.
87. Ware JE, Highway GW. SF-12 Health Survey (Version 1.0). *Management.*:1-8.
88. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care.* 1996;34(3):220-233. doi:10.2307/3766749.
89. Yeung TSM, Wessel J, Stratford PW, MacDermid JC. The timed up and go test for use on an inpatient orthopaedic rehabilitation ward. *J Orthop Sports Phys Ther.* 2008;38(7):410-417. doi:10.2519/jospt.2008.2657.
90. Halket A, Stratford PW, Kennedy DM, Woodhouse LJ, Spadoni G. Measurement properties of performance-specific pain ratings of patients awaiting total joint arthroplasty as a consequence of osteoarthritis. *Physiother Can.* 2008;60(3):255-263. doi:10.3138/physio.60.3.255.
91. D. Podsiadlo SR. The Timed “Up & Go”: A Test of Basic Functional Mobility for Frail Elderly Persons. *JAGS.* 1991;39:142-148.
92. Jger P, Zaric D, Fomsgaard JS, et al. Adductor Canal Block Versus Femoral Nerve Block for Analgesia After Total Knee Arthroplasty. *Reg Anesth Pain Med.* 2013;38(6):526-532. doi:10.1097/AAP.0000000000000015.

93. Szucs S, Iohom G, O'Donnell B, et al. Analgesic efficacy of continuous femoral nerve block commenced prior to operative fixation of fractured neck of femur. *Perioper Med (London, England)*. 2012;1:4. doi:10.1186/2047-0525-1-4.
94. The 2011 Knee Society Knee Scoring System ©. 2012;(December):1-9.
95. Ryd L, Kärrholm J, Ahlvin P. Knee scoring systems in gonarthrosis. Evaluation of interobserver variability and the envelope of bias. Score Assessment Group. *Acta Orthop Scand*. 1997;68(1):41-45. doi:10.3109/17453679709003973.
96. Mudumbai SC, Kim TE, Howard SK, et al. Continuous adductor canal blocks are superior to continuous femoral nerve blocks in promoting early ambulation after TKA. *Clin Orthop Relat Res*. 2014;472:1377-1383. doi:10.1007/s11999-013-3197-y.

Appendices

Appendix A: Ethics Approval

LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-14-180

PROJECT TITLE: Ultrasound guided motor sparing knee blocks with or without Dexmedetomidine for postoperative analgesia following total knee arthroplasty: a randomized double blind study

PRINCIPAL INVESTIGATOR: Dr. Sugantha Ganapathy

LAWSON APPROVAL DATE: April 25, 2014

Health Sciences REB#: 104373

Please be advised that the above project was reviewed by the Clinical Research Impact Committee and Lawson Administration and the project:

Was Approved

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill
V.P. Research
Lawson Health Research Institute

All future correspondence concerning this study should include the Lawson Approval Number and should be directed to Sherry Paiva, Research Administration Officer, Lawson Approval,

cc: Administration

**Western
Research**

Use of Human Participants - Revision Ethics Approval Notice

Principal Investigator: Dr. Sugantha Ganapathy

File Number: 104373

Review Level: Delegated

Protocol Title: Ultrasound guided motor sparing knee blocks with or without Dexmedetomidine for postoperative analgesia following total knee arthroplasty: a randomized double blind study

Department & Institution: Schulich School of Medicine and Dentistry/Anaesthesia, Western University

Sponsor:

Ethics Approval Date: January 02, 2014 Expiry Date: December 31, 2015

Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
Revised Western University Protocol	Received Jan 24, 2014	
Revised Letter of Information & Consent		2014/01/24
Other	pain dairy-Received Jan 24, 2014	

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced revision(s) or amendment(s) on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the University of Western Ontario Updated Approval Request Form.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

The Chair of the HSREB is Dr. Joseph Gilbert. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Signature

Ethics Officer to Contact for Further Information

This is an official document. Please retain the original in your files.

Western University Research Ethics Board (HSREB) - Dr. Gilbert

Appendix B: Letter of Information and Consent

Letter of Information and Consent Form

Study Title:

Ultrasound Guided Motor Sparing Knee Blocks for Postoperative Analgesia Following Total Knee Arthroplasty: A Randomized Blinded Study

Principal Investigators:

Dr S Ganapathy FRCP, Dr. James Howard FRCS

Co-investigators:

Orthopedic Surgeons: Dr. Brent Lanting, Dr. Ted Vasarhelyi, Dr. Steven MacDonald

Anesthesia: Dr. Kevin Armstrong Clinical fellows: Dr. Rakesh Vijayashankar Sondekoppam,

Dr. Vishal Uppal, Dr. Maria Lopera Vesquez

Other Co-investigators: Mr. Olawale Sogbein, Dr Dianne Bryant

Dept. of Anesthesiology and Perioperative Medicine

London Health Sciences Centre

University Hospital

Olawale Sogbein
University Hospital
MSc Candidate

The purpose of this letter is to provide you with information to help you decide whether you wish to participate in this research study conducted by the Departments of Anesthesiology and Perioperative Medicine and Department of Orthopedic Surgery, University of Western Ontario.

Your decision is completely voluntary and will not affect your medical care if you choose not to participate. It is important for you to ask questions and be aware of the research risks, benefits and alternatives.

Participant initials: _____

Motor sparing blocks TKJA , 2014

Your health care provider may be an investigator in this research study, and as an investigator, is interested in both your welfare and in the conduct of the study. You are not under any obligation to participate in any research project offered by your doctor.

The following pages explain the study itself and why we are doing it and your rights as a study participant in it. The final page is a consent form, which you will be required to sign if you choose to participate in this study. You will be given a copy of this Letter of information and consent form to keep.

WHY ARE WE DOING THIS STUDY?

The operation you are having (Total Knee Joint Arthroplasty, shortened to TKJA) is a very common one. However the first two to three days following the operation can be very painful. Severe pain following surgery can interfere with your physiotherapy and slow down your recovery. We are interested in evaluating two different methods of providing pain relief while you are in the hospital after a TKJA.

The first method is called periarticular infiltration which means that the surgeon will inject into your knee joint a mixture of local anesthetic (freezing), an NSAID's (anti-inflammatory drug) and morphine (pain killer) at the end of surgery. This method is our usual care and provides good quality pain relief without making the leg weak. Patients usually feel pain once this mixture wears off.

Another option for providing pain relief is called a nerve block. A nerve block is an anesthetic injection (freezing) targeted toward a certain nerve or group of nerves to treat pain. The purpose of the injection is to "turn off" a pain signal coming from a specific location in the body (in your case the knee). Imaging guidance, such as ultrasonography may be used to help the doctor place the needle in the right location so that you can receive maximum benefit from the injection. Sometimes, a nerve block can make your leg weak and increase the potential that you will fall down. Performing this block at the mid-thigh level can minimize leg weakness while providing good quality pain relief.

WHAT DOES THE STUDY INVOLVE?

To provide anesthesia during the operation you will receive a spinal anesthetic. This will numb the entire lower half of your body for about 4 hours. This is part of our usual care practice. In addition, your surgical procedure will not be modified as a result of your participation in the study. The group you are allocated to will determine the method of postoperative pain relief.

Participant initials: _____

Page 2 of 7

Motor sparing blocks TKJA , 2014

All patients will receive a block catheter pre-operatively and all patients will receive an injection into the knee at the end of surgery prior to waking up. What is injected through the catheter and into the knee joint is determined through randomization (flipping a coin).

	Local Infiltration Analgesia (Hospital Standard)	Motor Sparing Knee Block (Nerve Block)	Catheter in the adductor-canal block
GROUP 1	Freezing agent: -Ropivacaine -Ketorolac -Epinephrine -Morphine	Placebo (saline)	Started once front of the knee starts to hurt more than 6 out of 10 on pain rating scale.
GROUP 2	Placebo (saline)	Freezing agent: -Ropivacaine -Ketorolac -Epinephrine -Morphine	Started once front of the knee starts to hurt more than 6 out of 10 on pain rating scale.

**A placebo is a solution which looks like the study medication but contains no active ingredients. This is done to ensure that clinicians are blinded.*

Group 1 (Usual care): If you are assigned to this group, you will receive an injection of local anesthetic mixture near the joint done by the surgeon at the end of surgery before you wake up. These patients will receive a placebo substance (saline) in the block catheters.

Group 2 (Nerve block): Patients in this group will receive local anesthetic in the nerve block before the operation. This group will also receive a placebo solution (saline) injected into the knee joint at the end of surgery by the surgeon.

No matter which group you are in, if you begin to feel excessive pain in the front of your knee, the doctor or nurse can administer local anesthetic via the catheter and you will be connected to a pump that you control to deliver local anesthetic freezing for the next 36-48 hours. All patients will receive multiple oral pain killers called multimodal analgesia starting in the preoperative period for a total of 5 days.

Following the operation you will be followed up closely until you are discharged from hospital. You will be assessed on a regular basis for any pain or feelings of nausea. We will provide you with a pain diary for you to record pain levels at certain times following the surgery and to indicate the amount of pain medication that you have needed. On the morning after surgery and on the day you are discharged, we will conduct a standard test of your mobility (*TUG test*). To complete this test, you are asked to rise from a chair, walk a short distance, turn around, walk

Participant initials: _____

Page 3 of 7

Motor sparing blocks TKJA, 2014

back to the chair and sit down again. The research assistant will time how long it takes you to complete this task.

When you return to the surgeon's clinic at three months after your surgery you will receive a short questionnaire to assess progress in your general health. We will also ask about any complications since leaving the hospital.

POSSIBLE SIDE EFFECTS, RISKS, AND DISCOMFORTS:

Regional nerve blocks have been shown to be a very safe alternative to general anesthesia. However, just as general anesthesia carries risks, regional anesthesia entails certain risks too. Serious risks are very rare, but they are of a different nature to those of general anesthesia and the risks are detailed below. The numbers below indicate the risk of each problem. For example 1/10,000 means on average 1 in every 10,000 patients undergoing a nerve block will suffer that problem.

1. Failed block: The block may provide inadequate pain relief. This occurs in 5/100 to 10/100 of patients. If this occurs, alternative oral or intravenous medications such as morphine or dilaudid will be used to make you comfortable.
2. Risk of suffering some degree of bruising from the needle injection site – 1/10 to 1/100.
3. Temporary nerve irritation leading to an area of numbness or tingling persisting for up to a week – 1/100
4. Risk of suffering a temporary seizure due to the local anesthetic being too rapidly absorbed – very rare. 1/10,000 to 1/100,000.
5. Risk of suffering longer-term nerve damage lasting several months – very rare. 1/25000.
6. Risk of suffering permanent nerve damage – very rare – 1 in 1million.

Side effects from the sedation include short-term (a few minutes to a few hours) drowsiness, forgetfulness and sometimes minor temporary itching.

Wound infiltration and infusion of local anesthetic may be associated rarely with toxicity from absorbed local anesthetic, nerve injury and infection. The exact frequency of these problems is currently unknown. A member of the research team will explain all the details during your visit to pre-admission clinic.

EXPECTED DURATION OF THE STUDY AND NUMBER OF SUBJECTS EXPECTED TO PARTICIPATE:

There will be about 80 people in this stage of the study, which will be conducted at University Hospital, London. The study is expected to run for twelve months.

STUDY RESTRICTIONS/SUBJECT RESPONSIBILITIES:

Participant initials: _____

Page 4 of 7

Motor sparing blocks TKJA , 2014

London Health
Sciences Centre

As a study participant in a research study, you have certain responsibilities. Your responsibilities are to:

1. Follow procedures as instructed
2. If possible, answer the study related questions asked by the research team
3. Report all changes in your physical or mental condition during the course of the study, whether or not you feel they are related to the study procedures

The study doctor has the right to stop your participation in the study at any time, with or without your consent, if he or she feels that this is in your best interest.

POSSIBLE BENEFITS OF THE STUDY:

Participation in this study may or may not be of a direct benefit to you. It is possible your pain relief may be better as you will be very closely monitored while you are in hospital.

ALTERNATIVES:

If you decide not to participate in this study it will NOT prejudice your care. After discussion with your anesthesiologist you will receive the most appropriate anesthetic which will suit you the best for the procedure you are having done.

RIGHT TO WITHDRAW FROM OR REFUSE TO PARTICIPATE IN THIS STUDY:

Your participation in this study is completely voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with NO effect on your future care. We will keep any data collected as part while you were a participant even if you drop out later. You do not waive any legal rights by signing the consent form.

PRIVACY AND CONFIDENTIALITY:

All information will be kept confidential to the best of our ability. The company that takes care of the research database is EmPower Health Research. Your identifying information (name, mailing address, phone number, email address, date of birth) is being collected as part of your participation in this study. Your data is protected by a username and password. It travels in a scrambled format to a server (storage computer) that is located in Montreal, Quebec, Canada. The company that houses the server is a professional company (Netelligent) with extremely high standards of physical and virtual security. We want to let you know however, that even with this high level of security, there is always a remote chance that your information could be accessed or "hacked" by someone who is not supposed to have your information. The chance that this information will be accidentally released is small. In any publication, presentation or report, your name will not be used and any information that discloses your identity will not be released or

Participant initials: _____

Page 5 of 7

Motor sparing blocks TKJA, 2014

London Health
Sciences Centre

published. Representatives of The University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research.

Representatives of the University of Western Ontario Health Sciences Research Ethics Board and Health Canada may contact you or require access to your study-related records to monitor the conduct of the research. You do not waive any legal rights by signing the consent form. If you choose not to sign the consent form, you will not be included in this research study. You may choose to withdraw from the study even after consenting for the participation in the study.

RESEARCH RELATED INJURIES:

If physical injury occurs due to your involvement in this research, medical treatment will be available to you as per the standard care at our institution provided by OHIP. Compensation for lost wages and/or direct or indirect losses is not available.

COSTS:

There will be no additional costs to you as a result of being in this study. You will not be compensated for participation in this study.

QUESTIONS:

Before you sign the consent form, you should ask questions about anything that you do not understand. The study staff will answer questions before, during, and after the study.

If you have questions about this study or how it is being run, you should contact Dr. S. Ganapathy, the principal investigator [REDACTED] at London Health Sciences Centre, University Campus. You can also contact co-investigator Mr. [REDACTED]

If you have any questions about your rights as a research participant you may contact Dr. David Hill, Scientific Director, Lawson Health Research Institute [REDACTED]

In case of an emergency, please contact Dr. Sugantha Ganapathy at [REDACTED] OR go to the nearest hospital emergency department.

Participant initials: _____

Motor sparing blocks TKJA , 2014

Consent Form

Study Title: Ultrasound Guided Motor Sparing Knee Blocks For Postoperative Analgesia Following Total Knee Arthroplasty: A Randomized Blinded Study.

I have read the letter of information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

I will be given a copy of this information and consent form to keep.

Signature of participant: _____ Date: _____

Name of the participant: _____

Signature of person obtaining informed consent _____

Date: _____

Printed name of the person obtaining informed consent _____

Participant initials: _____

Motor sparing blocks TKJA , 2014

Appendix C: Image Permissions

Dear Olawale
OK!

Best regards
Joergen

Joergen B. Dahl, MD, DMSc, MBAex
Head, Associate professor
Department of Anaesthesia and Intensive Care Medicine
Bispebjerg and Frederiksberg Hospitals

Fra: Olawale Sogbein [REDACTED]
Dato: lørdag den 4. juli 2015 kl. 00.30
Til: "Jørgen B. Dahl" [REDACTED]
Emne: Image Permissions

Hello,

I am a Master's student at the University of Western Ontario in London, Ontario, Canada. For my Master's thesis I am conducting a study entitled "Motor Sparing Knee Blocks for Postoperative Analgesia Following Total Knee Arthroplasty- A Randomized Blinded Study" I was wondering if I could use the Figure 1(Cross-sectional ultrasonography image of the adductor canal...) and Figure 2(Cross-sectional MR scan of the adductor canal...) from "Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: preliminary results" by Lund, Jenstrup, Jaeger, Sorensen, and Dahl published in the Acta Anaesthesiol Scand 2011; 55: 14-19. Usage would be in the literature review section of my thesis, and full credit would be cited.

Thank you very much,

—
Olawale Sogbein
MSc Candidate
MES, BHSc (Hon.)
Western University

Hi Olawale,

You are welcome to use the two images you indicated in your thesis.

Best regards,
David Darling

On Fri, July 3, 2015 8:55 pm, Olawale Sogbein wrote:

> Hello,

>

>

> I am a Master's student at the University of Western Ontario in London,
> Ontario, Canada. For my Master's thesis I am conducting a study entitled
> "Motor Sparing Knee Blocks for Postoperative Analgesia Following Total
> Knee Arthroplasty- A Randomized Blinded Study" I was wondering if I could
> use the figure "Ligaments of the Knee" on the "Knee" page from your
> Encyclopedia of Science website. Usage would be in the literature review
> section of my thesis, and full credit would be cited.

>

>

> Thank you very much,

>

>

> --

> Olawale SogbeinMSc Candidate

> MES, BHSc (Hon.)

> Western University

>

>

Curriculum Vitae

Olawale Sogbein

EDUCATION

Master of Science	Kinesiology, Sports Medicine University of Western Ontario, London, ON September 2013 – August 2015
Master of Environmental Studies	Nipissing University, North Bay, ON September 2012-August 2013
Honours Bachelor of Science <i>Dean's List</i>	Health Sciences University of Ottawa, Ottawa, On Class of 2012

RESEARCH EXPERIENCE

University of Western Ontario London, ON Thesis Project 2013 – Present	University Hospital, London Health Sciences Centre <i>Under the supervision of Dr. Dianne Bryant and co-advisory of Dr. James Howard.</i> Conduct a randomized controlled trial investigating a motor sparing block in postoperative analgesia. Responsible for patient recruitment, follow-up, data collection and entry, statistical analysis.
Nipissing University North Bay, ON Research Assistant 2012 – 2013	<i>Under the supervision of Dr. Stephen Kariuki.</i> Assisted with the conducting of experiments and data collection.

CONFERENCES

Toronto, ON Presenter May 2014	<i>Bodies of Knowledge Graduate Student Conference</i> Presented thesis work regarding motor sparing blocks for postoperative analgesia following total knee arthroplasty.
London, ON	<i>Three-Minute Thesis Competition</i>

Presenter

April 2014

Presented a proposal for my thesis work regarding motor sparing blocks for postoperative analgesia following total knee arthroplasty.

TEACHING EXPERIENCE

University of Western Ontario
London, ON

Teaching Assistant

Winter 2014 and 2015

Introduction to Athletic Injuries

Kinesiology 2236B

University of Western Ontario
London, ON

Teaching Assistant

Fall 2013 and 2014

Medical Issues in Exercise and Sport

Kinesiology 4437A

HONOURS & AWARDS

2015

2013-2015

2014

2009-2012

Kinesiology Graduate Travel Award

Western Graduate Research Scholarship

Faculty of Health Science Travel Award

University of Ottawa Dean's Honour List