Postoperative pain is a significant consequence of total joint arthroplasty that can affect early mobilization, joint range of motion, and length of stay. Inadequate pain control can lead to secondary medical sequelae such as venous thromboembolic and cardiac events. Adequate control of pain following total joint arthroplasty is therefore paramount to a successful outcome and to patient satisfaction. Traditional postoperative analgesia with opioids or epidural anesthetics provides inconsistent results with significant side effects. Regional nerve blocks and multi-modal pain techniques have emerged as a way to address this issue. This review will consider the evidence for the use of regional nerve blocks for pain control after total knee and hip replacement, and examine the agents, administration routes and dosing protocols, along with the role of multi-modal analgesia in achieving optimal pain control after lower extremity joint arthroplasty.

**ABBREVIATIONS**

FNB: Femoral Nerve Block; TKA: Total Knee Arthroplasty; PCA: Patient Controlled Analgesia; SNB: Sciatic Nerve Block; ACB: Adductor Canal Block; THA: Total Hip Arthroplasty; LPB: Lumbar Plexus Block; LP: Lumbar Plexus; cLPB: Continuous Lumbar Plexus Block; cFNB: Continuous Femoral Nerve Block; PEC: Continuous Epidural Anesthesia; FIB: Fascia Iliaca Block; NSAID: Non-Steroidal Anti-Inflammatory; COX-2: Cyclo-oxygenase-2; NMDA: N-Methyl-D-aspartic Acid or N-Methyl-D-aspartate; PMDI: Periarticular Multimodal Drug Injection; VAS: Visual Analog Scale; TJA: Total Joint Arthroplasty

**INTRODUCTION**

Postoperative pain is a significant consequence of total joint arthroplasty that can affect early mobilization, joint range of motion, and length of stay. Inadequate pain control can lead to secondary medical sequelae such as venous thromboembolic and cardiac events. Adequate control of pain is therefore paramount to a successful outcome and to patient satisfaction. Historically, traditional postoperative analgesia was either intravenous or neuraxial, primarily with the use of opioids. Unfortunately, opioids provide inconsistent analgesia and can cause several common side-effects including sedation, confusion, constipation, nausea, vomiting, and pruritus. Epidurals containing local anesthetics with or without an opioid are superior for analgesia, but can cause severe hypotension, urinary retention, delayed ambulation, and there is a risk of developing an epidural hematoma with concomitant use of postoperative anticoagulation [1]. In addition to these direct medical issues, these side effects can have a significant financial impact and can increase overall costs due to delayed discharge and additional monitoring requirements. As a result, strategies have been developed to achieve adequate pain control while attempting to minimize side effects of opioids and epidural anesthesia. The purpose of this review is to discuss these strategies currently in common use for hip and knee arthroplasty patients.

Traditionally, the use of peripheral nerve blocks in the lower extremity has not been as widespread as in the upper extremity. This is partly due to anatomic considerations as well as the predominance of neuraxial anesthesia, which is not an option for upper extremity cases [2]. Unlike the brachial plexus, the nerves supplying the lower extremity are not clustered where they can be easily blocked with a relatively superficial injection of local anesthetic. Consequently, lower extremity blocks require specialized training and practice but they can reduce the need for opioids and epidural anesthesia. Advances in needles, catheters, nerve stimulator and ultrasound technology have facilitated localization of neural structures and improved success rates. This review will consider the evidence for the potential regional blocks for total knee and hip replacement and examine the agents, administration routes and role of multi-modal analgesia in achieving pain control after lower extremity joint arthroplasty.

**TOTAL KNEE ARTHROPLASTY**

**Femoral nerve blocks**

The Femoral Nerve Block (FNB) is a common method...
of analgesia for postoperative pain control after Total Knee Arthroplasty (TKA). First described by Labat in 1923, it is a relatively easy technique to master and can be performed by many anesthesiologists. The femoral nerve is the largest branch of the lumbar plexus, originating from the posterior branches of the L2 to L4 roots. The nerve passes anterior to the iliopectos muscle under the inguinal ligament and just lateral to the femoral artery and vein. It then divides into numerous branches in the proximal anterior aspect of the thigh and provides sensory innervation to the anterior aspect of the thigh and knee [3] (Figure 1).

As first described, the block is performed with the patient in the supine position, and the injection point is at the intersection of a line drawn from the anterior superior iliac spine to the pubic symphysis and a vertical line just lateral to the femoral artery [4] (Figure 2). Today, the advancement in nerve stimulation and ultrasound guidance has resulted in improved localization and overall block success [5]. The primary advantage of the FNB over epidural anesthesia is that it does not provide complete motor blockade to the non-operative leg, which may encourage earlier ambulation. It also avoids the risk of epidural hematoma that is associated with the use of anticoagulants simultaneously with epidural analgesia [6,7]. Femoral nerve blocks have also been shown to result in a reduced need for parenteral or oral analgesia to control pain as well as a reduction in reported pain levels.

Complications of FNBs include falls secondary to quadriceps weakness that may occur. The rate of falls reported in the literature after FNB ranges from 0.7% to 1.6%. Reoperation for injuries associated with falls, including ligamentous rupture, fracture, wound dehiscence, and mobile-bearing dislocation have a 0.4% incidence [8]. Additional complications of FNB include vascular injury, hematoma, femoral neuritis (0.59%), and a 0.2% risk of permanent nerve injury [9]. However, despite these potential complications, FNB has been successfully used for post-operative pain control after lower extremity total joint arthroplasty. A systematic review identified 23 randomized trials with 1016 patients and showed that FNB plus patient controlled analgesia (PCA) is superior to PCA alone or epidural infusion for postoperative analgesia in TKA.

Sciatic nerve blocks

Despite the advantages of FNBs, many contend that FNBs alone provide insufficient pain relief to the posterior knee after TKA [10]. This has led to the use of supplemental Sciatic Nerve Blocks (SNBs) in addition to FNBs for improved pain control.

The results of addition of SNB to FNB after TKA have been conflicting. Morin et al. reported on prospectively randomized patients undergoing TKA who received continuous FNB, combined FNB and SNB, or a psoas compartment block. The combined FNB and SNB resulted in lower postoperative opioid use but there was no difference in pain scores or functional outcomes among the groups [11]. Furthermore, they noted more problems while performing active exercises and a more unsteady gait with the addition of the sciatic nerve block. Other studies have found that SNB failed to show improved pain relief when added to a FNB, whether a single-dose or continuous nerve block was used [12]. Several meta-analyses and systematic reviews also concluded that SNB does not provide any analgesic advantage when added to FNB [13,14]. A more recent systematic review identified 391 patients in intermediate-quality studies, but still had inconclusive evidence to define the effect of adding SNB to FNB on analgesia and related outcomes for TKA [15]. A more recent prospective randomized study investigated the effect of adding a single-dose or continuous SNB to FNB in patients undergoing TKA. The addition of SNB did not improve time-to-discharge readiness or knee function, but did result in diminished opioid requirements and improved pain scores while ambulating [16]. Further high-quality studies are needed to evaluate the value of adding SNB to FNB in patients undergoing TKA to determine if they offer any substantial benefit.

Figure 1 Nerves of the Lumbar Plexus.

Figure 2 Femoral Nerve Block.
Selective tibial nerve blocks

In addition to concerns regarding the efficacy of SNB when combined with FNB, there are potential negative side-effects of SNB that can limit function, most commonly post-operative foot drop and leg motor weakness. Furthermore, surgeons have expressed concern that preoperative SNB can mask an injury to the peroneal nerve. Selective tibial nerve blocks have evolved as an alternative to SNB to augment FNB, with the idea that blocking only the tibial nerve component of the sciatic nerve would preserve peroneal nerve function and still provide adequate pain control. The sciatic nerve consists of tibial and peroneal nerve branches that diverge at a variable distance above the popliteal crease. The nociceptive innervation of the posterior knee joint arises from articular branches of both nerves [3]. A recent study investigated combining FNB with a selective tibial nerve block in the popliteal fossa compared with a combined FNB and SNB for patients undergoing TKA. The study found that tibial nerve block performed in close proximity to the popliteal crease avoided complete peroneal motor block and provided similar postoperative analgesia compared to sciatic nerve block [17]. A limitation, however, was that this study did not investigate functional outcomes or time to discharge. Further studies examining this combination of peripheral nerve blocks are needed to assess their ability to improve pain control and outcomes after TKA.

Adductor canal block

The adductor canal is an aponeurotic tunnel in the mid-thigh region. It travels between the anterior and medial compartments of the thigh and is bordered anteriorly by the sartorius, laterally by the vastus medialis and posteromedially by the adductor longus and magnus. The sensory saphenous nerve, the nerve to the vastus medialis, the medial femoral cutaneous nerve, the medial retinacular nerve, and the articular branches from the obturator nerve travel within the adductor canal. In addition, the femoral artery and vein also travel within the canal (Figure 3). The Adductor Canal Block (ACB) has become an area of interest in recent years for regional anesthesia in TKA patients. The main advantage of the ACB is that unlike a FNB, it is predominantly a sensory block [19] and has been shown to reduce pain and morphine consumption compared with placebo after TKA [20].

Several different techniques have been described, the most common being the trans-sartorial approach which blocks the nerve as it travels behind the sartorius muscle [20]. As previously discussed, FNBs lead to quadriceps muscle weakness with functional impairment and associated increased risk of falling postoperatively [21,22]. Adductor canal blocks have the advantage of preserving quadriceps muscle strength and ability to ambulate better than FNB, which reduces fall risk. In healthy volunteers FNB reduced quadriceps strength by 49% from baseline, compared with only 8% with ACB [23]. A recent randomized, double-blinded study in TKA patients showed that adductor canal block preserved quadriceps muscle strength better than FNB, without a significant difference in postoperative pain. There was no difference, however, in mobilization ability with ACB compared to FNB [24].
concluded that the risks of single injection LPB did not justify its use for THA [28].

In contrast to single injection LP blockade, continuous LP blocks (cLPB) have proven effective for long term post-operative analgesia following THA [29-31]. cLPB combined with patient controlled IV morphine PCA after THA resulted in lower patient reported pain scores and reduced morphine consumption over a 36 hour period when compared with PCA alone [31]. Marino et al showed cLPB combined with PCA provided superior pain control and lower morphine consumption over a 24 hour period when compared with PCA alone [30]. In both of these studies, the patients receiving cLPB received the block prior to surgery and the catheter remained in place post-operatively, limiting the studies by a lack of blinding of the treatment from the study investigators. Other studies have demonstrated less positive effects. Ilfeld et al. conducted a randomized double blind study in which continuous LPB was compared with a sham cLPB for post-operative analgesia following THA [29]. Catheters were placed for all patients and utilized for anesthetic delivery intra-operatively. Following surgery, the catheters remained in place for all patients with two infusion solutions, local anesthetic and saline. The catheters were continued for four days post-operatively. The results showed that while the group of patients receiving four days of anesthetic LPB had a significantly shorter length of stay, there was no significant difference in post-operative pain scores, or oral and IV opioid use between the two groups.

Femoral nerve blocks for THA

Due to the potential risks of the psoas compartment block, other approaches to blocking the lumbar plexus have been developed. One such approach is the femoral nerve block, which utilizes the femoral canal to deliver local anesthetic to the lumbar plexus. Singelyn et al compared continuous Femoral Nerve Block (cFNB) with continuous epidural anesthesia (PECA) and PCA alone for pain control following THA and found that cFNB did not provide any greater pain relief than PCA or PECA [32]. Other studies comparing cFNB to cLPB have yielded contradictory results. Marino et al compared cFNB with cLPB and PCA alone for post-operative analgesia after THA and found that although cFNB and cLPB reduced morphine consumption, only cLPB resulted in lower pain scores [30]. In contrast, Ilfeld et al. compared cFNB with cLPB for THA and found the two techniques produced comparable analgesic effects [33]. Two possible explanations were given to account for the contradictory results of the two studies. One explanation offered was that the use of different needles for catheter placement affected the outcomes, with Ilfeld et al. contending that more accurate placement is achieved with their choice of needle. The second possible explanation is that a scheduled post-operative administration of a long acting opioid to both groups in the study may have reduced the difference in pain scores between the two groups. Further studies are needed to determine the role of femoral nerve block after total hip replacement, and similar to their use after TKA concerns for potential fall risk must be considered.

Fascia iliaca block

Another approach to lumbar plexus blockade is the Fascia Iliaca Block (FIB). The FIB is a field block where local anesthetic is delivered underneath the fascia iliaca lateral to the femoral nerve. The block distributes a large volume of local anesthetic cephalad up the fascial plane with the goal of blocking the femoral nerve, lateral femoral cutaneous nerve and more unlikely, the obturator nerve. A modified FNB first developed for use in children, [34] the FIB has proven effective as analgesia for the acute pain of hip fracture [35-37]. However, to date there is little evidence of its efficacy for post-operative analgesia following THA. In one randomized controlled trial, a single injection FIB did not result in lower pain scores or reduced morphine consumption when compared to a sham FIB in which a single injection of saline was administered [38]. In another study, a modified FIB was used with a more proximal needle placement. The modified FIB resulted in no significant difference in morphine consumption at 3 and 6 hours post- operatively, but it did lead to significantly reduced opioid consumption at 12 and 24 hours [39]. Additional studies are needed to determine the role of FIB after THA.

Local anesthetics and concentrations

Local anesthetics act by binding to the intracellular portion of sodium channels thereby inhibiting sodium influx through ion channels in the neuronal cell membranes. This ultimately prevents depolarization and signal conduction resulting in loss of sensation in the area supplied by the nerve [40]. Local anesthetics have an effect on all nerve fibers. The degree to which nerve fibers are “susceptible” to local anesthetic action is related to a combination of the nerve fiber diameter and the degree of myelination. Pain transmitting nerve fibers tend to be thinner and either unmyelinated or lightly myelinated. The smaller diameter lends readily to local anesthetic diffusion resulting in faster onset of action. Myelinated nerves are also more easily blocked than unmyelinated ones. They have a smaller area of exposed surface membrane which allows for more rapid and complete blockade than for an unmyelinated nerve of similar diameter [41].

Anesthesiologists can individualize peripheral and neuraxial nerve block regimens for total joint arthroplasty procedures using the variety of short and long acting local anesthetics currently available. Local anesthetics are available for use in varying concentrations as well. In general, the duration of action is affected by the concentration of the local anesthetic as well as the volume injected. Duration of action can also be prolonged with additives such as epinephrine or a corticosteroid, typically dexamethasone [42]. Bupivacaine, a long-acting amide local anesthetic, is one of the most commonly used local anesthetics. However, concerns
over the risk of cardiotoxicity causing hypotension, arrhythmias and even cardiac arrest eventually led to the development of other long-acting local anesthetics. Ropivacaine is an amide local anesthetic with a very close pharmacodynamic profile to equipotent doses of bupivacaine. Differential sensory and motor block is only apparent at low concentrations (0.2% and less). The primary benefit of ropivacaine is its lower risk of cardiotoxicity in the event of inadvertent intravascular injection. The higher therapeutic index leads to an improved safety profile compared with bupivacaine [43].

A level-I study investigated the effect of FNB with either 0.25% ropivacaine or 0.25% bupivacaine added to a spinal anesthetic in TKA. There was no difference in opioid consumption, pain scores, or motor and/or sensory blockade up to 10 hours postoperatively between the groups. However, 30% of patients in the 0.25% bupivacaine group had persistent motor blockade at 10 to 24 hours after the block. They concluded that both agents are effective local anesthetics for peripheral nerve blocks [44]. In another study, ropivacaine and bupivacaine showed similar anesthetic and analgesic effects, but a significantly faster onset time was found for ropivacaine (13 vs. 17.5 minutes, p<0.001) [45]. The optimal concentration of ropivacaine is another issue for consideration. A study by Paauwe et al. showed no differences in pain scores, motor blockade, or ambulation between femoral infusions of ropivacaine 0.2% and 0.15% in TKA [7]. A previous pilot study demonstrated inadequate analgesia and no advantage associated with the use of a ropivacaine concentration less than 0.1% [46]. A study of 120 TKA patients using three different concentrations of ropivacaine in a continuous FNB showed that ropivacaine 0.1% provided ineffective analgesia, while 0.2% and 0.3% provided equivalent analgesia. There were no significant differences in motor blockade, mobilization, or ropivacaine plasma concentrations, which always remained below toxic levels. This study also demonstrated that initial infusion rates should be adjusted to 15 mL/h to obtain effective analgesia [47]. Another study evaluated different concentrations of ropivacaine (0.12%; 0.14%; 0.16%; 0.18%; 0.20%; 0.22% or 0.50%) in single-dose femoral-sciatic nerve blocks. The authors concluded the 0.20% or higher ropivacaine doses provided satisfactory postoperative analgesia, but the 0.50% group had a significantly higher rate of motor blockade compared to all other doses [48].

CONTINUOUS VERSUS SINGLE DOsing

Postsurgical pain lasts for many days. Because local anesthetic action lasts for 18 to 24 hours after a single shot injection, alternate delivery methods were developed for continued postsurgical pain management. Indwelling nerve block catheters can be placed adjacent to the nerve and a local anesthetic is infused through a portable infusion pump. Several studies have investigated the differences between single dose and continuous infusion for various nerve blocks. Cappelleri et al. studied continuous SNB compared with single-injection SNB in a randomized, blinded study of patients undergoing TKA with lumbar plexus block. They found that continuous SNB improved analgesia, decreased morphine use, and improved early rehabilitation compared with single-injection SNB. Single-dose SNB patients also used 72% more opioids and walked less than their counterparts during the first 48 hours postoperatively [49]. A recent study by Albrecht et al. investigated the difference between continuous and single-dose FNB in TKA in 99 patients. They were unable to demonstrate that varying the concentration and volume of a fixed-dose ropivacaine infusion for continuous FNB influenced time to discharge readiness or improved functional outcomes when compared with a conventional single-injection FNB after TKA [50]. However, this study was terminated prematurely due to a change in institutional protocols and may have been underpowered.

Ambulatory pumps

As attempts to minimize hospitalization time following total joint replacement continue, several novel methods have been developed to allow patients to be discharged home earlier. One such method is the use of perineural blocks. Unlike intravenous or epidural analgesics, perineural nerve blocks may be continued following hospital discharge on an ambulatory basis using a portable infusion pump [51,52]. Ilfeld et al. reported on 50 patients undergoing TKA randomized to 4-day ambulatory continuous FNB or single night continuous FNB followed by saline placebo infusion. They found that a 4-day continuous ambulatory FNB decreased the time required to reach discharge criteria by 53% compared with an overnight hospital-only continuous FNB [53]. A multicenter, randomized, triple-masked, placebo-controlled study by the same group showed that extending a continuous FNB from overnight to over 4 days decreases the time to reach each of three important discharge criteria (adequate analgesia, independence from intravenous opioids, and ambulation greater than 30 minutes) by an estimated 20%. There were no reported femoral nerve palsy the day following catheter removal or at the 6-week surgical postoperative visit [54].

Multimodal analgesia

Multimodal analgesia is a multidisciplinary approach to pain management that maximizes the synergistic effect of treatment with pain medications, while diminishing the negative side effects, particularly opioid-related effects by attempting to minimize their use [55,56]. This balanced analgesia protocol includes the use of drugs of different classes that act at different sites within the central and peripheral nervous system (Table 1). NSAIDs, COX-2 inhibitors and acetaminophen have become important non-opioid adjuvants in the perioperative analgesia protocol. Anticonvulsants such as gabapentin and lyrica as well as NMDA antagonists, such as ketamine have also been increasingly utilized as part of multimodal analgesia regimens (Table 2). Combining peripheral or neuraxial anesthetic techniques with non-opioid agents and the use of opioid agents for breakthrough pain results in improved pain control, diminished stress response, and decreased opioid requirements after total joint arthroplasty [57,58]. Many of the protocols recommend a preoperative oral dose of an anticonvulsant, a COX-2 inhibitor and acetaminophen before the procedure. Ideally, the patient also receives a peripheral nerve block in conjunction with a spinal or epidural anesthetic. Postoperatively, the patient then continues the oral regimen of the multimodal cocktail of drugs with the addition of an IV and oral opioid only as necessary.

In a recent study, 36 patients undergoing minimally invasive TKA were randomized to receive either a multimodal analgesia therapy with a periarticular injection or hydromorphone PCA.
A recent meta-analysis included 21 randomized studies, with pooled results showing the PMDI group had better pain relief, less opioid consumption, larger range of motion, and lower rates of nausea and vomiting than the placebo group. No significant difference was seen in regard to the length of hospital stay between the two groups. The authors recommended using PMDI as part of the pain management plan after TJA [65]. Other studies comparing PMDI to control or placebo injections in patients undergoing simultaneous bilateral TKAs have demonstrated mixed results. Koh et al. studied 55 patients randomized to receive PMDI or no injection during bilateral TKAs. The PMDI group experienced a lower pain level during the night of operation and on the first postoperative day, but no differences in pain levels, function, or patient satisfaction were noted between the groups afterwards [66]. A larger prospective, double-blind, randomized study looked at 286 patients who received either PMDI or placebo injections in patients undergoing TKA. There were no differences between groups in pain scores, satisfaction, range of motion, or blood loss at all times after surgery [67]. Consensus on whether PMDI offers clinically relevant pain relief is still lacking and further studies are needed.

**DISCUSSION AND CONCLUSION**

Adequate pain control is essential to recovery after total joint replacement. It affects postoperative joint rehabilitation and overall surgical outcome. Additionally, as the focus in medicine increasingly shifts towards linking physician and hospital

### Table 1: Location and Mechanism of Action of Multimodal Analgesia Agents.

<table>
<thead>
<tr>
<th>Location</th>
<th>Inhibition Targets</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Tissue</td>
<td>Prostaglandins, Bradykinin, Substance P</td>
<td>NSAIDs, Local anesthetics</td>
</tr>
<tr>
<td>Peripheral Nerves</td>
<td>Unmyelinated C fibers, Myelinated A fibers</td>
<td>Local anesthetics</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>Dorsal root ganglia, Dorsal horn cells</td>
<td>Opioids, Gabapentinoid α-agonists, NMDA antagonist</td>
</tr>
<tr>
<td>Brain</td>
<td>Spinohalamic tracts, Cortex</td>
<td>Opioids, Acetaminophen, NSAIDs, α-agonists, NMDA antagonist</td>
</tr>
</tbody>
</table>


### Table 2: Anesthetic Agents and Mechanisms of Action.

<table>
<thead>
<tr>
<th>Agent Type</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs (e.g. ketorolac)</td>
<td>Inhibit cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) and the synthesis of prostaglandins and thromboxanes throughout body</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Inhibit prostaglandin synthesis in CNS</td>
</tr>
<tr>
<td>Opioids (e.g. fentanyl)</td>
<td>Bind to opioid receptors μ, κ, δ (mu, kappa, and delta) in CNS; some also block the re-uptake of norepinephrine and serotonin (e.g. tramadol)</td>
</tr>
<tr>
<td>Local anesthetics (e.g. ropivacaine)</td>
<td>Bind to the intracellular portion of Na+ channels and block Na+ influx, preventing depolarization of neuronal cell membranes</td>
</tr>
<tr>
<td>Gabapentinoids (e.g. gabapentin)</td>
<td>Bind to the α2β-1 subunit of the voltage-dependent Ca2+ channel, resulting in a reduction of Ca2+ influx at nerve terminal</td>
</tr>
<tr>
<td>NMDA antagonist (e.g. ketamine)</td>
<td>Block glutamate and/or glycine binding sites on CNS neurons, allowing diminished pain perception; dissociative anesthesia</td>
</tr>
<tr>
<td>α-agonists (e.g. dexmedetomidine)</td>
<td>Inhibits the release of norepinephrine in CNS, causing sedation, relaxation, and analgesia without respiratory depression</td>
</tr>
</tbody>
</table>

1Non-Steroidal Anti-Inflammatory
2Cyclo-oxygenase-2
3Cyclo-oxygenase-1
4Central Nervous System
5N-Methyl-D-aspartic acid or N-Methyl-D-aspartate
reimbursement to patient satisfaction scores, good pain control and methods to attain it will continue to grow in importance. Continued efforts to develop the ideal strategy to achieve this for each individual patient, while minimizing side effects are critically important to optimizing the results for these quality of life improving procedures.

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