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Updates on multimodal analgesia and regional anesthesia for total knee arthroplasty patients

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The subspecialty of regional anesthesiology and acute pain medicine (RAAPM) is in a position to lead changes that may impact the current opioid crisis. At the hospital level, RAAPM experts can implement evidence-based multimodal analgesic clinical pathways featuring regional anesthesia. Multimodal analgesia consists of using two or more analgesic modalities targeting pain pathways at various levels to improve pain control, while also aiming to reduce opioid utilization and related adverse effects. These types of pathways or protocols have been widely applied in the joint replacement population. This review focuses on the current state of the evidence regarding individual elements of a multimodal analgesic pathway for patients with total knee arthroplasty including new regional anesthesia techniques like the IPACK (Infiltration between the Popliteal Artery and Capsule of the Knee) block and suggests future research directions to improve the clinical care of this surgical population in the future.

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Introduction

In 2010, more than 100 million surgical procedures were performed in the United States and more than 98% of these patients received opioids during hospitalization [1,2]. Surgery itself has been identified as a risk factor for instigating chronic opioid use [3], and both opioid-naïve and opioid-tolerant patients can be affected [4]. One large study of all Veterans Healthcare Administration patients who underwent surgery in 2011 found that greater preoperative levels of opioid use are associated with progressively longer time to opioid cessation postoperatively [5]. When attempting to predict the risk of long-term opioid use after surgery, the incidence varies based on preoperative patient characteristics and the type of surgery [6]. Patients who undergo total knee arthroplasty (TKA), total hip arthroplasty, cholecystectomy, mastectomy, and other common surgeries have an increased risk for chronic opioid use after surgery, with TKA being the highest risk [6]. For TKA patients, long-term opioid use is also associated with an increased risk of knee revision surgery in the first year following initial arthroplasty [7].

The subspecialty of regional anesthesiology and acute pain medicine (RAAPM) is in a unique position to lead changes that may impact the current opioid crisis. At a national level, RAAPM anesthesiologists can participate in the development of outcome measures that promote the use of multimodal analgesia; advocate for sensible procedure-specific opioid-prescribing guidelines; educate clinicians in nonopioid pain management techniques including regional anesthesia; and generate the evidence needed to support meaningful policies and changes in clinical practice. Locally, at the hospital level, RAAPM experts can implement evidence-based multimodal analgesic clinical pathways [8]. Multimodal analgesia consists of using two or more analgesic modalities targeting pain pathways at various levels to improve pain control, while also aiming to reduce opioid utilization and related adverse effects [9]. These types of pathways or protocols have been widely applied in the joint replacement population. This review focuses on the current state of evidence on individual elements of a multimodal analgesic pathway for TKA patients and suggests future research directions to improve the clinical care of this surgical population in the future.

Regional anesthesia versus regional analgesia

For the purpose of this review, we mainly address regional *analgesic* techniques as a component of multimodal analgesia for the perioperative management of TKA patients rather than regional *anesthesia* for intraoperative care. Intraoperatively, there are convincing data to support the use of neuraxial anesthesia as the first choice over general anesthesia for TKA patients [10,11]. The odds of developing pulmonary compromise, cardiac complications, pneumonia, all-cause infection, and acute kidney injury; requiring mechanical ventilation postoperatively or needing a blood transfusion; or resulting in death 30 days after surgery are all decreased for TKA patients with neuraxial anesthesia when compared to those with general anesthesia [10]. When neuraxial and general anesthesia are combined, the odds of pulmonary compromise, all-cause infection, need for postoperative mechanical ventilation, and death 30 days after surgery remain decreased when compared to that in general anesthesia alone [10].

Multimodal analgesia

Any evidence-based clinical pathway for TKA patients must begin with multimodal analgesia [12,13]. The 2016 guidelines developed by multiple anesthesiology and pain medicine societies for postoperative pain management recommend patient education, a pain management plan emphasizing multimodal analgesia, and patient information about opioid tapering after hospital discharge [14]. For joint arthroplasty patients in particular, the use of more than two modes of analgesia compared to an opioid-only regimen is associated with decreased odds of respiratory complications, length of stay, and dose of prescribed opioid after surgery [15]. While opioids remain to be part of the overall pain management plan for major surgery like TKA [8], this review focuses on the nonopioid modalities. When creating a multimodal analgesic protocol for TKA patients, several categories of nonopioid analgesic agents are available (Table 1).

Table 1
Nonopioid modalities available for inclusion in multimodal analgesic clinical pathways for patients with total knee arthroplasty.

Class	Mechanism of Action	Options	Frequency	Considerations
Nonpharmacologic	Variable	Patient Education Compression Cryotherapy Acupuncture Electrical stimulation	Routine	No clear guidelines
NSAIDs	Nonselective COX-1,2 inhibition Selective COX-2 inhibition	Ketorolac Ibuprofen Celecoxib	Routine	Renal insufficiency, gastric ulcers, platelet dysfunction, cardiovascular disease
Acetaminophen	Central prostaglandin synthesis inhibition	Acetaminophen (Paracetamol)	Routine	Hepatic dysfunction
Gabapentinoids	Binding to alpha-2-delta subunits of voltage-dependent calcium channels	Gabapentin Pregabalin	If indicated	Renal impairment
NMDA Antagonists	N-methyl-D-aspartate blockade	Ketamine Magnesium	If indicated	Severe psychiatric disorders, increased intracranial or intraocular pressure (ketamine only)
Local and Regional Analgesia	Sodium channel blockade	Spinal/Epidural Lumbar Plexus ± Sacral Plexus Femoral Nerve ± Sciatic Nerve Femoral Nerve ± LIA Adductor Canal ± LIA Adductor Canal ± IPACK LIA Only	Routine	Allergy to local anesthetic, site infection, available resources and training level of staff

NSAIDs = nonsteroidal anti-inflammatory drugs; NMDA = N-methyl-D-aspartate; LIA = local infiltration analgesia; IPACK = infiltration between the popliteal artery and capsule of the knee.

Nonpharmacologic modalities including patient education

Before delving into the wide variety of medications that may be prescribed for pain management postoperatively, we should first address "drug-free" interventions. Nonpharmacologic modalities such as cryotherapy, compression, acupuncture, and transcutaneous electrical nerve stimulation may offer analgesic benefits for TKA patients [16], although clear guidelines have not been established [17]. Patient education and engagement in pain management may be as important as the medications and interventions we employ [18]. First, setting realistic expectations for the goals of postoperative pain management before surgery is important. Explaining to patients that the goal is not to be "pain free" but rather a manageable pain level to facilitate early rehabilitation is key. A recent article in The New York Times details how a German anesthesiologist explained to an American patient why her outpatient postoperative pain would be managed only without opioids: "Pain is a part of life. We cannot eliminate it nor do we want to. The pain will guide you. You will know when to rest more; you will know when you are healing" [19]. Having conversations like this that normalize opioid-sparing analgesia and highlight the short- and long-term benefits of minimizing opioids may help patients make decisions about their own pain management. While multimodal analgesic protocols have become more common, they can be confusing for patients trying to navigate the multitude of options. One study has shown that patient education using a cognitive aid that clearly lists the elements of the pain management regimen in lay terms can decrease inpatient opioid use following TKA [20]. Patient education should also be available where regular people go for information—the Internet. There is little information available for patients online about regional anesthesia options for perioperative pain management, and what is available is often written above recommended reading levels [21]. If patients do not know about this opioid-sparing option, they cannot ask for it. In general, regional anesthesia continues to be underutilized even in cases like TKA when it clearly offers benefits [22]. A direct-to-patient educational strategy may prove invaluable in decreasing the disparity of regional anesthesia access in the future.

Nonsteroidal anti-inflammatory drugs

There is overwhelming evidence supporting the use of nonsteroidal anti-inflammatory drugs (NSAIDs) as an integral part of multimodal pain management for a variety of surgeries [25,26]. NSAIDs produce their anti-inflammatory and analgesic effects by blocking central and peripheral prostaglandin production by cyclooxygenase (COX) inhibition. Preoperative administration of NSAIDs has been consistently shown to decrease postoperative pain and opioid consumption and increase patient satisfaction compared to placebo [26]. The efficacy of postoperative administration of NSAIDs has also been demonstrated to improve pain scores, decrease opioid consumption, and improve physical therapy outcomes for patients undergoing TKA [27]. Caution must be exercised in patients with renal insufficiency, gastric ulcers, and platelet dysfunction. For patients with a history of gastric ulcers, selective COX-2-inhibiting agents like celecoxib may be preferred [23]. Use of NSAIDs in patients with a history of coronary artery disease should at least warrant careful consideration. Prudent recommendations limit routine NSAID use to 48 h in patients at risk for postoperative cardiovascular events and avoid high doses [24].

Acetaminophen

Acetaminophen is the most commonly prescribed analgesic for the treatment of acute pain in the United States [25]. Acetaminophen primarily inhibits central prostaglandin synthesis and only minimally affects peripheral COX enzymes [26]. Perioperative administration of acetaminophen for patients undergoing a range of surgeries decreased opioid consumption and pain scores, even when only a single dose was administered preoperatively [27,28]. A combination of analgesics from different classes may provide additive analgesic effects with fewer side effects than when a single therapeutic drug is used. Because acetaminophen and NSAIDs have different mechanisms of action, the combination may offer superior analgesia (decreased pain intensity and analgesic supplementation) compared with either drug alone [29]. The intravenous formulation of acetaminophen may be used for patients who cannot tolerate oral intake or will be fasting for an extended period of time; otherwise, the oral formulation may be preferred [30,31]. A recommended dosing regimen for a surgical patient with normal liver function is 1 g of acetaminophen preoperatively followed by 1 g every 6 h postoperatively. Daily dose should be decreased in patients with hepatic dysfunction.

Gabapentinoids

Gabapentinoids including gabapentin and pregabalin act by binding to alpha-2-delta subunits of voltage-dependent calcium channels in presynaptic afferent neurons [32]. Their anti-allodynic and anti-hyperalgesic properties are used for treating neuropathic pain. These properties may also be beneficial in acute postoperative pain. Preoperative administration has consistently been found to reduce postoperative pain, opioid consumption, and opioid-related adverse effects for a variety of surgeries [33,34]. Commonly reported adverse effects, even with a single preoperative dose of gabapentinoids, include sedation and dizziness [35], which may preclude routine administration. Although there may be benefits in de novo administration of gabapentinoids perioperatively, an optimal dosing regimen has not been determined. Indications may include preoperative chronic opioid therapy or a pre-existing chronic pain condition (e.g., neuropathic pain). One review recommends pregabalin over gabapentin, as it may have the added advantages of improved sleep and decreased anxiety [38]. The review suggests a dosing regimen of a single dose of 150 mg pregabalin 1–2 h preoperatively with continuation postoperatively for several days only when needed [38]. There are no absolute contraindications to gabapentin or pregabalin. However, doses should be decreased in patients with renal impairment, and patients treated with opioids and gabapentinoids concurrently may warrant careful monitoring [36]. Gabapentinoids have been associated with abuse potential [37].

N-methyl-D-aspartate receptor antagonists

Ketamine is a phencyclidine derivative originally developed as an intravenous anesthetic. Ketamine acts through a variety of receptors: N-methyl-D-aspartate (NMDA), acetylcholine, gamma aminobutyric acid, mu opioid, and others [38]. The use of intraoperative subanesthetic doses of ketamine has been associated with decreased pain intensity and rescue analgesic requirements [39] in the immediate perioperative period and decreased opioid consumption for up to six weeks postoperatively [40,41]. One challenge in implementing subanesthetic doses of ketamine in a multimodal analgesic protocol is the variability in described dosing regimens in published studies. The multi-society guideline on management of postoperative pain recommends the use of ketamine for patients undergoing major surgery, opioid-tolerant patients, or patients with contraindications to opioids [14]. More recently, the American Society of Regional Anesthesia and Pain Medicine has issued consensus guidelines on the use of intravenous ketamine for acute pain management, which provide clinicians practical advice based on available evidence [38]. When applying published doses of subanesthetic ketamine intraoperatively, context is important. The commonly applied intravenous regimen of 0.5 mg/kg bolus followed by 0.25 mg/kg/h is based on a study conducted by De Kock and colleagues in abdominal perineal resection patients; on average, patients weighed 70 kg, and surgery lasted for 4 h, which means that the maximum dose was approximately 105 mg [42]. Potential side effects include hallucinations, nightmares, sympathetic activation, and excessive salivation. Contraindications include severe psychiatric disorders and increased intracranial or intraocular pressure.

Magnesium may also offer nonopioid analgesia through NMDA receptor antagonism. A meta-analysis of 20 randomized controlled trials (RCTs) found the systemic administration of perioperative magnesium reduced postoperative pain and opioid consumption [43]. Perioperative intravenous administration of magnesium has been found to improve postoperative analgesia in a variety of surgeries [44–46] and may prolong spinal blockade [47]. One recommended dosing regimen consists of a magnesium sulfate 30–50 mg/kg bolus, followed by 8–10 mg/kg/h intraoperative infusion [48]. Side effects of magnesium may include dizziness, headache, nausea, vomiting, shivering, and cardiovascular events but are not common with perioperative administration [43], given the doses used should be below toxic levels [49].

Local and regional analgesia

Local anesthetics can be used in a variety of techniques to provide targeted nonopioid analgesia. Over time, these techniques have evolved in terms of selectivity, as the goal of optimal pain control has become balanced with the goal of early mobility [50] (Fig. 1).

Neuraxial techniques

ASA practice guidelines for acute pain management in the perioperative setting include specific mention of neuraxial techniques as a component of multimodal analgesia for patients who undergo major surgeries including lower extremity arthroplasty due to decreased odds of developing postoperative cardiac complications, pulmonary complications, and prolonged ileus [9]. To provide complete regional analgesia for TKA, the nerve roots L3 to S2 must be covered, which provide peripheral nerve branches and can be divided into anterior and posterior groups [50]. For TKA patients, a single dose of intrathecal morphine may reduce pain scores up to 24 h after administration [51]. Patients require postoperative monitoring for respiratory depression after the administration of intrathecal morphine. Where it is available, a potential alternative is diamorphine, which may provide similar analgesia and may be associated with less respiratory depression [52]. While there may be advantages favoring more selective blocks over neuraxial blocks for unilateral lower extremity surgery [53,54], neuraxial techniques do provide effective analgesia for TKA patients [55,56] and can be performed by every anesthesiologist without the need for specialized equipment or training. Given that approximately three-quarters of patients in the United States receive general anesthesia alone without any regional analgesia [10], neuraxial techniques should not be completely abandoned if these are the only forms of regional anesthesia available [57]. Contraindications to neuraxial anesthesia include infection

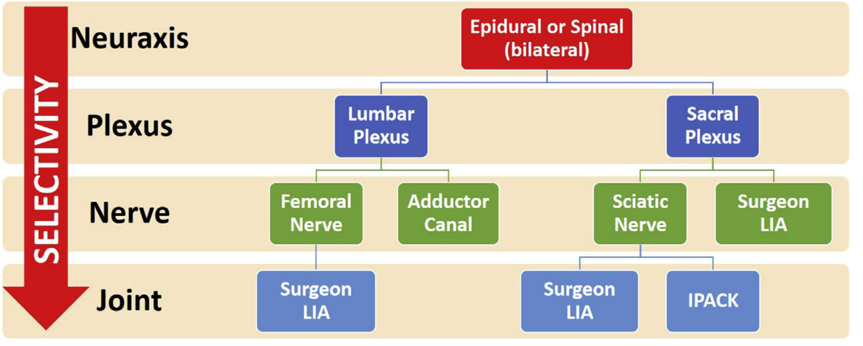

Fig. 1. Regional analgesic options for TKA patients moving from least selective to most selective; LIA = local infiltration analgesia; IPACK = Infiltration between the Popliteal Artery and Capsule of the Knee.

at the injection site, bleeding diathesis, known left ventricular outflow obstruction, hypovolemia, increased intracranial pressure, and patient refusal [58].

Peripheral regional analgesia

Peripheral regional analgesic techniques consist of nerve and plexus (lumbar and sacral) blocks and can be performed unilaterally to select for the operative limb (Fig. 1). Unlike neuraxial block techniques, no single peripheral nerve or plexus block can provide complete analgesia of the lower limb. When used in a multimodal analgesic regimen, peripheral nerve block (PNB) techniques can result in improved quality of recovery, early discharge after ambulatory surgery, decreased hospital length of stay, lower pain scores, and decreased overall need for supplemental analgesics including opioids [59,60].

The choice of single-injection versus continuous nerve block has been addressed by the multi-society guidelines for the management of postoperative pain [14]; for major surgery with an expectedly long duration of pain, continuous blocks are preferred. Continuous peripheral nerve block (CPNB) techniques have been studied for decades, and they extend the duration of targeted local anesthetic-based analgesia beyond what is feasible with single-injection nerve block techniques even with the use of adjuvants [59,61]. An additional advantage of CPNB over single-injection blocks is titratability, which allows personalization of local anesthetic dosing to an individual patient's needs. A prospective cohort measuring postoperative pain on the first day after surgery in more than 50,000 patients in 179 different surgeries reported that the highest pain scores occur after orthopedic and trauma procedures involving the extremities [62]. For patients who undergo TKA, moderate to severe pain may last for several days, and more than half of patients may report persistent pain at 3 months [63]. These data suggest that TKA patients may be ideal candidates for CPNB. However, being able to provide CPNB for patients on a regular basis requires a system that may not be available for various reasons in every practice setting [64], and implementation of new CPNB programs remains challenging [65].

When choosing which peripheral regional analgesic techniques to offer patients, many factors have to be considered. For a complete block of the lower extremity, a combination of lumbar plexus and parasacral (sacral plexus) blocks can be performed for knee surgery [66]. While this can provide complete analgesia after TKA, the major disadvantage is that this combination renders the limb insensate and prevents active mobilization [67]. Although more distal targets, femoral nerve and sciatic nerve blocks produce a similar effect and have the same disadvantage [68]. With the increasing use of multimodal analgesia, the continuing need for a sciatic nerve block for analgesia after TKA has come under question [69]. Evidence supports analgesic efficacy of a sciatic nerve block, but the benefits may only be clinically relevant for a day or two after surgery [67,70] and may be provided by alternative methods [71]. Femoral nerve blocks have a well-established body of evidence supporting their analgesic efficacy for TKA patients but have come under fire in the last several years due to concerns over fall risk as the expected time point for the first postoperative ambulation moves much earlier [72]. As a result, more distal and selective PNB techniques of the femoral nerve branches have emerged [73,74] and are commonly referred to as "adductor canal blocks" within the regional anesthesia and orthopedic surgery community. Although these selective techniques are technically performed in the distal femoral triangle and proximal to the anatomic adductor canal [75], we will also refer to them as "adductor canal blocks" for the purposes of this review. The adductor canal contains more than just the saphenous nerve, and anatomic studies demonstrate that the nerve to vastus medialis and other nerve branches are also located in this compartment and contribute to the innervation of the knee [76]. An alternative technique involves a distal adductor canal injection and has been referred to the "popliteal plexus block" [77]; a cadaver study has demonstrated spread of injectate from the adductor canal into the popliteal fossa with coverage of the genicular branch of the posterior obturator nerve [78]. The use of adductor canal blocks for TKA patients is increasing [79], as data support advantages over femoral nerve blocks in terms of quadriceps muscle preservation and physical therapy achievement without sacrificing pain control when a multimodal analgesia protocol is employed [80,81].

Absolute contraindications to peripheral regional anesthesia include allergy to local anesthetics or patient refusal. Relative contraindications include an active infection at the site of the injection, inability to cooperate, pre-existing neurological deficits along the distribution of the intended block, and anticoagulation or bleeding disorders for deep blocks [82]. In these latter situations, careful consideration of risks and benefits is warranted.

Local infiltration analgesia

Local infiltration analgesia (LIA) is a local anesthetic administration technique performed by the surgeon in close proximity to the operative site. For TKA, the LIA technique involves injection of dilute local anesthetics with adjuvants [83,84] within multiple layers surrounding the knee joint (the posterior capsule, retinacular layer, and subcutaneous tissue) [83]. Within a multimodal analgesia regimen, LIA can be used as the sole method of local anesthetic administration [84]; however, combining LIA with PNB reliably produces better outcomes for TKA patients [85,86]. LIA may eliminate the need for sciatic nerve blockade in practices where a combination of PNB techniques has been used for postoperative analgesia after TKA [71], since the durations of action of these two techniques are similarly less than one day [87]. Compared to techniques in regional anesthesia and analgesia, LIA does not require anesthesiologists with specialized skills or special equipment, and this may be an advantage in certain practice settings. Across the United States, PNB is generally underutilized for TKA [88], and LIA is one method to ensure that every TKA patient has access to local anesthetic as part of an opioid-sparing multimodal analgesic regimen for pain management. Although liposomal bupivacaine has been described for use in LIA for TKA patients, a Cochrane review has not determined a clear difference in analgesia between liposomal bupivacaine and plain bupivacaine in surgical site infiltration [89], arguably because the often-advertised 72-h duration is inconsistent and rarely reproducible.

Infiltration between the popliteal artery and capsule of the knee

Infiltration between the popliteal artery and capsule of the knee or "IPACK block" is a new technique developed by Dr. Sanjay Sinha, an anesthesiologist in Hartford, CT, USA, for TKA patients [90]. The IPACK block can be used in place of surgeon-administered LIA to provide analgesia of the posterior knee. It is typically performed by a regional anesthesiologist with ultrasound guidance (Fig. 3) and combined with PNB technique of the lumbar plexus, either a femoral nerve or an adductor canal block [91]. Few published studies to date have investigated the IPACK block. Two prospective studies suggest benefits such as decreased pain scores and opioid consumption favoring the use of IPACK when compared to no infiltration on the first day after TKA [92,93]. The optimal volume or dose of local anesthetic for the IPACK block is not currently known, but one cadaver study suggests that volumes in excess of 20 ml may spread to the terminal branches of the sciatic nerve [94].

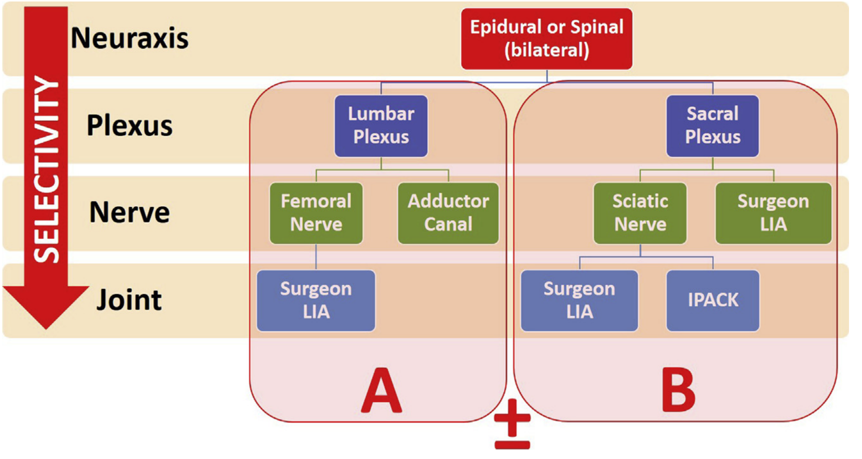

Fig. 2. Regional analgesic options for TKA organized by selectivity: one technique from Box A is required; one technique from Box B can be combined with a technique from Box A for additional analgesia but is optional.

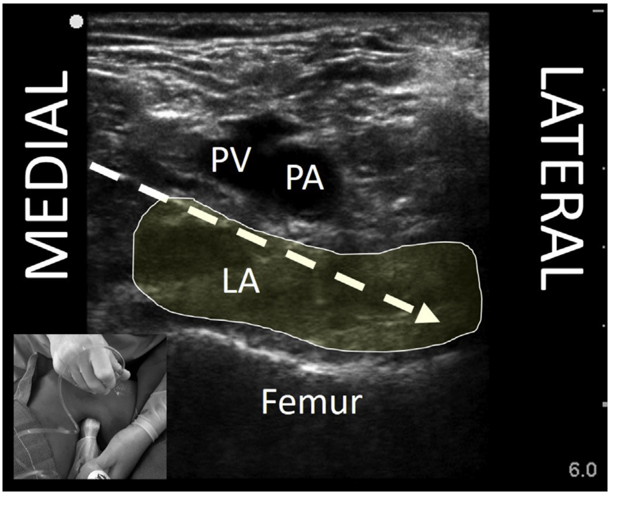

Fig. 3. Sonogram demonstrating the IPACK (Infiltration between the Popliteal Artery and Capsule of the Knee) block; dashed arrow and inset box demonstrate needle trajectory from medial to lateral; LA = local anesthetic; PV = popliteal vein; PA = popliteal artery.

Putting it all together

Every institutional clinical pathway for TKA requires a solid foundation in multimodal analgesia [12]. Table 1 provides a general checklist with categories of modalities that should be considered. Those labeled "Routine" should be used in every TKA patient without a contraindication, and those labeled "If indicated" can be added for the appropriate patient. Choosing the local and regional analgesic can seem daunting given all of the different options. However, this decision is dependent on multiple factors (e.g., staff training, equipment, and logistics) and can be addressed systematically. When deciding between multiple techniques for the same indication, one approach is to use a pragmatic framework using the following criteria: 1) increasing access; 2) enhancing efficiency; 3) decreasing disparities; and 4) improving outcomes [57]. Weights or points can be applied to each category and competing techniques can be scored separately, and these scores can then be compared to each other to aid in decision-making. Alternatively, Fig. 2 offers a more practical approach for TKA. When creating a multimodal analgesic protocol, one local or regional analgesic technique in Box A is *required*; a second local or regional analgesic technique from Box B can be combined for additional analgesia but is *optional*.

Future directions for TKA pain management

Much of the research on pain management strategies for TKA has focused on the acute post-operative period. While evidence supports the efficacy of regional analgesic techniques in the short term, published studies have not shown long-term benefits after both single-injection PNB and CPNB [95,96]. Given the natural trajectory of pain after TKA, these results may not be surprising. In a prospective, observational study, TKA patients who report higher maximal pain scores on the first 8 postoperative days have a higher likelihood of developing persistent postsurgical pain (PPSP) [63]. Approximately 11% of TKA patients 3 months after surgery develop chronic persistent pain with a neuropathic component [63]. Unlike patients on a normal recovery trajectory whose maximal pain scores decrease after postoperative day 5, patients who develop severe chronic pain with a neuropathic component experience an increase in pain at day 5 [63].

Addressing the problem of pain in the subacute period for TKA patients has received much less focus than that during the immediate postoperative period and represents a tremendous opportunity for research and clinical innovation. In theory, the subacute period represents a vulnerable time for patients recovering from surgery, and inadequate pain management may lead to the development of PPSP [97]. A transitional pain service (TPS), first described at the Toronto General Hospital in 2015, is a novel pain service that provides surveillance and early intervention with the goal to prevent PPSP and long-term opioid dependence [98]. The TPS identifies patients at risk based on perioperative pain, opioid use, and negative affect and involves in their care at every point in the perioperative continuum up to 6 months after surgery [98]. The TPS is a multidisciplinary team consisting of pain medicine specialists, advanced practice nurses, psychologists, and physiotherapists offering a range of interventions for high-risk patients. To date, the TPS has been successful in impacting patients' pain trajectories, preventing the transition from acute to chronic pain in some patients, improving pain and function, and decreasing opioid consumption.

For post-TKA patients who have greater than normal pain preventing rehabilitation and experience difficulty with weaning opioids, one promising new intervention is the use of percutaneous peripheral nerve stimulation (PNS) [99]. Although neuromodulation has been used extensively and successfully in the treatment of chronic pain, its use in acute pain management is a bourgeoning new field [100]. Procedurally, there are many similarities between ultrasound-guided CPNB and ultrasound-guided PNS lead placement except that PNS leads do not have to be as close to the target nerve or plexus [101]. Leads are approved for 60 days of use. In a study of TKA patients with pain insufficiently treated with oral analgesics, patients 8–58 days postoperatively had their pain decreased by an average of 93% at rest and 30% with active knee motion without motor weakness [99,100].

Summary

For TKA patients, optimal postoperative pain management requires a multimodal approach including regional anesthesia, a subspecialty that continues to evolve rapidly. Despite ample evidence showing the multitude of benefits of applying regional analgesia, its underutilization in the United States for a common surgery like TKA highlights an area that needs improvement. As new regional analgesic techniques like the IPACK block continue to emerge, applying practical tools to evaluate their potential utility should help clinicians assemble the multimodal analgesic protocol that is correct for their practices. Future research will need to explore new interventions and care models that will aid patients in the subacute period when they exhibit abnormal pain trajectories to prevent the development of persistent postsurgical pain.

Practice points

- The opioid crisis offers an opportunity for regional anesthesiology and acute pain medicine specialists to take a leadership role and make a positive impact.
- The use of a multimodal analgesic pathway that combines systemic nonopioid medications and regional anesthesia techniques is associated with improved pain scores, lower opioid requirements, shorter hospital stays, and fewer complications for a variety of surgeries like total knee arthroplasty.
- Regional anesthesia for total knee arthroplasty remains underutilized despite well-established benefits.
- Utilizing a pragmatic framework or other decision support tool may help clinicians select the combination of elements that will work best in a multimodal analgesic protocol at their institutions.
- The subacute period represents a vulnerable period of time for patients recovering from surgery when abnormal pain trajectories can be identified, and a transitional pain service may provide timely intervention to prevent the progression to persistent postsurgical pain and long-term opioid dependence.

Research agenda

- Various combinations of elements lead to multiple different multimodal regimens; comparative effectiveness studies of these different regimens in specific practice settings (e.g., private practice, and academic) are needed.
- The feasibility of applying pragmatic criteria in comparing new techniques in regional anesthesia and acute pain medicine needs to be demonstrated, and the resulting outcomes of those decisions along with practical implementation deserve further exploration.
- For TKA patients recovering from surgery in the subacute period, early detection methods (e.g., home monitoring) to identify patients who are experiencing abnormal pain trajectories are needed.
- New techniques like the IPACK block should be studied in rigorous randomized clinical trials with a placebo control to determine efficacy and head-to-head against active comparators to measure effectiveness.
- New technologies like peripheral neuromodulation may have beneficial effects on TKA patients' long-term outcomes, but large prospective studies are required.
- Model options for creating a transitional pain service in different practice settings, including tools for detecting patients at risk for developing chronic pain, are needed.

Conflicts of interest

None of the authors has any conflicts of interest to declare.

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