

# Anesthesia and Analgesia Practice Pathway Options for Total Knee Arthroplasty

## *An Evidence-Based Review by the American and European Societies of Regional Anesthesia and Pain Medicine*

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**Abstract:** In 2014, the American Society of Regional Anesthesia and Pain Medicine in collaboration with the European Society of Regional Anesthesia and Pain Therapy convened a group of experts to compare pathways for anesthetic and analgesic management for patients undergoing total knee arthroplasty in North America and Europe and to develop a practice pathway. This review is intended to be an analysis of the current literature to assist individuals and institutions in designing a pathway for total knee arthroplasty that is based on existing evidence and expert recommendation and may be customized according to individual settings.

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Total knee arthroplasty (TKA) is one of the most commonly performed orthopedic procedures, with an estimated more than 700,000 total knee replacements (TKRs) performed annually in the United States. The annual expected growth rate of TKA is 7.9% in the United States and 5.3% to 14.7% in the main European countries.<sup>1</sup> Patients undergoing TKA report improved health-related quality of life and functional status.<sup>2–4</sup> Unfortunately, it is known to cause moderate to severe pain in most patients and is therefore regarded as one of the most painful orthopedic procedures.<sup>5</sup> In addition, patients who are identified as at risk of chronic

pain may benefit from aggressive perioperative pain management in an attempt to prevent central sensitization.<sup>6</sup> The extensive increase in the number of patients undergoing TKA requires specific customized management of care. Clinical pathways are tools created to organize care of well-defined groups of patients while maintaining a high quality of efficient care during a well-defined, limited episode of care.<sup>2</sup> An effective TKA pathway would link the current evidence to individual practices with the goal of having a positive impact on perioperative outcomes (Fig. 1). In 2014, the American Society of Regional Anesthesia and Pain Medicine (ASRA) in collaboration with the European Society of Regional Anaesthesia and Pain Therapy (ESRA) convened a group of experts to compare pathways for anesthetic and analgesic management for patients undergoing TKA between North America and Europe and develop a practice pathway. It became immediately clear that standardized pathways are not ubiquitous in Europe or North America. Rather, each practice was using a combination of different techniques dictated by the orthopedic surgeons, anesthesiologists, or simply the needs of the site. The panel quickly determined that it was going to be impossible to define or compare a specific pathway on either continent. Therefore, this review is intended to be an analysis of the current literature to assist individuals and institutions in designing a pathway for TKA that is based on existing evidence and expert recommendation and may be customized according to individual settings.

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## METHODS

The ASRA and ESRA panelists were chosen based on their demonstrated expertise in various issues related to anesthetic (neuraxial vs general) and analgesic (eg, multimodal analgesia, peripheral nerve blocks [PNBs]) management for patients undergoing TKA. Panelists received no compensation for their contributions; nor did any declare a conflict of interest pertinent to the topic. Panelists were charged with performing an extensive review of the literature; summarizing and presenting their findings at the 2014 American Society of Regional Anesthesiology and Acute Pain Medicine Conference, Chicago, Illinois; and producing an article based on their scholarly work. A comprehensive review of the subtopics (anesthesia type and outcomes, PNBs, infiltrative techniques, and multimodal oral analgesia) was performed, including publications involving comparative techniques, efficacy, and complications. In each section, the authors created their work with a combination of literature review and experience-based opinion. This document is not intended to define the standard of care and is not a formal systematic review. Rather, it is intended to provide a scoping review of specific components of a regional anesthesia pathway for TKA.<sup>7</sup>

## RESULTS

### Anesthesia Type and Outcomes

The discussion regarding the choice of anesthesia and the potential impact on outcomes has been ongoing for many decades, and much controversy still remains.<sup>8</sup> A number of studies including clinical trials, meta-analyses, and population-based investigations have compared anesthetic (general vs neuraxial vs peripheral) and analgesic (neuraxial, PNBs, infiltration, and multimodal medication) options (Table 1). Despite significant additions to our knowledge in recent years, many questions remain, and important caveats need to be considered when interpreting the data.<sup>15</sup>

For example, with perioperative practices substantially differing between institutions, results of both randomized trials conducted in single-center settings and population-based investigations may have limited applicability to highly specialized practices, which may have developed protocols with good outcomes. Whereas the former may be burdened by lack of external validity, the latter sources of information, representing population-based averages, may lack applicability to a specific institution. It must also be noted that anesthetic and analgesic techniques represent only a small piece of the many interventions that influence major perioperative outcomes.

Until recently, evidence regarding the impact of the type of anesthesia on perioperative outcomes relied on a number of relatively small, often single-institutional investigations widely considered underpowered to detect differences in perioperative morbidity and mortality. More recently, however, a meta-analysis involving 28 studies and 1538 patients performed by Macfarlane et al<sup>16</sup> focusing on randomized controlled trials (RCTs) involving TKR patients concluded that “there was insufficient evidence from RCTs alone to conclude that anesthetic technique influenced mortality, cardiovascular morbidity, other than postoperative hypotension, or the incidence of deep venous thrombosis and pulmonary embolism when using thromboprophylaxis.” Furthermore, the authors did not find a difference in blood transfusions or length of operating time but improved pain management profiles and possibly decreased length of stay (LOS) attributable to neuraxial

anesthesia/analgesia. The inability to identify significant differences in major complications, however, was likely related to the relatively low sample size in the included studies.

With the advent of large database research, many of the previous limitations regarding sample size and external validity could be overcome, but at the expense of the inability to determine causality and take into account important clinical cofounders. In this context, an analysis of population-based administrative data from hundreds of hospitals in the United States including information on more than a quarter of a million TKA patients suggested that the risk of perioperative complications was significantly reduced when neuraxial anesthesia was used compared with general anesthesia.<sup>17</sup> Benefits of neuraxial anesthesia included an 83% lower mortality risk as well as similar reductions in the odds of pulmonary complications. Other benefits were found for lung infections and for gastrointestinal and renal complication risk. Interestingly, patients receiving a combination of neuraxial and general anesthesia had risk of various complications between those for neuraxial and general anesthesia alone. Advantages in LOS and cost were also observed. In addition, the study showed that approximately only one fourth of patients actually received a neuraxial anesthetic, pointing toward a potentially large positive impact on the health care system if the use of neuraxial anesthesia was to be expanded. With the inability to establish causal relationships, however, the potential attributable impact remains speculative.

Using various databases, other authors were able to draw similar conclusions. Without specifically differentiating between hip and knee arthroplasties, Chang et al<sup>18</sup> observed higher surgical site infection (SSI) risk among joint arthroplasty patients receiving general compared with neuraxial anesthesia in a cohort of 3081 Taiwanese patients. Similarly, Liu et al<sup>12</sup> linked the use of neuraxial versus general anesthesia to reduced pneumonia and systemic infection risk using the American College of Surgeons National Surgical Quality Improvement Program database. Working with data from the same source,<sup>12</sup> Pugely et al<sup>13</sup> found that short-term complication risk was higher in those receiving general versus neuraxial anesthesia for TKR. A recent retrospective case-control study undertaken to confirm or refute these findings found no difference in the incidence of SSI in patients undergoing total joint arthroplasty under general versus neuraxial anesthesia.<sup>7</sup> In this study, Kopp et al<sup>7</sup> also examined the effects of PNBs on SSI and found no significant effect. However, increasing body mass index and current smoking were found to significantly increase the incidence of SSI in patients undergoing lower-extremity total joint arthroplasty. A recent meta-analysis that included 13 studies concluded that the use of neuraxial anesthesia was associated with a significant reduction in the incidence of postoperative SSI compared with general anesthesia in TKA and total hip arthroplasty (THA).<sup>19</sup> Additional studies have linked neuraxial anesthesia to be independently associated with reduced need for critical care services (odds ratio [OR], 0.55; 95% confidence interval [CI], 0.51–0.6) as well as inpatient falls (OR, 0.70; 95% CI, 0.56–0.87).<sup>10,20</sup> It has to be mentioned, however, that, although population-based analyses seem to produce results favoring the use of neuraxial anesthesia, not all studies show better outcomes for all complications. Furthermore, clinical trial results from highly specialized institutions may show good outcomes in terms of recovery profiles with general anesthesia.<sup>11</sup>

A recent retrospective, propensity score–matched cohort study also suggests a strong association between spinal anesthesia and a lower 30-day mortality, as well as a shorter hospital LOS after elective TKA or THA.<sup>21</sup> The propensity score matching allowed the authors to minimize the baseline differences between groups, therefore limiting the treatment selection bias that is often present in retrospective studies.

- ☑ Decrease pain
- ☑ Decrease hospital length of stay
- ☑ Decrease cost
- ☑ Decrease morbidity & mortality
- ☑ Decrease the use of resources
- ☑ Improve long-term functional outcomes
- ☑ Decrease in-hospital falls
- ☑ Decrease surgical site infection
- ☑ Decrease rate of blood transfusion
- ☑ Decrease the incidence of chronic pain
- ☑ Improve patient satisfaction

FIGURE 1. Goals of a TKA pathway.

**TABLE 1. General Versus Regional Anesthesia in TKA**

Year	Author	Title/Findings	Type	No. Patients	Journal
2016	Perlas et al <sup>21</sup>	Anesthesia Technique and Mortality After Total Hip or Knee Arthroplasty: A Retrospective, Propensity Score–Matched Cohort Study	Cohort	10,868	<i>Anesthesiology</i>
2015	Fleischhut et al <sup>22</sup>	Lower 30-d mortality, shorter LOS with spinal anesthesia Variability in Anesthetic Care for Total Knee Arthroplasty: An Analysis From the Anesthesia Quality Institute	Observational	108,625	<i>Am J Med Qual</i>
2014	Liu et al <sup>23</sup>	Differences in anesthetic care by patient and provider characteristics are prevalent Peripheral Nerve Blocks Versus General Anesthesia for Total Knee Replacement in Elderly Patients on the Postoperative Quality of Recovery Regional anesthesia with sedation facilitates faster postoperative recovery compared with general anesthesia	RCT	213	<i>Clin Interv Aging</i>
2014	Memtsoudis et al <sup>10</sup>	Inpatient Falls After Total Knee Arthroplasty: The Role of Anesthesia Type and Peripheral Nerve Blocks	Observational	191,570	<i>Anesthesiology</i>
2013	Harsten et al <sup>11</sup>	Peripheral nerve block use is not associated with inpatient falls Recovery After Total Intravenous General Anesthesia or Spinal Anesthesia for Total Knee Arthroplasty: A Randomized Trial	RCT	120	<i>Br J Anaesth</i>
2013	Liu et al <sup>12</sup>	General anesthesia showed more favorable recovery effects than spinal anesthesia Neuraxial Anesthesia Decreases Postoperative Systemic Infection Risk Compared With General Anesthesia in Knee Arthroplasty	Observational	16,555	<i>Anesth Analg</i>
2013	Pugely et al <sup>13</sup>	Neuraxial anesthesia was associated with lower odds for complications compared with general anesthesia Differences in Short-term Complications Between Spinal and General Anesthesia for Primary Total Knee Arthroplasty	Observational	14,052	<i>J Bone Joint Surg Am</i>
2012	Stundner et al <sup>14</sup>	General anesthesia was associated with higher risk of complications compared with spinal anesthesia Comparative Perioperative Outcomes Associated With Neuraxial Versus General Anesthesia for Simultaneous Bilateral Total Knee Arthroplasty	Observational	15,687	<i>Reg Anesth Pain Med</i>
2007	Napier et al <sup>24</sup>	Neuraxial anesthesia was associated with lower rates of blood transfusions and, by trend, decreased morbidity Postoperative Benefits of Intrathecal Injection for Patients Undergoing Total Knee Arthroplasty	2-Group comparison	85	<i>Orthop Nurs</i>
2006	Chu et al <sup>25</sup>	The overall effect of pain control was greater with intrathecal injections vs general anesthesia Postoperative Outcome in Chinese Patients Having Primary Total Knee Arthroplasty Under General Anaesthesia/Intravenous Patient-Controlled Analgesia Compared to Spinal-Epidural Anaesthesia/Analgesia	RCT	60	<i>Hong Kong Med J</i>
2004	Kudoh et al <sup>26</sup>	Regional anesthesia was associated with superior pain relief compared with general anesthesia A Comparison of Anesthetic Quality in Propofol+Spinal Anesthesia and Propofol+Fentanyl Anesthesia for Total Knee Arthroplasty in Elderly Patients	RCT	150	<i>J Clin Anesth</i>

Continued next page

TABLE 1. (Continued)

Year	Author	Title/Findings	Type	No. Patients	Journal
1996	Williams-Russo et al <sup>27</sup>	Propofol-spinal anesthesia provided better and faster recovery than propofol-fentanyl anesthesia Randomized Trial of Epidural Versus General Anesthesia: Outcomes After Primary Total Knee Replacement	RCT	262	<i>Clin Orthop Relat Res</i>
1995	Williams-Russo et al <sup>28</sup>	Epidural anesthesia is associated with faster postoperative rehabilitation Cognitive Effects After Epidural vs General Anesthesia in Older Adults. A Randomized Trial	RCT	262	<i>JAMA</i>
1992	Sharrock et al <sup>29</sup>	Type of anesthesia does not affect the magnitude or pattern of postoperative cognitive dysfunction Fibrinolytic Activity Following Total Knee Arthroplasty Under Epidural or General Anesthesia	RCT	21	<i>Reg Anesth Pain Med</i>
1991	Jørgensen et al <sup>30</sup>	No effect of anesthetic technique was found on clot formation and fibrinolytic activity Antithrombotic Efficacy of Continuous Extradural Analgesia After Knee Replacement	RCT	48	<i>Br J Anaesth</i>
1991	Mitchell et al <sup>31</sup>	Use of continuous extradural analgesia was associated with a lower incidence of deep vein thrombosis Prevention of Thromboembolic Disease Following Total Knee Arthroplasty. Epidural Versus General Anesthesia	RCT	72	<i>Clin Orthop Relat Res</i>
1991	Sharrock et al <sup>32</sup>	The incidence of proximal vein thrombosis was significantly lower with epidural anesthesia compared with general anesthesia Effects of Epidural Anesthesia on the Incidence of Deep-Vein Thrombosis After Total Knee Arthroplasty	Observational	705	<i>J Bone Joint Surg Am</i>
1990	Nielsen et al <sup>33</sup>	Use of epidural anesthesia reduced the risk of proximal thrombosis Lower Thrombosis Risk With Epidural Blockade in Knee Arthroplasty	RCT	36	<i>Acta Orthop Scand</i>
1990	Nielson et al <sup>34</sup>	The incidence of thrombosis was 2/13 in the epidural vs 10/16 in the general anesthesia group ( $P < 0.05$ ) Long-term Cognitive and Social Sequelae of General Versus Regional Anesthesia During Arthroplasty in the Elderly General anesthesia poses no more risk to long-term mental function than regional anesthesia	RCT	64	<i>Anesthesiology</i>

## Anesthesia Type and Outcomes in Subpopulations

Although less extensively studied, recent population-based analyses have identified benefits of neuraxial anesthesia over general anesthesia in subpopulations of patients undergoing TKA.<sup>35–39</sup> Patients with sleep apnea have been shown to benefit from having a neuraxial compared with a general anesthetic. Neuraxial anesthesia was associated with a reduction of major complications. Interestingly, the use of PNBs also decreased the need for critical care services after surgery.<sup>39</sup> For patients undergoing bilateral TKA, the use of neuraxial anesthesia was associated with an independent decrease in the need for blood transfusions (OR, 0.52; 95% CI, 0.45–0.6) but did not affect overall complication rates significantly.<sup>14</sup> Finally, a study examining whether there are beneficial effects of neuraxial anesthesia in patients across various age groups and/or levels of comorbidity burden suggested that this was indeed the case. Although the incidence of major complications was found to be significantly higher among older and sicker patients (26.1%) compared with the younger group without cardiopulmonary disease (4.5%), the use of neuraxial anesthesia was independently associated with better outcomes across all age and comorbidity cohorts.<sup>37</sup> It must be mentioned that some of the previously mentioned studies included both hip and knee arthroplasty patients in their cohorts, but in each case, the procedure type was taken into account during adjustment steps, thus rendering results relevant for TKA patients.

## Peripheral Nerve Blocks

Although epidural infusion was historically a popular analgesic option, limitations involving anticoagulation (eg, epidural hematoma),<sup>40,41</sup> opioid adverse effects (eg, nausea and pruritus),<sup>42</sup> hemodynamic issues (eg, hypotension),<sup>42</sup> and catheter-related complications (eg, unilateral nonoperative side insertion)<sup>43</sup> have left PNBs as a standard, commonly used alternative. Peripheral nerve block techniques have been shown to reduce perioperative complications.<sup>44</sup> In addition, they have proven to decrease the time to discharge readiness, conserve hospital resources, and improve patient satisfaction.<sup>45–47</sup> Single-injection femoral nerve blocks (FNBs) have been widely used to provide potent analgesia, but in doing so, they simultaneously induce profound quadriceps weakness for the duration of the injected local anesthetic. Continuous FNBs have been shown to provide a longer duration of analgesia than single-injection FNB.<sup>3</sup>

The quests for fast-track surgery, younger patients undergoing TKA, and early patient mobilization have been drivers for change in the management of postoperative pain. Years ago, as regional anesthesia was gaining popularity, it was common to combine a posterior lumbar plexus block (psoas) with a sciatic block to provide complete unilateral analgesia for patients undergoing TKA.<sup>48</sup> Although the analgesia provided was ideal, changes in postoperative thromboprophylaxis and recommendations to treat these blocks similarly to epidurals had an impact on this practice.<sup>41</sup> To decrease the risk of bleeding, yet maintain a similar degree of analgesia, FNBs, often in combination with a sciatic block, became commonplace. More recently, the impact of quadriceps weakness in the postoperative period has led practitioners to seek alternatives to femoral block that result in less quadriceps weakness. The ability to selectively block the sensory articular branches, or a combination of these, to the knee joint using ultrasound guidance without or with minimal motor impairment is an appealing option.

For surgical procedures such as TKA and anterior cruciate ligament reconstruction, randomized controlled clinical trials have focused on selective ultrasound-guided saphenous and obturator nerve blocks and reported significant reductions in postoperative pain management and opioid consumption.<sup>49–52</sup> This is not

surprising because the saphenous nerve can be easily visualized with ultrasound from the proximal thigh<sup>53</sup> at the level of the lesser trochanter and distally to the adductor canal.<sup>54</sup> It is notable that the adductor canal block (ACB) described by Lund et al<sup>55</sup> has been proven to have a significant pain-reducing effect in some studies evaluating TKA<sup>56,57</sup> but that other studies have failed to detect a similar effect.<sup>58</sup> Despite these conflicting results, many clinical centers have started to use ACBs after TKA, thereby replacing femoral catheters and lessening the postoperative quadriceps weakness.

Studies involving volunteers and surgical patients have conclusively established a decrease in quadriceps weakness after a single-injection ACB compared with the femoral nerve.<sup>54</sup> In 2 trials involving healthy volunteers, ACB decreased quadriceps strength less than 8% from baseline, compared with greater than 49% for femoral blocks, leading to improved mobilization.<sup>59,60</sup> Similarly, dramatic results are reported for surgical patients after TKA, without compromising analgesia to a statistically significant degree.<sup>56,61,62</sup> However, because of the protocol designs, it is possible that ACBs provided undetected inferior analgesia within the first 4 postoperative hours compared with femoral blocks,<sup>56,61,62</sup> and in fact, evidence for this supposition is provided in a study involving a single initial local anesthetic bolus and subsequent perineural local anesthetic infusion.<sup>63</sup>

Although the ACB as described by Lund et al<sup>55</sup> has exhibited very promising results, there have been some controversy and academic discussion as to what actually constitutes a block into the adductor canal, how the adductor canal can be clearly identified, and whether local anesthetic should be injected into the femoral triangle or adductor canal proper.<sup>64,65</sup> One must remember that the most common type of surgical approach for TKA involves a medial parapatellar arthrotomy and that the human knee joint is innervated by an anterior and a posterior group of sensory nerves. The most important anterior group of sensory nerves for this procedure can be targeted, based on solid anatomical evidence, with a selective low-volume block in the femoral triangle to anesthetize the saphenous nerve, the medial retinacular nerve (the terminal branch of the medial vastus muscle nerve), and the anterior branch of the medial femoral cutaneous nerve.<sup>66</sup>

Detailed cadaveric studies of the adductor canal consistently showed that the medial vastus nerve enters a separate fascial tunnel in the fascia covering the medial vastus muscle and superficial to the vastoadductor membrane.<sup>66</sup> When this fascial tunnel is opened, it can be seen that the entire tunnel is superficial to the vastoadductor membrane. Thus, an injection into the true adductor canal will not anesthetize the medial vastus nerve. Thus, a block in the femoral triangle seems to be more appropriate.

To determine the optimal point of injection of local anesthetic in the mid thigh for maximal sensory inhibition and minimal motor impairment, it is preferable to use internal landmarks visible by ultrasound.<sup>67</sup> With this technique, it is possible to ensure blockade of both the saphenous and the medial vastus nerve when injecting into the femoral triangle cephalad to the apex of the said triangle and not into the adductor canal missing to anesthetize the medial vastus nerve.

Perineural catheters have also been inserted into the adductor canal,<sup>55,61</sup> with randomized placebo-controlled investigations demonstrating the analgesic potential of continuous blocks after knee arthroplasty.<sup>68,69</sup> The results from studies comparing adductor and femoral catheters for knee arthroplasty provide a more complex picture compared with the single-injection data. The first randomized trial found that subjects with an adductor canal catheter retained 52% of their baseline quadriceps strength 24 hours after catheter insertion, compared with only 18% for subjects with a femoral catheter ( $P = 0.004$ ).<sup>57</sup> In contrast to the single-injection studies, no benefits on mobilization were identified.<sup>57</sup> A second

randomized trial reported improved mobilization at 24 hours for subjects with adductor canal versus femoral catheters<sup>70</sup>; however, the study protocol design makes the data for continuous blocks questionable,<sup>71</sup> and its results require future confirmation. Two additional randomized trials documented both improved mobilization (eg, standing, sitting) and ambulation with continuous adductor canal versus femoral infusions, but inferior analgesia at rest<sup>63</sup> and during physical therapy.<sup>72</sup> As with any technique, there is the potential for complications, and the ACB is not unique. Severe and relatively long-lasting muscle weakness due to myotoxicity has been reported in 3 patients after continuous ACBs.<sup>73</sup> These cases were diagnosed based on clinical presentation, imaging, and neurophysiologic studies (not biopsy proven) and represent a divergence from the previously accepted belief that local anesthetic myotoxicity was not clinically relevant in humans. Further study on the incidence and mechanism is important.

### Sciatic Nerve Block for TKA

The sciatic nerve block (SNB) is used as a supplement to the FNB for complete analgesia after TKA. Although most of the knee is innervated by branches of the femoral nerve, the posterior compartment of the knee is supplied by branches of the sciatic nerve. Despite the tenable anatomic explanation of the analgesic contribution, SNB has been associated with considerable controversy. The main concern is whether the analgesic value of an SNB outweighs concerns of concomitant motor and sensory loss of the lower leg.<sup>74</sup>

Previous observational and retrospective studies and small RCTs, searching for the analgesic value of an additional SNB, revealed conflicting results. In a systematic review, Abdallah and Brull<sup>75</sup> found insufficient evidence to qualitatively define the effect of adding SNB to FNB for analgesia, but the authors noted that the quality of the included studies was low to moderate. Recent RCTs with larger groups of patients showed a significant reduction in postoperative opioid consumption, less opioid-induced adverse effects, and significantly lower resting and dynamic pain scores. These effects persisted during the first 24 hours after a single-injection SNB and even longer when continuous SNB was used.<sup>76–80</sup> When compared with local infiltration analgesia (LIA) of the posterior capsule, SNB resulted in a significant opioid-sparing effect during and after the first 8 postoperative hours of TKA.<sup>81</sup>

Most recently, a systematic review and meta-analysis demonstrated evidence in favor of adding SNB to FNB for TKA.<sup>82</sup> Data from 386 patients retrieved from 8 RCTs proved that the addition of an SNB (single-injection or continuous) reduced the cumulative postoperative morphine equivalent consumption up to 24 hours after general and spinal anesthesia. This meta-analysis also demonstrated significant reduction in pain after a single-injection SNB during the first postoperative 8 hours.

However, despite these benefits, there are concerns related to the motor and sensory block of the lower leg, limiting a widespread use in clinical TKR pathways. Sciatic nerve block may disguise perioperative nerve injury of the lower leg and may cause a delay in early detection and treatment of surgically induced nerve injury. The reported incidence of surgical nerve injury after TKR, usually common peroneal nerve palsy, is 0.8% to 10%.<sup>83</sup> In a large prospective study of orthopedic patients, incidence of transient nerve injury after PNB was 8%, whereas permanent nerve injury was very rare (0.05%) and non-block related.<sup>84</sup> Also, in a prospective audit of more than 7000 PNBs, incidence of late neurologic complications was 0.5%, including block-related incidence of only 0.04%.<sup>85</sup> Neurologic complications after PNB are 10 to 100 times more likely to be related to nonblock causes.<sup>86</sup> Several

patient- and surgery-related risk factors of peroneal nerve injury after TKR have been identified, such as valgus deformity, flexion contracture, previous neuropathy or radiculopathy, rheumatoid arthritis, tourniquet use, constrictive dressing, and postoperative hematoma.<sup>83,87,88</sup> A 20-year cohort study demonstrated an unchanged risk of nerve injury after TKR when any PNB technique was used.<sup>89</sup>

In the context of an accelerated TKR pathway, concerns have been expressed about inability to ambulate on the day of operation after an additional SNB.<sup>90,91</sup> Remarkably, no delay in discharge or functional outcome was found when SNB was combined with FNB.<sup>76,82</sup> Ambulation on the first postoperative day after SNB was significantly impaired in some patients compared with local infiltration techniques of the posterior capsule but did not differ from the second postoperative day until discharge.<sup>82</sup> Also, no difference was found in time to discharge among groups with single injection, continuous SNB, or no SNB.<sup>76,82</sup>

### Infiltrative Techniques for TKA

Epidural and perineural catheter techniques are very effective in controlling postoperative pain after TKA; however, these techniques require technical expertise and are associated with block failures, as well as require postoperative catheter management by acute pain service. Despite increased use of ultrasound-guided nerve blocks and their well-documented superior analgesic efficacy, some anesthesiologists have been unable to introduce these techniques in routine clinical practice. In recent years, several infiltrative techniques have received increasing attention as “simple” and less invasive local anesthesia–based alternatives as stand-alone or as part of multimodal regimens to treat TKA postoperative pain. A significant proportion of surgical pain originates from the joint and surgical wound; therefore, it would be logical to use local anesthetics to provide site-specific analgesia while allowing ambulation without motor weakness. In addition, there are animal studies that demonstrate the benefit of LIA with multiple drug combinations in a rat model of knee surgery.<sup>92</sup> These techniques can be single-dose or catheter techniques and are usually surgeon administered.<sup>93</sup>

Liposome bupivacaine is a long-acting formulation of bupivacaine HCl approved in the United States for infiltration directly into a surgical wound. When infiltrated into the knee joint during a TKA, liposome bupivacaine resulted in less apparent quadriceps femoris weakness than a single-injection ropivacaine FNB (although it also provided inferior analgesia) and therefore theoretically may decrease the risk of falling.<sup>94</sup> Unfortunately, 4 RCTs found no evidence of improving post-TKA analgesia using liposome versus unencapsulated bupivacaine, suggesting, at least until additional data with positive results are reported, that no additional benefits are provided infiltrating the knee joint with liposome bupivacaine if bupivacaine HCl is an option.<sup>95–98</sup>

There is currently no liposome local anesthetic approved within the United States for use in PNBs. However, 1 phase 2 study suggests that single-injection FNBs with liposome bupivacaine can provide duration of action of more than 72 hours in healthy volunteers.<sup>99</sup> A phase 3, multicenter RCT demonstrated a treatment effect of at least 72 hours in subjects undergoing TKA, with statistically and clinically relevant analgesic benefits provided versus placebo up to 24 hours (minimal differences at time points after 24 hours).<sup>100</sup> Comparisons with a single-injection or continuous FNB are lacking but will be required to demonstrate the relevance of liposome bupivacaine FNBs if such a formulation is ultimately approved by the US Food and Drug Administration.

### Wound Catheter Infusion Techniques

Wound catheter infusion techniques are well established in the management of postoperative pain for a variety of surgical

procedures for more than 15 years.<sup>101</sup> A 2006 systematic review of 44 RCTs including 16 RCTs of patients undergoing major orthopedic surgery concluded that the technique was associated with improved analgesia, reduced opioid use, increased patient satisfaction, and perhaps reduced hospital stay. No major adverse effects were reported, and the rates of wound infection were similar to those in the control group (0.7%).<sup>102</sup> A more recent meta-analysis of 14 RCTs (756 patients) focused on ropivacaine for wound catheter infusion; the authors noted consistent evidence of effective analgesia and opioid sparing across a wide range of surgical procedures including TKA.<sup>103</sup> Plasma concentration of local anesthetic was below toxic levels, despite 8 to 20 mg/h ropivacaine infusion for 48 hours.<sup>103</sup>

Wound catheter infusion techniques should preferably be called surgical-site catheter techniques because the catheters are not always strictly in the surgical wound. In clinical practice, catheters have been placed through the surgical wound into deeper layers and in cavities (subcutaneous, subfascial, subacromial, intra-articular, intraperitoneal, preperitoneal, intraosseous, etc).<sup>104</sup>

**Local Infiltration Analgesia**

Despite its name, the original LIA technique is not only infiltration of local anesthetic but also a multicomponent optimization package including several components of enhanced postoperative recovery protocols. A mixture of ropivacaine, ketorolac (where available), and epinephrine is infiltrated into all tissues subject

to surgical trauma, and a catheter is often placed intra-articularly for 24 hours for top-ups of the mixture. The LIA technique has shown favorable results when compared with traditional methods of pain relief such as epidural analgesia, intrathecal morphine, and FNB.<sup>93</sup> A systematic review of 27 RCTs on LIA for TKA and THA showed that LIA for TKA was associated with reduced pain scores and opioid requirements up to 72 hours after surgery.<sup>105</sup>

**Multimodal Oral and Intravenous Analgesia**

Total knee arthroplasty surgical procedures produce tissue inflammation, triggering the production of prostaglandins (PGs),<sup>106</sup> particularly PGE<sub>2</sub>, which have been implicated in acute postoperative pain. There are several additional mediators released including histamine and bradykinin.<sup>107</sup> Increased sensitivity to painful stimuli is mediated by repetitive release of excitatory amino acids (glutamate and aspartate). In addition, the expression of c-fos, nitric oxide synthase, and cyclooxygenase 2 (COX-2) genes leads to sensitization. Multimodal analgesic techniques use individual agents that interact with the various mediators or their targets to produce pain relief.<sup>108,109</sup> The goal is to reduce or eliminate the use of opioids because there are reports of increased morbidity and mortality from prescribed opioids.<sup>110</sup> A large number of nonopioids are available such as acetaminophen (paracetamol), nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, ketamine, and glucocorticoids.<sup>111</sup> Literature on the topic has demonstrated the benefits of multimodal analgesia but does not address the potential problems

**TABLE 2. Perioperative Analgesics**

Drug	Analgesic Dose	Dosing Interval	Maximum Daily Dose	Comments
Acetaminophen (paracetamol)	500–1000 mg PO	q 4–6 h	3000 mg	As effective as aspirin; 1000 mg more effective than 650 mg in some patients
<b>NSAIDs</b>				
Celecoxib	400 mg initial, then 200 mg PO	q 12 h		Celecoxib is a COX-2 inhibitor
Ibuprofen	200–400 mg PO	q 4–6 h	3200 mg	200 mg equal to 650 mg of aspirin or acetaminophen
Naproxen	500 mg PO	q 12 h	1000 mg	250 mg equal to 650 mg of aspirin, but with longer duration
Ketorolac	15–30 mg IM/IV	q 4–6 h	60 mg (>65 y); 120 mg (<65 y)	Comparable with 10 mg morphine; reduce dose in patients <50 kg or with renal impairment; total duration of administration is 5 d
Ketamine	0.15–0.3 mg/kg IV			CNS effects are possible
Gabapentin	300–1200 mg PO	Preop		Adjust dose based on age and creatinine clearance; can be used in the postoperative period
Pregabalin	150–300 mg PO	Preop		Adjust dose based on age and creatinine clearance; can be used in the postoperative period
<b>Opioids*</b>				
Extended-release oxycodone	10–20 mg PO	q 12 h		Limit to a total of 2 doses to avoid accumulation and opioid-related adverse effects
Extended-release morphine	15–30 mg PO	q 8–12 h		Limit to a total of 2 doses to avoid accumulation and opioid-related adverse effects
Oxycodone	5–10 mg PO	q 4–6 h		Combination products* of oxycodone/acetaminophen (Percocet, Tylox) and oxycodone/aspirin (Percodan) are also available
Hydromorphone	2–4 mg PO	q 4–6 h		Also available as Dilaudid suppository (3 mg) with 6- to 8-h effect
Hydrocodone	5–10 mg PO	q 4–6 h		All preparations contain acetaminophen* or ibuprofen
Tramadol	50–100 mg PO	q 6 h	400 mg; less in cases of renal or hepatic disease	Combination product of tramadol/acetaminophen (Ultracet) is also available

\*Recommend starting with immediate-release opioids.

CNS indicates central nervous system; IM, intramuscular; IV, intravenous; PO, per os (by mouth); preop, preoperative; q, quaque (every).

of combining multiple drugs.<sup>112,113</sup> Meta-analysis has shown **beneficial** analgesic effects when **opioids are combined** with **nonopioid analgesics**<sup>114</sup> (Table 2).

### Nonsteroidal Anti-inflammatory Drugs: COX-2 Inhibitors and Acetaminophen

Nonsteroidal anti-inflammatory drugs are **among the most widely used** analgesic medications **in the world** because of their ability to reduce pain and inflammation. The mechanism of action of the NSAIDs is inhibition of PG production by either **reversible** or **irreversible** acetylation of the **COX enzyme**. Administration of **COX-2 inhibitors** in the perioperative period has consistently demonstrated decreased opioid consumption postoperatively and **improved outcomes** in joint replacement, such as range of motion.<sup>115</sup> It is ideal to **continue the COX-2 inhibitor** after major surgery for a **period of at least 2 weeks**, coinciding with the **duration** of the **surgical inflammatory process**.

### Injectable NSAIDs

**Ketorolac** tromethamine is an NSAID with activity at **both COX enzymes**, thus blocking PG production. **Ketorolac** is available for **enteral**, ophthalmic, and **parenteral** delivery. Ketorolac has an **onset** of action of approximately **10 minutes**, **peak** analgesic effect at **2 to 3 hours**, and analgesic **duration of 6 to 8 hours**, making it attractive for postoperative analgesia. It has been used to treat mild to severe pain after major surgical procedures. Ketorolac has been used as an adjuvant in arthroplasties as a means to provide multimodal pain management by reducing the amount of opioid consumed.<sup>116,117</sup>

**Caution** is warranted in patients with **renal insufficiency** and **elderly** patients in whom the creatinine clearance is impaired. Another route of administering ketorolac is **intranasal**. Intranasal ketorolac has been shown to provide analgesia characterized by **rapid onset** and duration of **6 to 8 hours**.<sup>118</sup> The rapid onset and improved analgesia seen with intranasal ketorolac may be due to higher penetration of the cerebrospinal fluid via the cribriform plate; higher cerebrospinal fluid levels of NSAIDs have been associated with enhanced analgesia.

Recently, an injectable form of ibuprofen was developed and approved by the Food and Drug Administration for use in patient care. Intravenous ibuprofen has not been well studied; however, its ability to inhibit the COX enzymes is likely to produce effects similar to ketorolac. The **bleeding properties** of injectable NSAIDs need to be **considered** in the perioperative period, especially in patients concomitantly receiving systemic anticoagulation.

### Acetaminophen

Acetaminophen (**paracetamol**) produces its analgesic effect by **inhibiting central PG synthesis** with **minimal inhibition** of **peripheral PG synthesis**.<sup>119</sup> Often labeled as an NSAID, acetaminophen and NSAIDs have important differences such as acetaminophen's **weak anti-inflammatory** effects and its generally poor ability to inhibit COX in the presence of high concentrations of peroxides, as are found at sites of inflammation,<sup>120,121</sup> as well as it does **not** have an adverse effect on **platelet function**<sup>122</sup> or the **gastric mucosa**.<sup>121</sup> The **comparative efficacy** of different analgesics has also been shown **to vary with the type and extent of surgical procedure**.<sup>123</sup> A qualitative systematic review comparing acetaminophen and NSAIDs in postoperative pain management found NSAIDs to be **superior after dental surgery**, with **similar results** after **knee surgery**.<sup>124</sup> **Intravenous acetaminophen** has reliable bioavailability and **onset** of meaningful pain relief of **25 to 27 minutes** in patients undergoing orthopedic surgery.<sup>125</sup> With a **greater central role of action** **than** the commonly used **NSAIDs**, acetaminophen

may be combined with COX-2 inhibitors or NSAIDs as part of a multimodal regime. A systematic review investigating the **combination of acetaminophen and NSAIDs** concluded that the **combination** confers **superior analgesia** than either drug alone.<sup>126</sup>

### Gabapentinoids

The anticonvulsant class of medications includes both gabapentin and pregabalin. These medications have been shown to be effective in treating a number of chronic pain states<sup>120,127</sup> and, more recently, acute postoperative pain. Gabapentin, 1-(aminomethyl) cyclohexane acetic acid, is a structural analog of the neurotransmitter  $\gamma$ -aminobutyric acid. Pregabalin is the active *S*-enantiomer of racemic 3-isobutyl  $\gamma$ -aminobutyric acid, **modifying voltage-gated calcium channels** in a similar manner to gabapentin. These medications may produce their antinociceptive effect by **inhibiting calcium influx** via these channels, subsequently **inhibiting** the release of excitatory neurotransmitters such as **substance P** and **calcitonin gene-related peptide**. These receptors may also play an important role in the development of chronic pain because presynaptic voltage-gated calcium channels are up-regulated in the dorsal root ganglia after surgical trauma, leading to central sensitization.<sup>121</sup> In fact, pregabalin has been shown in animal models to **reduce postoperative hyperalgesia**.<sup>128</sup>

Perioperative use of pregabalin has been shown to **decrease** the incidence of **chronic pain after TKA**.<sup>129</sup> A **preoperative dose** of **300 mg** was likely **too high** because several patients became **sedated** (which is the most common adverse effect of this class of drugs). Randomized controlled trials have determined that **lower doses of pregabalin** are **more useful**, avoiding excessive sedation, particularly in the elderly patients.

### Ketamine

Ketamine is a well-known agent used by anesthesiologists for both general anesthesia and sedation for the past 3 decades. Ketamine's mechanism of action is as a **noncompetitive N-methyl-D-aspartate receptor antagonist**. With the discovery of the *N*-methyl-D-aspartate receptor and its links to nociceptive pain transmission and **central sensitization**, there is a renewed interest in using ketamine as a potential antihyperalgesic agent. Although **high doses (>2 mg/kg)** of ketamine **have been implicated** in causing **psychomimetic effects** (excessive sedation, cognitive dysfunction, hallucinations, nightmares), subanesthetic or low doses (**<1 mg/kg**) of ketamine have demonstrated **significant analgesic efficacy without** these **adverse** effects. Furthermore, there is **no evidence** to indicate that **low-dose ketamine** exerts **any adverse effect** on respiration, cardiovascular function, nausea, vomiting, urinary retention, and constipation/postoperative ileus.

Recent systematic reviews have concluded that **low-dose ketamine** as the **sole analgesic** agent reduces pain after intravenous, intramuscular, and subcutaneous administration. In contrast, there is little evidence to support low-dose epidural ketamine by itself for postoperative analgesia.<sup>130</sup> There is a growing body of evidence that **low-dose ketamine may play an important role** in **postoperative pain management** when used as an **adjunct** to opioids, local anesthetics, and other analgesic agents.<sup>112</sup> Ketamine in combination with either parenteral or epidural opioids not only reduces postoperative opioid consumption but also **prolongs and improves analgesia**.<sup>131</sup> Although extensive **data are lacking**, there are suggestions that low-dose ketamine infusions during the perioperative period **may reduce the incidence of chronic pain**.<sup>132</sup>

### Strategies to Decrease the Risk of Falls After TKA

A critical component of optimizing joint function after knee arthroplasty is postoperative ambulation and flexion.<sup>133-135</sup> This



importance stems from the effects of immobilization on muscles and synovial joints, including muscular and cartilage atrophy, ligament weakening, and adhesion formation.<sup>136</sup> Because these damaging changes begin immediately after surgery, physical therapy, which is heavily dependent on ambulation, is usually initiated as soon as possible (often in the afternoon the day of surgery).<sup>137,138</sup> It is generally accepted that joint pain limits patients' ability to ambulate,<sup>56</sup> and therefore, providing potent analgesia is a high priority during physical therapy sessions.

Within the first decade of widespread use, case reports within the surgical literature suggested a link between continuous FNBs and falls.<sup>139,140</sup> Doubt was cast on the importance of these case reports when a large retrospective study revealed little difference in the rate of falls between no regional analgesic and single-injection FNBs (incidence, 0.8%–1.6%).<sup>10</sup> However, given the limitations of the database used for this retrospective investigation, single-injection and continuous PNBs could not be differentiated,<sup>141</sup> and it remains unknown what percentage, if any, of the “peripheral nerve blocks” included a perineural local anesthetic infusion.

Unfortunately, additional studies that were able to distinguish between the 2 techniques have found an association between continuous, but not single-injection, FNBs and falls. One retrospective study found that TKA patients without any regional analgesic or a single-injection FNB had similar risks of falling, but the addition of a continuous FNB increased the OR of falling to 4.4 ( $P = 0.04$ ).<sup>142</sup> Two meta-analyses involving psoas compartment and femoral catheters after knee and hip arthroplasty reported ORs of 3.9 and higher than 5.5 over single-injection blocks and perineural infusions of less than 12 hours.<sup>90,143</sup> Lastly, a retrospective study reported no falls in patients at a single institution in the 3 years before the implementation

of a continuous PNB program, compared with a 2.7% incidence in the 4 years after the program's implementation.<sup>144</sup> Taken together, these investigations suggest that continuous PNBs involving the femoral nerve may be associated with an increased risk of falling over a single-injection or no nerve block after knee arthroplasty.

Remaining unknown is the underlying cause of this difference in fall risk.<sup>141</sup> Although joint proprioception, sensory ability, and motor strength are all decreased during perineural infusion, to what degree each contributes to the risk of falling is undetermined. Nevertheless, various risk factors for falling have been identified, other than continuous PNBs, including increasing age,<sup>10,142</sup> general anesthetic (vs spinal),<sup>10</sup> major comorbidities (eg, anemia risk still increased even after transfusion),<sup>10,145</sup> obesity (body mass index,  $>30 \text{ kg/m}^2$ ),<sup>142</sup> and male sex.<sup>10</sup> Various steps have been demonstrated to decrease the risk of falling, including medical (eg, delirium prevention, nutrition, minimization of medications) and physical (eg, bed rails, nonslip flooring, decreasing bed height, access to call light) interventions.<sup>146</sup> Interventions specifically within the purview of anesthesiologists include educating health care providers regarding continuous PNBs (eg, physical therapists, nurses, surgeons),<sup>47</sup> requesting a knee immobilizer during ambulation,<sup>147</sup> educating patients and their families,<sup>148</sup> and possibly having both patients and nursing staff sign “contracts” prohibiting unassisted ambulation.<sup>149</sup>

There are various steps that will minimize the effects of continuous PNBs on the lower extremity. The first involves the choice of local anesthetic. When delivered via perineural catheters in various anatomic locations, ropivacaine appears to provide similar analgesia to bupivacaine as long as the dose is increased by approximately 50%.<sup>150–154</sup> In addition, although the evidence

#### **Preoperative Holding Area**

- Acetaminophen: 1000 mg PO
- Celecoxib: 400 mg PO (if 18–64 years old and GFR  $> 50 \text{ ml/min}$ )
- Consider Gabapentin 600 mg or Pregabalin 100 mg PO
- Consider Oxycodone (immediate release): 5–10 mg PO

#### **Intraoperative**

- Preferred spinal anesthetic (not required) with sedation
- Consider peripheral nerve blockade (single injection vs continuous infusion)
- Consider surgeon administered periarticular infiltration of local anesthetic
- Consider IV ketamine injection of 0.5 mg/kg +/- ketamine infusion of 0.1 mg/kg/hour
- Dexamethasone: 4 mg IV
- Granisetron: 0.1 mg IV OR Ondansetron: 4 mg IV, +/- Droperidol: 0.625 mg IV
- Fentanyl: up to 250 mcg IV, +/- Hydromorphone: up to 1 mg IV PRN for analgesia

#### **PACU**

- Fentanyl: 25 mcg IV PRN OR Hydromorphone: 0.2 mg IV PRN for pain  $\geq 4$
- Acetaminophen: 1000 mg PO or IV (if last dose  $\geq 6$  hours)
- Ketamine: 10 mg IV once PRN for pain  $\geq 4$
- Oxycodone (IR): 5 mg PO for pain  $\leq 4$  OR 10 mg PO for pain  $\geq 5$  (one dose prior to discharge)

#### **Floor Care**

- Acetaminophen: 1000 mg PO every 6 hours (650 mg for age  $> 75$ )
- Ketorolac: 15 mg IV every 6 hours for 4 doses (if GFR  $> 50 \text{ ml/min}$ ) or other NSAID
- Tramadol: 50–100 mg PO OR Oxycodone: 5–10 mg PO OR Hydromorphone: 2–4 mg PO (PRN pain)
- Fentanyl: 25 mcg IV PRN for breakthrough pain  $\geq 7$ ; up to 3 doses
- +/- Continuous peripheral nerve catheter infusion

Abbreviations: PACU, Post Anesthesia Care Unit; IV, intravenous; PO, per os; PRN, pro re nata (as necessary); GFR, glomerular filtration rate; all pain scores listed refer to the numeric rating scale (0 to 10).

**FIGURE 2. Sample multimodal analgesia total joint pathway.** All pain scores listed refer to the numeric rating scale. GFR indicates glomerular filtration rate; PACU, postanesthesia care unit; PO, per os (by mouth); PRN, pro re nata (as necessary).

regarding motor block is mixed,<sup>150–152,154,155</sup> there is strong evidence that the duration of bupivacaine is 2 to 3 times that of ropivacaine.<sup>155</sup> Therefore, if ropivacaine is used for a perineural infusion and negatively influences mobilization, the infusion pump may be paused until resolution of the undesirable effects, allowing for more effective titration compared with a bupivacaine infusion. Minimizing local anesthetic dose/mass will also decrease unwanted adverse effects. This can be accomplished by minimizing the basal infusion rate while providing patient-controlled bolus doses to reinforce analgesia for breakthrough pain.<sup>156–159</sup> It also remains unknown if the addition of a single-injection or continuous SNB increases the risk of falling<sup>76–78,160–162</sup>; although until illuminating data are published, it seems prudent to minimize local anesthetic dose/mass just as for femoral perineural infusion.<sup>163</sup>

Unfortunately, although some practitioners have tried to decrease quadriceps weakness by decreasing local anesthetic concentration, data from multiple randomized controlled investigations demonstrate that it is dose, not concentration (or basal rate), that determines continuous block effects.<sup>163,164</sup> Relatedly, providing local anesthetic as automatic, repeated bolus doses does not change block effects compared with a continuous basal infusion, as long as the total dose remains constant.<sup>156,165,166</sup> Similarly, no additive has demonstrated improved analgesia and/or decreased motor block, including epinephrine<sup>167–169</sup> and clonidine.<sup>170–172</sup>

One of the most promising fall-reduction interventions is converting continuous femoral to adductor canal nerve blocks, owing to the demonstrated reduction of induced quadriceps weakness.<sup>57,173</sup> At the time of this writing, 6 RCTs were published comparing continuous femoral and adductor canal nerve blocks,<sup>9,57,63,70,72,173</sup> with 3 demonstrating increased ability of standing, sitting, ambulating, and climbing stairs for subjects with an adductor canal infusion.<sup>9,57,63,70</sup> Regardless, although there is a hypothetical reduction in fall risk with adductor infusion, this association remains solely theoretical and requires additional study because no RCT to date demonstrates a reduction in falls between the 2 catheter locations.<sup>9,57,63,70,72,73</sup>

Lastly, new applications of existing technologies providing post-TKA analgesia may provide similar or superior analgesia to continuous peripheral nerve blockade without increasing the risk of falling. For example, ultrasound-guided percutaneous peripheral nerve stimulation offers the promise of blocking pain signals at the level of the spinal cord, without inducing a motor, sensory, or proprioception block.<sup>174,175</sup> Similarly, there is evidence that cryoneurolysis of the superficial, sensory-only anterior femoral cutaneous and infrapatellar saphenous nerves provides post-TKA analgesia without any weakening of the quadriceps femoris muscle.<sup>176,177</sup> In addition, several nonpharmacologic approaches have been investigated for post-TKA analgesia. These encompass neuromuscular electrical stimulation, which is electrical stimulation of muscles to produce contraction, and transcutaneous electrical nerve stimulation, as well as cooling therapies and compression, which show promise in the management of post-TKA pain. Additional research is required to define the analgesic efficacy of these modalities along with the incidence of complications and comparisons with other post-TKA analgesic techniques.

## DISCUSSION

Clinical pathways are tools created to organize care of a well-defined group of patients while maintaining high-quality, efficient care during a well-defined, limited episode of care. A collaboration of experts from ASRA and ESRA has reviewed the existing literature and presents in this review the components of a comprehensive, up-to-date, and evidence-based clinical pathway. This

review is intended to assist individuals and institutions in designing a pathway for TKA that is based on existing evidence and expert recommendation and may be customized according to individual settings (Fig. 2).

Multimodal analgesia involves the concurrent use of more than 1 class of medication to target different mechanisms of analgesia and has been advocated to improve analgesia through additive or synergistic effects while reducing opioid-induced adverse effects.<sup>108,109</sup> The goal is to reduce or eliminate the use of opioids, which are well recognized as having many unacceptable adverse effects. Many contemporary pathways include PNBs and/or peripheral nerve catheters. Although there is considerable disagreement on the optimal PNB or combination of nerve blocks, we can conclude that single-injection and continuous ACBs induce less quadriceps weakness compared with their femoral counterparts. Conversely, there are limited data suggesting that femoral blocks and catheters provide superior analgesia. Therefore, health care providers must determine the relative importance of analgesia versus quadriceps strength and mobilization ability. More studies are needed to determine what role periarticular infiltrative techniques will play in a multimodal pathway. The promise of simplicity may entice providers to rely on these less invasive local anesthesia–based alternatives as stand-alone or as part of multimodal regimens to treat TKA postoperative pain.

Unfortunately, adequately powered prospective RCTs comparing neuraxial versus general anesthesia in TKA patients are lacking. Recent population-based data suggest, however, that neuraxial anesthesia may be associated with superior results for most but not all outcomes compared with general anesthesia. It is noteworthy that some clinical investigations provide evidence of good outcomes when general anesthesia is being used, suggesting that individual practice patterns can achieve adequate results with either technique. Although no definitive answer is available regarding the best anesthetic practice for TKA, little, if any, evidence exists that neuraxial is inferior to a general anesthetic. Thus, in the absence of contraindications and assessment of associated risk, neuraxial anesthesia may represent a preferable approach in the treatment of patients undergoing TKA, although highly specialized practices maintain excellent outcomes with either approach. Studies elucidating the mechanisms by which neuraxial anesthesia may produce advantageous results, as well as investigations regarding evaluating the long-term outcome of these patients, are urgently needed to enhance our knowledge on this topic further.

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