Comprehensive Analysis of Pain Management after Total Knee Arthroplasty

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Total knee arthroplasty (TKA) has been much improved recently and it is regarded as one of the most common and successful surgical procedures that provides pain relief and improves function in patients with severe knee arthritis. However, recent studies have reported that 15%–20% of patients are not satisfied after TKA without evident clinical or radiological findings and the most common causes of patient dissatisfaction include residual pain and limited function. The evaluation and treatment of painful TKA relies on a thorough understanding of the origin by careful evaluation, and a systematic approach is essential to efficiently and effectively resolve the pain. Periarticular injections (PAIs) and nerve blocks are gaining popularity because they are associated with less side effects than systemic regimens. The analgesic efficacy and safety of PAI compared with nerve blocks for postoperative pain management still remain controversial. Therefore, more study is needed to determine if any changes in the regimen of the injection or technique could provide added benefit to long-term functional improvement beyond the perioperative period.

Keywords: Knee, Arthroplasty, Pain, Management

Introduction

Total knee arthroplasty (TKA) has been much improved recently and it is regarded as one of the most common and successful surgical procedures that provides pain relief and improves function in patients with severe knee arthritis. However, recent studies have reported that 15%–20% of patients are not satisfied after TKA in spite of no evident clinical or radiological findings, and the most common causes of patient dissatisfaction include residual pain and limited function. Therefore, appropriate pain control after TKA can be expected to enhance early functional recovery and improve patient satisfaction.

Nowadays, several risk factors and mechanisms of persistent pain after TKA are being proposed and targeting of the patients at risk might help to manage these patients. Significant progress has also been made in improving analgesia and pain control, but various protocols are still not well understood. In this review article, risk factors and mechanisms of painful TKA will be assessed and pain management protocols would be summarized.

Definition and Mechanism of Painful TKA

Pain could be defined as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.” It could imply that pain is a complex and multifactorial experience that involves multiple organ systems. An increased amplification of pain is related to tissue injury, blood pressure, impaired pain regulatory systems and proinflammatory states. All chronic pain was once acute, but not all acute pain becomes chronic. The transition is complex and involves pre-, intra- and postoperative, psychosocial, socio-environmental and patient-related genetic factors.

Five predictors contribute to chronic postsurgical pain (CPSP): preoperative pain at the operated area, preoperative pain elsewhere in the body (such as spine or hip), acute postoperative
pain, capacity overload, and comorbid stress symptoms such as anxiety, rumination, magnification, and helplessness. \(^{12}\) Nociceptive and neuropathic pain would be closely related to this process. Nociceptive pain is caused by the ongoing activation of sensory neurons in response to a noxious stimulus such as injury, disease, or inflammation. On the contrary, neuropathic pain is caused by aberrant signal processing in the peripheral or central nervous system and is broadly categorized as peripheral or central in origin.\(^ {11}\)

Patients with TKA frequently show pain elsewhere in the body.\(^ {10}\) Chang et al.\(^ {36}\) reported that lumbar radiating pain during an activity may be a source of poor outcome after TKA. The risk factors for the development of CPSP are controversial, but more intense postoperative pain is seen in association with central sensitization, younger age, obesity, and female gender.\(^ {25}\) Sensitization is a non-adaptive processing of nociceptive inputs and has a vital role in the etiology of neuropathic pain.\(^ {6,11}\) This contributes to pain in patients with osteoarthritis of the knee; this explains the discordance between the intensity of pain and the severity of the osteoarthritis on radiographs as well as the discrepancy between a satisfactory postoperative radiographic appearance and unexplained persistent pain after TKA.\(^ {16-18}\) Chronic use of the opioid also causes a state of nociceptive sensitization called 'opioid-induced hyperalgesia.'\(^ {19}\) Those who have the possibility of developing neuropathic pain might benefit from specific management with antihyperalgesic drugs such as ketamine or gabapentinoids.

A recent study showed that chronic non-orthopedic conditions such as fibromyalgia, migraine, irritable bowel syndrome, chronic low back pain, a head injury or stroke are more commonly found in patients with poor outcome after TKA. Those conditions are all causes of stress, leading to a combination of psychological distress and amplification of pain. These mechanisms are poorly understood, but are characterized by pain associated with abnormalities of motor function, autonomic balance, neuro-endocrine function and sleep.\(^ {6,20}\).

### Evaluation of Painful TKA

Full assessment of both the surgical and non-surgical factors that can cause pain after TKA is essential in addition to multidisciplinary team approaches that involve orthopedic surgeons, physical therapists, pain management physicians, and primary medical doctors.\(^ {29}\) Laskin\(^ {22}\) categorized etiologies of pain after TKA based on their temporal associations as follows: start-up pain, pain on weight bearing, early postoperative pain, pain associated with full flexion, pain with stair climbing or descent, rest pain, and continuous postoperative pain. Start-up pain may be related with loosening of components. Pain that is activity related may indicate a mechanical etiology and suggest instability if it is associated with recurrent swelling. In contrast, pain that is constant and not alleviated with rest and activity modification should raise suspicion of underlying periprosthetic joint infection. Pain with stair climbing can be caused by extensor mechanism pathology. Pain that begins within the first year after TKA suggests infection, instability, malpositioned implants, or soft tissue impingement. In contrast, pain that begins more than 1 year postoperatively suggests wear, osteolysis, aseptic loosening, or infection. Extraarticular sources of knee pain include the spine, hip, vessels, and complex regional pain syndrome. If pain was radiated to the thigh or down to the foot, it may have been referred from the lumbar spine or hip. Pain described as burning, tingling, prickling, shooting, electric shock-like, squeezing, spasm, or cold may indicate a neuropathic origin.\(^ {11}\)

### Regimens for Pain Control after TKA

Pain control regimens after TKA include oral or parenteral anesthesia, intravenous patient-controlled analgesia (PCA), nerve blocks, periartricular injections (PAIs), and continuous epidural or intraarticular analgesia.\(^ {13-26}\) Among them, nerve blocks and PAIs are gaining popularity because they are associated with little side effects than systemic regimens and this review article will focus on these regimens. PCA is widely used with morphine, but its drawbacks include somnolence, nausea, vomiting, ileus, constipation, pruritis, urinary retention, hypotension, and respiratory depression which can also affect the patient’s ability to effectively participate in physical therapy.\(^ {27,28}\) Epidural analgesia may produce spinal headache, neurogenic bladder, hypotension, and contralateral leg numbness.\(^ {27,29}\)

#### 1. Periartricular Injection

PAI has been reported to be effective in controlling immediate postoperative pain without the systemic side effects associated with systemic opioids.\(^ {24,30-32}\) The goal of PAI is to decrease pain at the central and peripheral levels while minimizing side effects, facilitating patient participation in postoperative rehabilitation, allowing earlier discharge, and improving overall function outcome.\(^ {27,33}\) The agents used in PAIs typically include local anesthetics, opioids, non-steroidal anti-inflammatory drugs, and corticosteroids optionally.\(^ {24-36}\) However, the advantages of each medication and the additive or synergistic effects of each medica-
tion are still not well known.

Kelly et al. performed a randomized controlled trial (RCT) to compare the clinical efficacy of multimodal approaches with ropivacaine, epinephrine, clonidine, and ketorolac. They concluded that the multimodal pain control protocol involving an intraoperative PAI containing ropivacaine, epinephrine, clonidine, and ketorolac showed better early postoperative pain control than the protocol used in a control group (ropivacaine and epinephrine). However, the difference between group A (ropivacaine, epinephrine, ketorolac, and clonidine) and group B (ropivacaine, epinephrine, and ketorolac) was questionable. In a RCT of Kim et al., the gold standard for drug combination was evaluated. Among 6 tested protocols, a combination of ropivacaine, morphine, and ketorolac in a PAI showed a significantly stronger and sufficiently synergistic analgesic effect without adding methylprednisolone in TKA.

Another clinical trial examined the effect of liposomal bupivacaine in the use of PAI. Liposomal bupivacaine is a novel composition in which the drug is dissolved into liposomes that release the medication in a controlled fashion slowly over a period of 96 hours. It was shown to reduce opioid use after the surgery when it was used with femoral nerve block (FNB) in TKA. With the ongoing evolution of regional anesthesia and the development of ultrasound guidance, success rates have increased, complications have been minimized and various techniques have become more popular. However, the optimal nerve block, combination with other blocks or other modalities, and single- or multiple-shot techniques are still being debated.

2. Nerve Blocks (Regional Anesthesia)

Regional anesthesia techniques seem to be an ideal method to deliver intraoperative analgesia and to minimize postoperative pain. However, it has been questioned by some authors because of side effects, such as impairment of motor function and risk of falls, risk of infection, and neurological complications. With the ongoing evolution of regional anesthesia and the development of ultrasound guidance, success rates have increased, complications have been minimized and various techniques have become more popular. However, the optimal nerve block, combination with other blocks or other modalities, and single- or multiple-shot techniques are still being debated.

FNB is frequently used to control postoperative pain after TKA. It showed superior outcomes to opioid-based analgesia. Compared with epidural analgesia, it showed similar analgesia but caused less nausea and vomiting and better patient satisfaction. However, continuous blockade of the femoral nerve induces weakness of the quadriceps that raises the risk for falls and increases the risk of infection. However, a recent cohort study indicated that peripheral nerve blocks do not necessarily increase the likelihood for falls. The superiority of single shot vs. continuous FNB is questionable, but continuous blockade could induce weakness of the quadriceps more easily. Therefore,
adjustment of continuous infusion with a rather low-dose regimen may effectively minimize quadriceps weakness\(^{48}\). In case of insufficient pain control despite FNB, sciatic nerve block appeals to be a suitable option to optimize pain management\(^{48}\). However, the use of an additional sciatic nerve block is controversial and it should be determined by individuals based on the consideration of advantages (improved analgesia and reduction of opioids) and disadvantages (risk of nerve injury and motor weakness)\(^{48,52-54}\).

Adductor canal block (ACB) was devised with the idea of performing a conduction block on the sensory branches of the femoral nerve and avoiding the disadvantage of motor impairment\(^{48}\). However, clinical studies are only recently available and still sparse. A recent meta-analysis reported that ACB remains an attractive alternative to FNB for pain control and motor strength preservation after TKA, but the anatomical location of the adductor canal needs to be better defined to ensure consistency in the type of block performed. It was concluded that they cannot safely suggest that an ACB provides optimal outcomes in comparison to FNB until aforementioned factor is completely understood\(^{55}\). Therefore, it is too early to recommend ACB for pain management after TKA even though it has the potential to replace FNB as a gold standard of pain management after TKA\(^{56}\).

The analgesic efficacy and safety of PAI compared with FNB for postoperative pain management in TKA still remains controversial. Recent two meta-analyses also reported a little different conclusions. In a meta-analysis performed by Wang et al.\(^{57}\), single shot FNB showed better pain relief in the early postoperative period compared with single shot PAI and continuous PAI provided postoperative analgesia comparable to that of continuous FNB. No significant difference was seen in regard to the complications between the two methods. However, in the meta-analysis of the Albrecht et al.\(^{58}\), there were no clinical differences in functional outcome or rates of complications. PAI provided similar postoperative analgesia after TKA to FNB; however, they pointed out the low number of trials that sought complications. One interesting article was published by Youm et al.\(^{8}\). They reported that PAI was more effective than FNB during the early (0–8 hours) postoperative period after TKA. However, patients treated with PAI experienced rebound pain at 24 hours. Therefore, they concluded that the combination of PAI and FNB may provide greater postoperative pain management than either alone for the first 24 hours after TKA.

**Conclusions**

The evaluation and treatment of painful TKA relies on a thorough understanding of the origin by careful evaluation, and a systematic approach is essential to efficiently and effectively resolve the pain. The preoperative assessment of risk factors might lead to individualization of perioperative management. PAs and nerve blocks are gaining popularity because they are associated with little side effects than systemic regimens. The superiority blocks with regard to analgesic efficacy and safety for postoperative pain management in TKA still remains controversial. Therefore, more research is needed to determine if an addition or a change in the regimen of the injection or technique could provide added benefit to long-term functional improvement beyond the perioperative period.

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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