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Multimodal Pain Management in Total Knee Arthroplasty
A Prospective Randomized Controlled Trial

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ABSTRACT

We analyze the effects of a multimodal analgesic regimen on postoperative pain, function, adverse effects and satisfaction compared to patient-controlled analgesia (PCA). Thirty-six patients undergoing TKA were randomized to receive either (1) periarticular injection before wound closure (30 cc 0.5% bupivacaine, 10 mg MSO_4, 15 mg ketorolac) and multimodal analgesics (oxycodone, tramadol, ketorolac; narcotics as needed) or (2) hydromorphone PCA. Preoperative and postoperative data were collected for VAS pain scores, time to physical therapy milestones, hospital stay length, patient satisfaction, narcotic consumption and medication-related adverse effects. The multimodal group had lower VAS scores, fewer adverse effects, lower narcotic usage, higher satisfaction scores and earlier times to physical therapy milestones. Multimodal pain management protocol decreases narcotic usage, improves pain scores, increases satisfaction and enhances early recovery.

Recent years have brought forth significant innovations in total knee arthroplasty procedures, including perioperative and postoperative analgesic and rehabilitation protocols. Despite these advances, perioperative pain control continues to be suboptimal following total knee (TKA) and total hip (THA) arthroplasties [1–5]. Large doses of parenteral narcotics, a mainstay in many pain management strategies, can be associated with significant adverse effects including constipation, nausea, vomiting, dizziness, urinary retention and respiratory depression [6–10]. In addition, opioid-induced respiratory depression and hypoxia are associated with myocardial ischemia, tachycardia, delirium, delayed wound healing and increased infection rates [11,12]. Opioid effects and side effects are potentiated in the elderly due to modified volumes of distribution and reduced drug clearance, and total joint arthroplasties are most frequently performed in elderly patients [12,13]. Traditionally, postoperative protocols for total joint arthroplasty were based on a general anesthetic and parenteral patient-controlled analgesia (PCA). In recent years, efforts have centered on multimodal analgesic protocols to improve early postoperative pain control, while decreasing the associated adverse effects [14–18].

Inadequate pain management has become a national focus, including being declared the fifth vital sign by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [19–21]. Increasing postoperative pain is associated with increased hospital stays and readmissions, lower patient satisfaction, longer time to physical therapy milestones and diminished range of motion [8,10,20,22,23]. Considering the extensive innervation of bone and the cuts involved in total joint arthroplasty procedures, it is not surprising that postoperative pain control is a significant concern following total knee and hip arthroplasty [17,24].

Recent investigations have examined a variety of pain management protocols for THA and TKA, including so-called minimally invasive surgical techniques, continuous epidurals, indwelling peripheral nerve catheters (regional block), intraarticular injections, and periarticular injections [3,7,8,10,14–18,20,25–30]. Although regional nerve blocks and continuous epidurals have been shown to be superior to PCA in postoperative pain control; disadvantages include diminished muscle control, falls, immobility and longer time to physical therapy milestones, as well as hypotension, urinary retention, nerve damage, missed compartment syndromes and difficulties associated with VTE prophylaxis protocols [8,28,29,31–33]. In an attempt to avoid these complications, approaches such as peri- and intraarticular injections have attempted to target the origin of the pain, minimizing systemic side effects while maximizing the potential for immediate mobility and muscle control. Although intraarticular infusion pumps and injections can accomplish these goals, they can often be associated with prolonged wound drainage, suboptimal improvement in pain control, and unclear benefit in early postoperative function [7,25,30,34,35].

Pain management becomes increasingly important as patients, surgeons and institutions pursue the shared lofty goals of so-called fast-track recovery programs that include specialized early therapy protocols, early discharge to home and rapid recovery. We

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hypothesize that local infiltration analgesia and multimodal pain management in minimally invasive TKA will achieve improved pain control, lower narcotic consumption, decreased systemic side effects, improved overall satisfaction, earlier time to physical therapy milestones and shorter hospital stays compared to minimally invasive TKA and PCA parenteral narcotics in fast-track total knee recovery.

Methods

Patients and Randomization

We performed a randomized controlled trial of patients undergoing minimally invasive primary total knee arthroplasty at a single institution. For our purposes, minimally invasive indicates the use of custom-modified instrumentation, a quadriceps sparing arthrotomy that does not extend beyond 1 cm proximal to the patella and surgical techniques that focus on soft tissue protection. Inclusion criterion were patients desiring rapid rehab and early discharge with tricompartmental knee disease undergoing TKA scheduled as first case of the day. Patients were excluded from participation if they had known allergies to medications used in the study, history of or current drug addiction or abuse, history of or current psychiatric illness or medical conditions limiting physical therapy participation.

The study was approved by the institutional review board (IRB), and all subjects gave written consent after receiving both an oral and a written explanation of the study protocol. Patients undergoing minimally invasive TKA were prospectively randomized to one of two study arms using sealed, opaque envelopes that were opened during surgery once the implant was in place. Following the operation, patients were interviewed by an independent investigator who was blinded to the treatment groups and was not present during the operation or randomization process. Patient interviews occurred on postoperation days zero, one and two as well as at a 3-week follow-up appointment.

Multimodal and PCA Protocols

The night before surgery, all participants received 5 mg of Coumadin. Sixty minutes prior to surgical incision, all patients received vancomycin and cefazolin (Ancef) dosed by weight. Prior to surgery, each patient was evaluated by a practicing anesthesiologist who decided upon the method of anesthesia during the operation, which was subsequently verified prior to incision. For epidural or spinal anesthesia, lidocaine 2% with HCO_3 was used, with discontinuation of epidural catheters at the end of the operation.

All operations were performed by the senior author using the same surgical techniques and the same posterior stabilized design (Genesis II, Smith and Nephew, Memphis TN). All patients received the same immediate postoperative management in the recovery room using intravenous morphine or hydromorphone administered at the discretion of the anesthesiologist. All patients were transitioned on the morning of expected hospital discharge from their assigned analgesic protocol to oral pain control with oxycodone (Oxycontin), hydrocodone-acetaminophen (Vicodin) and tramadol (Ultram) to also be continued after discharge.

Patients in both groups performed the same rapid recovery physical therapy protocols including evaluation on the evening of surgery and twice daily on successive inpatient days. Completion of specific physical therapy milestones determined when patients were eligible for discharge.

Patients randomly assigned to the multimodal group received the following protocol (Table 1):

Intraoperative: Periarticular injection prior to wound closure consisted of 30 cc 0.5% bupivacaine, 10 mg MSO_4 and 15 mg ketorolac. The injection was placed around the posterior capsule in the posteromedial and posterolateral soft tissues, synovium, pes anserinus and iliotibial band at Gerdy's tubercle.

Postoperative: Multimodal pain management consisted of scheduled oxycodone 10 mg orally every 12 h, tramadol 50 mg orally every 6 h, ketorolac 15 mg parenterally every 12 h, hydrocodone 5 mg orally as needed and hydromorphone 1 mg parenterally as needed for rescue. Prophylactic antiemetics were administered consisting of ondansetron (Zofran) 4 mg parenterally every 8 h and metoclopramide (Reglan) 10 mg parenterally every 8 h as needed.

Table 1
Multimodal and PCA Pain Management Protocols.

	Multimodal	PCA
Intraoperative injection	30 cc 0.5% bupivacaine, 10 mg MSO_4 and 15 mg ketorolac	None
Postoperative inpatient medications		
Pain management	Oxycodone 10 mg orally every 12 h Tramadol 50 mg orally every 6 h Ketorolac 15 mg IV every 12 h Hydrocodone 5 mg orally as needed Hydromorphone 1 mg IV as needed	Hydromorphone PCA Hydromorphone 1 mg IV as needed
Antiemetic prophylaxis	Ondansetron 4 mg IV every 8 h Metoclopramide 10 mg IV every 8 h as needed	
Medications after discharge	Oxycodone, hydrocodone-acetaminophen and tramadol	

Patients randomly assigned to the control group received the following protocol (Table 1):

Intraoperative: No periarticular injection.

Postoperative: Pain management with hydromorphone PCA and hydromorphone 1 mg parenterally as needed. Dosing was altered as needed with management goal of VAS score $\leq$4. The same prophylactic antiemetics as the multimodal group were administered (ondansetron (Zofran) 4 mg parenterally every 8 h and metoclopramide (Reglan) 10 mg parenterally every 8 h as needed).

Patient Outcome Measures

Preoperative and postoperative data were collected on postoperative days zero, one and two as well as during the 3-week follow-up appointment. Measures consisted of the Visual Analog Scale (VAS) pain score, narcotic consumption, medication-related adverse effects, time to physical therapy milestones, length of hospitalization and patient satisfaction score. For each patient, the Oxford Knee Score was calculated prior to the operation, and a standardized preoperative questionnaire was administered [36]. The total narcotic usage was standardized using a reference analgesic dose of morphine (10 mg IM) to calculate conversion factors, and equianalgesic dosages were determined as previously reported (Table 2A) [37,38]. All medications were accounted for, including anesthesiologist-administered narcotic and local infiltration analgesia medications. Physical therapy milestones included active straight leg raise, time until patient first gets out of bed, ambulation about the hospital room with or without assistance, ambulating 100 feet and ability to climb stairs.

Statistical Analysis

Statistical analysis was performed with two-tailed *t*-tests and 95% confidence intervals. Based on results from other similar studies [17], we anticipated an average decrease in VAS score of 0.8 in the treatment group. With this expected value, a power analysis was