How Can We Best Balance Pain Control and Rehabilitation After Knee Replacement?

Colin J. L. McCartney, MBChB, PhD, FRCA, FRCPC, and Patrick Wong, MD, FRCPC

Total knee arthroplasty (TKA) is a common, painful surgical procedure that requires high-quality anesthesia and postoperative pain control to facilitate early rehabilitation. In the past, common barriers to early rehabilitation after TKA included pain, nausea, and dizziness, which often were related to basic analgesic methods that used opioid analgesics alone. The more recent use of multimodal analgesic techniques and peripheral regional anesthesia has allowed significant reduction in opioid requirements and improved pain control while reducing major side effects.[1]

Commonly used peripheral regional anesthesia techniques for TKA include femoral and sciatic nerve blocks (both single-injection and continuous techniques). These techniques provide profound pain control after major knee surgery but require careful titration to avoid impairment of motor function.[2,3] In addition, their use requires extra training and resources and can provide a significant barrier to use in many institutions.

More recently, periarticular infiltration and local infiltration analgesia (LIA) have demonstrated promise as simple, surgically administered methods of providing pain relief that do not impair motor function.[4] Since the initial description, LIA has been investigated against various analgesic modalities (Table 1).[5–26] Many of these studies have confirmed the analgesic benefit of LIA, but comparisons against methods such as femoral and/or sciatic nerve block have been less conclusive.[5,19,27,28] Persisting concern about exacerbating motor weakness and impairment of rehabilitation has led many practitioners to evaluate more distal techniques such as blocks of the saphenous nerve in the adductor canal (adductor canal block [ACB])[29] or tibial nerve block in the popliteal fossa.[30] Studies on the ACB to date have demonstrated similar analgesic benefits without motor impairment compared with both single-injection and continuous femoral nerve block techniques.[31–36] In 2013, Andersen et al.[25] demonstrated that the addition of ACB to LIA led to better analgesia and earlier ambulation over LIA alone. For that reason, many practitioners are moving to the use of the ACB in preference to femoral nerve block to avoid motor impairment.

In this issue of *Anesthesia & Analgesia*, Sawhney et al.[26] further our knowledge of the ACB by comparing, in a randomized and blinded fashion, the combination of ACB and local infiltration to either technique alone for patients having TKA. Although they found no difference in pain control with the addition of ACB to LIA for pain at rest, there was a significant reduction in pain in walking when the 2 techniques were used together. There was also a significant reduction in IV hydromorphone consumption in the combination group. Reassuringly, the addition of ACB did not cause any impairment in distance walked compared with LIA alone. Finally, the use of ACB alone (without LIA) led to poor pain control compared with the other 2 groups, suggesting that the use of ACB alone (without LIA) should be avoided. Disappointingly but not surprisingly, the beneficial effects of adding a single-shot ACB to LIA disappeared by postoperative day 2.

The results of this study add to previous findings that demonstrate the analgesic benefits of the ACB when added to LIA. The lack of negative impact of the ACB on ability to ambulate should facilitate early recovery. Moreover, reduction in opioid consumption with the addition of ACB to LIA will lead to reduction in opioid-related adverse effects, further improving the ability to ambulate. Sawhney et al.[26] advance our knowledge of the field by further demonstrating the analgesic benefit of the ACB when added to LIA alone for TKA. Use of the ACB should therefore be strongly considered for patients having TKA because of the benefits to pain control and reduction in opioid consumption without impact on rehabilitation.

Although Sawhney et al.[26] are to be commended for this advance in knowledge, further studies are required to continue to evaluate the place of ACB for early recovery after knee surgery. Few studies have evaluated ACB for knee procedures other than TKA.[37–39] Because Sawhney et al.[26] were unable to show any benefits of adding ACB to LIA beyond postoperative day 1, a continuous ACB technique should be the focus of further future investigations to examine whether benefit can be extended.[36] The impact of these advanced peripheral nerve blocks on discharge readiness[40] and ability to manage TKA patients at home needs further evaluation. Furthermore, the safety of additional multiple

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Table 1. Evidence for Local Infiltration Analgesia Alone or in Addition to Other Peripheral Nerve Block Techniques for Total Knee Arthroplasty

Study	Results
Initial detailed description for LIA (case series, no control group)	
LIA (intraop + postop)[4]	Pain score ≤3/10 for >80% of patients up to POD 2
RCTs with LIA (modified from Marques et al.[5])	
LIA (intraop) versus placebo[6–10]	Decreased pain at rest and with activity on POD 1; no difference on POD 2
LIA (intraop + postop) versus placebo[11–15]	Decreased pain at rest and with activity on POD 1 and POD 2
LIA (intraop) versus ssFNB[16–18]	No difference in pain at rest or with activity on POD 1 or POD 2
LIA (intraop + postop) versus cFNB[19–21]	No difference in pain at rest or with activity on POD 1 or POD 2
LIA (intraop) + ssFNB versus ssFNB alone[22–24]	No difference in pain at rest on POD 1 or 2; no difference in pain with activity on POD 2
RCTs with LIA and ACB	
LIA (intraop) + ACB catheter versus LIA alone[25]	ACB catheter + LIA produces improved pain control, ambulation, and sleep compared with LIA alone
LIA (intraop) versus LIA + ACB versus ACB alone[26]	ACB + LIA produces lower pain scores with ambulation on POD 1 and 2. ACB (without LIA) has higher pain score at rest or with knee flexion on POD 1.

ACB = adductor canal block; cFNB = continuous femoral nerve block; intraop = intraoperative direct injection; LIA = local infiltration analgesia; POD = postoperative day; postop = postoperative infiltration via indwelling catheter; RCT = randomized controlled trials; ssFNB = single-shot femoral nerve block.

local anesthetic techniques with regard to local anesthetic toxicity needs to be examined.

In summary, TKA is a painful procedure that requires good pain relief for optimal recovery. Sawhney et al.[26] demonstrate that ACB is a useful addition to LIA alone for improving pain control and reducing opioid consumption without causing significant impact to early rehabilitation. This study adds to a growing body of literature demonstrating the analgesic benefits of ACB without impairing the all-important analgesic "balance" that is vital for successful recovery after TKA.

DISCLOSURES

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REFERENCES

1. McCartney CJ, Nelligan K. Postoperative pain management after total knee arthroplasty in elderly patients: treatment options. Drugs Aging 2014;31:83–91
2. Charous MT, Madison SJ, Suresh PJ, Sandhu NS, Loland VJ, Mariano ER, Donohue MC, Dutton PH, Ferguson EJ, Ilfeld BM. Continuous femoral nerve blocks: varying local anesthetic delivery method (bolus versus basal) to minimize quadriceps motor block while maintaining sensory block. Anesthesiology 2011;115:774–81
3. Brodner G, Buerkle H, Van Aken H, Lambert R, Schweppe-Hartenauer ML, Wempe C, Gogarten W. Postoperative analgesia after knee surgery: a comparison of three different concentrations of ropivacaine for continuous femoral nerve blockade. Anesth Analg 2007;105:256–62
4. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. Acta Orthop 2008;79:174–83
5. Marques EM, Jones HE, Elvers KT, Pyke M, Blom AW, Beswick AD. Local anaesthetic infiltration for peri-operative pain control in total hip and knee replacement: systematic review and meta-analyses of short- and long-term effectiveness. BMC Musculoskelet Disord 2014;15:220
6. Han CD, Lee DH, Yang IH. Intra-synovial ropivacaine and morphine for pain relief after total knee arthroplasty: a prospective, randomized, double blind study. Yonsei Med J 2007;48:295–300
7. Zhang J, Jiang Y, Shao J, Shen H, Wang Q, Zhang X. Effect of periarticular multimodal drug injection on pain after total knee arthroplasty. J Clin Rehabil Tissue Eng Res 2007;11:8678–82
8. Fu P, Wu Y, Wu H, Li X, Qian Q, Zhu Y. Efficacy of intra-articular cocktail analgesic injection in total knee arthroplasty—a randomized controlled trial. Knee 2009;16:280–4
9. Fu PL, Xiao J, Zhu YL, Wu HS, Li XH, Wu YL, Qian QR. Efficacy of a multimodal analgesia protocol in total knee arthroplasty: a randomized, controlled trial. J Int Med Res 2010;38:1404–12
10. Chen Y, Zhang Y, Zhu YL, Fu PL. Efficacy and safety of an intraoperative intra-articular magnesium/ropivacaine injection for pain control following total knee arthroplasty. J Int Med Res 2012;40:2032–40
11. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, Varin F. A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. J Bone Joint Surg Am 2006;88:282–9
12. Andersen KV, Bak M, Christensen BV, Harazuk J, Pedersen NA, Søballe K. A randomized, controlled trial comparing local infiltration analgesia with epidural infusion for total knee arthroplasty. Acta Orthop 2010;81:606–10
13. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. Acta Orthop 2010;81:354–60
14. Spreng UJ, Dahl V, Hjall A, Fagerland MW, Ræder J. High-volume local infiltration analgesia combined with intravenous or local ketorolac+morphine compared with epidural analgesia after total knee arthroplasty. Br J Anaesth 2010;105:675–82
15. Essving P, Axelsson K, Åberg E, Spännar H, Gupta A, Lundin A. Local infiltration analgesia versus intrathecal morphine for postoperative pain management after total knee arthroplasty: a randomized controlled trial. Anesth Analg 2011;113:926–33
16. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. J Arthroplasty 2007;22:33–8
17. Meftah M, Wong AC, Nawabi DH, Yun RJ, Ranawat AS, Ranawat CS. Pain management after total knee arthroplasty using a multimodal approach. Orthopedics 2012;35:e660–4
18. Ng FY, Ng JK, Chiu KY, Yan CH, Chan CW. Multimodal periarticular injection vs continuous femoral nerve block after total knee arthroplasty: a prospective, crossover, randomized clinical trial. J Arthroplasty 2012;27:1234–8

19. Toftdahl K, Nikolajsen L, Haraldsted V, Madsen F, Tønnesen EK, Søballe K. Comparison of peri- and intraarticular analgesia with femoral nerve block after total knee arthroplasty: a randomized clinical trial. Acta Orthop 2007;78:172–9
20. Carli F, Clemente A, Asenjo JF, Kim DJ, Mistraletti G, Gomarasca M, Morabito A, Tanzer M. Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. Br J Anaesth 2010;105:185–95
21. Affas F, Nygårds EB, Stiller CO, Wretenberg P, Olofsson C. Pain control after total knee arthroplasty: a randomized trial comparing local infiltration anesthesia and continuous femoral block. Acta Orthop 2011;82:441–7
22. Krenzel BA, Cook C, Martin GN, Vail TP, Attarian DE, Bolognesi MP. Posterior capsular injections of ropivacaine during total knee arthroplasty: a randomized, double-blind, placebo-controlled study. J Arthroplasty 2009;24:138–43
23. Koh IJ, Kang YG, Chang CB, Do SH, Seong SC, Kim TK. Does periarticular injection have additional pain relieving effects during contemporary multimodal pain control protocols for TKA? A randomised, controlled study. Knee 2012;19:253–9
24. Mahadevan D, Walter RP, Minto G, Gale TC, McAllen CJ, Oldman M. Combined femoral and sciatic nerve block vs combined femoral and periarticular infiltration in total knee arthroplasty: a randomized controlled trial. J Arthroplasty 2012;27:1806–11
25. Andersen HL, Gyrn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. Reg Anesth Pain Med 2013;38:106–11
26. Sawhney M, Mehdian H, Kashin B, Ip G, Bent M, Choy J, McPherson M, Bowry R. Pain after unilateral total knee arthroplasty: a prospective randomized controlled trial examining the analgesic effectiveness of a combined adductor-canal peripheral nerve block with periarticular infiltration versus adductor-canal nerve block alone versus periarticular infiltration alone. Anesth Analg 2016;122:2040–6
27. Fowler SJ, Christelis N. High volume local infiltration analgesia compared to peripheral nerve block for hip and knee arthroplasty—what is the evidence? Anaesth Intensive Care 2013;41:458–62
28. Spangehl MJ, Clarke HD, Hentz JG, Misra L, Blocher JL, Seamans DP. The Chitranjan Ranawat Award: periarticular injections and femoral and sciatic blocks provide similar pain relief after TKA: a randomized clinical trial. Clin Orthop Relat Res 2015;473:45–53
29. Jenstrup MT, Jæger P, Lund J, Fomsgaard JS, Bache S, Mathiesen O, Larsen TK, Dahl JB. Effects of adductor-canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. Acta Anaesthesiol Scand 2012;56:357–64
30. Sinha SK, Abrams JH, Arumugam S, D'Alessio J, Freitas DG, Barnett JT, Weller RS. Femoral nerve block with selective tibial nerve block provides effective analgesia without foot drop after total knee arthroplasty: a prospective, randomized, observer-blinded study. Anesth Analg 2012;115:202–6
31. Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, Patt ML, Goon AK, Lee YY, Ma Y, Yadeau JT. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. Anesthesiology 2014;120:540–50
32. Hanson NA, Allen CJ, Hostetter LS, Nagy R, Derby RE, Slee AE, Arslan A, Auyong DB. Continuous ultrasound-guided adductor canal block for total knee arthroplasty: a randomized, double-blind trial. Anesth Analg 2014;118:1370–7
33. Shah NA, Jain NP. Is continuous adductor canal block better than continuous femoral nerve block after total knee arthroplasty? Effect on ambulation ability, early functional recovery and pain control: a randomized controlled trial. J Arthroplasty 2014;29:2224–9
34. Grevstad U, Mathiesen O, Valentiner LS, Jaeger P, Hilsted KL, Dahl JB. Effect of adductor canal block versus femoral nerve block on quadriceps strength, mobilization, and pain after total knee arthroplasty: a randomized, blinded study. Reg Anesth Pain Med 2015;40:3–10
35. Zhang W, Hu Y, Tao Y, Liu X, Wang G. Ultrasound-guided continuous adductor canal block for analgesia after total knee replacement. Chin Med J (Engl) 2014;127:4077–81
36. Shah NA, Jain NP, Panchal KA. Adductor canal blockade following total knee arthroplasty-continuous or single shot technique? Role in postoperative analgesia, ambulation ability and early functional recovery: a randomized controlled trial. J Arthroplasty 2015;30:1476–81
37. Chen JY, Li N, Xu YQ. Single shot adductor canal block for postoperative analgesia of pediatric patellar dislocation surgery: a case-series report. Medicine (Baltimore) 2015;94:e2217
38. Ahl El MS. Femoral nerve block versus adductor canal block for postoperative pain control after anterior cruciate ligament reconstruction: a randomized controlled double blind study. Saudi J Anaesth 2015;9:279–82.
39. Espelund M, Grevstad U, Jaeger P, Hölmich P, Kjeldsen L, Mathiesen O, Dahl JB. Adductor canal blockade for moderate to severe pain after arthroscopic knee surgery: a randomized controlled trial. Acta Anaesthesiol Scand 2014;58:1220–7
40. Machi AT, Sztain JF, Kormylo NJ, Madison SJ, Abramson WB, Monahan AM, Khatibi B, Ball ST, Gonzales FB, Sessler DI, Mascha EJ, You J, Nakanote KA, Ilfeld BM. Discharge readiness after tricompartment knee arthroplasty: adductor canal versus femoral continuous nerve blocks—a dual-center, randomized trial. Anesthesiology 2015;123:444–56

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Pain After Unilateral Total Knee Arthroplasty: A Prospective Randomized Controlled Trial Examining the Analgesic Effectiveness of a Combined Adductor Canal Peripheral Nerve Block with Periarticular Infiltration Versus Adductor Canal Nerve Block Alone Versus Periarticular Infiltration Alone

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BACKGROUND: Total knee arthroplasty is a painful surgery that requires early mobilization for successful joint function. Multimodal analgesia, including spinal analgesia, nerve blocks, periarticular infiltration (PI), opioids, and coanalgesics, has been shown to effectively manage postoperative pain. Both adductor canal (AC) and PI have been shown to manage pain without significantly impairing motor function. However, it is unclear which technique is most effective. This 3-arm trial examined the effect of AC block with PI (AC + PI) versus AC block only (AC) versus PI only (PI). The primary outcome was pain on walking at postoperative day (POD) 1.

METHODS: One hundred fifty-one patients undergoing unilateral total knee arthroplasty were included. Patients received either AC block with 30 mL of 0.5% ropivacaine or sham block. PI was performed intraoperatively with a 110-mL normal saline solution containing 300 mg ropivacaine, 10 mg morphine, and 30 mg ketorolac. Those patients randomly assigned to AC only received normal saline knee infiltration.

RESULTS: On POD 1, participants who received AC + PI reported significantly lower pain numeric rating scale scores on walking (3.3) compared with those who received AC (6.2) or PI (4.9) ($P < 0.0001$). Participants who received AC reported significantly higher pain scores at rest and knee bend compared with those who received AC + PI or PI ($P < 0.0001$). The difference in pain scores between participants who received AC + PI and those who received AC was 2.83 (95% confidence interval, 1.58–4.09) and the difference between those who received AC + PI and those who received PI was 1.61 (95% confidence interval, 0.37–2.86). On POD 2, participants who received AC + PI reported significantly less pain on walking (4.4) compared with those who received AC (5.6) or PI (5.6) ($P = 0.006$). On POD 2, there was no difference between the groups for pain at rest or knee bending. Participants who received AC used more IV patient-controlled analgesia on POD 0. There was no difference between the groups regarding distance walked.

CONCLUSIONS: Participants who received AC + PI reported significantly less pain on walking on PODs 1 and 2 compared with those who received AC only or PI only. (Anesth Analg 2016;122:2040–6)

Effective pain management is essential for early mobilization and rehabilitation after total knee arthroplasty (TKA). Multimodal analgesia, including spinal analgesia, peripheral nerve blockade, periarticular infiltration (PI) of the knee joint intraoperatively, opioids, nonsteroidal antiinflammatory drugs (NSAIDs), acetaminophen, and gabapentinoids, has been shown to manage postoperative pain after arthroplasty effectively.[1–3] However, the challenge of managing postoperative pain after TKA is to preserve motor function while providing adequate analgesia.[1,2,4]

The introduction of adductor canal (AC) peripheral nerve blocks to manage pain after TKA is relatively new. The AC is an aponeurotic space in the middle third of the thigh. It contains nerve branches that supply sensory innervation to the knee, including the posterior branch of the obturator nerve and the saphenous nerve. Blocking these nerves provides analgesia to the medial aspect but not to the lateral or posterior aspects, of the knee.[5–7]

Saranteas et al.[5] examined the effectiveness of an ultrasound-guided saphenous nerve block in 23 healthy volunteers. They reported that 22 of 23 of the volunteers had a complete sensory block, and none of the volunteers had motor block of the hip flexor or knee extensor.[5] Manickam et al.[6] examined the feasibility and efficacy of ultrasound-guided block of the saphenous nerve in the AC in 20 patients

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undergoing lower limb surgery. They reported that all 20 patients developed complete sensory block and no motor block.[6] AC block has also been compared with femoral nerve block and was found to have an early sparing of the quadriceps strength with no difference in pain intensity scores, analgesic use, or knee mobility.[3,8,9]

PI of the knee joint has been shown to improve pain management and to preserve motor function. With PI, the nerves, muscle, and tissue in the posterior, lateral, and medial aspects of the knee are infiltrated intraoperatively with local anesthetic, morphine, and ketorolac to provide analgesia.[10] Randomized controlled trials have reported that patients undergoing TKA who received PI (with ropivacaine/ketorolac/epinephrine versus saline) used less morphine postoperatively, had less pain, and a shorter length of hospital stay.[11–14]

Randomized controlled trials also have examined the effectiveness of intermittent PI compared with continuous femoral nerve block for TKA. These trials have produced mixed results; therefore, it is unclear whether PI provides similar or better analgesia compared with femoral nerve block. Toftdahl et al.[2] reported that patients who received intermittent PI (300 mg ropivacaine/30 mg ketorolac/0.5 mg epinephrine) reported lower pain intensity scores with physiotherapy, used less morphine, and were able to walk further on postoperative day (POD) 1 compared with those who received continuous femoral nerve block (10 mL/h ropivacaine 2 mg/mL). In contrast, Carli et al.[1] reported that on PODs 1 and 2, pain scores (at rest) and morphine use were less in the patients who received continuous femoral nerve block (0.2% ropivacaine 8 mL/h) compared with those who received continuous PI (0.2% ropivacaine 100 mL/ketorolac 30 mg/epinephrine 0.5 mg). Affas et al.[13] reported that the mean pain scores (at rest and movement) were similar for both patients who received either femoral nerve block with intermittent injection (ropivacaine 2 mg/mL) or intermittent intraarticular infiltration (150 mL ropivacaine 2 mg/mL/30 mg ketorolac/0.5 mg epinephrine).

These studies demonstrate that AC block decreases pain after TKA without impact on quadriceps function and PI is effective in managing postoperative TKA pain without impairing motor function. Perlas et al.[3] conducted a retrospective cohort study in which they examined the effect of analgesic modality after TKA. Patients who received femoral nerve block, PI, or PI + AC block charts were reviewed. Patients who received PI + AC block walked the longest distance on POD 1, and patients who received PI with or without AC block reported lower pain scores.[3] Andersen et al.[15] combined these analgesic techniques by comparing the effect of a continuous saphenous nerve block with ropivacaine versus saline, in addition to PI, on pain and ambulation. They reported that patients who received ropivacaine in their AC block reported lower pain scores on movement and rest and no difficulty with ambulation. No published prospective randomized trials, however, have compared single-injection AC block with PI to PI only to AC nerve block only.

The purpose of this trial is to examine the effectiveness of AC block with PI compared with PI only compared with AC nerve block only on pain after unilateral TKA. The primary outcome of this trial was pain on walking, using a 0 to 10 numeric rating scale (NRS) at POD 1. We hypothesized that there would be no difference between the 3 groups with regard to pain scores on walking, resting, or knee bending.

METHODS

This study design was a prospective, surgeon- and observer-blinded, randomized controlled trial. Research Ethics Board approval was obtained at North York General Hospital, Toronto, Ontario. The study was registered with ClinicalTrials.gov (NCT01797588). Between May 31, 2013, and February 28, 2014, all patients who were scheduled for primary TKA were identified in the preoperative assessment clinic and invited to meet with the research assistant in a private office, who would confirm eligibility, explain the study, and obtain informed written consent. The inclusion criteria were age 18 years or older, ASA physical status I to III, and able to speak, read, and understand English. The exclusion criteria were contraindication to neuraxial and/or regional anesthesia, allergy to local anesthetics, chronic pain unrelated to their knee joint, chronic (3 months or longer) opioid use, and preexisting neuropathy involving the operative site.

After consent was obtained, participants' baseline demographic information was collected and randomly assigned to 1 of the 3 groups via a web-based computerized block randomization service (randomize.net). Group 1 received both an AC peripheral nerve block and intraoperative PI (AC + PI). Group 2 received an AC block and intraoperative saline infiltration (AC). Group 3 received 2 mL local anesthetic injected into the skin in the area of the AC and intraoperative PI. All participants, orthopedic surgeons, members of the acute pain service, and outcome assessors were blinded to the group allocation. Only the anesthesiologist responsible for intraoperative care and the anesthesia assistant performing the AC block/sham block were aware of the randomization. The pharmacy department prepared the blinded PI solution.

On the day of surgery, all participants received a premedication consisting of acetaminophen 1000 mg, celecoxib 200 mg, and gabapentin 300 mg on arrival at the day surgical unit. Participants were transferred to a designated block room to undergo peripheral nerve block and spinal anesthesia. AC block was performed under conscious sedation with fentanyl 50 μg and midazolam 1 mg. The medial aspect of the patient's thigh was prepared for a block using 2% chlorhexidine. With both the hip and knee flexed at 45 degrees, the leg was externally rotated. The AC was identified using a Sonosite-Flex linear HFL38X-6MHz™, Bothell, WA, ultrasound probe. All patients then received a subcutaneous injection of 2 mL of 1% lidocaine to anesthetize the skin at the AC site. Patients assigned randomly to AC block had the block performed through the anesthetized skin using a 22G facet tip, 50-mm Pajunk SonoTAP™ needle (Pajunk, Germany). A total of 30 mL of 0.5% ropivacaine was injected into the canal. For participants randomly assigned to receive a sham block, the procedure stopped after they received 2 mL of 1% subcutaneous lidocaine to anesthetize the skin at the AC site. All participants received a standard spinal anesthetic using a 25G Pajunk Spinal needle and 2 mL of 0.5% bupivacaine with 0.1 mg preservative-free morphine.

Intraoperative sedation was administered with a propofol infusion. Participants also received IV dexamethasone

8 mg and ondansetron 4 mg to reduce postoperative nausea and vomiting (PONV). The PI solution was administered by the surgeon during the TKA. A total of 6 different surgeons were involved in the administration of the infiltration solution for their respective patients. All surgeons were trained to perform the PI technique in a similar manner. A blinded 110-mL PI solution bag was prepared by the pharmacy and delivered to the operating room (OR). The PI solution bag

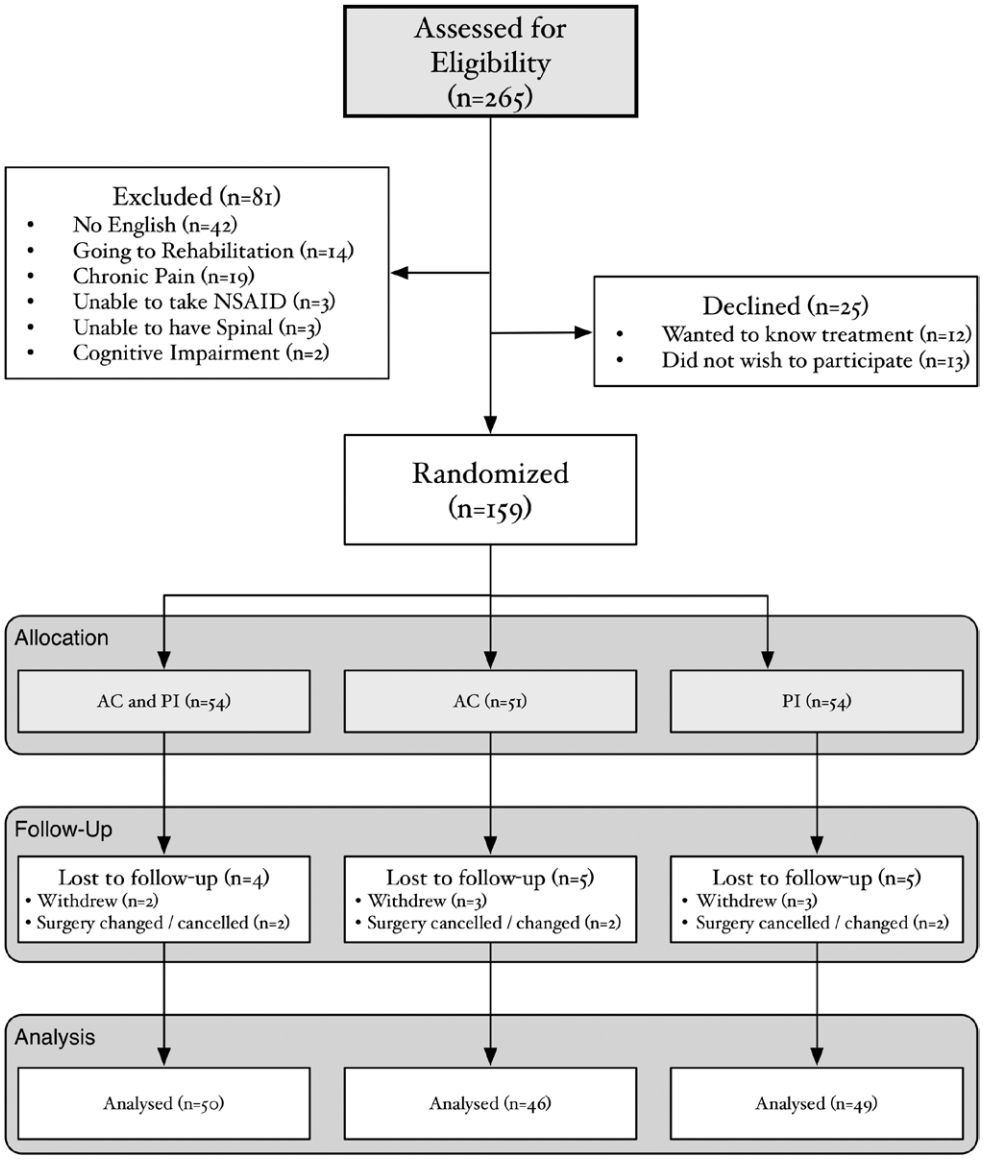

Figure 1. Consolidated Standards of Reporting Trials Statement flow diagram. AC = adductor canal; NSAID = nonsteroidal antiinflammatory drug; PI = periarticular infiltration.

Table 1. Patient Demographics

	AC + PI (*n* = 54)	AC (*n* = 51)	PI (*n* = 54)	Total (*n* = 159)	*P* value between groups
Age, y	68.3 (±9.7)	66.4 (±9.6)	67.6 (±9.4)	67.0 (±9.5)	0.58
Female sex	33 (61%)	31 (60.8%)	36 (66.7%)	100 (62.9%)	0.78
Education					
Less than high school	5 (9.3%)	2 (3.9%)	3 (5.56%)	10 (6.3%)	0.51
High school	19 (35.2%)	19 (37.3%)	17 (31.5%)	55 (34.6%)	0.82
College/university	30 (55.6%)	30 (58.8%)	33 (61.1%)	93 (58.5%)	0.84
Pain intensity (0 to 10 NRS)					
Preoperative pain at rest	1.41 (±1.9)	2.2 (±2.4)	1.8 (±2.2)	1.8 (±2.2)	0.15
Preoperative pain with movement	4.99 (±2.4)	5.4 (±2.5)	5.7 (±2.3)	5.4 (±2.4)	0.31

Values are presented as mean (±SD) or *n* (%).
AC = adductor canal; NRS = numeric rating scale; PI = periarticular infiltration.

contained either 110-mL normal saline solution containing 300 mg ropivacaine, 10 mg morphine, and 30 mg ketorolac or 110 mL saline 0.9%. The surgical team was blinded to the contents of the study bag. A 20-mL aliquot was injected into the posterior capsule and the medial and lateral ligaments just before implantation; after insertion of the implants, another 20 mL was infiltrated into the capsule and retinacular tissues. The remaining solution (approximately 60 mL) was used to infiltrate the muscle and subcutaneous tissues. Postoperative analgesia was standardized to hydromorphone patient-controlled analgesia (PCA; 0.2 mg bolus, 5-minute lockout, and a 4-hour maximum of 6 mg), celecoxib 200 mg every 12 hours, acetaminophen 1000 mg every 6 hours, hydromorphone control released 3 mg every 12 hours, and gabapentin 100 mg every 8 hours. Participants did not receive an NSAID if their creatinine was elevated. Creatinine was monitored daily, and the NSAID was discontinued if the creatinine was elevated during the participant's hospital stay. This multimodal regimen was administered until discharge to home, with the exception of hydromorphone PCA that was discontinued on POD 2 or earlier. Once hydromorphone PCA was discontinued, oral hydromorphone immediate release 1 to 2 mg as needed was prescribed for breakthrough pain.

Outcomes were measured on PODs 1 and 2 by a research assistant or by the primary investigator. Outcomes examined included pain intensity, analgesic consumption, motor function, pain-related interference with activities, and length of stay. Baseline demographic information was collected at the time of consent to participate in the trial in the preadmission clinic. Surgical data including side of TKA and anesthetic administered were collected from the chart postoperatively. Pain intensity was measured using the 0 to 10 NRS and included in the Brief Pain Inventory-Short Form (BPI-SF). In addition to the primary outcome of pain intensity with walking, we measured pain intensity at rest and with knee bending on PODs 1 and 2. Pain-related interference with activities was measured with a modified version of the BPI-SF interference subscale. Analgesic consumption was collected from the participant's electronic medication administration record and by recording the amount of breakthrough morphine or hydromorphone consumed via a PCA pump. All adjunct analgesics consumed, including acetaminophen, celecoxib, and gabapentin, were recorded per drug in milligram per day. Distance walked was measured in meters, as recorded by the physiotherapist or by the physiotherapy assistant on PODs 1 and 2. Length of stay in hospital was measured in hours from time of the surgery to time to discharge home.

Statistical Methodology

The primary outcome of this study was pain on walking on POD 1. With 3 equal groups, a pooled SD of 3 points on the 0 to 10 NRS, and a 2-tailed type I overall Bonferroni corrected error of 0.05, 48 individuals were required in the treatment arm. This would detect a difference of ≥2 points on the pain scale using the *t* test (independent samples) and a power of 80%. Accounting for a potential 15% attrition rate, a sample

Table 2. OR Data

	AC + PI (*n* = 50)	AC (*n* = 46)	PI (*n* = 49)	*P* value between groups
Right TKA, *n* (%)	26 (52)	21 (45)	19 (39)	0.58
Length of procedure, min	85.4 (±18.8)	90.9 (±17.1)	86.4 (±16.7)	0.95

Values are presented as mean (±SD) or *n* (%).
AC = adductor canal; OR = operating room; PI = periarticular infiltration; TKA = total knee arthroplasty.

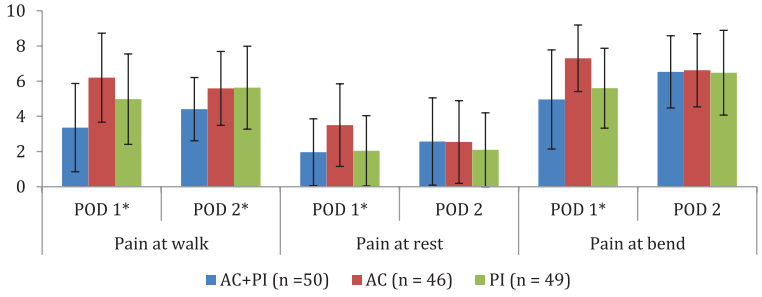

Figure 2. Pain scores (0–10 numeric rating scale: 0 = no pain, 10 = worst pain).

Table 3. Pain-Related Interference (Brief Pain Inventory, Interference Subscale)

	AC + PI (*n* = 50)	AC (*n* = 46)	PI (*n* = 49)	*P* value between groups
BPI total POD 1	6.71 (±7.10)	16.28 (±12.59)[a]	8.90 (±9.21)	<0.0001
BPI total POD 2	12.69 (±10.32)	13.54 (±10.64)	11.00 (±9.02)	0.46
Distance walked in meters POD 1	38 (±21.0)	20 (±15.8)[b]	34.5 (±31.5)	0.001
Distance walked in meters POD 2	61.7 (±36.8)	49.9 (±31.2)	58.7 (±32.5)	0.21

Values are presented as mean (±SD). *P* value was obtained from a 1-way analysis of variance. In groups determined to be significantly significant, a Bonferroni correction was applied to test for individual intergroup comparison.
AC = adductor canal; BPI = Brief Pain Inventory; PI = periarticular infiltration; POD = postoperative day.
[a]Value is significantly greater than that in the other 2 groups.
[b]Value is significantly less than that in the other 2 groups.

of 53 participants was required for each group. In total, 159 participants were recruited into this trial.

Data were analyzed using Statistical Analysis Software (SAS v.9.2; SAS Institute Inc., Cary, NC). The distribution of the data was analyzed for normality using histograms, quantile-quantile plots, and the Lilliefors test. Differences in mean scores between groups were assessed using 1-way analysis of variance (normally distributed data) and the χ^2 test for independence (categorical data). In comparisons with a group that was determined to be statistically significant, a Bonferroni-adjusted significance level of 0.0167 was calculated to account for the increased possibility of type I error because of multiple testing.

RESULTS

Two hundred sixty-five patients were screened for inclusion in this trial from June 2013 to March 2014. One hundred six patients did not meet the inclusion criteria or did not wish to participate. One hundred fifty-nine patients were included and randomly assigned to 1 of the 3 groups and 145 participants completed this trial (Fig. 1). Demographic information is presented in Table 1, and OR data are presented in Table 2. There were no significant differences between the groups in demographic information, including age, sex, and preoperative pain reported. There also were no significant differences between the groups in OR data.

On PODs 1 and 2, pain intensity on walking was significantly lower for participants who received both AC block and PI compared with participants who received PI block only or AC block only (Fig. 2). Participants who received AC block only reported significantly greater pain intensity scores than participants who received AC block and PI, PI only for pain intensity on walking, at rest, and with knee bending. On POD 1, participants who received AC + PI reported significantly lower pain on walking (3.3) compared with those who received AC (6.2) or PI (4.9). Participants who received AC reported significantly greater pain scores at rest and knee bend compared with those who received AC + PI or PI. The difference in pain scores between participants who received AC + PI and those who received AC was 2.83 (95% confidence interval, 1.58–4.09) and the difference between those who received AC + PI and those who received PI was 1.61 (95% confidence interval, 0.37–2.86). Participants who received AC block only also reported significantly greater pain-related interference with activities, as measured using a modified version of the BPI-SF interference subscale on POD 1. There were no differences between the 3 groups for pain-related interference with activities on POD 2 (Tables 3 and 4). There was no difference between the groups for the distance walked, with the mean distance walked on POD 1 and POD 2 being 31 and 57 m, respectively. No participant reported quadriceps weakness.

There were no differences between the 3 groups for the pre- and postoperative standing analgesics consumed on POD 0, POD 1, or POD 2 (Table 5). Participants who received AC only consumed more IV PCA hydromorphone on POD 0 and POD 1 (Tables 5 and 6). There were no documented cases of major or minor symptoms suggestive of local anesthetic systemic toxicity (LAST), and none of the participants reported symptoms of LAST when asked on POD 1. There were no differences between

Table 4. Group Comparisons for Pain Scores and Pain-Related Interference with Activities on POD 1

	Walk		Rest		Bend		Pain-related interference	
Group comparison	Significance	Difference (95% CI)	Significance	Difference (95% CI)	Significance	Difference (95% CI)	Significance	Difference (95% CI)
PI versus AC	No difference	−1.2 (−2.48 to 0.05)	Lower	−1.4 (−2.59 to −0.32)	Lower	−1.7 (−2.90 to −0.52)	Lower	7.39 (−12.29 to −2.49)
PI versus AC + PI	Greater	1.61 (0.37 to 2.86)	No difference	0.08 (−1.02 to 1.87)	No difference	0.64 (−0.53 to 1.80)	No difference	2.19 (−2.29 to 6.97)
AC versus AC + PI	Greater	2.83 (1.58 to 4.09)	Greater	1.54 (0.42 to 2.66)	Greater	2.34 (1.17 to 3.52)	Greater	9.58 (4.75 to 14.41)

The difference represents the difference in means between groups. CIs are Bonferroni corrected.
AC = adductor canal; CI = confidence interval; PI = periarticular infiltration; POD = postoperative day.

Table 5. Standing Preoperative and Postoperative Analgesics Consumed

	AC + PI (*n* = 50)	AC (*n* = 46)	PI (*n* = 49)	*P* value between groups
Hydromorphone CR POD 0, mg	2.6 (±0.98)	2.7 (±1.14)	2.6 (±1.00)	0.97
Hydromorphone CR POD 1, mg	5.9 (±1.85)	6.3 (±2.52)	5.6 (±1.17)	0.28
Hydromorphone CR POD 2, mg	5.1 (±2.58)	5.8 (±2.79)	5.7 (±2.25)	0.30
Acetaminophen POD 0, mg	1276.5 (±823.55)	1456.5 (±835.50)	1500.0 (±798.94)	0.35
Acetaminophen POD 1, mg	3509.8 (±1046.38)	3782.6 (±663.76)	3583.3 (±820.83)	0.28
Acetaminophen POD 2, mg	3215.7 (±1154.36)	3615.2 (±887.94)	3416.7 (±918.68)	0.14
Celecoxib POD 1, mg	168.0 (±84.37)	147.8 (±88.79)	166.7 (±75.32)	0.42
Celecoxib POD 2, mg	320.0 (±145.68)	302.2 (±146.80)	333.3 (±144.89)	0.58
Celecoxib POD 3, mg	284.0 (±162.08)	278.3 (±165.88)	283.3 (±164.17)	0.98
Gabapentin POD 0, mg	91.8 (±49.31)	104.3 (±55.60)	106.6 (±52.35)	0.33
Gabapentin POD 1, mg	246.94 (±84.41)	295.7 (±153.41)	257.4 (±87.83)	0.09
Gabapentin POD 2, mg	232.7 (±98.72)	284.8 (±187.34)	219.1 (±105.58)	0.05

Values are presented as mean (±SD).
AC = adductor canal; CR = control released; PI = periarticular infiltration; POD = postoperative day.

Table 6. Postoperative Analgesics Consumed, as Needed

	AC + PI (*n* = 50)	AC (*n* = 46)	PI (*n* = 49)	*P* value between groups
PCA hydromorphone POD 0, mg	0.2 (±0.4)	0.9 (±1.4)	0.2 (±0.5)	0.44
PCA hydromorphone POD 1, mg	1.8 (±1.9)	4.5 (±3.9)	2.6 (±2.7)	0.10
PCA hydromorphone POD 2, mg	1.5 (±2.1)	1.6 (±1.7)	2.3 (±4.6)	0.40
PCA hydromorphone total, mg	3.5 (±3.5)[a]	7.0 (±5.6)	5.0 (±6.9)	0.008
Hydromorphone IR per os POD 1, mg	0.3 (±1.1)	0.05 (±0.2)	0.09 (±0.4)	0.16
Hydromorphone IR per os POD 2, mg	1.5 (±2.2)	1.9 (±3.8)	1.07 (±1.2)	0.034

Values are presented as mean (±SD) or *n* (%). *P* value was obtained from 1-way analysis of variance. A Bonferroni correction was applied to test for individual intergroup differences. Analysis of variance assumptions were checked by using traditional residual plots and Lilliefors tests (all $P > 0.2$).
AC = adductor canal; IR per os = immediate release by mouth; PCA = patient-controlled analgesia; PI = periarticular infiltration; POD = postoperative day.
[a]Value is significantly lower than that in the other 2 groups.

the groups in the rates of opioid-related adverse effects of nausea, vomiting, or pruritus.

DISCUSSION

An optimal analgesic regimen for patients undergoing TKA provides adequate pain management while not limiting the patients' ability to ambulate. The AC block has gained increasing popularity because of its potential analgesic efficacy and its potentially limited impact on motor function.[3,5,6,8,9] PI of local anesthetics is reported to be effective in reducing pain after TKA compared with placebo.[2,10–14] In this trial, we compared 3 different methods of providing peripheral nerve block as part of an analgesic regimen that included a spinal anesthesia with intrathecal morphine and multimodal analgesics. Our results suggest that the combination of AC block and PI provides better pain relief and does not compromise ambulation compared with AC block only or PI block only. When the AC block is combined with PI, analgesia is improved because of the ability to provide local anesthetic to the anterior, medial, lateral, and posterior aspects of the knee, potentially providing more complete analgesia compared with using each technique individually. The results of this trial are similar to the results reported in other trials.[3,16]

As part of the multimodal analgesic regimen at our institution, patients receive an IV opioid via PCA postoperatively after TKA. All patients using IV PCA are closely monitored, as per our institutions policy, for pruritus, nausea, and vomiting. In this trial, the IV PCA use was greater in patients who received AC block only on PODs 0, 1, 2, and overall. Although opioid use was greater in this group, there was no difference in opioid-related adverse effects compared with the other groups including PONV. This finding could be related to the intraoperative administration of dexamethasone and ondansetron, which was included in our study protocol, to reduce PONV.

Limitations of this trial included only measuring distance walked once a day by the physiotherapist. If either the investigator or the research assistant walked with the physiotherapist and measured the distance walked, it would have provided more consistency, and possibly accuracy, in this measurement. Also, in our study, patients stated that they ambulated more than once a day; however, no attempt was made to assess distance walked for the entire 48-hour period, because these data were not extractable from the patient record. Providing each participant with a pedometer or other recording device would have assisted in collecting this information.

Using a combination of an AC and PI requires the use of a high total dose of local anesthetic with the potential for LAST. During this trial, participants were monitored closely and asked about signs and symptoms of LAST. No participants reported symptoms of LAST. This includes no reported changes in neurological status or evidence of cardiac toxicity. However, this trial was not powered to assess the safety of the combined AC + PI technique. We did not retrieve plasma levels of local anesthetic to assess for concentration of local anesthetic in the blood stream and thus cannot conclude there is no risk of LAST. The AC blocks also were not tested for sensory blockade because of the blinded nature of the study. Therefore, it is not known whether any of the AC blocks had failed. In addition, the AC blocks were performed by multiple anesthesiologists, and the PI infiltrations were performed by multiple orthopedic surgeons. Despite these limitations, the addition

of both AC block and PI has patient advantages when used in combination of with an already established multimodal regimen that includes opioids, gabapentinoids, and antiinflammatory drugs. The preservation of knee strength without the risk of perioperative leg weakness has the potential to reduce the risk of patient falls. Additional research on the safety of these analgesic techniques, including the risk of falls and the incidence of LAST, needs to be conducted. Future research and outcomes could focus on determining whether this analgesic regimen can result in early discharge from hospital and its impact on patient satisfaction. In this trial, we were specifically interested in examining pain in the acute postoperative period. Therefore, future trials could also assess patient outcomes at regular intervals for a longer period (i.e., 6 months or a year) to provide information on the long-term impact of these analgesic techniques. ■

DISCLOSURES

Name: Monakshi Sawhney, PhD, NP(Adult).
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Monakshi Sawhney has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.
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Attestation: Richard Bowry has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
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REFERENCES

1. Carli F, Clemente A, Asenjo JF, Kim DJ, Mistraletti G, Gomarasca M, Morabito A, Tanzer M. Analgesia and functional outcome after total knee arthroplasty: periarticular infiltration vs continuous femoral nerve block. Br J Anaesth 2010;105:185–95
2. Toftdahl K, Nikolajsen L, Haraldsted V, Madsen F, Tønnesen EK, Søballe K. Comparison of peri- and intraarticular analgesia with femoral nerve block after total knee arthroplasty: a randomized clinical trial. Acta Orthop 2007;78:172–9
3. Perlas A, Kirkham KR, Billing R, Tse C, Brull R, Gandhi R, Chan VW. The impact of analgesic modality on early ambulation following total knee arthroplasty. Reg Anesth Pain Med 2013;38:334–9
4. Lund J, Jenstrup MT, Jaeger P, Sørensen AM, Dahl JB. Continuous adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: preliminary results. Acta Anaesthesiol Scand 2011;55:14–9
5. Saranteas T, Anagnositis G, Paraskeuopoulos T, Koulalis D, Kokkalis Z, Nakou M, Anagnostopoulou S, Kostopanagiotou G. Anatomy and clinical implications of the ultrasound-guided subsartorial saphenous nerve block. Reg Anesth Pain Med 2011;36:399–402
6. Manickam B, Perlas A, Duggan E, Brull R, Chan VW, Ramlogan R. Feasibility and efficacy of ultrasound-guided block of the saphenous nerve in the adductor canal. Reg Anesth Pain Med 2009;34:578–80
7. Akkaya T, Ersan O, Ozkan D, Sahiner Y, Akin M, Gümüş H, Ateş Y. Saphenous nerve block is an effective regional technique for post-menisectomy pain. Knee Surg Sports Traumatol Arthrosc 2008;16:855–8
8. Joegar P, Dusaka Z, Fomsgaard JS, Hilsted KL, Bjerregaard J, Gyrn J, Mathiesen O, Larsen TK, Dahl JB. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. Reg Anesth Pain Med 2013;38:526–32
9. Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, Patt ML, Goon AK, Lee YY, Ma Y, Yadeau JT. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. Anesthesiology 2014;120:540–50
10. Vasarhelyi EM, Naudie D. Local infiltration in orthopaedic surgery. COA Bull 2012, Spring;96:22–3
11. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A. Reduced hospital stay, morphine consumption, and pain intensity with local infiltration analgesia after unicompartmental knee arthroplasty. Acta Orthop 2009;80:213–9
12. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. Acta Orthop 2010;81:354–60
13. Affas F, Nygårds EB, Stiller CO, Wretenberg P, Olofsson C. Pain control after total knee arthroplasty: a randomized trial comparing local infiltration anesthesia and continuous femoral block. Acta Orthop 2011;82:441–7
14. Busch CA, Shore BJ, Bhandari R, Ganapathy S, MacDonald SJ, Bourne RB, Rorabeck CH, McCalden RW. Efficacy of periarticular multimodal drug injection in total knee arthroplasty. A randomized trial. J Bone Joint Surg Am 2006;88:959–63
15. Andersen HL, Gyrn J, Møller L, Christensen B, Zaric D. Continuous saphenous nerve block as supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. Reg Anesth Pain Med 2013;38:106–11
16. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, Varin F. A multimodal analgesia protocol for total knee arthroplasty. A randomized, controlled study. J Bone Joint Surg Am 2006;88:282–9