Prospective randomized trial of continuous femoral nerve block with posterior capsular injection versus periarticular injection for analgesia in primary total knee arthroplasty

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Background: Femoral nerve block (NB) and periarticular injection (PI) are 2 common options for pain control after total knee arthroplasty (TKA). We performed a prospective triple-blinded randomized trial comparing continuous femoral NB to PI, with follow-up to 1 year.

Methods: Patients younger than 70 years of age who were scheduled to undergo elective primary TKA under spinal anesthesia between 2009 and 2010 were randomly allocated to receive either continuous femoral NB or PI. Patients in the NB group received ropivacaine through an NB catheter and a sham saline PI. The PI group received a PI of ropivacaine, morphine, ketorolac and epinephrine, and a sham saline infusion via an NB catheter. Both groups had standardized oral analgesia preoperatively, spinal anesthesia and sedation, and postoperative analgesia. Surgeons, anesthesiologists, patients and assessors were blinded to group assignment. Pain was measured twice daily on postoperative days 1 and 2, at rest and with motion, with a numeric rating scale. Patient satisfaction, pain (Oxford Knee Score) and range of motion were assessed at 1 year.

Results: There were 39 participants in the NB group and 35 participants in the PI group. There were no statistically significant differences between the groups at baseline. Statistically but nonclinically significant reductions in pain scores on postoperative day 2 and in narcotic need on the day of surgery were found in the PI group. Patient-reported satisfaction did not differ at any time point. At 1 year, knee flexion was significantly greater in the NB group than in the PI group (mean range of motion 120° v. 110°, $p = 0.03$).

Conclusion: There was no demonstrated improvement in pain control with the use of an NB versus PI when used with multimodal analgesia. Clinicians should opt for the modality that has the best efficiency for their surgical environment. ClinicalTrials.gov # NCT00869037

Contexte : Le bloc nerveux (BN) fémoral et l'infiltration périarticulaire (IP) sont 2 options d'usage courant pour maîtriser la douleur après l'arthroplastie totale du genou (ATG). Nous avons procédé à un essai prospectif randomisé à triple insu afin de comparer le BN fémoral et l'IP, avec un suivi allant jusqu'à 1 an.

Méthodes : Les patients de moins de 70 ans qui devaient subir une ATG élective sous épidurale entre 2009 et 2010 ont été assignés aléatoirement à un BN fémoral continu ou à une IP. Les patients du groupe soumis au BN recevaient de la ropivacaïne par un cathéter de BN et une IF simulée (solution saline). Le groupe soumis à l'IP recevait de la ropivacaïne, de la morphine, du kétorolac et de l'épinéphrine et une perfusion simulée (solution saline) par un cathéter de BN. Les 2 groupes avaient reçu une analgésie orale standard avant l'intervention, une anesthésie rachidienne avec sédatifs et une analgésie postopératoire. Les chirurgiens, les anesthésiologistes, les patients et les évaluateurs ne connaissaient pas l'assignation des agents aux différents groupes. La douleur a été mesurée 2 fois par jour aux jours 1 et 2 postopératoires, au repos et à la mobilisation, au moyen d'une échelle numérique. La satisfaction des patients, la douleur (questionnaire d'Oxford pour le genou) et l'amplitude de mouvement ont toutes été évaluées après 1 an.

Résultats : Le groupe soumis au BN comptait 39 participants et le groupe soumis à l'IP en comptait 35. Il n'y avait aucune différence statistiquement significative entre les groupes au départ. Des réductions statistiquement (et non cliniquement) significatives des scores de douleur au deuxième jour postopératoire et du recours aux narcotiques le jour de la chirurgie ont été notées dans le groupe soumis à l'IP. La satisfaction autodéclarée des patients n'a différé à aucun moment. Au bout de 1 an, la flexion du genou était significativement plus marquée dans le groupe soumis au BN que dans le groupe soumis à l'IP (amplitude de mouvement moyenne 120° c. 110°, $p = 0{,}03$).

Conclusion : On n'a démontré aucune amélioration de la maîtrise de la douleur avec l'utilisation du BN c. IP avec analgésie multimodale. Les médecins devraient opter pour la modalité qui offre le meilleur degré d'efficience en fonction de leur environnement chirurgical. ClinicalTrials.gov # NCT00869037

Total knee arthroplasty (TKA) is associated with considerable pain in the postoperative period.[1,2] This pain is most intense during the first few days after surgery but can last for several weeks to months, with varying intensity.[3] Analgesic regimens for pain after TKA have changed over time with the evolution and adoption of fast-track methodology[4,5] and with review of new evidence regarding the efficacy and safety of various regimens.[6–14]

An ideal analgesic regimen should meet the following requirements: (1) ensure minimal pain both at rest and with movement, (2) provide good analgesia beyond postoperative days 1 and 2, (3) avoid impairing motor function, (4) permit early weight bearing, physiotherapy and mobilization, (5) avoid the need for bladder catheterization, (6) avoid the requirement of prolonged parenteral administration of medications or fluids, (7) lack major adverse effects and (8) permit early commencement of pharmacologic prophylaxis of deep venous thrombosis.

There is no ideal analgesic technique for TKA; however, 2 commonly used approaches incorporate femoral nerve block or periarticular multimodal injection (PI). There is conflicting evidence as to which of these techniques is superior, owing to differences in the methods used for background or supplemental analgesia.[7,10]

Single-shot femoral nerve block provides effective analgesia in the first 24 hours after TKA.[6,10] The disadvantages with this approach are that the duration of analgesia does not cover the entire period of moderate to severe pain, the resultant quadriceps weakness can delay early physiotherapy and mobilization, it does not cover posterior knee pain, patients are at increased risk for falls, and it requires investment in infrastructure to maintain operating room efficiency.

Continuous femoral nerve block (NB) with low-dose local anesthetic infusion is an alternative to single-shot femoral nerve block.[9,10] Although the analgesia is of longer duration, other concerns are not completely alleviated with this approach.[10,12,13] The duration of analgesia has been shown to be unreliable beyond 36 hours, potentially owing to displacement of the nerve block catheter from its tissue plane during movement.[9,10]

Periarticular multimodal injection is very popular in centres that have adopted fast-track methodology.[11,13,14] It is very simple to perform, does not adversely affect operating room efficiency, does not cause any motor block, permits early commencement of pharmacologic prophylaxis of deep venous thrombosis, and has very few adverse effects other than inadvertent intravascular injection, a risk it shares with any NB technique. The duration of analgesia with PI is about 4–8 hours, but when PI is combined with an oral multimodal regimen, the transition is reported to be smooth, thereby permitting good longer-term analgesia.[12,13]

There is a paucity of data comparing the efficacy and safety of continuous femoral NB and PI when both groups have background oral multimodal analgesia. Longer-term follow-up is also not often reported. Furthermore, most studies report pain as assessed at fixed points during the day, which can be confounded by sporadic analgesia administration. The effectiveness of the 2 techniques as indices of reliability is often not reported.

In this triple-blinded randomized controlled trial (RCT) comparing continuous femoral NB to PI, we sought to address some of the above limitations by (1) incorporating a local anesthetic injection in the posterior knee capsule to cover posterior knee pain with femoral NB; (2) reporting worst pain experienced between fixed intervals; (3) reporting the number of patients who experience mild, moderate and severe pain in the 2 study groups; (4) reporting pain and procedural complications throughout the hospital stay and 1 year after TKA; and (5) reporting rehabilitation outcomes throughout the hospital stay and at 1 year. These measures enabled us to gather the important short- and long-term outcome data that will inform the process of adopting a reliable analgesic regimen for management of pain after TKA.

Our objective was to compare the analgesic efficacy of PI to that of continuous femoral NB, both combined with posterior capsular local anesthetic infiltration, when both groups have background multimodal analgesia. We hypothesized that continuous femoral NB would be superior to PI for the stated primary outcome measure.

Methods

Setting and design

The study was conducted by academic anaesthesiologists and surgeons at a community hospital between April 2009 and March 2010. Regional and local research ethics board approval was obtained, and participants were recruited with informed consent. Participants were randomly allocated in a concealed manner to either the NB group (multimodal analgesia + continuous femoral NB + intraoperative posterior capsular injection + sham PI) or the PI group (multimodal analgesia + PI + intraoperative posterior capsular injection + sham continuous femoral NB). Patients, physicians (surgeons and anesthesiologists) and outcome assessors were blinded to the interventions.

Inclusion and exclusion criteria

Eligible participants were patients younger than 70 years of age who were scheduled to undergo elective primary TKA under spinal anesthesia and had an American Society of Anesthesiologists Physical Status Classification System category of I, II or III.

We excluded the following patients: those who refused to consent to participate in the study; those with contraindications for regional anesthesia; those with preexisting

neurologic deficits; those with allergy or contraindication to any of the drugs used in the study; those undergoing revision knee arthroplasty; those with chronic pain or receiving narcotics for pain relief preoperatively; those with inflammatory arthritis; those with alcohol or other drug use disorder; those with psychiatric disorders; those who were unable to use the outcome assessment tools employed in the study; and those who were wheelchair bound or used a walker for mobilization preoperatively.

Intervention

In the NB group, continuous femoral NB was achieved with infusion of 20 mL of 0.2% ropivacaine as a loading dose, followed by infusion at 15 mL/h until postoperative day 1, then at 10 mL/h until postoperative day 2, when the catheter was removed. Sham PI was given with 0.9% saline, followed by a posterior capsular injection of 20 mL of 1% ropivacaine.

In the PI group, sham continuous femoral NB was performed with 0.9% saline at the same volume and rate as in the NB group. Periarticular and posterior capsular injection with a solution containing 300–400 mg of ropivacaine, 5 mg of preservative-free morphine, 30 mg of ketorolac and 0.3–0.4 mg of epinephrine, made up to 100 mL with 0.9% saline.[14]

In both groups, preoperative oral analgesia was given with controlled-release hydromorphone, celecoxib and acetaminophen. A continuous femoral NB catheter was placed under ultrasonographic or nerve stimulator guidance, or both, followed by standardized spinal anesthesia and sedation. Postoperatively, intravenous patient-controlled analgesia with hydromorphone was started on the day of surgery (postoperative day 0); oral analgesia with controlled-release hydromorphone, immediate release hydromorphone, celecoxib and acetaminophen was given from postoperative day 1 onward. Participants were allowed to use a cryocuff, and refractory pain was treated with intravenous infusion of ketamine. Physiotherapy was started in the morning of postoperative day 1 for all patients.

Primary outcome measure

The primary outcome measure was static and dynamic pain scores on postoperative days 1 and 2. Pain was assessed twice daily at specified times with a numeric rating scale (NRS). Pain at rest was also assessed preoperatively with the same NRS.

Secondary outcome measures

Secondary outcome measures were narcotic consumption until postoperative day 2; number of patients requiring ketamine or cryotherapy for intractable pain; number of patients with NRS pain scores in the mild (0–3), moderate (4–7) and severe (> 7) range[15] until postoperative day 2; incidence of narcotic-related adverse effects (nausea, vomiting, pruritis, euphoria/dysphoria, hallucination, respiratory depression) until postoperative day 2; number of patients able to ambulate with or without a walking frame on postoperative days 1 and 2; maximum knee flexion (active/passive) on postoperative days 1 and 2, at discharge and 1 year postoperatively; hospital length of stay; and patient satisfaction, assessed on postoperative days 0, 1 and 2, at discharge from hospital and at 1 year with a 10-point Likert scale ranging from 1 (completely unsatisfied) to 10 (completely satisfied). The Short Form Health Survey version 2 (SF-12v2) and Oxford Knee Score were administered preoperatively and 6 weeks, 6 months and 1 year after surgery.

At the completion of enrolment, we carefully reviewed all participant charts to assess for violations of the standard drug administration protocol. Participants with protocol violations were removed from the analysis.

Sample size

The standard deviation (SD) for pain scores with PI or continuous femoral NB in published studies is mostly in the range of 20–30 mm (2–3 on the NRS).[16] Assuming an SD of 3 on the NRS, a sample size of 36 participants per arm would be needed to detect a difference of 2 on the NRS, which would be considered clinically significant (2-sided, $\alpha = 0.05$, $\beta = 0.8$).[17] We targeted recruitment of 90 patients (45 per arm) to allow for dropouts and loss to follow-up.

Statistical analysis

We analyzed continuous variables using repeated-measures analyses of variance to compare groups for the primary outcome measure. We assessed nominal variables using the χ^2 test or Fisher exact test if matched cells were rare (expected frequencies < 5), and ordinal variables using the Kruskall–Wallis test. Statistical significance was set at $p < 0.05$.

RESULTS

We randomly allocated 92 patients to either the NB group ($n = 48$) or the PI group ($n = 44$) (Figure 1). Nine patients in both groups were removed from the study because of errors in randomization or schedule changes, or because they were deemed ineligible for the study based on the clinical opinion of the treating anesthetist at the time of surgery. The data for the 74 remaining patients (39 in the NB group and 35 in the PI group) were analyzed.

There were no statistically significant differences in the preoperative data between the 2 groups; however, there were trends toward participants in the PI group being

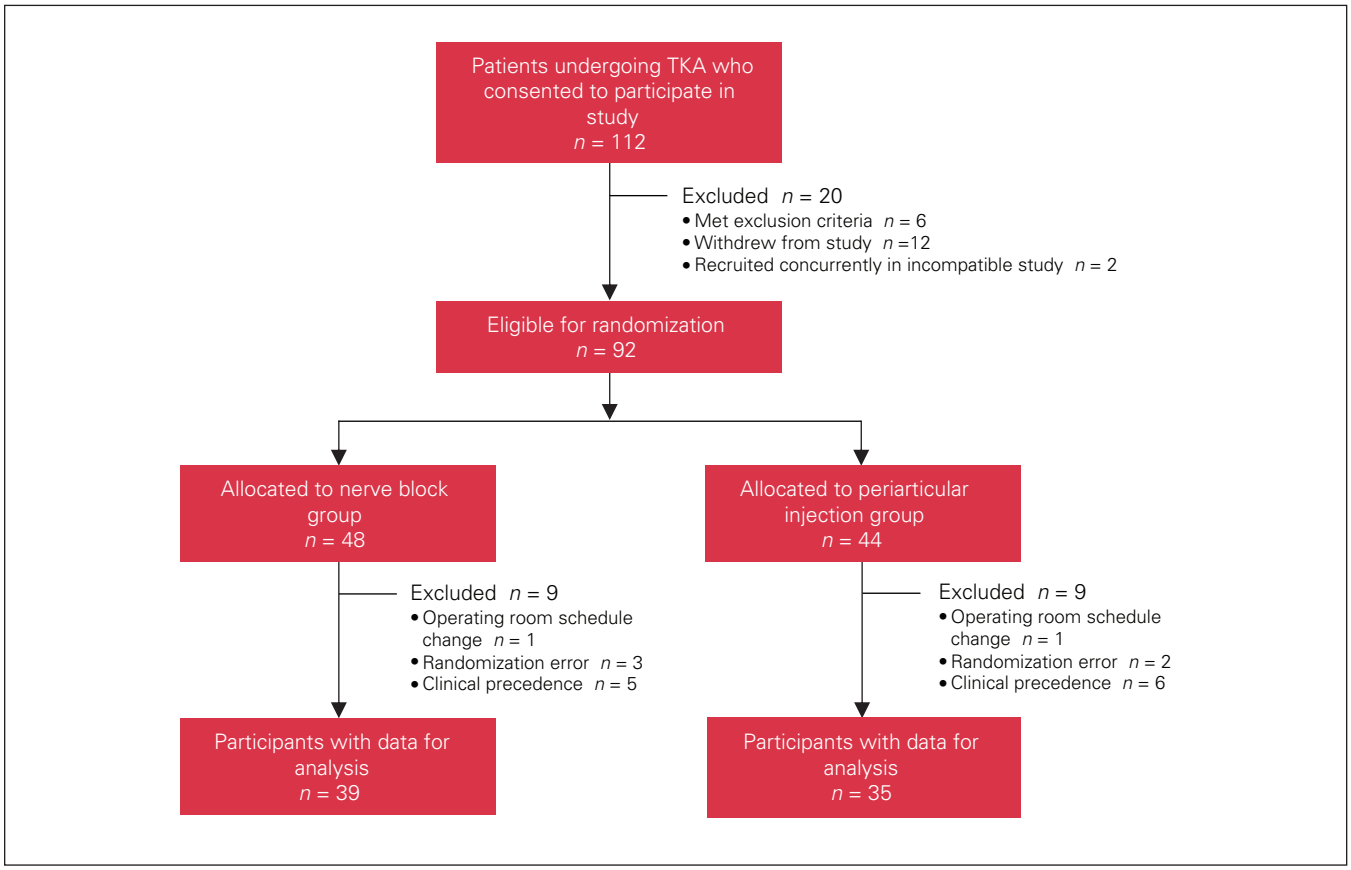

Fig. 1. Flow diagram showing patient selection and randomization.

younger, more obese and female than those in the NB group (p = 0.1, 0.2 and 0.2, respectively) (Table 1). There were no differences in preoperative pain scores between the 2 groups. Two patients in the PI group received gabapentin in the perioperative period, in violation of the study protocol. We analyzed the data with and without these participants and found no material differences in the results, so these participants were kept in the data set.

Pain and opioid consumption data are presented in Table 2. Pain at rest on the afternoon of postoperative day 2 was reported to be less with PI than with NB (p = 0.02). Pain with movement was similarly lower in the PI group than in the NB group on both the morning (p = 0.04) and afternoon (p = 0.03) of postoperative day 2. Worst pain experienced did not differ between the 2 groups when assessed as linear data. When pain scores were categorized as mild, moderate or severe, for worst pain experienced, more participants in the NB group than in the PI group reported severe pain on the morning of postoperative day 2 (p = 0.02) (Table 3). A similar trend was found for pain with movement on the morning and afternoon of postoperative day 2 (p = 0.06 and 0.07, respectively).

Participants in the NB group used a mean of 1.5 mg more intravenously administered hydromorphone than those in the PI group on postoperative day 0 (p = 0.02) (Table 2), but no differences in opioid consumption were noted between the groups on postoperative day 1 or 2. No differences were found in the use of cryotherapy (p = 0.4). Ketamine was not administered to any study participants. There were no differences in the severity of reported nausea or pruritis between the groups.

Knee range of motion during the hospital stay did not differ between the groups. There was no difference in time of first ambulation (p = 0.4) (Table 4) or in use of a walking frame. Length of hospital stay did not differ (4.0 d [SD 1.2 d] in the NB group v. 4.1 d [SD 1.4 d] in the PI group, p = 0.6). There was no difference between the groups in patient satisfaction scores on postoperative day 0, 1 or 2.

At 1 year, maximum knee flexion was significantly greater in the NB group than in the PI group (mean range of motion 120° [SD 11°] v. 110° [SD 22°], p = 0.03). Controlling for preoperative knee range of motion, gender, age and body mass index did not affect this result. No differences were found in SF-12 score, Oxford Knee Score rating, or patient-reported pain or satisfaction.

Discussion

We found between-group differences in our primary outcome of pain scores on postoperative day 2, with the PI group having average scores about 1 point lower than the NB group. The a priori assumption of clinical significance,

Table 1. Baseline characteristics of patients who underwent total knee arthroplasty with continuous femoral nerve block or periarticular injection for analgesia

Characteristic	Group; mean ± SD*		
	Continuous femoral nerve block *n* = 39	Periarticular injection *n* = 35	*p* value
Age, yr	61.0 ± 5.8	58.6 ± 6.6	0.1
Gender, no. (%) of patients			0.2
Female	23 (59)	26 (74)	
Male	16 (41)	9 (26)	
Body mass index	33.9 ± 7.8	36.8 ± 9.6	0.2
Preoperative pain score at rest†	5.9 ± 2.1	5.6 ± 1.9	0.5
Oxford Knee Score rating	30.8 ± 11.6	32.0 ± 10.3	0.7
Preoperative knee flexion, °	110 ±12	108 ± 15	0.6
Diabetes, no. (%) of patients	6 (15)	4 (11)	0.7

SD = standard deviation.
*Except where noted otherwise.
†Assessed with a numeric rating scale.

Table 2. Mean postoperative pain scores on numeric rating scale* and opioid requirements in the 2 groups

Variable	Group; mean ± SD		
	Continuous femoral nerve block	Periarticular injection	*p* value
Pain at rest			
Postoperative day 1			
Morning	2.6 ± 1.8	2.2 ± 1.7	0.4
Afternoon	2.9 ± 1.8	2.8 ± 1.5	0.9
Postoperative day 2			
Morning	3.2 ± 2.5	2.5 ± 1.4	0.1
Afternoon	2.8 ± 2.0	1.8 ± 1.3	0.02
Pain with movement			
Postoperative day 1			
Morning	4.8 ± 2.7	4.5 ± 2.7	0.7
Afternoon	5.9 ± 2.4	5.2 ± 2.4	0.2
Postoperative day 2			
Morning	5.7 ± 2.6	4.6 ± 1.9	0.04
Afternoon	5.4 ± 2.4	4.2 ± 1.8	0.03
Worst pain experienced			
Postoperative day 1			
Morning	5.6 ± 2.8	5.4 ± 2.8	0.8
Afternoon	6.6 ± 2.3	6.4 ± 2.6	0.7
Postoperative day 2			
Morning	6.7 ± 2.5	5.6 ± 2.0	0.04
Afternoon	6.3 ± 2.5	5.6 ± 2.2	0.2
Overnight total dosage of patient-controlled analgesia, mg	4.5 ± 3.2	3.0 ± 2.4	0.02
Total dosage of hydromorphone in hospital, mg†	67.2 ± 42.0	67.3 ± 40.5	0.99

SD = standard deviation.
*Rated from 0 (lowest) to 10 (highest).
†All delivery routes.

however, was 2 points of the primary outcome metric, indicating that, although there was a statistically significant difference, there was no clinical significance. The higher mean amount of patient-administered hydromorphone (by 1.5 mg) in the NB group on the day of surgery was also statistically significant, but, with no difference in the total dosage of hydromorphone or in adverse effects of opioids reported between the groups, the clinical significance of this difference is questionable. Pain scores were not specifically collected on the day of surgery, which makes this finding difficult to put into context. In addition, the time of day of the procedure was not recorded as part of the study and may have led to a difference between groups in the duration of postoperative care, which, in turn, may have led to a difference in mean hydromorphone dosage on the day of surgery.

Participants in the NB group had a mean of 10° more of maximum knee flexion at 1 year. The SD was more than twice as big in the PI group than in the NB group. There were trends in the PI group toward having more women and a higher body mass index. This may have played a role in knee flexion results, as a gynecoid adipose distribution, with potentially greater thigh girth, may have led to early soft tissue impingement and reduced final maximum knee flexion in these patients. However, controlling for these features in the analysis did not affect the relation between treatment group and range of motion at 1 year. There were no between-group differences in patient-reported outcomes, so although there may have been a difference in range of motion, participants in the PI group did not appear to perceive increased limitations.

Horn and colleagues[18] reported the cases of 16 patients who underwent bilateral staged TKA with single-shot bupivacaine femoral NB for the first operation and liposomal bupivacaine PI for the second procedure. They found differences between the groups in hospital length of stay, number of physiotherapy sessions to achieve discharge criteria and patient preference. These results may also be explained by the presence of contralateral disease in the femoral NB group. In addition, the single-shot NB would be expected to have a much shorter duration of action than the liposomal bupivacaine, which suggests the drug formulation was the differentiating feature, rather than the delivery technique.

Uesugi and colleagues[19] performed an RCT comparing single-shot femoral and sciatic NB to PI with ropivacaine, epinephrine, morphine and steroid among 210 patients undergoing TKA. Their findings were similar to ours, with discrete points when one or the other technique was statistically significantly superior but the magnitude of difference being of questionable clinical significance. In an RCT in 160 patients undergoing TKA, Spangehl and colleagues[13] found greater narcotic use among those who had PI than among those who had continuous femoral and sciatic NB on the day of surgery. Hospital length of stay was

Table 3. Categoric comparison of pain scores on numeric rating scale

Variable	NRS score;* no. of participants						*p* value†
	Continuous femoral nerve block			Periarticular injection			
	0–3	4–7	> 7	0–3	4–7	> 7	
Pain at rest							
Postoperative day 1							
Morning	28	11	0	27	8	0	0.6
Afternoon	26	13	0	22	13	0	0.8
Postoperative day 2							
Morning	22	15	2	27	8	0	0.1
Afternoon	25	11	1	31	4	0	0.06
Pain with movement							
Postoperative day 1,							
Morning	13	19	7	13	17	5	0.95
Afternoon	6	18	15	8	21	6	0.1
Postoperative day 2							
Morning	11	15	13	10	21	4	0.06
Afternoon	9	21	7	14	19	1	0.07
Worst pain experienced							
Postoperative day 1							
Morning	8	18	13	9	18	8	0.6
Afternoon	3	18	18	5	16	14	0.7
Postoperative day 2							
Morning	5	14	20	5	23	7	0.02
Afternoon	5	17	15	6	20	9	0.4

NRS = numeric rating scale.
*Rated from 0 (lowest) to 10 (highest).
†For difference between intervention groups.

Table 4. Time of first ambulation in the 2 groups

Time	Group; no. of participants	
	Continuous femoral nerve block	Periarticular injection
Postoperative day 1		
Morning	11	12
Afternoon	19	17
Postoperative day 2		
Morning	6	1
Afternoon	2	2
After postoperative day 2	1	3

shorter in the PI group, and patients in the NB group reported a higher rate of dysesthesia up to 6 weeks after surgery. Despite these findings, those authors concluded that there was no realized benefit of one intervention over the other. Two other smaller randomized studies showed similar results.[20,21]

There is a paucity of published data on the longer-term sequelae of analgesic techniques on TKA outcomes. Wegener and colleagues[22] reported on the Western Ontario and McMaster Universities Arthritis Index (WOMAC), Oxford Knee Score and visual analogue scale scores at 1 year. Our data on patient-reported outcome measures are consistent with theirs, but Wegener and colleagues[22] did not report any data on range of motion at 1 year.

Limitations

Strengths of this study include the randomized triple-blinded design and careful reassessment of all participant charts to identify any violations of the standardized drug administration protocol. Participants in whom a major violation of the study anesthesia or analgesia protocol occurred were excluded from analysis. Although this reduced the sample size, it also reduced the within-group variation and noise that would have occurred had the data been assessed as intention-to-treat.

Limitations include the fact that, despite randomized group assignment, there were still trends toward demographic differences between the 2 groups: the PI group trended toward being younger and female and having a higher body mass index. Women have been found to report higher pain scores on the visual analogue scale than men in the early postoperative period after TKA.[23–25] In addition, female gender has been associated with higher body mass index.[26] Older patients have been found to require less rescue medication than younger patients after total joint replacement.[27] Together, these findings suggest that a younger, more obese group with a higher predominance of women would have a higher degree of reported pain in the perioperative period, rather than the significantly lower pain scores observed in the present study. Based on this information, we believe that the demographic trends did not adversely affect our results.

Another limitation was the substantial number of participants removed from the study at the time of surgery. This was largely due to preference on the part of anesthesiologists at the study site for use of continuous femoral NB for patients with obstructive sleep apnea during the study period. Obstructive sleep apnea was not an exclusion criterion for the study but did result in roughly equal numbers of participants being removed from the 2 groups. In addition, the blinding of anesthesiologists and surgeons to drug administration prevented the double checks that typically occur in the operating room that would have prevented participants from receiving study drug via both delivery methods or no drug at all.

Conclusion

We found no clinically significant differences between continuous femoral NB and PI in the perioperative period despite finding statistically significant differences in some outcomes. The difference in range of motion observed at 1 year may have resulted from differences in the randomly assigned groups in addition to potentially being related to the type of analgesia strategy used. When deciding on the analgesic regimen for management of pain after TKA, surgeons and anesthesiologists should opt for the perioperative modality that has the best efficiency for their operating room environment.

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