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Femoral nerve catheter *vs* local infiltration for analgesia in fast track total knee arthroplasty: short-term and long-term outcomes

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Abstract

Background: The aim was to compare the effects on short-term and long-term pain and functional outcome of periarticular local anaesthetic infiltration (LIA) with LIA of the posterior knee capsule in combination with a femoral nerve block (FNB) catheter in patients undergoing total knee arthroplasty.
Methods: Eighty patients were randomised to one of two groups: Subjects in group LIA received periarticular LIA with ropivacaine 0.2% for postoperative analgesia; subjects in group FNB received LIA of the posterior capsule and a FNB catheter. The primary outcome parameter was functional capacity of the knee 12 months after surgery. Secondary parameters included mobility as determined by accelerometer data, pain, satisfaction with the analgesic regimen, hospital length of stay, and use of pain medication 3 and 12 months after surgery.
Results: There were no differences between groups in long-term functional capacity, patient satisfaction and hospital length of stay. In the first 2 days, subjects in group FNB had slightly lower pain scores and used less opioids, and subjects in group LIA had a higher level of accelerometer activity. Three and 12 months after surgery, subjects in group FNB had lower maximum pain scores and were less likely to use any pain medication 12 months after surgery.
Conclusions: Both techniques were similar regarding long-term functional outcome. Subjects in group FNB had slightly lower pain scores and lower opioid consumption after operation, lower maximum pain scores at 3 and 12 months, and were less likely to use any pain medication at 12 months.
Clinical trial registration: NCT01966263.

Keywords: local anaesthesia; arthroplasty; nerve block; postoperative pain

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Editor's key points

- Low postoperative pain, early mobilisation, and no persistent pain are aims of total knee arthroplasty.
- Short- and long-term benefits of different analgesic techniques need to be understood.
- Local anaesthetic infiltration was compared with femoral nerve block catheter, assessing up to 12 months post-surgery.
- Femoral nerve block catheter reduced pain severity and analgesic consumption 12 months after surgery.
- Techniques associated with less long-term analgesic use after surgery should be considered.

Total knee arthroplasty (TKA) reduces knee pain and improves knee joint function in patients with knee osteoarthritis.[1] TKA may be associated with severe postoperative pain, which in turn may slow rehabilitation and predispose to the development of persistent pain.[2,3] Perioperative pain protocols therefore focus on achieving optimal pain relief with a minimum of side effects; however, these goals may conflict with changing surgical perspectives with emphasis on early mobilisation and reduced length of hospital stay. Recently developed fast track protocols (enhanced recovery protocols) aim for shorter hospital length of stay and better functional recovery.[4] Fast track protocols that incorporate early mobilisation have been shown to improve functional recovery and patient satisfaction, and are associated with a lower incidence of thromboembolic adverse events.[5]

Femoral nerve block (FNB) provides good analgesia[6] and is considered the standard of care by many.[7,8] However, use of FNB has become disputable, because like epidural analgesia it might hamper early mobilisation.

Recent developments such as local infiltration analgesia (LIA) aim at providing adequate analgesia while avoiding motor impairment.[9] Several RCTs comparing LIA with FNB have been conducted, and three meta-analyses show no differences in the two techniques regarding postoperative analgesia and complication rates.[10–12] Although LIA might provide acceptable perioperative analgesia, there are no data on long-term functional recovery and persistent pain.

We performed a blinded RCT comparing periarticular LIA of the knee with LIA of the posterior knee capsule in combination with a FNB catheter in terms of functional outcome and pain in patients undergoing primary TKA. Primary outcome measure was knee function, tested with functional tests. Secondary outcomes were perioperative and long-term knee pain, use of analgesics, length of hospital stay, and patient-reported functional outcome by questionnaires.

Methods

This blinded randomised study was approved by the local Medica MREC (IRBN, Independent Review Board Nijmegen IRBN2013005) and registered with an international clinical trials registry (www.clinicaltrials.gov, NCT01966263) before onset of participant enrolment. Patients undergoing primary unilateral TKA were assessed for eligibility during preoperative screening visit. Patients were informed about the study and written informed consent was obtained from all patients. The study was conducted between November 2013 and November 2015 at the Sint Maartenskliniek, Nijmegen, The Netherlands, according to the Declaration of Helsinki and later revisions thereof and in accordance with the ICH guidelines for Good Clinical Practice.

Patients

Eligible participants were all adults aged 50–80 yr with ASA physical health classification 1–3. Patients presented with non-inflammatory knee osteoarthritis and were scheduled for fast track, primary, unilateral TKA under spinal anaesthesia. Exclusion criteria were defined as: any contra-indication for locoregional or spinal anaesthesia, traumatic osteoarthritis or rheumatoid arthritis requiring TKA, an active local or systemic infection, known intolerance or contraindication for local anaesthetics, paracetamol, NSAIDs or opioids, BMI >40 kg m^{-2}, inability to walk independently (inability to walk at least 10 m without a walking aid), undergoing contra-lateral TKA <1 yr, or undergoing another surgery <3 months, use of opioids or anti-neuropathic pain medication >1 yr, or physical, emotional, or neurological conditions that would compromise compliance with post-operative rehabilitation and follow-up.

Study procedure

Using a computer-generated sequence of random numbers in eight blocks of 10 and a sealed envelope technique, patients were randomised to one of two groups: group FNB or group LIA. The envelopes were opened just before surgery, when the patient arrived in the anaesthetic room. Patient, anaesthesiologist, and orthopaedic surgeon were informed about the study allocation. The physical therapists and research assistants who assessed the outcome variables were blinded for treatment allocation and the patient was instructed not to discuss the analgesic regimen with anyone.

Anaesthesia and surgical procedure

All surgeries were performed according to standard hospital protocol. In the anaesthetic room, standard monitoring (pulse oximeter, non-invasive BP, and ECG) was applied to all patients and i.v. access was established. Before spinal anaesthesia, patients in group FNB received a femoral catheter (Contiplex, B. Braun, Melsungen, Germany) with dual guidance (ultrasound and nerve stimulation). A correct position of the needle and catheter tip was verified by the spread 5–10 ml of NaCl 0.9% injected under ultrasound guidance. The catheter was secured with a transparent dressing with an antimicrobial gel pad.

In patients in group LIA, a sham femoral catheter was taped to the skin in a similar fashion as with patients in group FNB.

All patients received spinal anaesthesia with hyperbaric bupivacaine 0.5% (10 mg) in the sitting position. Upon completion of the subarachnoid injection, patients were turned to the lateral decubitus position, the side of surgery being dependent. This was maintained for 20 min to achieve a predominantly unilateral block, after which patients were turned to the supine horizontal position.

During surgery, patients received conscious sedation with propofol upon request. A pneumatic tourniquet was placed around the patient's thigh and inflated to 50 mm Hg above systolic BP with a maximum of 250 mm Hg. The knee was

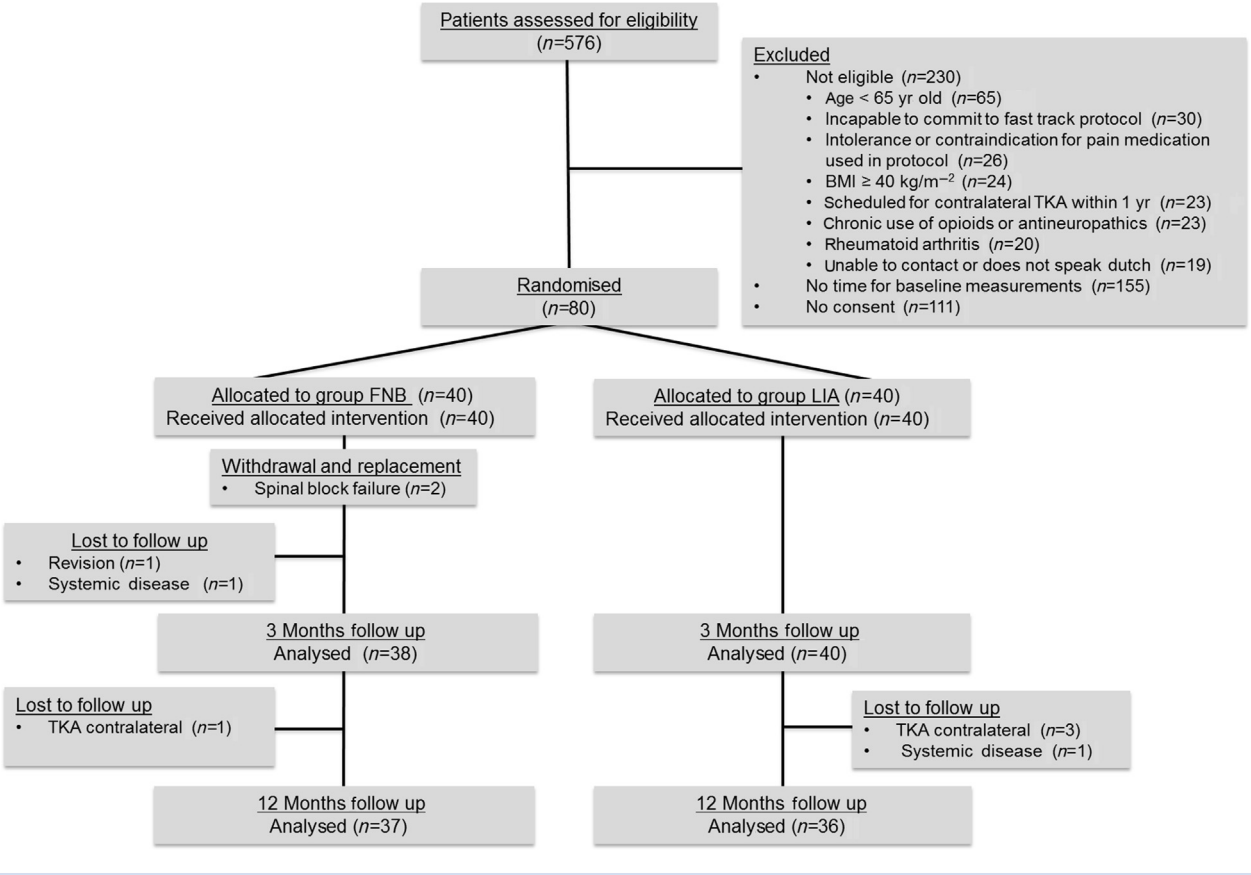

Fig 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

approached through medial parapatellar arthrotomy, and all patients received a Genesis II posterior-stabilised TKA (Smith & Nephew, Memphis, TN, USA) with patellar resurfacing.

Study interventions

After placement of the prosthetic components and before wound closure, patients in both groups received local infiltration of the posterior knee capsule with ropivacaine 0.2%, 100 ml plus epinephrine 1:200.000 to cover pain arising from the popliteal fossa. Immediately afterwards, patients in group FNB received a bolus of ropivacaine 0.2%, 20 ml via the femoral catheter, while patients in group LIA received local infiltration of the anterior capsule with ropivacaine 0.2%, 50 ml plus epinephrine 1:200.000 and of the subcutaneous tissue with ropivacaine 0.2%, 50 ml without epinephrine. Patients in group FNB received three additional boluses of ropivacaine 0.2% via the femoral catheter at 6 h intervals up to 18 h after the initial bolus injection.

Multimodal analgesia

All patients received oral multimodal analgesia consisting of paracetamol 1000 mg q.i.d., etoricoxib 90 mg once daily, and gabapentin 600 mg b.i.d. (300 mg if age >60 yr).

Breakthrough pain [numeric rating scale (NRS)>3] in the recovery room was treated with intravenous morphine.

At the orthopaedic ward, breakthrough pain (NRS>3) was treated with oxycodone 5–10 mg *ad libitum* (maximum of 60 mg 24 h^{-1} or 30 mg 24 h^{-1} if age >70 yr).

Rehabilitation and discharge criteria

Rehabilitation was according to the standard hospital fast track protocol. The protocol includes preoperative explanation of the protocol and instruction of the patients to ensure maximum involvement, short acting spinal anaesthesia, mobilisation within 4 h after operation, physical therapy twice daily, and evaluation of reaching the discharge criteria twice daily. Weight bearing mobilisation was started as soon as spinal anaesthesia had worn off and patients were encouraged to exercise. Patients were discharged when a set of discharge criteria was met (Supplementary Table S1).

Outcome measurements

Data collection, including conducting all functional tests, was done by blinded physical therapists and research assistants.

Functional capacity of the knee was assessed before operation, at hospital discharge, and at 3 and 12 months after operation using the Timed Up and Go Test (TUG), Stair Climbing Test (SCT) and the Six Minute Walking Test (6MWT). The TUG and SCT measure the time in seconds to perform predefined tests, and the 6MWT measures the distance in

meters. These tests have been validated for detection of improvement or deterioration in hip or knee function after surgery.[13] The functional tests were conducted by three blinded physical therapists, all tests were conducted in the same manner, in the same hall, using the same stairs and chair. At 3 and 12 months, the patients performed the functional tests just before their postsurgical follow-up visit to the orthopaedic surgeon at the outpatient clinic.

In addition, knee function was evaluated using the Lower Extremity Functional Scale (LEFS) and the Oxford Knee Score (OKS) before operation, at 6 weeks, and at 3 and 12 months after operation. At the same time intervals, fear of movement was measured using the Tampa Scale for Kinesiophobia (TSK), and quality of life was assessed using the EQ5D-3L and a Visual Analogue Scale (VASQL).

During hospital admission, a research assistant blinded for group allocation visited the patient twice daily at 8 am and 8 pm to assess postoperative pain by NRS (0=no pain, 10=worst possible pain). At each time point, patients were asked to rate their average pain during the previous 12 h period. In the morning of the first 2 postoperative days, an accelerometer was attached to the non-operated thigh and in the evening, it was taken off. Accelerometers were used to assess the level of activity: an accelerometer can detect body movements by measuring orientation and acceleration in three orthogonal planes; anteroposterior, mediolateral, and vertical. Hereby the intensity of activity over time can be estimated, and postures and transfers can be calculated by using the orientation of the meter in relation to the body.[14] The patients were instructed to continue their normal routine whilst wearing the accelerometer. Accelerometer data were either classified as 'active', which meant the accelerometer was in the upright position and moving, or 'resting', which was all other positions.

Twice daily the patients were visited by the physical therapist, who was blinded for group allocation, and who recorded the ability of the patient to mobilise.

At discharge, patients rated their satisfaction with the analgesic regimen on an NRS scale (0=very dissatisfied, 10=very satisfied), and range of motion (ROM) was calculated by the sum of knee flexion and extension as measured with a long-arm goniometer.

Pain and the use of analgesic medication for knee pain were assessed before operation, and at 3 and 12 months after surgery. Patients were asked to rate their average and their maximum pain in the 2 weeks preceding the contact moment on an 11-point numeric rating scale (NRS), ranging from no pain (0) to worst imaginable pain (10).

Sample size and statistical analysis

The null hypothesis of our study was that differences in anaesthetic technique for TKA do not affect long-term functional outcome. Of the three tests we used to evaluate functional capacity, the SCT has the largest variance.[15,16] To reduce the risk of insufficient power, we defined functional capacity of the knee 12 months after surgery as determined by SCT as the primary outcome parameter. Based on two studies,[15,16] the sample size necessary to detect at least a 30% difference with a 90% probability and $\alpha<0.05$ was 37 patients per group.

Allowing for patient withdrawal during the study period, we included 40 subjects per group.

Data were analysed using Stata version 13.1 (Stata Corporation, College Station, TX, USA) and are presented as mean (standard deviation). Knee function outcome scores were analysed using multiple regression models. Linear regression was used to investigate the effect of the analgesic technique on the use of pain medication. A multilevel regression model was used to investigate the effect of analgesic technique on pain scores after operation, during the first 2 postoperative days. Time, time squared, and baseline pain score were used as covariates in this model. The model used a random intercept, to allow for the clustering of the first four pain scores recorded after operation at 8 pm and 8 am within each patient. For this specific analysis, R version 3.4.3 was used as statistical software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Recruitment and flow of the patients is shown in a Consolidated Standards of Reporting Trials flow diagram (Fig. 1). All enrolled subjects received the allocated intervention. Subjects in both groups had similar patient and surgical characteristics. Distribution of baseline characteristics across the treatment groups is shown in Table 1 and adverse events in Supplementary Table S2.

Missing values

Average pain scores during hospitalisation

During the first 2 days, average pain scores were missed in one to three subjects because of absence during the regular visit. This concerned different patients every day. Missing average pain scores on the second day after surgery were because of patients being already discharged from the hospital.

Accelerometer data

Accelerometer data could not be obtained in all subjects because of technical failure. This concerned different subjects every day.

Functional capacity

Four subjects (two in each group) were discharged before the functional capacity tests could be performed and one subjects in group LIA was unable to perform the SCT on the day of discharge.

Table 1 Baseline characteristics. Displayed as mean (SD) or number of patients. FNB, femoral nerve block; LIA, local infiltration analgesia

	Group FNB (n=40)	Group LIA (n=40)
Sex, n, M/F	20/20	17/23
Age (yr) Mean (SD) [Range]	64 (6.9) [49–77]	66 (6.3) [53–80]
BMI (kg m^{-2})	30.0 (4.9)	28.4 (4.2)
ASA physical status n, 1/2/3	8/24/8	13/15/12
Side of surgery, n, left/right	22/18	17/23
Duration of surgery (min)	72 (16)	71 (11)
Tourniquet time (min)	55 (11)	56 (14)
Hospital length of stay (days)	3.2 (1.1)	3.0 (0.9)

Table 2 Functional performances displayed as mean (SD) and adjusted differences for baseline performance. 6MWT, 6 minute walk test; CI, confidence interval; FNB, femoral nerve block; LIA, local infiltration analgesia; ROM, range of motion; SCT, stair climbing test (primary outcome measure); TUG, timed up and go test

	Group FNB	N	Group LIA	N	Adjusted difference between means (95% CI)	P−value
SCT (s)						
Baseline	21.8 (11.3)	40	17.1 (6.8)	40		
Discharge	66.3 (25.9)	38	54.2 (24.7)	37	−8.2 (−19.8 to 3.5)	0.166
3 Months	16.8 (6.4)	37	17.4 (10.4)	38	2.4 (−1.5 to 6.3)	0.222
12 Months	13.8 (4.7)	37	14.3 (7.1)	36	1.9 (−0.7 to 4.5)	0.153
TUG (s)						
Baseline	10.1 (2.9)	40	9.0 (2.3)	40		
Discharge	21.7 (8.1)	38	19.6 (7.3)	38	−1.6 (−2.1 to 2.0)	0.380
3 Months	8.3 (1.5)	37	8.5 (2.4)	38	0.4 (−0.5 to 1.3)	0.356
12 Months	7.6 (1.2)	37	7.8 (1.9)	36	0.5 (−0.2 to 1.1)	0.197
6MWT (m)						
Baseline	394 (97)	40	432 (99)	40		
Discharge	203 (69)	38	219 (66)	38	8 (−22 to 38)	0.603
3 Months	440 (81)	37	447 (72)	38	−13 (−44 to 16)	0.368
12 Months	505 (84)	36	489 (71)	36	−32 (−64 to −0.4)	0.047
ROM (°)						
Baseline	107 (17)	40	111 (13)	40		
Discharge	74 (15)	38	72 (17)	38	−2 (−9 to 5)	0.569
3 Months	106 (13)	37	102 (13)	38	−5 (−11 to 1)	0.106
12 Months	112 (17)	37	112 (12)	36	−1 (−8 to 5)	0.580

At 3 months, one subject from group FNB was excluded from continued data collection because of revision surgery of the knee; one subject from group FNB withdrew from follow up because of the development of a malignancy. One subject in group FNB and two in group LIA missed the appointment at 3 months. None of these subjects had missed the functional capacity tests at discharge.

At 12 months, a third subject from group FNB and three subjects from group LIA were excluded from continued data collection because of TKA of the contralateral knee between 3 and 12 months. In group LIA, one subject withdrew from follow up at 12 months because of the development of a severe eye disorder requiring intensive treatment. One subject from group FNB was unable to perform the 6MWT because of severe backache. These subjects were not those with missing values at discharge and 3 months.

Average and maximum pain scores at 3 and 12 months

The missing values for average and maximum pain scores at 3 and 12 months concern the patients who missed the 3-month appointment, withdrew from follow up, or were excluded from continued data collection for reasons mentioned earlier.

All missing values were classified as completely at random, except for missing pain scores on postoperative Day 2 because of hospital discharge.

Long-term outcome variables

Functional capacity

Patients in both groups showed a major improvement in performance of functional knee capacity over time (Table 2).

Knee function and quality of life

Knee function as measured by LEFS and OKS improved over time in both groups. Knee function was comparable between the groups and there were no statistically significant differences at any of the time intervals. The same trend was found regarding quality of life as evaluated by EQ5D-3L and VASQL, and fear of movement as measured by TSK.

Table 3 NRS Pain scores at 3 and 12 months, displayed as mean (SD) and differences between means adjusted for baseline pain score. CI, confidence interval; FNB, femoral nerve block; LIA, local infiltration analgesia; NRS, numeric rating scale

	Group FNB	N	Group LIA	N	Adjusted difference between means (95% CI)
Baseline					
NRS average pain	4.7 (2.3)	40	3.9 (2.2)	40	
NRS maximum pain	7.2 (1.5)	40	6.7 (2.2)	40	
3 Months					
NRS average pain	2.4 (2.1)	38	2.8 (1.7)	37	0.7 (−0.1 to 1.5)
NRS maximum pain	3.8 (2.8)	38	4.6 (2.2)	37	1.2 (0.0−2.4)
12 Months					
NRS average pain	1.1 (1.8)	37	1.5 (2.0)	36	0.5 (−0.4 to 1.4)
NRS maximum pain	1.8 (2.4)	37	3.0 (2.6)	36	1.4 (0.2−2.6)

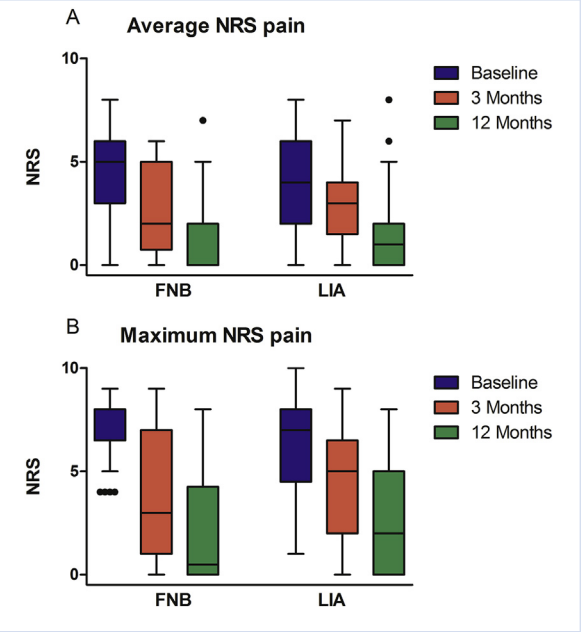

Fig 2. Box plots for NRS average (a) and maximum (b) pain scores at baseline, 3 and 12 months. • Represents outliers outside 1.5× inter-quartile range. FNB, femoral nerve block; LIA, local infiltration analgesia; NRS, numeric rating scale.

Pain

Average and maximum pain scores decreased over time in both groups. Maximum pain scores, but not average pain scores, were slightly lower in group FNB at 3 and 12 months after surgery; P=0.047 and P=0.021, respectively (Table 3 and Fig. 2).

Use of analgesics

Three months after surgery, there was no difference between the groups in the use of analgesics. Twelve months after surgery, patients in group LIA were almost six times more likely to use analgesic medication for pain in the operated knee compared with patients in group FNB [odds ratio 5.9; 95% confidence interval (CI) 1.1–31.7; P=0.037] (Table 4).

Short-term outcome variables

Postoperative pain and opioid use

Group FNB showed lower mean pain scores during the first 2 postoperative days, multilevel analysis revealed a difference of 0.95 (95% CI: 0.39–1.51, P=0.001) (Fig. 3). Similarly, a difference in favour of the FNB group was found for maximum pain scores (difference 1.22; 95% CI: 0.41–2.02; P=0.003).

Also, group FNB showed lower opioid consumption on the day of surgery and the day after surgery. Table 4 displays data on postoperative analgesic use. Oxycodone consumption on the day of surgery was 6.1 (8.9) mg in group FNB *vs* 10.9 (10.3) mg in group LIA (adjusted difference between means 4.8, 95% CI: 0.5–9.0). Oxycodone consumption on the day after surgery was 15.9 (12.4) mg in group FNB *vs* 28.6 (20.2) mg in group LIA (adjusted difference between means 12.8, 95% CI: 5.3–20.2).

There was no difference in patient satisfaction with the analgesic regimen [8.5 (1.1) in group FNB *vs* 8.1 (1.3) in group LIA].

Postoperative activity

Group FNB showed lower activity levels on the day of the surgery and the first postoperative day as measured by accelerometry. Time spent active on the day of surgery was 2.3 (2.4) min in group FNB *vs* 4.4 (2.9) min in group LIA (adjusted difference between means 2.2, 95% CI: 0.9–3.4). Time spent active on the day after surgery was 20.5 (14.9) min in group FNB *vs* 27.7 (14.1) min in group LIA (adjusted difference between means 7.2, 95% CI: 0.5–13.9).

Mobilisation

There was no difference between the groups in the ability to mobilise. ROM on the day of discharge was equal between groups FNB and LIA [74 (15) degrees and 72 (16) degrees, respectively], and there was no difference in hospital length of stay (Table 1).

Serious adverse events

None of the subjects showed any sign of local anaesthetic systemic toxicity (LAST). One falling incident was recorded. A patient in the FNB group mobilised unattended shortly after her return to the ward. The effects of spinal anaesthesia may not have been fully resolved at this time and may have contributed to the fall.

Discussion

We found no differences between groups (FNB and LIA) in functional recovery at 6 weeks, 3 months, and 1 yr after operation. These results agree with several other studies, although differences in methodology and the time of follow up exist.[17,18]

We found that maximum pain scores at 3 months and 1 yr after surgery were slightly but significantly higher in group LIA, and the odds of taking any pain medication for knee pain 1 yr after surgery was almost six times higher in the LIA group. Patients in group FNB also had lower pain scores and less opioid consumption in the immediate postoperative period. As postoperative pain is a possible risk factor for the development of chronic pain,[2,19] the possibility of a causal relation is intriguing and should be kept in mind. However, as our study was neither powered nor designed to detect the influence of anaesthetic technique on postoperative pain and chronification of pain after TKA, further study will be necessary to elucidate this.

Studies analysing the effect of analgesic technique on long-term recovery after TKA are scarce; most studies comparing FNB and LIA focus mainly on differences in the early postoperative period. Although pain and opioid consumption in the immediate postoperative period are important issues from a perspective of patient comfort and satisfaction, the effect of analgesic technique on long-term parameters such as functional recovery and pain is equally essential.

Regarding short-term outcome, we found that subjects in group FNB had lower pain scores and less oxycodone use on the first day and night after operation, and on the day after

Table 4 Rescue analgesic use during hospitalisation and analgesic use at 3 and 12 months follow up. In hospital oxycodone used was added up per patient for each day. Data are expressed as mean (standard deviation). FNB, femoral nerve block; LIA, local infiltration analgesia, CI: confidence interval

	Group FNB	N	Group LIA	N	Adjusted difference between means (95% CI)
Postoperative, in hospital, oxycodone use (mg)					
Day of surgery	6.1 (8.9)	40	10.9 (10.3)	40	4.8 (0.5–9.0)
Day after surgery	15.9 (12.4)	40	28.6 (20.2)	40	12.8 (5.3–20.2)
Day 2 after surgery	15.1 (16.7)	40	13.0 (15.6)	40	2.1 (−9.3 to 5.1)
Analgesic use at 3 months (no/yes)					
Paracetamol	29/9	38	25/13	38	
NSAID	37/1	38	32/6	38	
Opioids	35/3	38	33/5	38	
Other	37/1	38	37/1	38	
Overall use of pain medication at 3 months (no/yes)					
Total	28/10	38	22/16	38	
Analgesic use at 12 months (no/yes)					
Paracetamol	36/1	37	32/7	39	
NSAID	37/0	37	35/4	39	
Opioids	35/2	37	38/1	39	
Other	36/1	37	39/0	39	
Overall use of pain medication at 12 months (no/yes)					
Total	35/2	37	30/9	39	

surgery. The issue of the optimal analgesic regimen for fast track TKA is controversial.

Our results agree with Carli and colleagues[17] and Kovalak and colleagues,[20] who report less opioid use and lower pain scores in the first 2 days after operation when comparing femoral nerve catheter combined with LIA of the posterior part of the knee with LIA of both the posterior and anterior area of the knee. However, other studies reported better analgesia with LIA compared with FNB alone.[11,21–23] A possible explanation for this difference is the combination of FNB with local infiltration of the posterior capsule. Different branches of the femoral, obturator, and sciatic nerve contribute to the innervation of the knee[24] and FNB alone does not provide analgesia of the sciatic part of the knee. The addition of a sciatic nerve block has been shown to provide better analgesia than FNB alone[25] and local infiltration of the posterior capsule likely has a comparable effect.

Although the difference between the groups in pain scores and opioid use is statistically significant, the clinical relevance in the immediate postoperative period may be argued. Pain scores were low in both groups, and patient satisfaction with the analgesic technique was equally high.

Subjects in group FNB showed less activity as measured with the accelerometer on the first 2 days, but ROM at hospital discharge was similar between groups, as were length of hospital stay and functional test scores. Early mobilisation is believed to promote recovery after TKA and is one of the key features of fast track rehabilitation protocols. In our study we measured the time subjects spent active (standing, walking) using accelerometry, an objective way to measure physical activity.[26] Our data show that subjects in group FNB were less active on the day of surgery and the first postoperative day. However, the total amount of time spent active during the first day was short in both groups, on average 20 and 28 min during a 12 hour interval (8 am until 8 pm). As there was no difference between the groups on hospital length of stay, the clinical relevance of this difference in mobility is questionable.

Because of the potential of FNB to interfere with muscle strength, there is concern that the risk of falling is increased. We observed one falling incident in group FNB. This happened when the subject contrary to instructions, mobilised unattended at a time that spinal anaesthesia may not have been fully resolved. We did not observe any other falling incidents.

The dose of ropivacaine 400 mg we use for LIA is high, and well above the maximum recommended dose of 3–4 mg kg^{-1} for most patients. Although pharmacokinetic studies involving LIA with ropivacaine 400 mg for TKA found free ropivacaine concentrations to remain below the toxic threshold[27,28] and we observed no signs of LAST in any of our subjects, it may be prudent to consider reducing the dose of ropivacaine in patients with a low body weight, or in patients who are otherwise at an increased risk for LAST.

Our study has several limitations. We used a combination of ropivacaine and epinephrine for LIA, but around the world LIA mixtures vary in composition, additives, and dose of local anaesthetic; also, we opted for an intermittent bolus technique in the FNB group, whereas others may favour a continuous infusion. Our results, therefore, are not necessarily representative for different LIA mixtures and different modes of application.

Although the total dose of ropivacaine in both groups is comparable, the systematic difference between the two methods of pain relief may favour the FNB group because these patients received three additional boluses with local anaesthetic up to 18 h after surgery, whereas patients in group LIA only received 'single shot' infiltration at the end of surgery. To counteract this difference, an intra-articular catheter allowing similar top-ups would have been necessary in the LIA group. However, intra-articular catheters are controversial because of fear of an increased risk of infection, and for that reason, are not used in many orthopaedic centres, including ours. Therefore, despite this systematic difference between the two techniques, a comparison is still relevant from a clinical perspective.

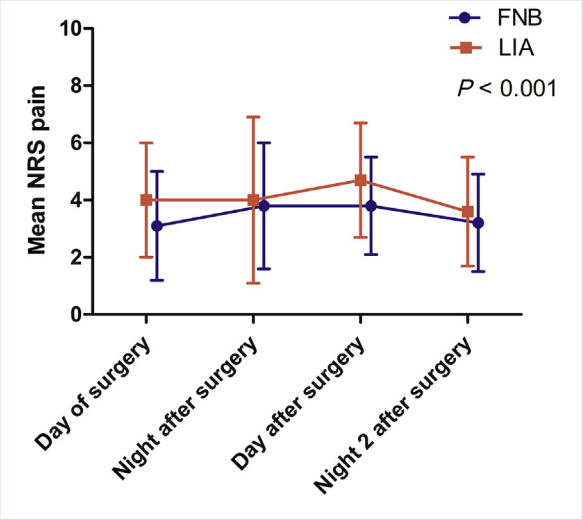

Fig 3. Postoperative pain scores during hospitalisation. Postoperative pain scores were assessed twice daily by a blinded research assistant. Data are plotted as means with standard deviation. Multilevel analyses on presented pain scores, corrected for baseline pain scores showed a significant pain reduction in group FNB (P=0.001). FNB, femoral nerve block; LIA, local infiltration analgesia; NRS, numeric rating scale.

For ethical reasons, we refrained from inserting femoral catheters in subjects randomised to group LIA, taping a sham catheter to the skin instead. Although an *in vivo* placebo catheter would have been a better option with respect to blinding, it is our opinion that the risk of an invasive sham catheter would not justify the benefits. Thus, the subjects were not blinded to group allocation.

The treating anaesthetists and surgeons were also not blinded. Given the study design, blinding of the anaesthetists was not possible. Blinding the operating room personnel, including the surgeons, would have necessitated sham infiltration of the anterior capsule and subcutaneous tissue with normal saline in the FNB group, causing unnecessary swelling. In addition, it would have made the LIA procedure more complicated with different injectates for the anterior part of the knee for the two groups, increasing the risk of unintentional protocol violation. However, because the physical therapists and the research assistants collecting the data were blinded and none of the anaesthetists, surgeons, or operating room personnel were involved in outcome measurements or data collection, we believe these limitations have not affected our results. Furthermore, performance on physical tests such as the 6MWT, SCT, and TUG is not only determined by knee function *per se*, but also by factors such as age, sex, BMI, and possible health issues. Because we used a randomisation procedure we assume that possible confounders were distributed equally among the groups.

Another limitation is that we asked subjects at the 3 and 12 months visits to rate their average and maximum pain in the 2 weeks preceding the contact moment, and this is a potential cause of recall bias. A pain diary would have reduced this risk, but would also have been much more time consuming for the patients. As post-surgery pain was a secondary outcome, we chose not to use a pain diary, but a less burdensome method instead.

In conclusion, FNB and LIA are comparable techniques regarding short-term and long-term functional outcome after TKA. There were no differences in SCT between the two groups, nor in the other functional capacity tests. We found that FNB compared with LIA provides slightly better pain relief and less oxycodone use on the first day and night after TKA, and on the day after surgery. Three and 12 months after surgery, patients in group FNB had lower maximum pain scores and were significantly less likely to use any pain medication 12 months after surgery. Further study is needed to determine if this relation is causal or spurious.

Authors' contributions

Conceived of the study: M.G.E.F., G.J.S., R.S.
Participated in study design: M.G.E.F., P.J.C.H., R.S.
Data collection: M.G.E.F., S.M.K.B.
Performed statistical analysis: M.G.E.F., S.M.K.B.
Processed the data: S.M.K.B.
Helped with the data analysis: P.J.C.H.
Participated in coordination of the study: R.S.
Drafted the manuscript, read and approved the final manuscript: all authors.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.bja.2018.05.069.

Declaration of interest

The authors declare that they have no conflicts of interest.

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