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Continuous Femoral Nerve Blockade or Epidural Analgesia After Total Knee Replacement: A Prospective Randomized Controlled Trial

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Because postoperative pain after total knee replacement (TKR) can be severe, we compared the analgesic efficacy of continuous femoral nerve blockade (CFNB) and continuous epidural analgesia (CEA) after TKR in this prospective randomized trial. Patients undergoing TKR under spinal anesthesia were randomized to receive either a femoral infusion of bupivacaine 0.2% (median infusion rate 9.3 mL/h) ($n = 53$) or an epidural infusion of ropivacaine 0.2% with fentanyl 4 μg/mL (median infusion rate 7.6 mL/h) ($n = 55$). Adjuvant analgesics were oral rofecoxib and oxycodone and IV morphine. Pain, nausea and vomiting, hypotensive episodes, motor block, range of knee movement, and rehabilitation milestones were assessed postoperatively. There were equivalent pain scores, range of movement, and rehabilitation in both groups. There was significantly less nausea and vomiting in the CFNB group ($P < 0.002$). The CFNB group received more rofecoxib ($P < 0.04$) and oxycodone ($P < 0.005$) than the CEA group. The operative limb displayed more motor block than the nonoperative limb in both groups at the level of the hip and knee for up to 48 h ($P < 0.05$, Mann-Whitney *U*-test), but there was no difference between groups in the nonoperative limb. CFNB is an effective regional component of a multimodal analgesic strategy after TKR.

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Postoperative pain after total knee joint replacement (TKR) can be severe. Two studies have demonstrated that continuous femoral nerve blockade (CFNB) provides postoperative analgesia and functional recovery that is comparable to continuous epidural analgesia (CEA) after TKR with fewer side effects (1,2). However, the clinical setting in which both studies were conducted included prolonged rehabilitation programs that differ from current practice in many institutions where early aggressive mobilization and short inpatient stays are routine (3). In addition to the different practice environment, previous investigations have involved relatively small numbers of patients. This prospective, randomized controlled study was designed to compare the analgesic efficacy and the ability to mobilize patients on postoperative days 1–5 using CFNB or CEA after TKR in our clinical practice.

Methods

After institutional ethics committee approval, patients scheduled to undergo primary TKR were invited to participate in the study. Exclusion criteria included the following: inability to give informed consent for language or cognitive reasons; contraindications to neuraxial blockade (including patient refusal, platelet count $<100 \times 10^9$/L or coagulopathy); contraindications to CFNB (e.g., infection overlying the injection site or previous femoro-popliteal bypass surgery); and contraindication to any study drugs.

Patients were randomized to either the CFNB group or the CEA group. The random allocation sequence was computer generated in permuted blocks of four and enclosed in sequentially numbered, opaque, sealed envelopes. The primary anesthetic

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technique in both groups was spinal anesthesia with 12.5–17.5 mg of bupivacaine 0.5%. Intraoperative sedation with midazolam was given at the discretion of the treating anesthesiologist. Patients and treating clinicians were not blinded as to study group randomization.

In the CFNB group, CFNB was established before spinal anesthesia. Using an aseptic technique, the femoral artery was located immediately caudad to the inguinal ligament. An insulated 18-gauge Tuohy needle (Contiplex® Tuohy Continuous Nerve Block Set; B Braun, Bethlehem, PA) was inserted just lateral to the artery and the femoral nerve located using a peripheral nerve stimulator (Stimuplex® HNS11; B Braun, Freiburg, Germany), with a quadriceps twitch at <0.6 mA (300 ms, 2 Hz) considered an acceptable response. Twenty-five mL of bupivacaine 0.25% with adrenaline 1:400 000 was injected incrementally and a 20-gauge catheter was then advanced 10–15 cm beyond the needle tip, stopping if resistance was felt.

Patients in the CEA group received a combined spinal-epidural anesthetic at the L2-3 or L3-4 interspace (CSEcure 16-gauge/27-gauge Combined Spinal/Epidural Minipack; Portex, Hythe, UK). No anesthetic was injected through the epidural catheter preoperatively.

In the recovery room, patients in the CFNB group had a femoral infusion of bupivacaine 0.2% commenced at 0.1 $mL \cdot kg^{-1} \cdot h^{-1}$, with a patient-controlled anesthesia (PCA) bolus of 0.05 mL/kg and a 60-min lockout period. When there was regression of sensory blockade below T8 and initial recovery of motor function and hemodynamic stability, patients in the CEA group had an epidural infusion of ropivacaine 0.2% plus fentanyl 4 μg/mL commenced at 6–10 mL/h in recovery. The acute pain service varied the infusion rate so as to maintain sensory blockade covering the surgical site.

All patients were assessed by the acute pain service three times daily. Local anesthetic infusions were continued until the morning of postoperative day 3 (with the operative day being day 0). Oral adjuvant analgesia consisted of rofecoxib 50 mg (Vioxx®; Merck Sharp & Dohme, Granville, Australia) daily and oxycodone 10–15 mg (Endone®; Boots Healthcare Australia Pty. Ltd., North Ryde, Australia) every 4 h, as required. If analgesia was inadequate despite oral adjuncts, an IV morphine infusion was commenced. If there was no evidence of a sensory block to ice, the local anesthetic infusion was ceased.

Postoperative mobilization followed the hospital clinical pathway. This protocol was as follows: sit out of bed on a chair on postoperative day 1, ambulation with a walking frame on postoperative days 2–3, ambulation with crutches and increased distance on postoperative day 4 and stairs on postoperative day 5 in preparation for discharge. Patients were reviewed by a physiotherapist twice daily. During initial mobilization on postoperative day 1, the ability to sit out of bed, wound drainage and hypotensive episodes were recorded by physiotherapists and nursing staff. Hypotensive episodes were defined as a change in systolic blood pressure from lying to standing of more than 20%, clinical signs consistent with hypotension on standing (such as feeling faint and diaphoretic) necessitating an immediate return to bed without a standing arterial blood pressure being recorded, or being hypotensive while supine. It was anticipated that patients would be discharged between postoperative days 5 and 6. Thromboprophylaxis was achieved with low molecular weight heparin dalteparin sodium 5000 IU (Fragmin; Pfizer Australia Pty. Ltd, West Ryde, Australia) given subcutaneously daily commencing on the evening of surgery.

Passive knee flexion, using a Continuous Passive Motion (CPM) machine (Smith & Nephew Kinetic Optima and Prima, Tournes, France) commenced on the day of surgery, and active flexion and extension exercises the following day. CPM was used according to the clinical pathway, increasing by 15 degrees of flexion with each application until 90 degrees of flexion was achieved. Active knee flexion was measured on postoperative days 1–5 using a large-size goniometer. Physiotherapists recorded power in lower limb muscle groups on postoperative days 1 and 2 using a 6-point scale of muscle power (0 = no muscle action; 1 = flicker movement only; 2 = unable to overcome gravity; 3 = able to overcome gravity; 4 = able to overcome gravity and moderate resistance; 5 = assessor unable to manually overcome the muscle power). Readiness for discharge was assessed according to the following criteria: 90° of active knee flexion, grade 3 or more knee extension strength, independent mobilization with 2 crutches on the flat and on steps, and independence with a home exercise program.

Visual analogue scale (VAS) pain scores were recorded on postoperative days 1 and 2 at rest, during CPM and during active physiotherapy. Other data collected included: patient characteristics, technical difficulties with block insertion, the achievement of physiotherapy milestones, nausea scores on postoperative days 1 and 2 (0 = no nausea; 1 = nausea only; 2 = nausea and vomiting) and the technical success of the blocks was evaluated by assessing sensory block to ice on postoperative days 1 and 2 (CEA group: upper limit of dermatomal block; CFNB group: presence of blockade over the anterior midthigh). Local anesthetic and adjuvant analgesic dosages were recorded, as was the incidence of early cessation of local anesthetic infusion (prior to postoperative day 3).

Table 1. Patient Characteristics

	CFNB (n = 53)	CEA (n = 55)
Age (yr)	69 (10)	71 (9)
Male/Female	26/27	25/30
Height (m)	1.67 (0.10)	1.65 (0.10)
Weight (kg)*	91 (16)	84 (18)
BMI	33 (6.1)	31 (5.2)
BMI >30	34	28

Values are mean (SD) or n.
CFNB = continuous femoral nerve blockade; CEA = continuous epidural analgesia; BMI = body mass index (kg/m).
* $P = 0.048$.

Assuming a baseline VAS pain score of 30 and a standard deviation (SD) of 25 (1), and using a two-tailed sample size analysis, we calculated that to detect a 50% reduction in pain scores with a power of 80% and an α-value of 0.05, we would require 44 patients in each group (Stata7 software, Stata Corporation, Texas). To allow for increased variability in primary outcome, 112 patients were recruited. All analyses were on an intention-to-treat basis. Statistical analysis was performed using StatView® Version 4.5 software (Abacus Concepts, Berkeley, CA). Parametric data were compared using Student's t-test, with a Bonferroni correction for multiple comparisons. Nonparametric data were compared using a Mann-Whitney U-test or Fisher's exact test as appropriate. Data are expressed as mean (SD) or median (interquartile range [IQR]). A P value of < 0.05 was considered significant.

Results

One-hundred-and-twelve patients were randomized between February 2001 and March 2003. Of these, four patients' data were not included in the analysis. One patient's data, from the CEA group, was lost. Three patients from the CFNB group were withdrawn after protocol violations. One was discovered to have severe aortic stenosis before anesthesia and two randomized patients were actually scheduled for hemiarthroplasties and were withdrawn. Of the remaining 108 patients, 53 were assigned to the CFNB group and 55 to the CEA group. Patient characteristics are shown in Table 1.

The VAS pain scores at rest, during CPM, and during physiotherapy on postoperative days 1 and 2 are depicted in Figure 1. There was no significant difference in pain scores between groups at any time (Mann-Whitney U-test). In the CEA group, preoperative localization of the epidural space was unsuccessful in 2 patients (3.6%), who received spinal anesthesia and postoperative IV morphine PCA. Two patients in the CEA group had inadvertent dural punctures with the Tuohy needle. In one of these, the epidural catheter was successfully inserted on a second attempt. Neither patient suffered a postdural puncture headache. The median cephalad extent of the sensory blockade in the CEA group was T11 and T12 on postoperative days 1–2 respectively. Four patients in the CFNB group and five in the CEA group had a successful block initially but had their infusions ceased earlier than planned as a result of catheter dislodgement.

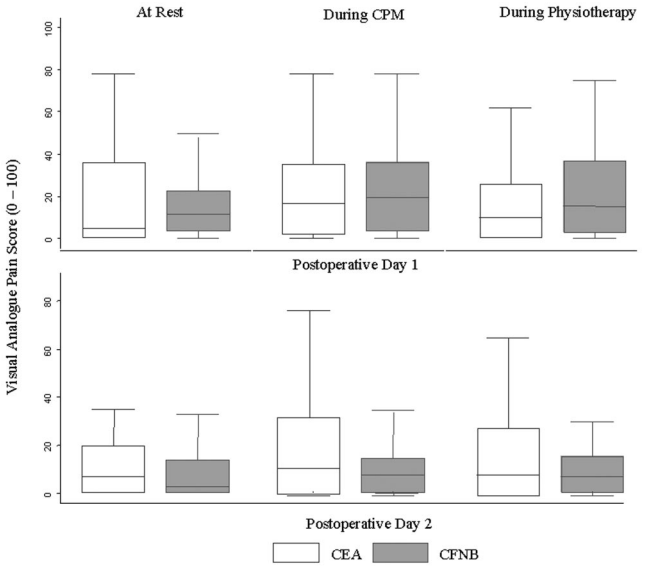

Figure 1. Visual analog pain score (0–100) measured at rest, during continuous passive movement (CPM), and during physiotherapy on postoperative days 1 and 2. CFNB = continuous femoral nerve blockade; CEA = continuous epidural analgesia. Boxes represent median and interquartile range; whiskers represent the 5th to 95th percentiles.

Analgesic drug dosages are shown in Table 2. Patients in the CFNB group received more oxycodone (21 [15] versus 13 [12] mg, $P = 0.005$) and rofecoxib (92 [48] versus 70 [60] mg, $P = 0.04$) than did those in the CEA group. The CEA group received a fentanyl with a mean dosage of 1.74 mg. There was no difference between groups in the number of patients requiring IV morphine (CFNB 12 versus CEA 11) or in the mean dosage of morphine (CFNB 44 mg versus CEA 53 mg). Patients in the CFNB group received a median bupivacaine infusion rate of 9.3 mL/h, whereas those in the CEA group received a median ropivacaine/fentanyl infusion rate of 7.6 mL/h.

More patients in the CEA group than in the CFNB group suffered nausea or vomiting and the nausea score was higher in the CEA group compared with the CFNB group (Table 2).

There were no differences between groups in volume of blood collected in wound drains (CFNB 821 [469] versus CEA 676 [472] mL) or in hemoglobin concentrations (CFNB 91 [38] versus CEA 92 [35] g/L) on postoperative day 1.

Table 2. Pharmacology, Side Effects and Postoperative Recovery

	CFNB (n = 53)	CEA (n = 55)	P value
Pharmacology			
Oxycodone (mg)	21 (15)	13 (12)	0.005
Rofecoxib (mg)	92 (48)	70 (60)	0.04
Fentanyl (mg)	–	1.74	
Patients requiring morphine	12	11	NS
Dosage (mg)	44 (30)	53 (28)	0.45
Local anesthetic infusion rate (ml/h)	9.3	7.6	
Nausea score	0.3	1.1	0.007
Hypotensive episodes	1	5	NS
Active knee flexion			
Postoperative day 1	54 (18)	52 (17)	NS
Postoperative day 2	67 (19)	65 (16)	NS
Postoperative day 3	73 (17)	77 (13)	NS
Postoperative day 4	80 (15)	83 (14)	NS
Postoperative day 5	81 (14)	82 (18)	NS
Technical success regional block (%)*			
Postoperative day 1	96	96	NS
Postoperative day 2	92	88	NS
Catheter dislodgement	4	5	NS
Hospital length of stay	5.3 (1.1)	5.4 (1.1)	NS

Values are mean (SD) or n.
CFNB = continuous femoral nerve blockade; CEA = continuous epidural analgesia.
* Evaluated with sensory block to ice.

More patients in the CFNB group were able to sit out of bed on postoperative day 1 compared with the CEA group (89% versus 70%, $P = 0.03$). The most common reason observed by the physiotherapists was excessive motor block (0 patients in the CFNB group versus 7 patients in the CEA group). In both groups, the operative limb displayed significantly more intense motor blockade than the nonoperative limb at the level of the hips and knees for up to 48 h ($P < 0.05$, Mann-Whitney U-test). In the operative limb, the only difference between groups was a more intense quadriceps motor block in the CFNB group than in the CEA group on postoperative day 2 ($P = 0.001$). In the nonoperative limb, there was no difference in motor block between groups (Fig. 2).

Postoperative range of movement in the operative knee is reported in Table 2. There were no significant differences between groups during postoperative days 1–5. There was also no difference between groups in the number of patients who achieved 90 degrees of flexion on CPM by postoperative day 3 and who could walk with crutches by postoperative day 4 or climb one step by postoperative day 5.

There was no difference between groups in hospital length of stay (mean of 5.3 days in CFNB group versus 5.4 days in CEA group).

Three patients suffered significant complications, with no difference between groups. One patient in the CFNB group had a non-ST elevation myocardial infarction that was treated conservatively. He was not hemodynamically compromised and the femoral infusion continued unchanged, providing good analgesia. A second patient in the CFNB group was hypotensive while supine. He had a cardiac conduction defect and required insertion of a permanent pacemaker. His femoral infusion was also continued. One patient in the CEA group was found to be hypotensive (60/40 mm Hg) and bradycardic, though still conscious, on the evening of surgery, 2 h after commencement of the epidural infusion. The patient's spinal-epidural block

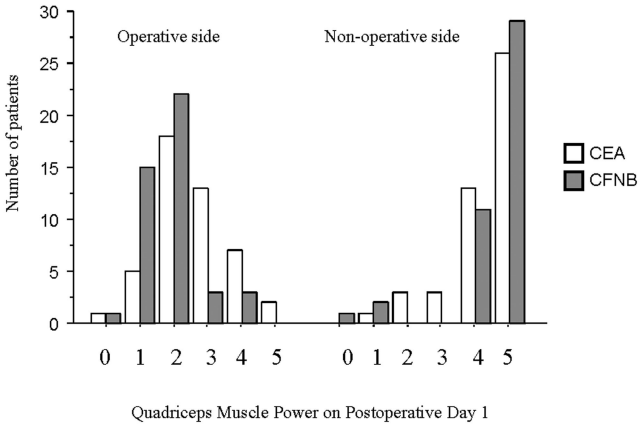

Figure 2. Quadriceps muscle power for operative and nonoperative sides on postoperative day 1. Muscle power scale: 0 = no muscle action, 1 = flicker movement only, 2 = unable to overcome gravity, 3 = able to overcome gravity, 4 = able to overcome gravity and moderate resistance, 5 = assessor unable to manually overcome the muscle power. $P < 0.001$ for difference in quadriceps muscle power between operative and nonoperative sides regardless of group.

had reached dermatome T3. The epidural infusion was discontinued and he was successfully resuscitated and admitted to the intensive care unit overnight without any sequelae. There were no neurological complications or perioperative deaths.

Discussion

This study showed equivalent analgesia between CFNB and CEA after TKR, consistent with previously published data (1,2). It demonstrates an improved side effect profile with a reduced incidence of nausea and vomiting using CFNB. This is the largest study addressing this question, with three times as many patients per group as earlier comparable studies. Furthermore, it demonstrates equivalence of analgesia in a practice setting of rapid rehabilitation and short hospital stay more similar to North American and Australian than European norms.

The physical characteristics of our surgical population are in contrast with those of other studies. Our patient population was obese with patients in the CFNB group having a mean body mass index (BMI) of 33 kg/m^2 compared with Capdevila et al.'s (2) CFNB patients having a mean BMI of 26 kg/m^2 . Singelyn et al.'s study (1) excluded patients with weight more than 100 kg, whereas this represented 28% of patients in our CFNB group. Despite the potential for procedural difficulties the frequent technical success rate (96% on postoperative day 1) and analgesic efficacy attests to the practicality of this technique even in obese patients. Moreover, the blocks were performed by a range of anesthesiologists without extensive expertise in this technique before the commencement of the study.

This is the first study to assess motor block with CFNB and CEA after TKR. The motor block was assessed on postoperative days 1 and 2 by unblinded physiotherapists using a motor power scale used routinely in their clinical care. In both study groups the operative lower limb exhibited more motor block than the nonoperative limb. Perhaps this motor block was a result of pain, stiffness, swelling, or other surgical factors and was not local anesthetic-induced weakness. Within the operative lower limb, the CFNB had a more intense quadriceps block than the CEA group. This may be central to the technique's efficacy, as it has been postulated that quadriceps spasm is a major source of pain after TKR. However, this blockade may interfere with early mobilization if weight bearing on the operative leg is required. In our practice, mobilizing on postoperative day 1 and 2 requires weight bearing only on the nonoperative leg, hence the potential advantage of a unilateral technique such as CFNB. However, despite the bilateral nature of CEA, no difference was found between groups in motor block affecting the nonoperative limb which may have resulted from the use of dilute local anesthetic mixtures used in the epidural infusions.

Postoperative range of movement and achievement of early rehabilitation milestones were similar in both groups. However, more patients in the CFNB group were able to sit out of bed on postoperative day 1, as dictated by the rehabilitation protocol. The most common reason reported by the physiotherapist for failure of patients from the CEA group to sit out of bed was motor block of the nonoperative lower limb, contradicting the more objective finding that the CEA group did not have more intense motor block. This contradiction may indicate bias, given the unblinded nature of the study. Alternatively, it may result from the misattribution of a sensory or proprioceptive block of the nonoperative limb as motor block.

Given the equivalent analgesia and rehabilitation, the side effect profile of the two techniques warrants further scrutiny. CEA was associated with more nausea and vomiting than CFNB. CFNB is unlikely to affect the autonomic nervous system, nor does it have any effect on the nonoperative lower limb, which is important for early mobilization in our practice. In addition, CFNB is not associated with neuraxial hematomas resulting from the concomitant use of low-molecular weight heparin and epidural catheters in orthopedic patients. Similarly, a femoral catheter does not complicate the treatment of postoperative complications such as myocardial infarction, which may involve anticoagulant drugs. This study had one such patient. Infection is a risk of any catheter technique and the insertion of femoral or epidural catheters requires a strict aseptic technique. One disadvantage of CFNB is that successful femoral nerve blockade will not block the entire operative limb, and thus should be considered as only one part of multimodal analgesia, not a stand-alone technique.

The limitations of this study include its nonblinded nature, which increases risk of bias. Only one regional analgesic technique was to be used in each patient. Therefore, the insertion of epidural and femoral catheters into all patients and the infusion of local anesthetic into one catheter and saline into the other, as would be required for a truly blinded study, was considered inappropriately invasive and therefore unethical. The use of different local anesthetics in the two groups could be described as a weakness in study design; however, our choice of local anesthesia used in the infusions and adjuncts added was evidence-based when possible. The CFNB group received bupivacaine 0.2%, which had been shown to be opioid-sparing and improve early mobilization (4). No similar study using ropivacaine for femoral infusions existed at the time of study design. In addition, the CEA group had fentanyl in the infusions, which may explain both the reduced requirement for oxycodone and rofecoxib and a more

frequent incidence of nausea and vomiting in this group compared with the CFNB group. The choice of ropivacaine in the CEA group followed standard practice for all epidural infusions in our institution, based on the less frequent incidence of motor block with ropivacaine compared with bupivacaine (5). The different modalities, continuous infusion in the CEA group and PCA in the CFNB, could also be described as a weakness in study design. However, studies comparing PCA with continuous mode for epidural analgesia in this surgical population indicate that, although the PCA mode confers the advantage of reduced local anesthetic consumption, there is no benefit in terms of efficacy or reduced incidence of side effects (6). Although we intended to run the infusions until the morning of postoperative day 3, we had a number of unintended early cessations (19% in the CFNB group versus 27% in the CEA group). The majority of these, however, occurred on day 2, when our primary outcome variables had already been collected.

In conclusion, in this study there was no difference in postoperative analgesia when CFNB was compared with CEA after TKR. CFNB can be recommended as an effective regional component of a multimodal analgesia strategy after TKR.

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References

1. Singelyn FJ, Deyaert M, Joris D, et al. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg 1998;87:88–92.
2. Capdevila X, Barthelet Y, Biboulet P, et al. Effects of perioperative analgesic technique on the surgical outcome and duration of rehabilitation after major knee surgery. Anesthesiology 1999;91:8–15.
3. Todd MM, Brown DL. Regional anesthesia and postoperative pain management: long-term benefits from a short-term intervention. Anesthesiology 1999;91:1–2.
4. Ganapathy S, Wasserman RA, Watson JT, et al. Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty. Anesth Analg 1999;89:1197–202.
5. Zaric D, Nydahl PA, Adel SO, et al. The effect of continuous epidural infusion of ropivacaine (0.1%, 0.2% and 0.3%) on nerve conduction velocity and postural control in volunteers. Acta Anaesthesiol Scand 1996;40:342–9.
6. Silvasti M, Pitkanen M. Patient-controlled epidural analgesia versus continuous epidural analgesia after total knee arthroplasty. Acta Anaesthesiol Scand 2001;45:471–6.