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A Prospective, Randomized, Blinded Trial to Compare Continuous Epidural Block and Femoral Nerve Block for Total Knee Arthroplasty

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Abstract

Objective: We conducted a prospective, randomized, and blinded trial to compare the perioperative quality of anesthesia and analgesia for Total Knee Arthroplasty (TKA) using either Epidural Analgesia (EA) or ultrasound-guided continuous Femoral Nerve Block (FNB).

Methods: Forty patients scheduled for TKA were randomized to two groups, EA or FNB. The initial local anesthetic doses for EA and FNB blocks were 5 mL and 20 mL 0.5% ropivacaine, respectively. After epidural or femoral nerve sheath catheterization, patients were anesthetized using propofol infusion and air-mixed 40% oxygen. A ProSealTM laryngeal mask airway was inserted and intravenous fentanyl was used as supplementary analgesia if necessary. After surgery, patients in both groups were administered an infusion of 4 mL/h 0.2% ropivacaine and 12.5 μg/h fentanyl via the epidural or femoral nerve catheter. We recorded the total doses of fentanyl administered during surgery, and the extent of postoperative pain using a visual analog scale (VAS) at rest and on movement until the third postoperative day (POD3).

Results: The mean doses of fentanyl administered during surgery in the EA and FNB groups were 106.6 ± 45.8 μg and 232.5 ± 84.7 μg, respectively [mean ± standard deviation; $p < 0.0001$]. Significantly lower VAS pain scores were reported during movement in the EA group on POD1 [EA vs. FNB=23 (0-77) vs. 47 (0-100), p=0.027] and POD2 [43 (0-70) vs. 63 (15-100), p=0.031].

Conclusions: Continuous epidural analgesia requires less fentanyl for TKA than FNB and is more effective for postoperative pain on movement.

Keywords: Ultrasound-guided block; Femoral nerve block; Epidural block; Total knee arthroplasty

Background

Recently, the number of orthopedic patients receiving epidural anesthesia (EA) has declined because of the increasing use of anticoagulant therapy, such as fondaparinux [1] and edoxaban [2], as prophylaxis against perioperative deep vein thrombosis. Alternative regional anesthetic techniques also have limitations: lumbar plexus block is associated with the risk of hematoma [3-5]. Recently, ultrasound-guided Femoral Nerve Block (FNB) has been adopted as a safe, reliable analgesic technique for Total Knee Arthroplasty (TKA). The additional precision in location of the nerve sheath afforded by ultrasound has been shown to reduce the volume of local anesthetic needed by 42% compared with FNB guided by nerve stimulation [6]. Although two previous studies have compared the postoperative effects of EA and FNB after TKA, the drug combinations and infusion rates in those studies differed from those used in our institution [7, 8]. The efficacy of opioids combined with local anesthetics for peripheral nerve block remains controversial. However, some studies have reported that the addition of fentanyl to 1.5% lidocaine [9] and 0.25% bupivacaine [10] can prolong analgesia in axillary brachial plexus block. There are also a few perioperative studies that have compared total opioid dose and postoperative analgesia in patients undergoing TKA.

This prospective, randomized, controlled and blinded study examined the role of EA or ultrasound-guided continuous FNB in patients undergoing unilateral TKA under general anesthesia. We compared the total fentanyl and propofol dose requirements in order to evaluate the intraoperative analgesic efficacy and side effects of each. We also compared–in a blinded evaluation– postoperative analgesic efficacy, frequency of analgesia, postoperative nausea and vomiting (PONV), Bromage scale, continuous passive motion (CPM), and satisfaction score on postoperative days (PODs) 0–3, using the same regimen for continuous EA and FNB.

Methods

After obtaining institutional ethics committee approval (Saitama Social Insurance Hospital, #112, 12 October 2007) and registration of the trial on a publicly accessible database https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?function=brows&action=brows&type=summary&recptno=R000013078&language=E; ID-UMIN000011166 R000013078, patients scheduled to undergo primary TKA were invited to participate in the study. Written informed consent was obtained from all subjects. Exclusion criteria included: inability to give informed consent for language or cognitive reasons; contraindications for neuraxial blockade, including patient refusal and platelet count of <100,000 cells/μl; contraindications for epidural block, such as current therapy with anticoagulant drugs or infection overlying the proposed injection site; and contraindications to any of the study drugs.

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Before surgery, 40 patients scheduled for TKA under general anesthesia were randomized by means of sealed envelopes into two groups: one received continuous EA (n=20), the other ultrasound-guided FNB followed by a continuous infusion (n=20). Neither the patients nor the three treating clinicians (MK, HM, YO) were blinded to the study group randomization. The initial local anesthetic doses for EA and FNB were 5 ml and 20 ml 0.5% ropivacaine, respectively. In the EA group, after infiltration anesthesia with 3–5 ml 1% lidocaine, an 18-gauge Tuohy needle (B Braun, Bethlehem, PA, USA) was inserted at the L2-3 or L3-4 interspace using a loss of resistance to saline technique, a catheter was inserted, and 5 ml 0.5% ropivacaine was injected. In the FNB group, after infiltration with 3-5 ml 1% lidocaine, a 18-gauge Tuohy needle (B Braun) was inserted just lateral to the femoral artery under ultrasound guidance, in plane approach, using a linear 9 MHz ultrasound probe (GE Logic BookXP, GE Healthcare, Tokyo, Japan). A quadriceps twitch at <0.5 mA (1 ms, 2 Hz) in response to peripheral nerve stimulation (Stimuplex HNS, B Braun AESCUCAP™, Tokyo, Japan) was used to confirm appropriate positioning of the needle tip in the vicinity of the femoral nerve. After localization of the nerve, 20 ml 0.5% ropivacaine was injected slowly, resulting in "donut" shapes around the nerve. Thereafter, a catheter was inserted until the end lay more than 5 cm beyond the needle tip. Its position close to the femoral nerve was checked by viewing the injection of a test dose of 0.9% NaCl with ultrasound, and once a satisfactory position had been obtained the Tuohy needle was removed. Having administered the blocks, the patient was covered with surgical drapes so as to disguise the location of the catheter, and the case was taken over by a second anesthesiologist. In both groups of patients, the second anesthesiologist checked the level of the block with an ice cube if there was an L1–3 sensory deficit.

All patients were anesthetized with a 3-4 μg/ml continuous Target-Controlled Infusion (TCI) of propofol (Diprifusor™) to permit the insertion of a ProSeal™ laryngeal mask airway using a bolus of intravenous (IV) fentanyl 50 μg without neuromuscular blockade. Patients were allowed to breathe a mixture of 40% oxygen in air spontaneously, and adequate depth of anesthesia was maintained with a propofol 2-3 μg/ml TCI infusion using bispectral index monitoring (BIS A2000, ver. 3.2; Aspect Medical Systems, Natick, MA, USA) <60. An additional 25–50 μg fentanyl was also administered via the blinded catheter for supplemental analgesia intraoperatively if needed, as indicated by tachypnea (respiratory rate >20/min), tachycardia >120/min, or hypertension (systolic pressure >140 mmHg). After surgery, 4 ml/h of 0.2% ropivacaine and 12.5 μg/h of fentanyl were administered via the respective catheters as a continuous infusion (96 ml and 300 μg/day, respectively) in both groups, using identical, pre-filled infusion pump sets (300 ml; Baxter Infuser BB series, LVBB 4 × 4, Tokyo, Japan), set at a basal infusion rate of 4 ml/h, with a 2 ml Patient-Controlled Analgesia (PCA) bolus and a 30 minute lock-out time.

The infusion was continued until the morning of POD 2 (with the operative day being day 0), and additional PCA boluses were administered for pain relief, if required. If PCA was inadequate, indicated by a visual analog scale (VAS) >3, further analgesia was provided by means of a 50 mg diclofenac sodium suppository every 6 h and/or 15 mg pentazocine intramuscularly twice daily, as required. For nausea and vomiting, 10 mg intravenous metoclopramide was administered every 8 h if requested by the patient. Femoral and epidural catheters were removed on the evening of POD 2 and more than 2 hours thereafter, thromboprophylaxis was initiated with 2.5 mg fondaparinux (GlaxoSmithKline, Middlesex, UK) given subcutaneously once daily.

Patients underwent passive knee flexion using a Continuous Passive Motion (CPM) machine (Smith and Nephew Kinetic Optima and Prima, Tournes, France) on PODs 2 and 3, and active flexion and extension exercises were started the following day. Continuous passive motion was tailored to individual requirements, administered in increments of 15° of flexion with each application until 90° of flexion was achieved. Active knee flexion was measured every morning at 10 a.m. on PODs 1–3 using a large goniometer. Nursing staff blinded to the patients' group allocation (the insertion site of the catheter was covered by gowns) recorded power in the lower limb muscle groups using the Bromage scale (0=able to flex knee and foot, 1=able to bend knee with foot flexion, 2=unable to flex knee but can still flex ankle, 3=unable to flex ankle). Visual analogue scale pain scores at rest and during movement (rehabilitation) were also recorded at 9 p.m. on the operative day and every morning at 10 a.m. on PODs 1–3. Other perioperative data collected from the anesthetic records by anesthesiologists blinded to the patients' group allocation (MK, HM, YO) included: patient characteristics, total doses of fentanyl, and propofol, minimum respiratory rate, minimum oxygen saturation (SpO_2), maximum end tidal CO_2, fluid volume, urine output, and blood loss during surgery. We also evaluated postoperative nausea and vomiting (PONV: 0=no nausea, 1=nausea only, 2=nausea and vomiting), frequency of PCA bolus and adjuvant analgesic administration, Bromage scale grades on the operated and non-operated sides, and CPM until 3 days had elapsed after TKA. Satisfaction scores (from 0 to 100 points) at discharge were also recorded. All data were collected by nurses or investigators blinded to patients' group allocations.

Parametric and nonparametric data were analyzed using Student's t-test and the Mann–Whitney U-test, respectively. A p value <0.05 was considered significant.

Results

No significant differences in patient characteristics were observed between the groups (Table 1). Perioperative data are shown in Table 2. Total fentanyl doses for EA and FNB were 106.6 ± 45.8 μg and 232.5 ± 84.7 μg, respectively [mean ± standard deviation, SD; p <0.0001]. There were no significant differences between the groups with regard to any of the other intraoperative outcomes measured. There were no significant differences between the two groups at rest on any POD in terms of pain scores, adjuvant analgesics, PONV, the Bromage scale, CPM and satisfaction scores (Figure 1, Table 3). In contrast, significantly lower VAS scores [median (range)] were found during movement in the EA group on POD 1 [EA vs. FNB=23 (0-77) vs. 47 (0-100), p=0.027] and POD 2 [43 (0-70) vs. 63 (15-100), p=0.031] (Figure 2).

Discussion

Our study is the first prospective, randomized, blinded trial to compare perioperative consumption of opioids and local anesthetics in patients undergoing TKA without sciatic nerve block receiving the same drug regimen for continuous EA and FNB. We found that patients receiving EA required 54% less fentanyl than those receiving

Group	EA (n=20)	FNB (n=20)
Age (Years)	72 ± 7	71 ± 8
Male Female	2:18	4:16
Height (cm)	151.4 ± 7.4	151.3 ± 8.0
Weight (kg)	57.5 ± 6.2	55.8 ± 10.3

Data are shown as mean ± standard deviation. There were no significant differences between the groups. Abbreviations: EA, epidural analgesia; FNB, femoral nerve block.

Table 1: Patient characteristics.

Group	EA	FNB	*p*-value
Anesthesia duration (min)	161.3 ± 19.9	174.6 ± 66.5	0.4
Operation duration (min)	105.5 ± 15.9	118.0 ± 63.8	0.4
Total fentanyl dose (μg)	106.3 ± 45.8	232.5 ± 84.7	<0.0001
Total propofol dose (mg)	811 ± 153	847 ± 252	0.58
Fluid volume (ml)	1296 ± 186	1213 ± 249	0.24
Blood loss (g)	189 ± 27	229 ± 27	0.32
Urine output (ml)	330 ± 195	254 ± 157	0.18
Minimum SpO_2 (%)	98.1 ± 1.3	98.0 ± 1.3	0.76
Minimum respiratory rate (/min)	6.0 ± 2.2	6.9 ± 2.4	0.27
Maximum $ETCO_2$ (mmHg)	53.7 ± 6.9	55.7 ± 7.5	0.39

Values are expressed as mean ± standard deviation. Total fentanyl dose for epidural anesthesia (EA) was lower than for femoral nerve block (FNB). Abbreviations: SpO_2, peripheral oxygen saturation; $ETCO_2$, end-tidal carbon dioxide concentration.

Table 2: Intraoperative data.

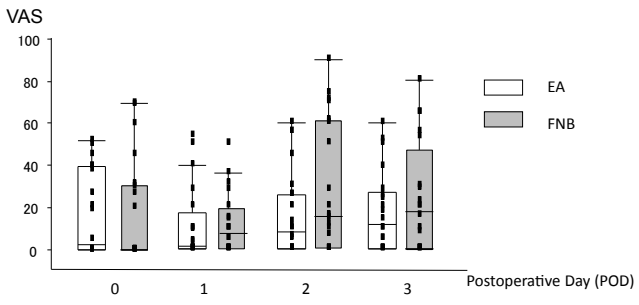

Figure 1: Postoperative visual analogue scale (VAS) pain scores at rest in the two groups [the dots and box plotting indicate individual data and 10, 25, 50, 75, 90% ranges, respectively]. No significant differences between groups were observed on any postoperative day (POD). Abbreviations: EA, epidural analgesia; FNB, femoral nerve block.

FNB. Epidural analgesia also appeared to afford better post-operative analgesia: the VAS for pain on movement reported by those receiving EA was 43% and 34% less on PODs 1 and 2, respectively, than those with a continuous FNB. No significant differences were found in other postoperative parameters between the groups.

Regional anesthesia and postoperative analgesia for TKA is commonly provided by means of FNB combined with sciatic nerve block [11], but the technique takes longer than FNB alone. Two studies have reported that FNB with sciatic nerve block can decrease morphine consumption in the immediate postoperative period compared with FNB alone [12,13]. However, Paul *et al.* [14] have expressed the opinion that the benefits of adding a sciatic block to FNB are unproven and need further study. Fowler *et al.* [15] could not detect any benefit in adding a sciatic block to a femoral nerve block in the first 24 h after surgery. To simplify the study design, we compared the analgesia afforded by continuous FNB without a sciatic block or by continuous EA using the same infusion rate and fentanyl dose.

In our study, VAS scores in both groups tended to be higher than those reported in previous studies. Barrington *et al.* [8] compared VAS and PONV scores in patients receiving continuous FNB and EA. The FNB and EA block regimes used in their study differed from ours. They chose an infusion rate of 9.3 ml/h for FNB and 7.6 ml/h for EA, and used 0.2% bupivacaine with no added opioid, whereas we used a standard infusion of 4 ml/h 0.2% ropivacaine with 12.5 μg/h fentanyl for both EA and FNB. Barrington *et al.* [8] reported mean VAS pain scores during movement of approximately 20 and 10 mm in both groups on PODs 1 and 2, respectively, approximately half the values in our study. This may have resulted from a two-fold higher local anesthetic infusion

	EA	FNB	*p*-value
Frequency of PCA/day			
POD-0	0 (0-2)	0 (0-1)	0.07
POD-1	0 (0-2)	0 (0-2)	0.98
POD-2	0 (0-1)	0 (0)	0.34
POD-3	0 (0)	0 (0)	1
Frequency of diclofenac 50mg suppository/day			
POD-0	0 (0-1)	0 (0-1)	0.68
POD-1	0 (0-2)	0 (0-2)	0.32
POD-2	0 (0-1)	0 (0-1)	0.29
POD-3	0 (0-1)	0 (0-1)	0.29
Frequency of pentazocine 15mg IM/ day			
POD-0	0 (0-1)	0 (0)	0.32
POD-1	0 (0)	0 (0-1)	0.32
POD-2	0 (0)	0 (0)	1
POD-3	0 (0)	0 (0)	1
PONV (0/1/2)			
POD-0	16/3/1	14/4/2	0.73
POD-1	8/1/11	8/6/6	0.07
POD-2	16/3/1	16/2/2	0.92
POD-3	20/0/0	20/0/0	1
Frequency of antiemetic drugs/day			
POD-0	0 (0-1)	0 (0-1)	1
POD-1	0 (0-2)	0.5 (0-2)	0.48
POD-2	0 (0)	0 (0)	1
POD-3	0 (0)	0 (0)	1
Bromage score [0/1/2/3] operative side			
POD-1	0/5/8/7	1/2/9/8	0.38
POD-2	1/5/7/7	0/4/10/6	0.55
POD-3	1/5/13/1	0/11/7/2	0.12
Bromage score [0/1/2/3] non-operative side			
POD-1	11/8/1/0	13/7/0/0	0.44
POD-2	15/5/0/0	13/7/0/0	0.49
POD-3	17/3/0/0	16/4/0/0	0.68
CPM (degree)			
POD-2	73.5 ± 14.8	72.3 ± 10.3	0.82
POD-3	79.5 ± 12.6	81.3 ± 13.0	0.66
Satisfaction Score (/100)	88.8 ± 13.4	88.1 ± 23.0	0.91

Values are expressed as mean ± standard deviation and median (interquartile range). Abbreviations: Abbreviations: EA, epidural analgesia; FNB, femoral nerve block; PCA, patient-controlled analgesia; POD, postoperative day; PONV, postoperative nausea and vomiting; CPM, continuous passive motion.

Table 3: Postoperative data.

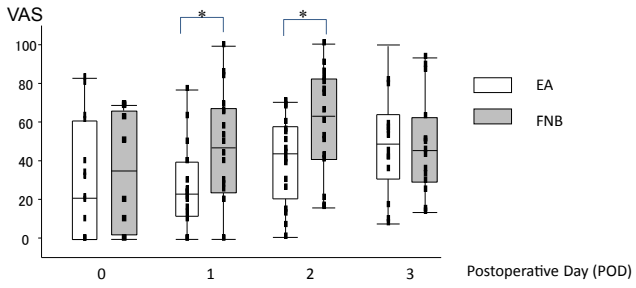

Figure 2: Postoperative visual analogue scale (VAS) pain scores during movement in the two groups [the dots and box plotting indicate individual data and 10, 25, 50, 75, 90% ranges, respectively]. *A significant difference was found on postoperative days (POD) 1 and 2 (p=0.027 and 0.031). Abbreviations: EA, epidural analgesia; FNB, femoral nerve block.

rate (9.3 ml/h) than that administered in our study (4 ml/h). Capdevilla *et al.* [16] compared the analgesic effects of continuous EA and FNB without ultrasound with those of intravenous PCA with morphine. According to their results, the median postoperative VAS scores for continuous FNB were approximately 30 and 25 mm at 24 and 48 hours, respectively, which were lower than our findings despite positioning of the catheter using both ultrasound and nerve stimulator guidance. Lower pain scores may have been the result of relatively high daily doses of morphine (36 mg) and clonidine (0.24 mg) used in their study.

Based on the results of a meta-analysis of randomized controlled trials, Paul *et al.* [14] concluded that FNB when complemented by PCA was more effective than PCA alone. Two groups reporting the results of clinical trials [9, 10] suggested that the additional analgesia afforded by the addition of opioids to local anesthetics is due to the presence of opioid receptors on peripheral neurons [17]. Therefore, we attempted to control pain using continuous FNB alone, without sciatic nerve block, by combining fentanyl with a local anesthetic.

Two studies have reported positive results with continuous FNB. Sundarathiti *et al.* [7] administered 8 ml/h 0.125% levobupivacaine for FNB, which provided superior analgesia than EA (0.125% levobupivacaine at the rate of 4 ml/h combined with 0.0125 mg/ml morphine). Morin *et al.* [13] administered 0.2% ropivacaine at the rate of 14 ml/h for continuous FNB. These previous studies suggest that a higher volume of local anesthetic combined with an opioid infused at approximately 10 ml/h may provide superior analgesia than EA alone [7, 16].

One of the side effects of nerve blocks using local anesthetics combined with opioids is postoperative nausea and vomiting (PONV), which is most likely caused by the opioid. Barrington *et al.* [9] found that PONV occurred less often during FNB than during EA. We administered the same dose of fentanyl (300 μg/day) via the epidural or perineural space, and noted no significant difference in the incidence of PONV. More than half the patients in both groups complained of PONV on POD 1. Therefore, antiemetic drugs, such as droperidol (2.5 mg/day) or metoclopramide (20–30 mg/day), should be added to the infusion pump for both EA and FNB.

Although Barrington *et al.* [8] reported seven patients with excessive motor block after EA, there were no significant differences in Bromage scale scores between the two groups. In our study, we found no difference in other rehabilitation milestones, Bromage scores (on the operative or non-operative side), and frequency of antiemetic use, CPM, or satisfaction scores between the groups.

Our study has certain limitations; there was no postoperative supplementary analgesic protocol: decisions about choice of analgesic, timing and route of administration were made individually. Furthermore, the long-term outcomes [18], including the effects on ADL, were not examined.

Conclusions

Femoral nerve block is safer than EA in patients taking anticoagulant therapy. However, we conclude that perioperative EA can significantly reduce the total dose of fentanyl and ropivacaine by approximately half compared with FNB. Both EA and FNB proved to be suitable techniques with which to supplement total intravenous general anesthesia in a spontaneously breathing patient. Using the same infusion pump settings, EA was more effective than FNB for postoperative pain during movement on PODs 1 and 2. Most patients receiving FNB complained of pain in the distribution of the sciatic nerve. Hence, the continuous FNB regimen requires further refinement to obtain as effective analgesia as EA, but without the disadvantage of PONV.

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