Adductor canal block versus femoral nerve block in unicompartmental knee arthroplasty: a randomized, double blind, prospective, comparative study

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Abstract

Background: Minimally invasive knee replacement surgery has grown in early twenty-first century to join international trend of ambulatory joint surgery. Both ultrasound-guided femoral nerve block (FNB) and adductor canal block (ACB) have excellent postoperative analgesia following uni-knee replacement. Minimal motor power affection facilitates early patient ambulation and rehabilitation. Therefore, the objective of this study is to evaluate and compare the functional recovery and analgesic efficacy of both techniques in uni-knee arthroplasty.

Methods: After University Review Board approval, informed written consent to participate in the study was obtained. Patients scheduled for unicompartmental knee arthroplasty (UKA) with combined spinal-epidural anesthesia were eligible for enrollment in this double blind, randomized trial. Patients received either FNB or ACB with a 20 cc of 0.5% of bupivacaine with 5 μg/ml epinephrine. Quadriceps muscle strength was measured as primary outcome using Medical Research Council scale (MRC). Postoperative pain with visual analog scale (VAS) and total morphine consumption was considered as secondary outcome, all recorded for 48 h post-anesthesia administration.

Results: Eighty patients were analyzed; quadriceps strength was significantly lower in the FNB group compared with ACB group especially at 12 postoperative hour (2 versus 4), respectively, \( p \) value < 0.05. There was no difference between the groups regarding postoperative. VAS at rest except at 24 h was significantly lower in FNB group with \( p \) value 0.003. The gate disturbance and the number of falls were significantly lower in the ACB group than the FNB group (2 compared to 9), respectively. There was no difference between groups regarding postoperative nausea, vomiting, and itching.

Conclusion: ACB preserved quadriceps muscle strength more than FNB, with reduced number of falls and without significant difference in pain relief. Therefore, ACB considered an alternative to FNB when given as supplemental postoperative pain control after unicompartmental knee arthroplasty.

Trial registration: This clinical trial was registered in the Pan African Clinical Trial Registry (PACTR) http://www.pactr.org/ as a prospective trial with the identification number PACTR201907788767332.

Keywords: Uni-knee arthroplasty, Femoral nerve block, Adductor canal block

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Background

Rational and background
Unicompartmental knee arthroplasty had varying degrees of acceptance since it was introduced three decades ago. With the publication of recent studies reporting 10 years’ survival rates exceeding 93%, the introduction of the mobile bearing form of the procedure, faster recovery than TKA, lower morbidity and mortality, and identifying the reasons for UKA revision such as overcorrection of the mechanical axis, thus, enthusiasm for UKA increased again (Mohammad et al., 2018; Ko et al., 2015; Murray et al., 2015).

Knee arthroplasties (KAs), whether total knee arthroplasty (TKA) or UKA involve extensive bone resection and soft tissue manipulations, and patients can suffer from severe pain during the early postoperative period. Proper pain control after KAs results in faster recovery, diminishes the risk of postoperative complications, and improves patient satisfaction (Korean Knee Society, 2012). Current pain management regimens following UKA include oral analgesics, periarticular injection, peripheral nerve blocks (PNBs), and intravenous patient-controlled analgesia (Ko et al., 2015). As PNBs provide effective and synergistic pain relief when used as a part of a multimodal regimen, they are considered to be an essential part of the current multimodal pain management protocol following knee arthroplasty (KA) (Pelt et al., 2014).

Given excellent pain relief and the opioid sparing effect, femoral nerve block (FNB) is commonly used as an analgesic supplement and is considered the regular PNB in patients undergoing KA. However, FNB is followed by a significant decrease in quadriceps muscle strength, with subsequent delay in mobilization, which is associated with the potential risk of falling. Recently, as the length of stay (LOS) in hospitals has been shortened by the performance of KA on an outpatient basis, a potent analgesia that preserves motor strength during early rehabilitation is becoming increasingly accepted as an essential part of the current perioperative practice following total knee arthroplasty (TKA). In this experience, a growing body of proof for UKA increased again (Mohammad et al., 2018; Ko et al., 2015; Murray et al., 2015).

Aim of the study
In this context, this study aimed to evaluate and compare the functional recovery and analgesic effect of adductor canal block (ACB) compared to femoral nerve block (FNB) following unicompartamental knee arthroplasty (UKA).

Patients and methods
After Institutional Review Board Approval of Al Fayoum University Hospitals and written informed consent, eighty-two (82) patients were allocated into two groups: group A, forty-one (41) patients received adductor canal block; group B, forty-one (41) patients received femoral nerve block. This clinical trial was registered in the Pan African Clinical Trial Registry (PACTR) as a prospective trial with the identification number PACTR201907788767332. It was carried out as multicenter study (Ain shams University Hospitals, Petroleum Medical Center, and El Fayoum University Hospitals) between March 2019 till March 2020 (about 12 months). Patients of either sex, aged 18–80 years, ASA I, II, and III who underwent elective unilateral (UKA) and with planned combined spinal epidural anesthesia (CSE), were included. Those with contraindications to neuro-axial blockade, contraindications to a FNB or ACB, coagulopathy, with absolute or relative contraindications to (UKA), e.g., inflammatory arthropathy, previous high tibial osteotomy (HTO) with overcorrection, with lesions of the cruciate ligaments, medial or lateral subluxation and tibial or femoral shaft deformity, patients with chronic opioid use (defined as daily or almost daily use of opioids for > 3 months), those with operative limb neuropathy, hypersensitivity, and/or allergies to local anesthetics or allergy to any of the study medications were excluded from our study.

Patient assessment
The patient’s quadriceps muscles strength was also assessed by a neurologic exam, based on a 6-point scale rated from 0–5 based on Medical Research Council (MRC) scale (0 = no contraction, 1 = flicker or trace of contraction, 2 = active movement with gravity eliminated, 3 = active movement against gravity, 4 = active movement against gravity and resistance, 5 = normal power) (James, 2007). Patients were instructed to extend their legs three times each, with a 30-s pause between each attempt. Sensory function along the distribution of the saphenous nerve (medial side of leg above the ankle) was assessed by pin-prick and temperature discrimination using the jagged edges of a broken tongue depressor and an alcohol swab in comparison with the non-operative side.

Patient preparation
After placement of 18 gauge i.v. cannula, 10 ml/kg Ringer’s lactate solution was given to the patients according to their hemodynamics. All patients were premedicated with i.v. 1 mg granisetron and 8 mg i.v. dexamethasone as antiemetic medications. All patients were sedated by 0.01 mg/kg midazolam and/or propofol 25–50 μg/kg/min when necessary before placement of the block or CSE.

Block technique
Group A, ACB
An ultrasound-guided ACB (20 cc of 0.5% of bupivacaine with 5 μg/ml epinephrine, via a 21-gauge 4-in. Stimuplex A needle; B. Braun Medical Inc., Melsungen, Germany) was performed at mid-thigh level, lateral to the femoral
artery, and deep to sartorius muscle using a high-frequency linear ultrasound transducer (10–12 Hz; SonoSite Turbo; SonoSite Inc., Bothell, WA), as described by Manickam (Manickam et al., 2009) (Fig. 1).

**Group B, FNB**

An ultrasound-guided FNB (20 cc of 0.5% of bupivacaine with 5 μg/ml epinephrine, via a 22-gauge 2-in. Stimuplex A needle; B. Braun Medical Inc.) was performed with a nerve stimulator guidance below the inguinal ligament. The femoral nerve was obviously discernable in all patients; the needle was introduced in plane similar to that described by Murray (Murray et al., 2010). The types of motor response and minimum current were remarked to ensure closeness of the injection drug to the nerve and to avoid intraneural injection. Ultrasound pictures were took to verify proper local anesthetic placement (Fig. 2).

**Anesthetic technique**

After end of the nerve block, all patients received (CSE) in the form of 2.5 cc of 0.5% hyperbaric bupivacaine (12.5 mg) as a spinal agent. Epidural anesthetic agent will be lidocaine 2% continuous infusion at rate of 2 mg/min (8 cc/h) intraoperatively according to the length of the procedure.

Regimen of multimodal analgesia postoperative was as follows: after the operation, the epidural infusion was adjusted as bupivacaine 0.06% 4 cc/h and increased according to the patients’ need up to 8 cc/h. Morphine 5 mg i.v. was given when patient VAS score is ≥ 3 by the nurse control system with at least 2-h interval, and the total doses were calculated. Acetaminophen 500 mg i.v. was given every 8 h. Additional doses of antiemetics, e.g., metoclopramide 10 mg and/or granisetron 1 mg i.v., were given when necessary.

**Measured parameters**

Quadriiceps muscle strength at 6, 8, 24, and 48 h post-anesthesia (block) administration was the primary outcome using the MRC scale. Pain scores using visual analog scale (VAS) (0–10) at 6, 8, 24, and 48 h post-anesthesia administration and total postoperative i.v. morphine consumption were considered as secondary outcomes. Additional data like sensory block duration (SBD); postoperative nausea and vomiting (PONV); time up to go (TUG); gait distance at 24 and 48 h post-anesthesia administration; incidence of complications including buckling, falls, neurologic symptoms, and local anesthetic toxicity; length of hospital stay (LOS); and patient satisfaction were also recorded. SBD was defined as time taken from completion of the block till first call for analgesia or VAS ≥ 3. TUG was defined as the time taken by the patient to stand up from a chair, walk a distance of 3 m without any support, and return to the chair (Kuang et al., 2016). Buckling was defined as a sudden and unintentional loss of postural strength and balance as seen by the staff, which may or may not have required the patient to support himself to prevent falling (Thacher et al., 2017).

**Methods of sample size calculation**

Depending on previous studies, a difference of 41% was detected between study groups concerning the quadriiceps strength which is the primary outcome in our study (Jaeger et al., 2013). G* power computer program version 3.1.9.2 was used to calculate the sample size required with 80% power, an alpha error of 0.05, and allocation ratio of 1 (Faul et al., 2009). A sample size of 37 patients
was calculated per each group. To compensate for drop outs, the sample size was increased by 10% to become 41 patients in each group.

Methods of randomization
Computer generated randomization and sealed opaque envelopes, aside from the researchers performing the blocks, all other investigators, anesthetist, surgeons, physical therapists, nurses, and the study participants were blinded to the randomization of each subject.

Statistical analysis
Statistical analysis was performed using SPSS version 21.0 (IBM, Armonk, NY, USA). Data were presented as mean (SD), median [Interquartile range (IQR)], or number of patients (%). Distribution of normality was assessed by using the Sharipo-Wilk test. Comparison between groups was made using independent t test or Mann-Whitney U test as appropriate. Categorical variables were assessed using chi-square test or Fisher exact test.

Results
The final cohort was eighty patients (forty patients) in each group as one patient in each group was converted intraoperative into TKR, so they were excluded from the study and further assessment. There were no significant differences between the two groups regarding the demographic or the baseline data except for the duration of surgery which might be attributed due to the variations between surgeons and center protocols. The total ratio of males to females in the two groups was 26 (32.5%)/54 (67.5%) (Table 1).

The motor power assessment was significantly higher in the ACB group than the FNB group at all the study time points (Table 2).

The gait distance was significantly higher in the ACB group more than the FNB group whether at 24 or 48 h post-anesthesia administration. Also, the TUG was significantly higher in the ACB group more than the FNB group. The number of falls was significantly lower in the ACB group than the FNB group (2 compared to 9). The two cases in the adductor canal group were for two females 53 and 59 years and BMI of 33 and 30, respectively, and both were at the right side. The nine cases of falls in the FNB groups were for 7 females and two males, 7 in the right side and two in the left side. Similarly, the number of buckling was significantly lower in the ACB group than the FNB group (8 compared to 17) (Table 3).

The rest of the measured parameters and complications showed no significant differences between the two groups (Tables 3, 4, 5, and 6).

Discussion
Numerous orthopedic centers have switched to ACB as the preferred regional anesthesia for KA as a postoperative pain control tool. Reducing the fall rate after KA was the major cause for this shift. There are recent publications supporting the use of ACB over FNB due to faster pain relief, greater quadriceps strength, earlier ambulation, greater average distance of ambulation during physical therapy, faster timed up and go test, and decreased LOS (Bolarinwa et al., 2018; Elkassabany et al., 2016).

In the current study, we compared the effect of ACB compared to FNB on the quadriceps motor power, postoperative analgesia, and complications in UKA surgeries,
and we found that ACB significantly preserved the quadriceps muscle strength and decreased the number of buckling and falls. Otherwise, no significant effect was found.

The adductor canal, also called the sub sartorial or Hunter’s canal, is an aponeurotic subway that starts at the apex of the femoral triangle and terminates at the adductor hiatus. It encloses the femoral vessels, the saphenous nerve (SN), and the nerve to the vastus medialis muscle (NVM). A recent cadaveric study showed that the SN and NVM were constantly present, while branches of the anterior obturator nerve were incongruously present (Koh et al., 2017). Moreover, the NVM shared profoundly in the innervation of the capsule of the knee through intramuscular, extramuscular, and deep genicular nerves (Laurant et al., 2016).

Strong evidence exists to support the claim that FNBs impair quadriceps strength postoperatively (Kim et al., 2014; Elkassabany et al., 2016; Shah & Jain, 2014; Grevstad et al., 2015; Edwards et al., 2019). Furthermore, a number of studies have established that ACBs significantly reserve the quadriceps motor function when compared to FNB after TKA, including a number of randomized controlled trials (RCTs) (Kim et al., 2014; Elkassabany et al., 2016; Shah & Jain, 2014; Grevstad et al., 2015; Edwards et al., 2019).

In the current study, our main outcome was the quadriceps muscle strength, and we found that ACB significantly preserved the motor power of the muscle compared to FNB in all study time points in the first 48 h post-anesthesia (block) administration.

Jaeger et al., in their study on 11 healthy volunteers, found that the ACB well-kept quadriceps muscle strength and enhanced early ambulation in comparison with FNB. In that study, the quadriceps muscle strength [the mean quadriceps maximum involuntary isometric contraction (MVIC) (0.5–6 h) post block] decreased 8% from baseline following ACB but 49% following FNB (Jaeger et al., 2013).

Moreover, Charous et al., in a study on healthy volunteers comparing the effect of FNB with basal infusion compared to repeated hourly bolus doses on quadriceps muscle strength, found a reduction of more than 80% with either method. They used a volume 30 ml of ropivacaine (0.1%) infused over 6 h through a perineural catheter (Charous et al., 2011).

Elkassabany et al. found that manual muscle grading tests were significantly higher on POD1 in the ACB group compared to that in the FNB (p = 0.001) (Wilcoxon-Mann-Whitney odds, 2.25 [95% confidence interval, 1.35–4.26]) which came in agreement with our outcomes. Similarly, Grevstad et al., in their study on 50 patients who underwent TKA with severe movement-related pain defined as having visual analog scale pain score greater than 60 mm during active flexion of the knee, reported that ACB provides a clinically pertinent and statistically significant rise in the quadriceps muscle strength for patients in severe pain after TKA. After block, the quadriceps maximum voluntary isometric contraction increased to 193% (95% confidence interval [CI], 143–288) of the baseline value in the ACB group and decreased to 16% (95% CI, 3–33) in the FNB.
group with an estimated difference of 178% (95% CI, 136–226), \( p < 0.0001 \) (Grevstad et al., 2015).

On the other hand, Kwofie et al. reported a preserved quadriceps strength and balance with ACB compared to FNB on a cohort of healthy volunteers (Kwofie et al., 2013).

In the current study, we used a manual observation tool for grading the quadriceps muscle power based on MRC scale because it was simple, reliable, and agreeing with available resources. Elkassabany et al. also used a manual muscle grading (Elkassabany et al., 2016). In contrary to our study, some studies preferred the use of the dynamometer as it was available, and they were accustomed to use it for grading of the muscle power (Kim et al., 2014; Jæger et al., 2013).

In our study, the incidence of buckling was 8 patients (20%) in the ACB group compared to 17 (42.5%) in the FNB group, and this difference was of statistical significance (\( p = 0.03 \)). This result came in agreement with Thacher et al. in their retrospective cohort study about the incidence of buckling and falls in knee surgeries. They found that the incidence of buckling was significantly lower in the ACB group (3 patients (2%)) compared to FNB group (17 patients (13%)) (\( p = 0.004 \)) (Thacher et al., 2017).

Also, we reported a significant difference in the incidence of falls between the two groups which was lower in the ACB group (2 patients (5%)) compared to the FNB group (9 patients (22.5%)) (\( p = 0.023 \)). Thacher et al. reported only one case of fall in the FNB group and no cases in the ACB group (Thacher et al., 2017). The difference between their results and ours could be attributed to the types of surgeries (UKA only in our study compared to different knee surgeries in theirs); and also, different group of populations, more males in their study (32% and 27%) compared to (12% and 14%) ours in ACB and FNB groups, respectively; and different races (Americans compared to Egyptians) with different physical fitness and sports practices and report bias by the patient or the relatives to the nurses or to the orthopedic residents.

Also, Bolarinowa et al., in their retrospective study on 1625 patients received whether ACB (791) or FNB with knee immobilizer (KI) (834) for TKA operations, reported also eleven (11) cases of falls in the FNB and one case of buckling.

### Table 3 Measured parameters

|                  | Group A (n = 40) | Group B (n = 40) | \( p \) value |
|------------------|-----------------|-----------------|--------------|
| SBD (min)**#     | 25.86 (5.89)    | 23.4 (7.63)     | 0.111        |
| Gait distance at 24 h (m)**# | 18.6 (5.7)   | 8.4 (3.3)     | 0.000**      |
| Gait distance at 48 h (m)**# | 31.63 (6.07) | 24.45 (5.43) | 0.000**      |
| TUG (s)**#       | 51.3 (13.5)     | 60.7 (16.7)     | 0.007**      |
| TMC (mg)**#      | 10.1 (6)        | 11.2 (5.6)      | 0.39         |
| Buckling (yes/no) | 8 (20%)/32 (80%) | 17 (42.5%)/23 (57.5%) | 0.03**  |
| Falls (yes/no)   | 2 (5%)/38 (95%) | 9 (22.5%)/31 (77.5%) | 0.023**    |
| LOS (days)**#    | 4.3 (0.9)       | 3.5 (1.1)       | 0.83         |
| Satisfaction     | 16.42 (1.21)    | 16.40 (1.27)    | 0.92         |

SBD sensory block duration, TUG time to up and go, TMC total morphine consumption, LOS length of stay

* \( p \) value < 0.05 is significant

#Data are presented as number (%)

**Data are presented as mean (SD)

### Table 4 VAS in the two study groups at rest at different study time points

|                  | Group A (n = 40) | Group B (n = 40) | \( p \) value |
|------------------|-----------------|-----------------|--------------|
| VAS 6h           | 0 (0–1)         | 0 (0–0)         | 0.32         |
| VAS 12h          | 0 (0–1)         | 1 (0–1)         | 0.15         |
| VAS 24h          | 2 (1–2)         | 1 (2–3)         | 0.003*       |
| VAS 36h          | 3 (2–3)         | 0.75 (2.25–3)   | 0.19         |
| VAS 48h          | 3 (3–4)         | 1 (3–4)         | 0.33         |

Mann Whitney U test

ACB adductor canal block, FNB femoral nerve block, VAS visual analog scale, IQR interquartile range

* \( p \) value < 0.05

### Table 5 VAS in the two study groups at movement at different study time points

|                  | Group A (n = 40) | Group B (n = 40) | \( p \) value |
|------------------|-----------------|-----------------|--------------|
| VASM 6h          | 1 (0–2)         | 1.75 (0.25–2)   | 0.15         |
| VASM 12h         | 3 (1–3)         | 3 (1–3)         | 0.69         |
| VASM 24h         | 3 (1–3)         | 3 (1–3)         | 0.71         |
| VASM 36h         | 4 (2–5)         | 4 (1–3–4)       | 0.11         |
| VASM 48h         | 4.5 (4.5–7.5)   | 1 (4–5)         | 0.06         |

Mann Whitney U test

ACB adductor canal block, FNB femoral nerve block, VASM visual analog scale on mobility, IQR interquartile range
only in the ACB. Surprisingly, Bolarinowa et al. reported 11 cases out of the 12 were after right side TKA compared to one case after left side TKA. Moreover, they noted that nine of twelve cases were female (Bolarinwa et al., 2018). In the same way, we noticed that falling was higher in the females (nine out of eleven), and also, the falls were more in the right (nine cases) side compared to two only in the left side.

In a RCT, which evaluated the risk of falling related to FNB as compared to ACB, reported no significant difference between the two groups on either POD1 or POD2 based on the Tinetti Gait and Balance instrument (Jaime, 2014), a tool designed to evaluate and identify elderly patients who are at elevated risk of falling (Elkassabany et al., 2016). These results could be returned to in that study; 24 out of 31 patients in the FNB group were labeled as high risk for falling compared to 21 out of 31 patients in the ACB group.

In a recent study, on 28 patients that had undergone UKA under spinal anesthesia with 1% 2-chloroprocaine with supplemental IPACK (Infiltration between the Popliteal Artery and Capsule of the Knee) plus distal femoral triangle block, physiotherapists reported no failure of mobilization due to motor block (Erskine, 2019).

In a study with magnetic resonance imaging on the ACB displayed that 30 ml injected through a catheter fills out the whole adductor canal. In the current study, we used a volume of 20 ml of 0.5% bupivacaine which was adequate and appropriate (Lund et al., 2011). Jæger et al. related the delayed and transient femoral motor response seen with the ACB in their study to the large volume (30 cc) that could result in diffusion to the motor fibers of the femoral nerve outside of the adductor canal (Jæger et al., 2013).

In our study, gait distance on POD1 was 18.6 (5.7) m in ACB compared to 8.4 (3.3) m, and this difference was significant. Also, it was 31.63 (6.07) m compared to 24.45 (5.43) m on POD2, and this difference was also significant.

Hanson et al., in their study on continuous ACB compared to placebo, found that the block group showed 236.5 ± 247 ft (72.13 m) on POD1 which was statistically non-significant from the placebo group. But, the block group showed improvement in maximum distance ambulated compared with that of the placebo group on POD2, 378.4 ft (115.41 m) compared to 243.7 ft (74.3 m) (p = 0.034) (Hanson et al., 2014). On the other hand, Elkassabany et al. found that the average distances of ambulation during the physical therapy (PT) and time to up and go were similar on POD1 and POD2 between the two groups (FNB and ACB) (Elkassabany et al., 2016).

Thacher et al., in their retrospective study about the risk of near falls between ACB and FNB, reported no significant difference between the two groups regarding the total distance walked in POD1 or POD2 during four physiotherapy sessions. It was about 63 ft (19.2 m) on POD1 in both groups and 94.87 ft (28.93 m) in ACB group and 82.8 ft (25.254 m) in FNB group on POD2. These results differ from us as there was no significant difference between the two groups. But, the total distance walked from their patients whether on POD1 or 2 was near to our results (Thacher et al., 2017).

**Conclusion**

ACB blocks significantly preserved the quadriceps muscle strength, significantly reduced the number of falls and near falls, significantly increased gait distances moved after 24 or 48 h post block, and significantly improved functional recovery more than FNB blocks when given as supplemental postoperative pain control after unicompartmental knee arthroplasties without significant effect on SBD, pain scores at rest or movement, total morphine requirements, LOS, or side effects.

**Limitations and recommendations**

Limitations of this study include the use of various functional measures, a limited long-term follow-up, and limited publications about unicompartmental hemi arthroplasties to compare with them. Further studies on unicompartmental knee arthroplasties are required as these types of operations are still done on limited scale.

**Abbreviations**

ACB: Adductor canal block; ASA: American Society of Anesthesiologist; CSE: Combined spinal epidural; FNB: Femoral nerve block; HTO: High tibial osteotomy; IPACK: Infiltration between the Popliteal Artery and Capsule of the Knee; KA: Knee arthroplasties; LOS: Length of stay; MRC: Medical Research Council; PNBs: Peripheral nerve blocks; PONV: Postoperative nausea and vomiting; SBD: Sensory block duration; TKR: Total knee replacement; TUG: Time up to go; UKA: Unicompartmental knee arthroplasty; VAS: Visual analog scale

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**Authors’ contributions**

SH and GA conceived the study and share in its design. JM undertook data collection, data capturing, and handling. IM coordinate data analysis with the assistance and review by GA. SH and JM drafted the manuscript. All authors read and approved the final manuscript.

**Table 6 Complications and satisfaction in the two study groups**

|                          | Group A (n = 40) | Group B (n = 40) | p value |
|--------------------------|-----------------|-----------------|---------|
| Nausea and vomiting (yes/no) | 13 (32.5%)/27 (67.5%) | 13 (32.5%)/27 (67.5%) | 1       |
| Itching (yes/no)          | 8 (20%)/32 (80%) | 10 (25%)/30 (75%) | 0.95    |

Hanson et al., 2014. "Postoperative pain control with adductor canal block for unicompartmental knee arthroplasties." Anesthesia and Analgesia, 119(2), 436-445.
