Challenge Journal of Perioperative Medicine

Research Article

Comparison of the analgesic effects of different bupivacaine concentrations in continuous femoral block after total knee arthroplasty surgery

Murat Unal [a,*], Serpil Şavlı Mete [b], Menşure Kaya [b], Abdurrahman Dünmez [c], Gülçin Özalp Şenel [b], Nihal Kadıoğulları [b]

[a] *Department of Anesthesiology and Reanimation, Samsun Education and Research Hospital, Samsun, Türkiye*
[b] *Department of Anesthesiology and Reanimation, Dr. Abdurrahman Yurtaslan Ankara Oncology Education and Research Hospital, Ankara, Türkiye*
[c] *Department of Anesthesiology and Reanimation, İzmir Tire State Hospital, İzmir, Türkiye*

ABSTRACT

Aim: In regional anesthesia practice, anesthesists' goal must be to use the lowest effective concentration of local anesthetics to provide sufficient pain relief while minimizing side effects and complications. This study was designed to compare the analgesic efficacy of two different concentrations of bupivacaine (0.125% and 0.1%) in continuous femoral block for postoperative analgesia.

Method: In this study, fifty patients were enrolled, all of whom underwent femoral nerve block catheterization. The block procedure involved the administration of 30ml of bupivacaine solution at a concentration of 0.25%. Following a thirty-minute interval post-block application, patients underwent knee surgery under general anesthesia. During the closure of subcutaneous tissues, an additional 10ml of bupivacaine solution was injected through the catheter. Two groups were formed based on the concentration of the solution administered: Group(0.125%) received bupivacaine at a concentration of 0.125%, while Group(0.1%) received it at a concentration of 0.1%. Subsequently, upon arrival at the postoperative care unit, infusion through the catheter commenced at a rate of 10ml/h-1, maintaining the same concentrations for both groups. In addition to the nerve block, all patients were provided with intravenous Patient Controlled Analgesia (PCA) devices containing morphine for pain management. Throughout the postoperative period, sensory and motor block levels, Numerical Rating Scale (NRS) values for static and dynamic pain assessment, total morphine consumption, morphine demand, as well as any observed side effects and complications, were meticulously recorded for analysis.

Results: Postoperatively the NRSstatic values at 24th and 48th hours and NRSdynamic values at the 24th hour were higher in Group(0.1%) and it was statistically significant($p<0,007$). And at 48th hour, morphine consumption was significantly higher in Group(0.1%) ($p<0,05$).

Conclusions: In our study, all patients across both experimental groups initially experienced satisfactory analgesia. However, within the 24-hour postoperative period, Group(0.1%) exhibited a decline in the quality of analgesia, necessitating increased utilization of rescue analgesics. This escalation in rescue analgesic use was associated with a higher incidence of adverse effects and reduced patient comfort levels within this group. Consequently, our findings indicate that the 0.125% concentration of bupivacaine yielded superior efficacy compared to the 0.1% concentration in the context of continuous femoral block administration.

ARTICLE INFO

Article history:
Received 27 October 2023
Revised 3 December 2023
Accepted 21 December 2023

Keywords:
Femoral nerve
Bupivacaine
Local anesthetics
Nerve blocks
Regional anesthesia

* *Corresponding author*. Tel.: +90-362 -311-1500 ; E-mail address: murat.unal@yahoo.com (M. Unal)
ISSN: 2980-292X / DOI: https://doi.org/10.20528/cjpm.2024.01.003

1. Introduction

While being used for achieving surgical anesthesia, regional anesthesia techniques are now commonly preferred for postoperative pain treatment as well. The advancements of pain therapy underscores the preference for central neuroaxial and peripheral nerve block techniques. Following total knee arthroplasty surgery, there happens notable pain, edema, and muscle spasm, with the initial 48 hours being particularly challenging. Effectively managing this pain is crucial for patients to regain muscle strength, enhance joint mobility, and facilitate early mobilization [1].

Postoperative pain therapy utilizes systemic intravenous drugs (opioids, nonsteroidal anti-inflammatory drugs, muscle relaxants, antidepressants, etc…), epidural blockage, and peripheral nerve blockage techniques. Intravenous methods provide sufficient analgesia at rest, but patients in motion may experience pain, and reflex spasm of the quadriceps femoris muscle that cannot be avoided. Hence, regional anesthesia techniques are often preferred. Advances in nerve stimulators, ultrasound-guided nerve locating techniques, and continuous analgesia with catheters have contributed to the successful application of nerve blockages [2-5]. In contemporary clinical practice, while nerve blockades traditionally relied solely on nerve stimulators, ultrasound-guided techniques have gained prominence and preference. This shift is attributable not only to the heightened success rates achieved with reduced procedural duration but also to the enhanced safety profile afforded by ultrasound guidance. Through real-time visualization of both nerves and peripheral tissues, ultrasound guidance ensures greater precision, mitigating the risk of inadvertent intraneural injection-induced nerve damage during the procedure [3].

The principal objective of rehabilitating patients following total knee arthroplasty (TKA) is to attain optimal extension and flexion range of motion within the knee joint. This endeavor is chiefly facilitated by the functionality of the quadriceps femoris muscle, which receives innervation from the femoral nerve.

In the realm of unilateral anesthesia or analgesia, femoral and sciatic nerve blockades stand out as efficacious modalities. Comparative investigations suggest parity in effectiveness between femoral block and epidural blocks for knee surgery. However, femoral block demonstrates a favorable profile with fewer observed side effects and complications, as evidenced by several studies [6-8].

In the context of employing regional anesthesia techniques for postoperative analgesia, local anesthetics, particularly bupivacaine, are predominantly utilized due to their accessibility and efficacy. Bupivacaine offers versatility in achieving desired effects through variations in concentration. Higher concentrations are conducive to achieving anesthesia, while lower concentrations are suitable for analgesia. The reduction of bupivacaine concentration serves to mitigate the incidence of side effects and complications. However, excessive reduction may compromise the efficacy of nerve blockade, leading to inadequate pain management. Hence, it is imperative to select a concentration that optimally balances pain reduction efficacy with minimal side effects and complications.

In this study, our aim was to compare 0.1% and 0.125% concentrations of bupivacaine in terms of analgesia, motor blockage, and side effects.

2. Material and Method

2.1. Study design

After obtaining ethical committee approval (AOEAH-EPKK No: 2007/3) and written informed consents from patients, 50 ASA I-III status participants aged 40 to 77, scheduled for elective total knee arthroplasty surgery between April-September 2007 were included to this study.

Exclusion criteria were, not being suitable for general anesthesia, those with mental retardation, a history of chronic analgesic usage, peripheral neuropathy, coagulation disorders, and local anesthetic allergy.

Before surgery, patients were informed about Numerical Rating Scale (NRS) and the use of Patient Controlled Analgesia (PCA) device.

2.2. Block performing

After all patients were evaluated for sensorial or motor neurologic deficiencies on the side that femoral block was to be applied and recorded as intact, all patients were premedication with 0.07mg/kg intramuscular midazolam before block application. Patients then assumed a supine position. The catheterization site, marked 1cm caudal to the inguinal ligament and 1cm lateral to the femoral arterial pulse, was sterilized, and 2ml of 1% prilocaine solution was subcutaneously infiltrated.

Femoral Block was performed with the nerve stimulator (Stimuplex-DIG©; Braun, Geisingen, Germany) which was set to 1.5mA output, 2Hz frequency, and 0.1ms for nerve location. A 50mm stimulating needle (Pajunk D-78187 set, Geisingen, Germany) was inserted at a 45-degree cephalic angle in the sagittal plane until quadriceps femoris muscle contraction was achieved. After reducing voltage and ensuring contraction at 0.5mA or less, 10ml isotonic saline was administered, and a 20-gauge catheter was placed, leaving 6-8cm in the femoral nerve sheath and secured with a suture. Thirty minutes before surgery, 30ml of 0.25% bupivacaine solution was administered through the catheter after a negative aspiration test.

2.3. Randomization

Patients were randomized into two groups by closed envelope method. Group(0.125%) patients were planned to receive 0.125% bupivacaine, and Group(0.1%) patients were planned to receive 0.1% bupivacaine through the femoral nerve block catheter.

2.4. Evaluation of outcomes

Before surgery, sensorial blockage was assessed in the anterior thigh for the femoral nerve, lateral thigh for the lateral femoral cutaneous nerve, and the knee's

medial and posterior regions for the obturator nerve using a cold object. Motor blockage was evaluated by testing resistance to knee extension (femoral nerve) and leg adduction (obturator nerve), noted as present or absent.

2.5. General anesthesia

After standard ASA monitoring (Electrocardiography, Hearth Rate, Non Invasive Blood Pressure, O_2 Saturation, EndtidalCO_2), general anesthesia induction began. Intravenous 1.5μg.kg^{-1} fentanyl, 4-6mg.kg^{-1} thiopental, and 0.1mg.kg^{-1} vecuronium were administered. Anesthesia was maintained with a 40% O2, 60% N2O, and 1.2MAC sevoflurane mixture after tracheal intubation. Intramuscular diclofenac was given post-induction to all patients.

During the operation, hemodynamic parameters were monitored every 5 minutes. A decrease in systolic blood pressure exceeding 30% of the baseline was considered hypotension and treated with 0.9% NaCl infusion, and if necessary, intravenous (iv.) 5-10mg of ephedrine was administered. Heart rates below 50 beats.min^{-1} were considered bradycardia and treated with 0.5mg iv. atropine.

2.6. Postoperative analgesia management and assessments

Towards the end of surgery, during subcutaneous tissue suturing, 10ml of 0.125% bupivacaine solution (Group (0.125%)) or 0.1% bupivacaine solution (Group(0.1%)) were administered via the femoral nerve catheter. In the Post-Anesthesia Care Unit (PACU), elastomeric infusion pumps (Easy pump 270ml, 10ml/hr., B Braun; Boulogne Cedex, France) containing 0.125% or 0.1% bupivacaine solutions, infused at a rate of 10ml/h, were connected to the catheters. All patients had intravenous Patient-Controlled Analgesia (PCA) with 0.5mg.ml^{-1} morphine programmed as a 1mg bolus dose with a 10-minute lockout time. Intramuscular diclofenac was given every 12 hours postoperatively to all patients.

Throughout the study, patients were assessed at 0, 2nd, 6th, 12th, 18th, 24th, and 48th hours for sensorial and motor blockage, total morphine consumption, morphine demand counts, static and dynamic NRS values. Side effects like local anesthetics toxicity, nausea, vomiting, itching, sedation, or complications such as hematoma, skin infection at the catheter entrance, occlusion, or catheter dislocation were recorded.

For thromboembolism prophylaxis, 40mg enoxaparin was subcutaneously administered to all patients 12 hours before surgery. The catheter was removed 48 hours after the operation if 12 hours have passed since the last enoxaparin dose.

2.7. Power analyses and statistical analyses

A pilot study was carried out on five patients in each group. As a result, a power calculation for a trial suggested that 25 patients would be needed in each group with a power of 0.8 and 95% confidence interval.

Statistical analysis employed SPSS 11.5 for Windows, utilizing Chi-square, Mann Whitney U, T test, repeated measures ANOVA tests. Statistical significance was set at $p<0.05$, and Bonferroni correction was applied as necessary. Data was presented as Mean± Standard Deviation, Median (Minimum-Maximum).

3. Results

Age, sex, weight, ASA and surgery durations of the patients in two groups were similar (Table 1).

NRS_{static} values were found to be significantly higher in Group(0.1%) at 24th and 48th hours, while $NRS_{dynamic}$ values were again found to be higher in Group(0.1%) only at 24th hour($p<0.007$)(Table 2).

Although morphine demand counts at 48th hour were not different between two groups, total morphine consumption values at 48th hour were higher in Group(0.1%) and it was found to be statistically significant ($p=0.04$) (Table 3).

Although nausea and vomiting counts were higher in Group(0.1%), the difference was not statistically significant ($p=0.852$, $p=0.091$).

Sedation scores of the patients were similar between groups.

Thirty minutes after femoral nerve block catheter was placed and local anesthetic drug was injected and just before the surgery started, sensorial and motor blockage status was evaluated. There were no significant differences in success of the block between both groups (Table 4).

Table 1. Patient characteristics and operation durations (mean ± SD, median (minimum-maximum)).

	Group(0.125%) (n=25)	Group(0.1%) (n=25)	p
Age (years)	63.3 ± 9.0	63.2 ± 7.4	0.923
Sex (M/F) (n)	3 / 22	2 / 23	1.000
Weight (kg)	83.6 ± 15.2	79.96 ± 13.8	0.351
Operation Duration (minutes)	113.0 ± 19.0	114.0 ± 17.7	0.849
ASA I / II / III (n)	2 / 11 / 12	2 / 18 / 5	0.102

* $p>0.05$

Table 2. NRS scores (median (minimum-maximum)).

	Group(0.125%) (*n*=25)	Group(0.1%) (*n*=25)	*p*
$NRS_{static\ (0\text{-}10)}$			
0 hour	0 (0-3)	1 (0-3)	190
2 h	0 (0-3)	1 (0-3)	0.265
6 h	1 (0-2)	1 (0-4)	0.388
12 h	0 (0-1)	1 (0-4)	0.160
18 h	0 (0-1)	1 (0-2)	0.095
24 h	0 (0-1)	1 (0-2)	0.001*
48 h	0 (0-1)	0 (0-1)	0.004*
$NRS_{dynamic\ (0\text{-}10)}$			
0 hour	1 (0-3)	1(0-3)	0.302
2 h	1 (0-5)	2(0-4)	0.668
6 h	1 (0-3)	2(0-5)	0.201
12 h	1 (0-3)	1(0-5)	0.325
18 h	1 (0-4)	1(0-5)	0.203
24 h	0 (0-2)	2(0-4)	0.002*
48 h	0 (0-3)	1(0-3)	0.028

NRS_{static}: NRS at rest. $NRS_{dynamic}$: NRS at motion.
* $p<0.007$ Bonferroni correction.

Table 3. Total morphine consumption and morphine demand at 48th hour (median (minimum-maximum)).

	Group(0.125%) (*n*=25)	Group(0.1%) (*n*=25)	*p*
Morphine demand at 48th hour (mg)	63.3 ± 9.0	63.2 ± 7.4	0.923
Total morphine consumption at 48th hour (mg)	3 / 22	2 / 23	1.000

* $p<0.05$

Table 4. Sensorial and motor blockage status 30 minutes after the block application.

	Group(0.125%) (*n*=25)	Group(0.1%) (*n*=25)	*p*
Femoral sensorial	25 (100%)	25 (100%)	-
Lateral cutaneous femoral	25 (100%)	24 (96%)	1
Obturator sensorial	25 (100%)	25 (100%)	-
Femoral motor	23 (92%)	20 (80%)	0.417
Obturator motor	21 (84%)	21 (84%)	1

* $p>0.05$

4. Discussion

After major knee surgeries, patients often endure severe pain linked to the reflex spasm of the quadriceps femoris muscle, highlighting the critical role of adequate analgesia for successful knee rehabilitation. Untreated pain impedes early mobilization and, subsequently, poses risks to surgical success. Peripheral nerve blocks, notably femoral or femoral+sciatic blocks, are preferred for postoperative analgesia due to better tolerance and fewer side effects, making them predominant choices after major knee surgery [6-8]. This study established effective analgesia for knee rehabilitation after total knee arthroplasty using 0.125% and 0.1% concentrations of bupivacaine in continuous femoral block.

The femoral block, with a low failure rate (Table 4), is an easily applicable technique [9,10]. Numerous factors affect the success of femoral nerve block, including the concentration and volume of the local anesthetic [11]. There are various statements in the literature about the

optimum drug concentration to be used in femoral block [12,13]. Beebe et al. [14] offers 0.125% bupivacaine at a rate of 5ml.h^{-1} infusion which does not prevent early ambulation of patients. The continuous infusion drug concentration can be lowered, but excessive reduction may compromise block quality and distribution [15]. Whereas high doses and volumes may lead to toxicity, which can be prevented by using the minimum effective dose [16]. No signs of toxicity were observed in our study, and side effects (nausea, vomiting, itching, sedation) from opioids showed no statistically significant difference between the two groups. However, the incidence of nausea and vomiting was higher in group (0.1%), potentially due to increased morphine consumption.

In our study, statistically higher NRS_{static} (24th and 48th hours) and NRS dynamic (24th hour) values were observed in group (0.1%) (p<0.008). At 48 hours, group (0.1%) had higher morphine rescue analgesic consumption compared to group (0.125%); (Group (0.125%)=10mg, Group(0.1%)=17mg) (p<0.05). While both groups achieved adequate analgesia, the higher morphine consumption in group (0.1%) suggested superior analgesic quality in group (0.125%).

Applying a femoral nerve sheath catheter with a nerve stimulator has a success rate of 80-100% [10,17]. Techniques such as ultrasound or x-ray assistance, as demonstrated by Behera et al. [18], enhance catheter application success. Numerous studies confirm that single-shot or continuous femoral blockage provides adequate analgesia, facilitates rapid rehabilitation, minimizes side effects, and reduces hospitalization time [14,19]. Until recently nerve blockages were being performed mostly with the assistance of nerve stimulators. But with these techniques there were always some risks like vascular puncture, repeated advancements of the needle for finding the nerve and nerve damages caused by intraneural injections. As the ultrasound assistance has begun, visualization of the nerves and peripheral tissues for performing these procedures had increased the success rates, shortened the time for performing the blocks and decreased the complications like vascular puncture or nerve damages [3]. One problem for the anesthesia practitioners is that ultrasound devices may not be easily accessible in daily practice. And whether single or assisted near ultrasound, classical techniques like nerve stimulator usage should be well known and be carefully used if needed.

Catheter usage is limited by the risk of infection. Tobias et al. [20] found that, after 48 hours, bacterial colonization occurred in 30-50% of adductor canal nerve block catheters. While our study did not conduct microbiological investigations, no local infection signs such as fever, erythema, or discharges were observed.

A rare complication of peripheral nerve block is neurologic deficit, occurring at a rate of 0.014-0.04% as O'Flaherty et al. [21] reported. In this study, 1 of 51 patients experienced femoral nerve palsy, resolving completely after 5 months of physiotherapy. The patient was excluded upon re-evaluation, revealing a history of past neuropathy.

To minimize costs and reduce side effects and complications, our goal should be using the minimum effective drug concentration. In our study, both 0.125% and 0.1% concentrations of bupivacaine in continuous femoral block achieved adequate postoperative analgesia. However, with 0.1% concentration, compared to 0.125%, the analgesia quality decreases after 24 hours, leading to increased rescue analgesic (morphine) consumption and more side effects. In conclusion, 0.125% concentration of bupivacaine proved to be the most effective dose with minimal side effects for continuous femoral analgesia.

As previously noted, ultrasonography-assisted techniques have demonstrated enhanced success rates; however, in routine clinical practice, accessibility to such devices may pose a challenge, as was the case in the circumstances under which this study was conducted. Nevertheless, regardless of prevailing limitations, scientific inquiry mandates the systematic evaluation of existing conditions, necessitating the collection of data for future investigative endeavors.

One of the limitations and weaknesses of our study pertained to the unavailability of an ultrasound device, which could have provided visualization of catheter locations and the distribution of local anesthetic solutions, thereby enhancing the accuracy of our assessments. Additionally, there may have been unintended bias in the evaluation of postoperative motor block status. This potential bias stemmed from the differences in the evaluators between preoperative and postoperative assessments. Preoperative assessments were conducted by the block performer, who possessed knowledge of the patients' baseline motor neurological status. In contrast, postoperative evaluations were conducted by night-shift doctors who were not privy to the patients' baseline status. The postoperative presence of dressing and bandaging on the leg might have contributed to this situation as well. Consequently, this discrepancy in evaluators may have introduced variability and potential inaccuracies in the assessment of postoperative motor blocks. Consequently, only preoperative motor block results were deemed statistically reliable and reported.

The mitigation of these limitations and the correction of these deficiencies would greatly contribute to the scientific evaluation of this subject matter. Future studies should endeavor to address these shortcomings by ensuring access to ultrasound technology for enhanced procedural visualization and consistency in the evaluation process across preoperative and postoperative assessments. Such endeavors would bolster the reliability and robustness of findings in this field.

5. Conclusions

In continuous femoral block, both 0.1% and 0.125% concentrations of bupivacaine exhibit efficacy in providing adequate analgesia while maintaining safety. However, the utilization of lower concentrations of bupivacaine correlates with a time-dependent decline in analgesic quality, accompanied by an increased demand for rescue analgesics, leading to heightened occurrence of side effects and diminished patient comfort. Consequently, our findings advocate for the preference of 0.125% concentration of bupivacaine as the more optimal choice for conducting continuous femoral block procedures.

Acknowledgements

None declared.

Funding

The authors received no financial support for the research, authorship, and/or publication of this manuscript.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.

Author Contributions

All of the authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; were involved in drafting the manuscript or revising it critically for important intellectual content; and gave final approval of the version to be published.

Data Availability

The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the ethics committee of AOEAH-EPKK No: 2007/3. All methods were performed in accordance with relevant guidelines and regulations.

REFERENCES

1. Bailey L, Griffin J, Elliott M, Wu J, Papavasiliou T, Harner C, Lowe W. Adductor canal nerve versus femoral nerve blockade for pain control and quadriceps function following anterior cruciate ligament reconstruction with patellar tendon autograft: A prospective randomized trial. *Arthroscopy*. **2019**; 35(3):921-929.
2. Morsy KM, Gad-Elrab FA, Elzohry AAM, Abdelhafeez AM. Effect of adding fentanyl to bupivacaine in femoral nerve block for post-operative pain in patient subjected to total knee replacement guided by ultrasound. *Anaesth Pain Med.* **2019**; 1(1):06-11.
3. Lewis SR, Price A, Walker KJ, McGrattan K, Smith AF. Ultrasound guidance for upper and lower limb blocks. *Cochrane Database Syst Rev*. **2015**; (9):CD006459.
4. Strid JMC, Sauter AR, Ullensvang K, Andersen MN, Daugaard M, Bendtsen MAF, Søballe K, Pedersen EM, Børglum J, Bendtsen F. Ultrasound-guided lumbar plexus block in volunteers; a randomized controlled trial. *BJA: Br J Anaesth*. **2017**; 118(3):430–438.
5. Ilfeld BM. Continuous peripheral nerve blocks: An update of the published evidence and comparison with novel, alternative analgesic modalities. *Anesth Analg.* **2017**; 124(1):308-335.
6. Vishwanatha S, Kalappa S. Continuous femoral nerve blockade versus epidural analgesia for postoperative pain relief in knee surgeries: A randomized controlled study. *Anesth Essays Res*. **2017**; 11(3):599-605.
7. Bugada D, Allegri M, Gemma M, Ambrosoli AL, Gazzerro G, Chiumiento F, Dongu D, Nobili F, Fanelli A, Ferrua P, Berruto M, Cappelleri G. Effects of anaesthesia and analgesia on long-term outcome after total knee replacement: A prospective, observational, multicentre study. *Eur J Anaesthesiol.* **2017**; 34(10):665-672.
8. Tetsunaga T, Sato T, Shiota N, Tetsunaga T, Yoshida M, Okazaki Y, Yamada K. Comparison of continuous epidural analgesia, patient-controlled analgesia with morphine, and continuous three-in-one femoral nerve block on postoperative outcomes after total hip arthroplasty. *Clin Orthop Surg*. **2015**; 7(2):164-170.
9. Sahin L, Korkmaz HF, Sahin M, Atalan G, Ultrasound-guided single-injection femoral nerve block provides effective analgesia after total knee arthroplasty up to 48 hours. *Agri.* **2014**; 26: 113-118.
10. MacLean D, Abdallah FW. Ultrasound-guided regional anesthesia. *Anesthesia & Analgesia.* **2017**; 125(4):1406.
11. Tulgar S, Selvi O, Senturk O, Serifsoy TE, Sanel S, Meydaneri S. Evaluation of analgesic regimens in total knee arthroplasty, retrospective study. *North Clin Istanb*. **2017**; 4(2):124-130.
12. Zhang T, Zhang T, Niu X. et al. Femoral nerve block using lower concentration ropivacaine preserves quadriceps strength while providing similar analgesic effects after knee arthroscopy. *Knee Surg Sports Traumatol Arthrosc.* **2023**; 31:4988–4995.
13. Veneziano G, Tripi J, Tumin D, Hakim M, Martin D, Beltran R, Klingele K, Bhalla T, Tobias JD. Femoral nerve blockade using various concentrations of local anesthetic for knee arthroscopy in the pediatric population. *J Pain Res.* **2016**; 9:1073-1079.
14. Beebe MJ, Allen R, Anderson MB, Swenson JD, Peters CL. Continuous femoral nerve block using 0.125% bupivacaine does not prevent early ambulation after total knee arthroplasty. *Clin Orthop Relat Res*. **2014**; 472(5):1394-9.
15. Iamaroon A, Tangwiwat S, Sirivanasandha B, Halilamien P, Lertpenmetha Y, Sirimaneewattana S, Surachetpong S, Puangchan S. Femoral nerve block using 0.25% or 0.5% bupivacaine for analgesia after arthroscopic anterior cruciate ligament reconstruction. *J Med Assoc Thai*. **2014**; 97(7):717-23.
16. Hussain N, McCartney CJL, Neal JM, et al. Local anaesthetic induced myotoxicity in regional anaesthesia: A systematic review and empirical analysis. *Br J Anaesth.* **2018**; 121:822–841.
17. Kim MK, Ko SH, Hwang YJ, Kwon DG, Jeon YS, Ryu DJ. Effectiveness of continuous femoral nerve block for pain relief after total knee arthroplasty: comparison with epidural patient-controlled analgesia and periarticular injection. *Journal of International Medical Research.* **2022**; 50(4).
18. Behera SK, Gunupuru B, Sahu L, Das S. Peripheral nerve stimulator versus ultrasound-guided femoral nerve block for knee arthroscopy procedures: A randomized controlled trial. *Cureus*. **2022**; 14(11):e32043.
19. Freccero DM, Van Steyn P, Joslin PMN, Robbins CE, Li X, Efremov K, Shukla P, Talmo CT, Bono JV. Continuous femoral nerve block reduces the need for manipulation following total knee arthroplasty. *JBJS Open Access.* **2022**; 7(3):e21.00155.
20. Lyngeraa TS. Bacterial growth from adductor canal block nerve catheters removed after 48 hours in situ. *BJA: Br J Anaesth*. **2015**; 115.
21. O'Flaherty D, McCartney CJL, Ng SC. Nerve injury after peripheral nerve blockade-current understanding and guidelines. *BJA Educ*. **2018**; 18(12):384-390.