The research protocol

Part 1

Project summary

Pain management after total knee arthroplasty (TKA) is essential to improve early mobilization, rehabilitation, and recovery. Continuous adductor canal (AC) block provides postoperative analgesia while preserving quadriceps strength. However, there have been inconsistencies regarding the optimal location for continuous catheter block. We compared continuous femoral triangle, proximal AC, and distal AC blocks for postoperative analgesia after TKA. Patients undergoing unilateral TKA were randomly assigned to three groups: femoral triangle, proximal AC, or distal AC. The surgeon performed periarticular local anesthetic infiltration. After surgery, an ultrasound-guided perineural catheter insertion procedure was performed. The primary endpoint was pain scores at rest during the time period of 8:00 AM to 9:00 AM on the first postoperative day. Secondary endpoints included pain scores at rest and during activity at other time points, quadriceps muscle strength, and opioid consumption. Ninety-five patients, 32 in the femoral triangle group, 31 in the proximal AC group, and 32 in the distal AC group, completed the study. Analysis of the primary outcome showed no significant difference in pain scores among groups. Secondary outcomes showed significantly lower pain scores at rest and during activity in the distal AC group than in the femoral triangle and proximal AC groups in the morning of the second postoperative day. Quadriceps strength and opioid consumption did not differ among groups. Continuous femoral triangle, proximal AC, and distal AC blocks in the setting of periarticular local anesthetic infiltration provide comparable postoperative analgesia after TKA.

Study goals and objectives

We designed this randomized, controlled, double-blind clinical trial to compare continuous femoral triangle, proximal AC, and distal AC blocks for postoperative analgesia after TKA. The proximal end of the AC was identified using ultrasound landmarks, and the locations of the femoral triangle and distal AC blocks were determined based on the patient's femur length using radiographs. Our primary endpoint was to compare postoperative pain scores, and the secondary endpoints included opioid consumption and quadriceps motor strength.

Study design

This research is the prospective randomised, double-blinded study.

Inclusion criteria: adult patients with an American Society of Anesthesiologists physical status of class I–III scheduled for elective, unilateral, primary TKA

Exclusion criteria: chronic opioid use (daily use for >1 month of 20 mg oral morphine equivalents), revision surgery, contraindications to spinal anesthesia or peripheral nerve blocks, and allergy to lidocaine or ropivacaine.

Expected duration: March 2020 and December 2021

Methodology

Assignments and interventions

Patients were randomly assigned to either the femoral triangle, proximal AC, or distal AC groups according to a computer-generated randomization sequence on the day of surgery.

Anesthesia and surgery protocol

Upon the patients' arrival at the operating room, routine monitoring was performed. The patients

received spinal anesthesia with 10–12 mg of 0.5% hyperbaric bupivacaine. Patients who requested intraoperative sedation received propofol at 30–50 μg/kg/min. Hypotension (>20% decrease in mean blood pressure from baseline) was treated with a bolus of ephedrine (4 mg) or phenylephrine (50 μg). All TKAs were performed via the medial parapatellar approach by a single surgical team. The surgeon performed periarticular local anesthetic infiltration with 150 mg of ropivacaine and 30 mg of ketorolac diluted with normal saline to a total volume of 50 mL. The first 20 mL of the mixture were injected into the posterior capsule, the medial and lateral collateral ligaments, and medial and lateral meniscus remnants, prior to implant placement. The remaining 30 mL were used to infiltrate the soft tissue around the knee, including the surrounding muscles, synovium, fat pad, and subcutaneous tissue, before wound closure. All patients received preoperative celecoxib (200 mg) orally and intraoperative doses of acetaminophen (1 g), tranexamic acid (1 g), and dexamethasone (5 mg) intravenously. In the ward, all patients received celecoxib 200 mg orally and acetaminophen 1 g intravenously every 12 h thereafter. Intravenous tramadol (50 mg) was administered as rescue analgesia. Patients received standard of care physical therapy sessions (twice on PODs 1 and 2) and were mobilized once on the day of surgery with caregiver assistance and ambulated as soon as possible on POD1.

Catheter insertion procedure

After surgery, the patient was transferred to a block room and routine monitoring was performed. All catheters were inserted under a full aseptic technique using a real-time ultrasound-guided in-plane approach by an experienced anesthesiologist. A multi-hole perineural catheter through a catheter-over-needle system (E-cath PLUS, PAJUNK® GmbH, Geisingen, Germany) and a linear 6–13-MHz ultrasound probe (HFL38xp, SonoSite Inc., Bothell, WA, USA) were used for all patients.

On ultrasound, the proximal end of the AC was defined as the intersection of the medial borders of the sartorius muscle and the adductor longus muscle (supplemental figure 1). In the femoral triangle group, the insertion site was determined at 2/15th the femur length above the proximal end of the AC along the long axis of the femur (figure 1A). In the proximal AC group, the insertion site was the proximal end of the AC (figure 1B). In the distal AC group, the insertion site was determined at 1/15th the femur

length below the proximal end of the AC along the long axis of the femur (figure 1C). In our hospital's TKA protocol, a full-length standing anteroposterior radiograph is obtained before admission. Based on this, femur length was measured from the top of the femoral head to the most distal end of the medial femoral condyle (supplemental figure 2).

In preliminary data from 10 patients, the mid-thigh was approximated at 2/15th of the femur length above the proximal end of the AC (supplemental table 1). In addition, an area 2 cm above the adductor hiatus was approximated at 1/15th of the femur length below the proximal end of the AC. The proximal end of the AC was identified by ultrasound and the length from the ASIS to the superior border of the patella was measured using a tape measure.

Following identification of the designated site, an 18-gauge cannula with an indwelling 21-gauge needle was advanced through the sartorius muscle with the needle tip positioned lateral to the saphenous nerve. To open a space for catheter insertion, 10 mL of 0.2% ropivacaine was injected via the needle for hydrodissection. A 21-gauge multi-hole E-catheter was inserted through an indwelling 18-gauge cannula. An additional 5 mL of 0.2% ropivacaine was injected during ultrasound imaging to ensure correct placement of the catheter tip between the artery and the deep fascia of the sartorius in the femoral triangle group or between the artery and the vastoadductor membrane (VAM) in the AC groups (supplemental figure 3). The catheter was secured with a sterile occlusive dressing and an anchoring device. During the 48-h postoperative period, 0.2% ropivacaine was infused via the perineural catheter at a basal rate of 6 mL/h, a 4 mL bolus, and a lockout time of 30 min using a portable, patient-controlled infusion pump. After the procedure, all patients were dressed with hospital uniform tops and bottoms to blind the group assignment.

Outcome measurement

The primary endpoint was pain scores at rest in the morning on POD1. The pain intensity at rest and during activity was evaluated using an 11-point numeric rating scale (NRS: 0 = no pain, 10 = worst

imaginable pain). The secondary endpoints included pain scores at other time points, quadriceps muscle strength, opioid consumption, and local anesthetic consumption. Pain scores and quadriceps strength were assessed at four time points: preoperative baseline, the morning (8:00-9:00 AM) of POD1, the afternoon (4:00-5:00 PM) of POD1, and the morning (8:00-9:00 AM) of POD2. The quadriceps strength of both legs was tested using a hand-held dynamometer (Lafayette Manual Muscle Test System, Lafayette Instrument Company, Lafayette, Indiana, USA). Patients were instructed to extend their knees twice, with a 30-second pause between each attempt. The maximum force achieved was used in the analysis. The consumption of tramadol was converted to oral morphine equivalents. Preoperative data collection included the Hospital Anxiety and Depression Scale (HADS) ranging from 0 to 21. The probable presence of anxiety or depression was defined as a HADS anxiety or depression subscale score ≥11.

Safety considerations

We excluded subjects who were thought to have the risk for spinal anesthesia or peripheral nerve blocks.

Exclusion criteria: contraindications to spinal anesthesia or peripheral nerve blocks, and allergy to lidocaine or ropivacaine

Data management and statistical analysis

We calculated the sample size required to detect a difference in NRS >3 among the three groups using pairwise comparison. Bonferroni correction was performed to adjust for the increase in type I error in multiple comparisons. Accordingly, 29 subjects were required in each group to achieve a statistical power of 90% at P-value of <0.0167. Therefore, 32 patients were enrolled in each group to account for a 10% dropout rate. The Shapiro–Wilk and Kolmogorov–Smirnov tests were used to confirm normality of the data distribution. One-way analysis of variance and the Kruskal–Wallis test were used to analyze parametric and nonparametric continuous variables, respectively. Post-hoc analysis was performed

using the t-test or Mann–Whitney test as appropriate and adjusted using the Bonferroni correction. Intergroup comparisons of categorical variables were conducted using Fisher's exact test or the chi-square test as appropriate. Continuous variables are presented as mean ± SD or median (interquartile range); categorical variables are presented as numbers (percentages). Statistical analyses were performed using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria), SPSS version 23.0, (IBM Corp., Armonk, NY), or MedCalc Statistical Software version 18.11.3 (MedCalc Software Ltd., Ostend, Belgium). Statistical significance (P) was set at <0.05.

Dissemination of results and publication policy

The principal investigator (Y.S.C.) will take the lead in publication.

Duration of the project

March 2020~ December 2021

Ethics

The Severance Hospital institutional review board (protocol number: 4-2019-1038) approved the study protocol (ClinicalTrial.gov, NCT04206150, December 20, 2019). This study was performed in accordance with relevant guidelines and regulations.

Informed consent forms

Written informed consent was obtained from subjects.

Part 2

Budget

The budget included the cost of the progress of the study.

Other support for the project

The authors declare no competing interests. This work was supported by a faculty research grant from the Yonsei University College of Medicine (grant number: 6-2020-0075). The funder was not involved in the study.

Collaboration with other scientists or research institutions

None.