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Comparison of postoperative pain in the first and second knee in staged bilateral total knee arthroplasty: Clinical evidence of enhanced pain sensitivity after surgical injury

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ABSTRACT

Staged bilateral total knee arthroplasty (TKA) may provide an ideal clinical model for the study of central sensitization. In staged TKA, hyperalgesia may be induced as a result of repeated surgical injury possibly via central sensitization, which can decrease functional outcomes. Therefore, we hypothesized that in staged bilateral TKA, patients would have greater pain in the second operated knee than in the first. Thirty patients undergoing staged bilateral TKA at a 1-week interval were enrolled. Postoperative pain, which was reported on the basis of a visual analog scale (VAS; primary outcome) at rest and at maximum knee flexion, and the amount of patient-controlled analgesic (i.v. fentanyl) and rescue analgesic (i.v. ketoprofen; secondary outcomes) administered during the 48 h after the operation, were compared between the first and second TKA. VAS scores at rest and at maximum knee flexion were greater on the second operated knee ($P < .001$ and $P < .01$, respectively). The cumulative amounts of patient-controlled analgesic and the rescue analgesic were greater in the second than in the first TKA ($P < .001$ and $P < .05$, respectively). Patients undergoing staged bilateral TKA experience greater postoperative pain in the second operated knee than the first. This suggests extension of hyperalgesia beyond the initially injured site to remote regions after surgical injury, in which central sensitization may be involved. Therapeutic approaches to reduce such hyperalgesia induced in the course of staged operations are required.

1. Introduction

Total knee arthroplasty (TKA) is a commonly performed orthopedic surgery to relieve pain and improve physical function in patients with knee osteoarthritis, and the number of TKAs performed is increasing dramatically [21,25]. Because osteoarthritis often involves both knees [9], bilateral TKA accounts for a considerable portion of all TKAs [30]. For bilateral TKA, staged sequential TKA at a 1-week interval is regarded as safe and efficient in terms of the complication rate, rehabilitation time, and duration of hospital stay [10,14].

However, because tissue damage can induce hyperalgesia via central sensitization [40], patients undergoing staged TKA may be at risk of hyperalgesia on the second operated knee as a result of repetition of surgical injury. This assumption that pain is greater in the second operated knee than in the first requires verification and is worthy of investigation because postoperative pain is associated with various morbidities [15], especially in patients who undergo TKA [17,31].

However, no studies to date have investigated whether previous surgical injury affects pain related to subsequent operations at a site remote from the previous surgery. This issue is related to the debate on whether increased pain sensitivity extends beyond the injured site to remote areas. Hyperalgesia at a remote region was once termed "tertiary hyperalgesia" as opposed to that within (primary hyperalgesia) or adjacent to (secondary hyperalgesia) the injured site [40]. Although primary and secondary hyperalgesia have been actively studied and their existence is generally agreed upon [19,26,39,40], there are only a few human data that support tertiary hyperalgesia [7,12], and its existence is questioned as a result of conflicting study results [26,27]. Hyperalgesia was detected at the site distant from the injured region in some studies [7,12], but not in others [26,27]. Because identical procedures are performed on both knees in bilateral TKA, greater pain in the second operated knee compared with the first could be interpreted as tertiary hyperalgesia, thus providing information regarding this controversial subject.

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In this study, we investigated whether patients experience greater pain in the second operated knee than in the first in staged bilateral TKA at a 1-week interval. Visual analog scale (VAS; primary outcome) and analgesic requirements (secondary outcome) of the first and second TKAs were compared.

2. Methods

This prospective, randomized, partiallyblinded, controlled trial was approved by the institutional review board and registered at ClinicalTrial.gov (NCT01457313). Patients scheduled for staged bilateral TKA at a 1-week interval under spinal anesthesia as a result of knee osteoarthritis, aged ⩽85 years, and with an American Society of Anesthesiologists physical status of I–II were enrolled (Fig. 1). Exclusion criteria were as follows: any contraindication to spinal anesthesia or femoral nerve block such as coagulopathy; conversion to general anesthesia; preexisting pain syndrome; abnormal liver function or renal test results; severe heart, liver, or renal disease; history of stroke or neurologic deficits; psychiatric disorder; chronic opioid use; drug dependency; allergy to study medications; inflammatory joint disease; previous surgery on or trauma of the knee; difference in preoperative VAS score of ⩾20 (at rest and at maximum knee flexion) between each side of the knee; body mass index of ⩾40 kg/m^2; and inability to comprehend the VAS or to use patient-controlled analgesia (PCA). The side of the knee to be operated upon first was determined randomly by a closed, opaque envelope method in a right–left ratio of 1:1.

While monitoring the electrocardiogram, pulse oximetry, noninvasive arterial blood pressure, femoral nerve block, and spinal anesthesia were performed by one experienced anesthesiologist who was blinded to the study protocol. For femoral perineural catheterization, an 18-gauge Tuohy needle was inserted below the fascia iliaca and close to the femoral nerve using an in-plane approach under real-time ultrasonography guidance [33]. Proper needle tip placement was confirmed by observing the spread of 0.9% saline 3 mL below the fascia iliaca and anterior to the femoral nerve [33]. A catheter was advanced 3 cm past the needle tip. A test dose of 5 mL of 2% lidocaine mixed with 5 μg of epinephrine was administered via the femoral nerve catheter [20]. After 5 min, loss of cold sensation to an alcohol swab in the sensory region of the ipsilateral femoral nerve and at the anterior thigh was confirmed [20]. A lumbar subarachnoid block was then performed with 15 mg of 7.5% levobupivacaine at the L3–L4 or L4–L5 intervertebral space in the lateral decubitus position to achieve sensory blockade to cold and pinprick above the T10 dermatome.

The same surgical technique, prosthesis, and rehabilitation protocol were used in both knees of each patient. All TKA procedures were performed by one experienced orthopedic surgeon (blinded to the study protocol) using the standard medial parapatellar approach with a tourniquet. A posterior-stabilized prosthesis (Genesis II; Smith & Nephew, Memphis, TN, USA) with a fixed-bearing system was used in every TKA. In all cases, the patella was resurfaced, and implant fixation was carried out with bone cement. A compressive dressing was applied, and a subcutaneous closed suction drain was kept in place for the first 24 h. In terms of rehabilitation, patients began walking with crutches or a walker and performing active and passive range-of-motion exercises 48 h after the operation.

Our institutional analgesic modality for postoperative pain of TKA comprised preemptive analgesia, periarticular injection during the TKA procedure, continuous femoral nerve blockade, i.v. PCA, postoperative oral analgesics, and i.v. rescue analgesics. Preemptive analgesia comprised 10 mg of dexamethasone i.v. (for control of postoperative pain and emesis), 200 mg of oral celecoxib, 75 mg of pregabalin, and 650 mg of acetaminophen, which were administered about 40 min before anesthetic induction. By the end of the TKA procedure (after fixation of all prostheses), a periarticular injectate (total of 300 mg of ropivacaine, 10 mg of morphine, 30 mg of ketorolac, 300 μg of 1:1000 epinephrine, and 750 mg of cefuroxime) was infiltrated in divided doses into the sheath of the medial and lateral collateral ligament and posterior capsule, synovium, capsule, quadriceps muscle, subcutaneous tissue, and joint capsule [22]. At the end of the operation, i.v. PCA (2000 μg

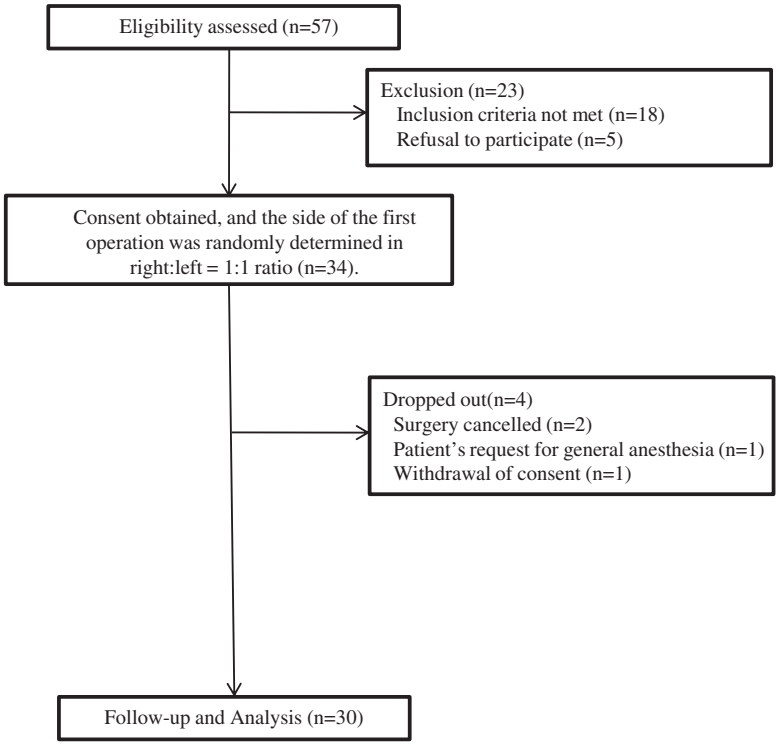

Fig. 1. Consort flow chart illustrating patient enrollment.