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Prediction of postoperative pain by preoperative pain response to heat stimulation in total knee arthroplasty

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ABSTRACT

It has been estimated that up to 54% of the variance in postoperative pain experience may be predicted with preoperative pain responses to experimental stimuli, with suprathreshold heat pain as the most consistent test modality. This study aimed to explore whether 2 heat test paradigms could predict postoperative pain after total knee arthroplasty (TKA). Patients scheduled for elective, unilateral, primary TKA under spinal anesthesia were consecutively included in this prospective, observational study. Perioperative analgesia was standardized for all patients. Outcomes were postoperative pain during walk: from 6 to 24 hours (primary), from postoperative day (POD) 1 to 7 (secondary), and from POD 14 to 30 (tertiary). Two preoperative tonic heat stimuli with 47°C were used; short (5 seconds) and long (7 minutes) stimulation upon which patients rated their pain response on an electronic visual analog scale. Multivariate stepwise linear and logistic regressions analyses were carried out, including 8 potential preoperative explanatory variables (among these anxiety, depression, preoperative pain, and pain catastrophizing) to assess pain response to preoperative heat pain stimulation as an independent predictor for postoperative pain. A total of 100 patients were included, and 3 were later excluded. A weak correlation [rho (95% confidence interval); *P* value] was observed between pain from POD 1 to 7 and pain response to short [rho = 0.25(0.04 to 0.44); *P* = .02] and to long [rho = 0.27 (0.07 to 0.46); *P* = .01] heat pain stimulation. However, these positive correlations were not supported by the linear and logistic regression analyses, in which only anxiety, preoperative pain, and pain catastrophizing were significant explanatory variables (but with low R-squares; 0.05 to 0.08). Pain responses to 2 types of preoperative heat stimuli were not independent clinically relevant predictors for postoperative pain after TKA.

1. Introduction

There is general agreement regarding a documented large interindividual variability in postoperative pain responses [4,6,9,24]. The basis of this variability is complex and might involve both psychological factors and somatic factors in the form of preoperative function in the nociceptive system and the peripheral and central inflammatory response. Preoperative prediction of postoperative pain is relevant because acute postoperative pain may be an important factor in the transition from acute to chronic pain states [18] and because identification of high pain responders may help to individualize and improve postoperative pain management [16]. Also, preoperative identification of high pain responders may be helpful to design enriched trials for assessment of new analgesics.

It has been estimated that up to 54% of the variance in postoperative pain experience may be predicted with preoperative quantitative sensory testing (QST), ie, basal pain perception (nociceptive response) to experimental physical stimuli [36]. The predictive strength of nociceptive testing might be higher than reported for single-factor analyses of demographics (eg, age), preoperative factors (eg, preoperative pain) and psychological factors (eg, anxiety, depression, and pain catastrophizing) [36]. Pain response to suprathreshold thermal stimuli (ie, pain beyond patient threshold) has been suggested to be the most consistent test modality, compared with pressure and electrical stimuli and lower phasic thermal stimuli evaluating warmth and heat pain detection thresholds [3].

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However, traditional QST is comprehensive and time consuming, calling for simple and fast methods in order to be feasible in daily clinical practice [36].

Recently, an increased preoperative pain response to short tonic heat pain stimulation was found to be a risk factor for postherniotomy pain [1]. In the present study, we aimed to explore whether a simplified preoperative tonic heat pain test paradigm could predict postoperative pain after the painful total knee arthroplasty (TKA). We hypothesized that dependency exists between pain response to preoperative heat pain stimulation and postoperative pain in TKA patients.

2. Methods

2.1. Patients and study design

The trial was approved by the regional ethics committee and the Danish Data Protection Agency, and was registered at http://www.clinicaltrials.gov (reg. no NCT01179204). Oral and written informed consent was obtained from all patients, and the study was carried out in accordance with the principles of the Helsinki Declarations.

Ethnic Danes ages >18 years and scheduled for elective, unilateral, primary TKA under spinal anesthesia by 3 orthopedic surgeons at Hvidovre University Hospital, Copenhagen, Denmark, were consecutively screened for inclusion in the study (August 2010 to September 2011). Exclusion criteria were history of alcohol or drug abuse, daily use of glucocorticoids or strong opioids (morphine, fentanyl, hydromorphone, ketobemidone, methadone, nicomorphine, oxycodone, and pethidine), rheumatoid arthritis, central or peripheral neurologic diseases potentially influencing pain perception, body mass index >40, dementia or other cognitive dysfunction, psychiatric diseases including treatment for anxiety or depression, malignant diseases, and previous surgery in the area of the nociceptive testing (potentially affecting sensory function).

Included patients were scheduled for an interview and nociceptive testing 1 to 2 weeks preoperatively. To ensure similar test conditions, patients were instructed to take no pain medication (of any kind) 48 hours before the nociceptive testing. The design was a single-center, prospective, consecutive, observational cohort study.

2.2. Outcomes measures

Dependency between pain response to preoperative heat pain stimulation and postoperative pain was evaluated. The primary outcome was pain from the knee during walk from 6 to 24 hours postoperatively, and the secondary outcome was pain from the knee during walk from postoperative day (POD) 1 to 7. In an attempt to assess subacute pain, a tertiary outcome—pain from the knee during walk from POD 14 to 30—was also included. Pain was assessed after 5-meter walk using the 100-mm visual analog scale (VAS; 0 = no pain and 100 = worst pain imaginable; subjective rating by patients). Pain during walk was chosen over pain at rest because pain on movement exerts the most direct adverse impact on postsurgical functional recovery [30], and thus might be more clinically relevant than pain at rest. The assessment at 6 hours was chosen to achieve the earliest possible pain assessment during walk, without running a risk of the residual effect of the spinal anesthesia (motor blockade) hindering walk. The primary outcome was the average of 2 pain assessments by an investigator at 6 and 24 hours, the secondary outcome was the average of 13 pain assessments on a questionnaire morning (8 am) and evening (10 pm) from POD 1 to 7 (average of not missing values), and the tertiary outcome was the average of 2 pain assessments on telephone interviews at POD 14 and POD 30. For the primary and tertiary outcome no missing values were accepted; for the secondary outcome a maximum of 3 missing values was accepted. At every time point throughout the study a VAS value of 100 was registered if patients were unable to walk due to pain from the operated knee.

2.3. Preoperative nociceptive testing

A thermal heat stimulus (Modular Sensory Analyzer, Somedic AB, Hörby, Sweden) and a contact heat thermode with a size of 12.5 cm^2 was used as previously described in herniotomy patients [1]. In this previous study, warmth and heat pain detection thresholds (5 of each) were determined, as well as pain responses to 4 short (5 seconds) tonic heat pain stimuli for each temperature of 45°C, 46°C, 47°C, and 48°C (administered in a semi-randomized order; 16 in total) in both the groin region (operation site) and on the ipsilateral forearm (control area) [1]. In the study, only pain response to the short tonic heat pain stimulus was found to be a risk factor for postherniotomy pain (not warmth and heat pain detection thresholds), but for all temperatures used (45°C, 46°C, 47°C, and 48°C) and at both test regions (groin and arm results were highly correlated) [1]. Therefore, to facilitate the potential usefulness in daily clinical practice, our preoperative nociceptive test paradigm was simplified, using only tonic heat pain stimuli with only 1 temperature (47°C), and only 1 test site. The heat probe was applied on the thigh 16 cm above the upper patellar border, as previously described by the group [23], on the site of surgery.

Preceding the nociceptive testing (and final inclusion), to ensure similar test conditions, all patients confirmed taking no pain medication for the previous 48 hours. The nociceptive testing consisted of 4 short (5 seconds) [1] and 1 long (7 minutes) [23,35] tonic heat pain stimuli. Tests were performed in a closed and quiet room with light subdued and with fixed temperature (20°C to 24°), with patients positioned in a semireclined position. First, to get the patient to become familiar with the test procedure, a short heat pain stimulus was applied on the contralateral leg. Second, the short heat pain stimuli were performed on the site of surgery. The probe temperature was ramped up from baseline temperature on 32°C at a rate of 5°C/s until 47°C was reached, and then maintained for 5 seconds. At the end of the 5-second period, patients rated their pain intensity on an electronic VAS, and the probe temperature was decreased to 32°C at a rate of 5°C/s. The 4 short heat pain stimuli were performed with 30-second intervals, and the average was calculated. After a 2-minute pause, the long heat pain stimulus began. Again, probe temperature was ramped up from 32°C at a rate of 5°C/s until 47°C was reached, and then maintained for 7 minutes. Patients rated their pain intensity on an electronic VAS continuously throughout the 7-minute period, and the mean VAS area under the curve (AUC) was calculated. If patients requested removal of the probe due intolerable pain before the test period was over, the maximum pain (VAS = 100) was noted in the 5-second test and for the remaining time in the 7-minute test.

All preoperative tests and postoperative pain recordings were done by 1 of 2 investigators using instruction sheets to standardize test procedures. Patients were unaware of the test result throughout the study, and the investigator assessing postoperative pain was blinded to preoperative measurements.

2.4. Preoperative interview

At a preoperative interview preceding the nociceptive tests, the following were registered: age, gender, body mass index, American Society of Anesthesiology physical score, smoking habits, average preoperative pain (last week) from the knee at rest and during walk (with the visual analog scale), the duration of knee pain

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