Protocol

Acute Postoperative Pain and Catastrophizing in Patients Undergoing Unicompartmental Knee Arthroplasty - A Prospective, Observational, Single-center, Cohort study

Protocol ID: UKAPCS

Brief title: Acute Postoperative Pain and Catastrophizing in Patients Undergoing Unicompartmental Knee Arthroplasty

ClinicalTrials.gov ID: NCT05510947

The protocol is based on three previous studies involving pain after total knee arthroplasty of which one is published and two are being prepared for publication. The studies are approved by the Local Ethics comity: De Videnskabsetiske Komiteer for Region Hovedstaden (H-18034756, H-18034778, and H-18034782), by the knowledge-Centre for Data Protection (reference numbers VD-2018-528, VD-2019-04, and VD-2019-05), and by the Danish Medicine Agency (DKMA) (EudraCT-numbers 2018-002634-20, 2018-002635-23, and 2018-002636-25).

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Introduction

Background

Primary knee arthroplasty is a frequently performed procedure and is expected to increase in numbers over the next decade [1, 2]. Advantages of unicompartmental knee arthroplasty (UKA) compared to total knee arthroplasty (TKA) include shorter hospital stays, faster recovery [3-6], fewer infections and readmissions [6-9], and lower costs [9]. The length of hospital stay after UKA is variable, but an increased length of hospitalization has been associated with more complications and higher readmission rates [10]. A recent study has shown that the main reasons for continued hospitalization beyond 24 hours after surgery are pain and lack of mobilization [11]. Strategies to decrease the length of stay after UKA should thus be aimed at improved analgesia and postoperative mobilization.

There is a large interindividual variability in the postoperative pain response. It is well documented in TKA-surgery that high pain responders (HPR), evaluated using the Pain Catastrophizing Scale (PCS), have higher postoperative pain responses compared to low pain responders (LPR) [12-15]. Recently, it has been shown that HPR patients undergoing TKA benefit from a larger preoperative dose of glucocorticoid compared to a previously recommended dose [16]. Interestingly, the same difference has not been found in LPR patients (Nielsen et al.: IN PREPARATION, clinicaltrials.gov ID NCT03758170, EudraCT 2018-002634-20, VEK H-18034756). These HPR patients constitute a vulnerable high-risk patient group and potentially benefit from targeted treatment [17].

Currently, the distribution of HPR- and LPR patients and their association with acute pain following UKA is not well investigated. The generated knowledge from this research project is essential to determine how studies with analgesia interventions should be designed. In the future, this will contribute to targeting treatment for high-risk patient groups to reduce pain and improve postoperative mobilization, and ultimately decrease the length of hospital stay in patients undergoing UKA. By targeting treatment, potential overtreatment is also avoided.

Aim

To investigate the prevalence of high- and low-pain responders, defined by a PCS score > 20 and ≤ 20 respectively, as well as the acute postoperative course of pain for these groups after unicompartmental knee arthroplasty.

Study design

Prospective observational single-center cohort study.

Sample size

120 patients

Outcomes

Primary outcome

- Ratio between HPR:LPR patients defined as patients with PCS > 20 and PCS ≤ 20 respectively

Secondary outcomes

- Incidence of moderate to severe pain (VAS > 30 mm) during a 5-meter walk test 24h postoperatively in LPR patients
- Incidence of moderate to severe pain (VAS > 30 mm) during a 5-meter walk test 24h postoperatively in HPR patients

- Differences between HPR- and LPR patients for the following variables:
    - Incidence of moderate to severe pain (VAS > 30 mm) during a 5-meter walk test 24h postoperatively
    - Incidence of moderate to severe pain (VAS > 30 mm) at rest 24h postoperatively
    - Cumulated pain upon ambulation in a 5-meter walk test day 2-7
    - Cumulative use of rescue-analgesics per day in hospital day 0 to discharge, and at home from day of discharge to day 7
    - Quality of sleep, lethargy, dizziness, and nausea pre- and postoperatively from day 0 to day 7
    - Length of stay (LOS) in hospital

Inclusion criteria

- Primary unilateral UKA
- Age ≥ 18 years
- Ability to participate in the study (understand written and spoken Danish language, self-reported pain, and satisfaction)
- Filled out the Pain Catastrophizing Scale preoperatively
- Signed written informed consent form

Exclusion criteria

- Mental disability that could impair a patient's decision-making capability of giving informed consent and not enabling valid data collection
- Insulin-treated diabetes mellitus
- Patients with known diagnoses of schizophrenia, ongoing psychosis, bipolar disease and/or a history of ongoing anti-psychotic treatment
- Patients with modulated pain-reception (experience) based on other diseases or injuries, e.g. spinal cord or brain injury, severe polyneuropathies, or neurologic disorder
- Peripheral nerve block per- or postoperatively

Study location

The inclusion will take place at the Dept. of Orthopaedic Surgery, Arthroplasty unit at Hvidovre Hospital, Capital Region of Denmark.

Timespan

Expected start of project: September 1, 2022

Expected end of data collection: July 1, 2023

Expected end of data analysis: September 1, 2023

Study plan

In the outpatient clinic, the screening procedure will be performed among patients planned to UKA by the surgeons. Patients will be asked if they may be contacted with the purpose of participating in a research project. Patients will undergo a preliminary examination where, as a standard procedure, the patient will receive a PCS questionnaire. Patients will be informed of the research project either in the outpatient clinic or by phone from an investigator.

All patients will receive verbal and written information about the project. All patients must give a signed informed consent on paper prior to inclusion to participate in the study.

Study specific

Study-specific tests include an evaluation of pain at hospital, and at home using the electronic pain diary.

Data collection

Data protection

All patient-related information will be treated confidentially, and data will be pseudoanonymized. Signed informed consent from participating patients will be stored at the Anesthesiologic Dept. 542, Hvidovre Hospital, in a locked cabinet. All electronic data will be stored in REDCap.

Collected variables

During the hospital stay, data will be collected by contacting the patient at the Orthopaedic Dept. and by accessing the electronic patient journal. After discharge patients will be asked to fill out an electronic pain diary until 7 days after the operation. The following variables will be collected:

- Number of participating patients (CONSORT)
- Pain during rest (VAS 0-100 mm), measured preoperatively, 24 h postoperatively, and twice a day from day 2 to 7
- Pain upon ambulation in a 5-meter walk test (VAS 0-100 mm), measured preoperatively, 24 h postoperatively, and twice a day from day 2 to 7
- Quality of sleep, lethargy, dizziness, and nausea pre- and postoperatively from day 0 to day 7.
- PCS score
- Preoperative analgesia
- Use of rescue-analgesia from day 0 to day 7
- Type and dose of analgesia from day 0 to day 7
- Length of stay (LOS) in hospital, and reasons for prolonged stay (>2 postoperative days)
- Demographical data (gender, age, height, weight, co-morbidity, American Society of Anesthesiologist (ASA) score).
- Surgical data (date of surgery, indication, surgical time, procedure information, intraoperative bleeding, transfusion data, perioperative analgesics)
- Deviations from standard treatment

Statistics

Power calculation

There is no relevant acute pain data from UKA patients, thus, sample size estimates are based on data from TKA patients. The pain response is expected to be higher in a TKA population, although this is not known. However, the relative difference in pain between HPR- and LPR patients is not necessarily different in UKA patients. We are not familiar with the ratio between HPR- and LPR-patients based on PCS score in UKA, and thus a power calculation will be associated with substantial uncertainty. For this reason and because of the descriptive hypothesis-generating nature of the study, we will include 120 patients.

Data analysis

Dichotomic data will be tested using chi-square test or Pearson's exact test and presented as odds ratio or proportion with two-sided 95% confidence intervals. Continuous data will be tested for

normal distribution using visual inspection of Q-Q plots and histograms and using the Kolmogorov–Smirnov test. Differences in data will be tested with unpaired t-test or Mann-Whitney U-test depending on normal distribution. Uni- and/or multivariate analyses will be performed to test independent variables. A *P*-value < 0.05 is considered significant. Statistical calculations will be made using either R statistical software (Open source) or SPSS statistics (IBM, New York, USA).

Financial conditions

Expenses are borne by Henrik Kehlet who has received funding from the Candys Foundation.

Publication

Based on the data, one or more manuscripts will be made for the purpose of publication in an international Peer-Reviewed journal. Results will be published independent of the findings. Authorship and co-authorship will be distributed according to the Vancouver Recommendations (International Committee of Medical Journal Editors). The order of authors will be as follows:

Anders Deichmann Springborg, Christian Bredgaard Jensen, Kirill Gromov, Anders Troelsen, Henrik Kehlet, Nicolai Bang Foss.

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