Comparing unicompartmental to total knee arthroplasty in medial gonarthritis: study protocol for 2-year follow-up of a randomized controlled trial

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Abstract

Background and objectives: Since the 1990s, unicompartmental knee arthroplasty (UKA) are again starting to gain interest worldwide. A mere 3.5% of all knee arthroplasties performed in Sweden 2014 were UKAs, whereas up to 25% had knee osteoarthritis isolated to the medial side. Reasons for this discrepancy might be that UKAs are considered more technically demanding, thus requiring more surgical training, and that long-term survival of these implants has been inferior compared to total knee arthroplasty (TKA). This has been addressed by improving surgical instruments and discontinuation of underperforming implants, and by improving surgical technique including mini-invasive incision and patient selection. In support of using the less surgically invasive UKA, a few cohort studies show less pain, fewer hospital days, and faster rehabilitation. However, to the best of our knowledge, there is a lack of high quality randomized clinical trials (RCTs) showing unequivocal clinical superiority of UKA compared to TKA. The aim of the present study is to compare changes in muscle mass, strength, performance based measures (PBMs), and patient reported outcome measures (PROMs) in patients randomized to UKA or TKA.

Design: A 2-year follow-up RCT.

Methods: The study will include 80 patients with medial knee osteoarthritis, aged 50 years or more, who will be scheduled for a knee replacement and equally randomized to either TKA or UKA.

Outcome measures: The primary outcome is muscle mass change at 6 weeks, 6, 12 and 24 months post-operatively measured by computed tomography. Secondary outcomes are PBMs, PROMs, muscle strength, and 3D motion analysis at the same occasions.

Discussion: Although patients subjected to total hip arthroplasty are typically satisfied with their surgical results, patients with TKA are less so. It is of importance to improve surgical procedure, and less invasive surgery of the knee might be a solution.

Ethics and dissemination: The study has been approved by the Regional Ethics Committee in Stockholm (DNR: 2014/1895-31/3) and will be conducted in accordance with the ethical principles of the Declaration of Helsinki. All patients will sign a consent form after being given oral and written information of the study. Patient recruitment began in November 2015 and will end in December 2019. Data collection will complete in June 2021. We plan to present results in open access scientific publications and at scientific conferences and meetings.

Trial registration: The study protocol was registered with ClinicalTrials.gov (identifier: NCT 02563756) on September 18, 2015. Protocol version: 1.0.

Key words: randomized controlled trial; unicompartmental knee arthroplasty; total knee arthroplasty; muscle mass; CT; performance based function; patient reported outcome measures; muscle strength; 3D analysis

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INTRODUCTION

Background

The end stage treatment of medial knee osteoarthritis (OA) is a clinical challenge. The management mainly evolves along two different approaches, unicompartmental (UKA) and total knee arthroplasty (TKA). As of yet there is no irrefutable scientific evidence to state which of these methods is superior in terms of patient satisfaction and recovered physical function. Despite evidence of decreased postoperative morbidity and socioeconomic burden after UKA, there is a hesitance amongst orthopedic surgeons. The main reason for this is probably the historically inferior long-term survivorship of UKA compared to TKA in national registries as well as it being technically more demanding. Consequently, several authors have advised against UKA based strictly on revision rate as the end-point. However, due to the retrospective and cumulative nature of registries, the 10-year survivorship of modern UKA versus TKA will not be at hand within the present decade. While the majority of patients with knee OA report reduced pain and improved function following TKA, nearly one out of five reports persistent disability, including impaired function and reduced quality of life. The reasons for the inferior clinical results are not well understood.

In Sweden, UKA surgeries have been constant around 3.5% of the total amount of knee arthroplasties, while in up to 25% of these patients, the OA is confined to the medial joint compartment. However, an increasing number of UKAs are performed in the United States and Denmark, a resurgence brought about by the mainstream introduction of minimally invasive (MIS) techniques in the late 1990s. Improved surgical technique using MIS and a more stringent patient selection, combined with an improved design of both implants...
Aim and hypotheses
The aim of the present study is to determine whether patients with medial knee OA would benefit from UKA compared to TKA in terms of muscle mass and strength, physical function as well as patient perceived function. The primary outcome measure is muscle mass changes as determined by computed tomography (CT). Secondary outcome measures are changes in performance based measures (PBMs) and patient reported outcome measures (PROMs) in patients randomized to either UKA or TKA.

Methods/Design
Study design and setting
This is a randomized controlled trial (RCT) where patients meeting the inclusion criteria after written consent will be randomized to surgical treatment with either TKA or UKA. Participants are assigned individual trial identity code numbers to anonymize documented data, and the code key is kept in locked storage at the Department of Orthopedics, Karolinska Institutet. Clinical report forms (CRFs) using these code numbers are used to document clinical data. Data are continuously transferred onto password-protected spread-sheet files on servers accessible for authorized researchers only (CA, MH). The manuscript is prepared for publication following the SPIRIT Checklist.

Participants and recruitment procedures
All patients with a medial OA, scheduled for a knee replacement at the Orthopedic Department at Karolinska University Hospital Huddinge, Stockholm, Sweden will be screened consecutively for participation and assessed by an orthopedic surgeon. If all inclusion criteria and none of the exclusion criteria (Table 1) are met they will be invited to participate in the study. They will receive oral and written information about the trial and those who provide a written informed consent will be included.

Anterior cruciate ligament (ACL) insufficiency is an exclusion criterion and is defined as a confirmed ACL injury, a reconstructed ACL, a positive Pivot shift or discovered perioperatively. A patient with symptomatic OA of the other knee or any hip will be excluded in order not to influence the outcome measurements. If the participants have had a well-functioning arthroplasty more than one year prior to inclusion, this will not be an exclusion criterion.

Radiological classification
Standard X-rays will be performed for staging of OA preoperatively and for measurement of hip-knee angles (HKA) pre- and 6 months postoperatively. Two experienced orthopedic surgeons provide the radiologic classification of OA according to the modified Kellgren and Lawrence’s classification (KL) ranging from grade 1–4. Radiographs defined as KL scores of 3 to 4, will be sub-classified by incorporating data from individual scores of joint space narrowing (JSN) and bone attrition. Thus, a KL grade 3 radiograph with mild JSN will be graded as 3a, and radiographs with more severe JSN as 3b. A KL grade 4 radiograph demonstrating complete loss of joint space will be graded as 4a if there is no bone attrition and 4b if subchondral bone attrition existed.

Follow-up
The timing of pre- and postoperative evaluations and types of investigations are outlined in Figure 1.

Randomization, blinding, and allocation concealment
The participants will be stratified in two equally large groups, below or above 65 years of age at operation. The person generating the allocation sequence will be different from those enrolling and assigning participants, and plays no further role in the study. Patient randomization will be performed by urn randomization according to Schulz et al. This ensures a randomization achieving balance in size between the groups while preserving most of the unpredictability compared with simple randomization. The generated sequence will be concealed in numbered, sealed, opaque envelopes. Randomization will be performed following the decision to include the patients, before surgery. The envelope with the lowest number in the stack will be opened in the presence of the main investigator the same day as the patient decides to participate in the study. The randomization list with code numbers will be kept in the same place as the original results. Blinding will be performed when deemed possible i.e., during the functional tests by hiding the operated knee in an opaque stocking. The evaluating
physiotherapist will not be the same as the ones assisting the participants in the postoperative training. Blinding will be not possible in the 3D motion analysis or in the CT measurements since the evaluator can easily recognize the type of surgery by the different scars and the appearance on CT images, and the motion analysis requires markers attached to the bare skin at the knee.

**Interventions**

Patients will be randomized to either undergo a TKA using a conventional medial arthrotomy or a UKA using a mobile bearing prosthesis through a mini-invasive arthrotomy.

The TKA implant used in the resent study is a cruciate retaining implant and includes a non-rotating metal backed tibial platform, and patella will not be resurfaced (PFC; De Puy Synthes, Warsaw, IN).

The UKA in the present study is one of the top performing UKA from our national registries, allowing a minimally invasive surgical technique, the Oxford Partial Knee, ZIMMER BIOMET (Zimmer Biomet, Warsaw, IN). The UKA implants will be uncemented if the bone quality is sufficient. Patients randomized to UKA will be operated by an experienced consultant using a technique developed by Goodfellow and colleagues. The operating surgeons perform UKAs with a rate of 20–30 annually. The TKAs will be performed by any senior orthopedic surgeon at our clinic, all experienced knee arthroplasty surgeons.

**Muscle measurements**

It is well known that knee OA patients develop a profound muscular weakness as their disease progresses, but the magnitude and distribution of the muscle atrophy pre- and postoperatively is far less clear. It can be hypothesized that knee extensors and flexors would be preferentially deteriorated in knee OA patients. Atrophy will result in decreased cross-sectional area (CSA) and an increase in fatty infiltration shown as a reduced radiological attenuation (RA). Using CT measurements, we will describe muscle CSA and RA of the thigh, hip, and calf at standardized levels (at the lower end of the sacroiliac joint, mid-thigh 20 cm above the knee joint line and mid-calf 13 cm below the knee joint line). CSA of multiple muscle groups will be measured in CT images and mean area will be calculated. This is a commonly accepted way to determine muscle volume and fat infiltration, indicative of muscle atrophy. The patient will be measured in a standard position and will rest in the supine position for 30 minutes before examination to allow for fluid equalization.

We will be able to compare changes in muscle CSA and RA in the operated limb with the healthy contralateral limb, and also describe the relationship between radiological deterioration and performance in functional testing.

Interestingly, Mizner et al. stated that muscular weakness in patients with knee OA was markedly aggravated at 1 month after TKA. Our first postoperative assessment after 6 weeks aims to quantify those changes in contractile muscle and function linked to the surgical trauma of TKA relative to UKA, since this may have an important impact both on early function and long-term recovery.

**Performance based measures**

PROMs reflects what a person perceives he or she can perform,
and PBMs reflect what a person actually can achieve. To balance the discrepancy between patient reported function and actual functional ability, we will use both types of measurements in this trial. The majority of recommended PBMs evaluate bilateral performance, like chair rises and climbing stairs. Orthopedic patients, however, typically display unilateral symptoms and a following weight bearing asymmetry (WBA) between limbs. A greater WBA is correlated with a poorer functional mobility over all, more severe knee pain and muscle impairment. We therefore aim to use a performance test battery, including both bilateral and unilateral tasks, tailored for the evaluation of knee OA patients prior and after surgery. The bilateral analyses used in this study include the prioritized analyses in an internationally agreed test battery for assessing physical function in patients with knee OA according to Osteoarthritis Research Society International (OARSI).

**Five times and 30-second sit to stand**
We will use this test to determine the patient’s exhaustibility in a repeated everyday activity. The patient will begin to sit on a standard stool (height 44 cm) without arm or back support. From sitting position, the patient will stand up completely with fully extended hips and knees and then return back down to sitting again. This will be counted as one repetition. The patient will not be allowed to use his or her arms for support. This will be repeated as many times as possible during 30 seconds. Only complete repetitions will be counted. If the patient needs to use a hand on the chair to get up to stand, this will be marked on the test protocol.

**Timed up and go**
This test will determine a patient’s ability to perform an everyday task. The patient will rise from a standard armchair, walks three meters on level ground, turns and returns to sitting in the same chair. The total time needed to start from sitting back to sitting again will be recorded. The test will be performed twice and the best time will be recorded.

**40-meter walk test**
This test is designed to evaluate the maximum walking speed in a somewhat complicated situation, such as walking among other people or inside a building. The patient will be asked to walk a distance of 40 meters, turn and walk back four times as fast as they can, thus completing a total distance of 40 meters. This will be timed in seconds and if the patient needs to use walking aids, this will be recorded.

**6-minute walk test**
A test commonly used in clinical practice that has demonstrated good measurement properties in OA populations. It is generally considered the best test for determining the patient’s ability to walk longer distances. The patient will be asked to walk as far as possible within a 6 minute time period, with the investigator walking alongside the patient and measuring the time and distance. It will be conducted on a level course and repeated testing should be conducted on the same course.

**Balance and reach forward test**
This is a demanding test that examines the patients’ balance, coordination and leg strength unilaterally. The patient will put his weight on one leg (starting with the affected) while reaching forward with the non-weight bearing leg as far as possible and touch the floor with his heel, and this will be repeated three times. The rater will measure the distance and the maximum reach will be recorded. Ninety percent of the maximum reach will be calculated and marked with a tape on the floor. The patient then will reach forward with the heel and touch beyond the 90% mark as many times as possible in 30 seconds; the number of repetitions will be recorded. Time until the first 10 repetitions will be also recorded. If the patient needs to hold a hand for balance, this will be allowed and marked in the protocol.

**Step-down forward**
This test aims to determine the patients’ ability to walk down a normal flight of stairs. The subject will put weight on the limb being tested, reach down and touch the ground with the non-weight bearing heel, and return to starting position. This will be repeated for 30 seconds; the number of repetitions will be recorded as well as the time taken until the first 10 repetitions will be recorded. If the patient needs to hold a hand for balance, this will be allowed and marked in the protocol. All patients will try to step down from a height of 16 cm, a standard step height in a flight of stairs. If the patient is not able to perform repetitions at this height, we will decrease the height in steps of 4 cm until the patient is able to complete one acceptable series of repetitions. The step-down forward and the balance and reach tests both showed excellent inter- and intrarater reliability in a test-retest validation study as previously conducted by our group (Nordbeck et al., in manuscript).

**Three-dimensional (3D) motion analysis**
3D motion analysis provides detailed information on movement patterns and gait that cannot be assessed by clinical observation. Gait analysis will be performed with a movement analysis system and two pressure-sensitive plates in the floor. The patient will walk barefoot at self-selected pace along a 12-meter long marked path. Thirty-four reflecting markers will be attached to the patient with adhesive tape. Markers will be recorded with nine cameras at different angles (VICON Motion Systems Ltd., Oxford, UK). Joint angles will be recorded in ankle, knee, and hip in three dimensions and torque, force and center of gravity will be calculated. 3D movement analyses will also be performed during the PBMs.

**Muscle strength**
Muscle strength will be evaluated with a Biodex System 3 dynamometer (Biodex Medical Systems Ink, Shirley, NY, USA). First isokinetic testing with three rounds of a maximum extension will be followed by a flexion. Then, the patient will perform three maximum extensions and flexions for 3 seconds against a non-moving lever.

**Outcome measurements**
The main outcome measure for early evaluation of arthroplastic surgery has traditionally been reduced pain, accompanied by measurements of restored range of motion and joint realignment. In the last decades, there has been an increasing focus on PROs addressing aspects of patient satisfaction, including perceived function, return to activity, health perception, and health related quality of life. We will collect...
PROM data at five occasions; pre-operatively, 6 weeks, and 6, 12 and 24 months postoperatively.

**KOOS**

It is a knee specific instrument evaluating the patient’s perspective in the short and long term after a knee insult. The self-administered questionnaire is divided into five separate subscales addressing: pain, function in daily life (ADL), function in sports and recreation, knee related quality of life, and other symptoms. Each subscale generates a final score ranging from 0–100 where 100 represents “best” and 0 “worst”. It has been thoroughly tested regarding validity and reliability and is in use worldwide in the evaluation of arthroplasty and different arthroscopic treatments.52-54

**OKS**

The Oxford Knee Score is a validated and widely used instrument to assess function and outcomes after interventions in patients with osteoarthritis of the knee.50 It is a 12-item self-administered questionnaire originally developed for follow-up of patients receiving TKA, translated and validated for Swedish.51

**Forgotten joint score**

It is a 20-item test developed to address the problem with ceiling effects that hampers many other PROMs. It claims to be able to describe to what degree the patient forgets about his operated knee in everyday life, as one does with our innate knees. It also has the ability to describe differences in improvement among patients with the best results especially when it comes to pain, compared to the Western Ontario and McMaster Universities subscales (WOMAC), KOOS, and OKS.52-54

**EQ-5D**

A self-administered general quality of life questionnaire addressing everyday life and health related activities of daily life, not specific for osteoarthritis of the knee.55 The instrument consists of a visual analogue scale and five items concerning mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The final health state is calculated using an index score where -0.594 is the worst possible health and 1 is full health. We will use the Swedish value sets to obtain a single index value for health state.56

**VAS**

Pain intensity will be measured using Visual Analogue Scale (VAS). The VAS score ranges from 0 (representing no pain) to 100 mm. Pain assessment will be done pre- and postoperatively during the functional tests as well as in rest. We will also note pain daily during the hospital stay. At preoperative assessment and then at follow up, the patient will be asked to rate his or her pain at rest as a median of the preceding week.57

**Rehabilitation**

All participants will follow a standardized supervised exercise program during 7 weeks. It includes progressive strength training following a regime described by Jakobsen et al.58 It consists of two sessions per week of approximately 45–50 minutes of active training when time for instructions and transitions between exercises are deducted. Participants will be also encouraged to follow a home exercise program.

**Statistical analysis**

**Sample size estimation**

CT measurements of RA have shown high test-retest reliability, with reported variance of less than 1%33 and muscle CSA less than 2%.34 To discriminate a 5% change, 15 individuals would suffice. The smallest clinically relevant changes in muscular strength by 10% will demand groups of 30 individuals.

A minimal important change (MIC) for KOOS and its subscales is currently not completely established. However, an MIC of 8–10 is considered appropriate. For calculating statistical power and sample sizes, an SD of 15 will be used.49 Elderly or more functionally impaired groups tend to have greater within-group variation than younger or healthier groups. We believe that our study group will be fairly homogenous, owing to our strict inclusion and exclusion criteria. Based on these numbers, in a between groups comparison using parametric data, an MIC of 8–10 and an SD of 15 will yield a minimum of 37 observations in each group to be able to detect a difference of 8 points in KOOS score. We estimate a drop-out rate of 10%, which would demand 40 persons in each group. This is in line with current research using the same instrument.59

Data analyses will be performed using IBM SPSS Statistics version 22 (IBM, Chicago, IL, USA). A significance level was set at \( P < 0.05 \). Depending on data distribution, means with standard deviation (SD) and medians with range will be used to describe the explored variables. Parametric methods will be used for normally distributed data while non-parametric methods will be used for data showing different patterns of distribution. Normal distribution of the data will be assessed using Shapiro-Wilk’s test and Q-Q plots. Fisher’s exact test will be used to determine whether the proportion of patients differs between the groups with regards to the KL classification of OA severity. One-way ANOVA, adjusted for baseline values, will be used to compare postoperative differences between groups.

Those eligible patients who refuse the study will receive the type of arthroplasty they prefer. We will record their gender, age, and reason for not participating, to be compared at group level with the participants to examine the possibility of study bias.

An interim analysis regarding the CT measurements will be performed at a total of 40 patients included. If we find clinically relevant changes in muscle atrophy, the CT measurements will be discontinued. Results will be analyzed based on an ‘intention-to-treat’ basis, participants will be analyzed according to the primary allocated group.

**Compensation**

Both treatment arms will be part of normal clinical practice at our clinic. In the event of patients suffering harm as a consequence of the study, the participants will be eligible to receive compensation from LÖF (Landstingets Ömsesidiga Försäkringsbolag). Löf is a mutual insurance company owned by its policy holders, the Swedish counties and regions.

**Ethics and dissemination**

**Ethical approval and consent to participate**

The study will be conducted in accordance with the ethical principles of the Declaration of Helsinki.60 The Regional Ethics Committee in Stockholm approved the study (DNR: 2014/1895-31/3). All participants will sign a consent form
after being given oral and written information of the study. The trial designed and initiated and is being performed as an academic investigation and was registered at ClinicalTrials.gov (NCT 02563756). The guidelines of the CONSORT Statement will be followed. Any important protocol modifications will be communicated to the Regional Ethics Committee and the registration at ClinicalTrials.gov will be updated.

Dissemination

We plan to present results in open access scientific publications and at scientific conferences and meetings.

DISCUSSION

Whereas patients receiving total hip replacements are typically satisfied with surgery, patients receiving TKA are less satisfied. Nevertheless, after years of knee pain and deteriorating function, the overall patient satisfaction improves with TKA. Therefore, it is reasonable to state that TKA is an effective end stage OA treatment, although it is mandatory to find ways to further improve patient satisfaction. Controversy still prevails regarding the long-term functional outcome of UKA, especially in relation to the risk of revision. If an alternative method is to be broadly introduced, its superior clinical results must be irrefutable. Our hypothesis is that the tissue sparing nature of UKA is beneficial to the patient in terms of preservation of muscle mass, strength and function leading to greater patient satisfaction. This is a presentation of a prospective RCT. It gives detailed information on the planned study, the design and the planned ways of analyzing data.

TRIAL STATUS

Patient recruitment is ongoing at the time of submission.

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Author contributions

MH and HEB conceived the project and procured project funding. CA will be responsible for coordination of the trial. NMC provided input on trial design and manuscript disposition. JP aided in data collection and added insight on functional testing. CA, HEB, MH and NMC provided feedback on drafts. All authors read and approved the final manuscript for publication.

Conflicts of interest

The authors declare no competing interests.

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Institutional review board statement

The study will be conducted in accordance with the ethical principles of the Declaration of Helsinki. The Regional Ethics Committee in Stockholm approved the study (DNR: 2014/1895-31/3).

Declaration of patient consent

The authors certify that they will obtain all appropriate patient consent forms. In the form, the patients will give their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Reporting statement

This study follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidance for protocol reporting.


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