INTRODUCTION

Hip osteoarthritis (OA) is a musculoskeletal disorder associated with joint pain, functional impairments, decreased muscle strength, and reduced quality of life with a prevalence of 11% in the general population.1–9 Hip OA is the leading cause for total hip arthroplasty (THA) with more than one million procedures performed annually worldwide.10 The procedure has been described as the surgery of the century,11 resulting in high patient satisfaction and large effect sizes for reducing pain, improving physical function, and increasing quality of life.12–17 However, up to 23% of the patients report long-term pain, and deficits in physical function and muscle strength may persist after THA.18–21 Moreover, there is a risk of severe complications after THA,19 with the cumulative incidence of hip dislocations being 3.5%.22

In clinical guidelines exercise is recommended as first-line treatment,23–27 and meta-analyses have displayed small to moderate effect sizes for reducing pain, improving physical function, and increasing quality of life in patients with hip OA.28–32 Moreover, supervised exercise with high compliance to the American College of Sports Medicine (ACSM) recommendations for
resistance training has been shown to result in superior outcomes compared with exercise performed with uncertain compliance. Progressive resistance training (PRT) is considered safe, feasible, appears to moderately improve multiple outcomes, and may be of clinical relevance in patients with hip OA. However, exercise may be underutilised in clinical practice and current treatment selection in patients with hip OA is based on low-level evidence as no randomised controlled trials (RCTs) have directly compared THA to non-surgical treatment. This comparison is important in order to ensure that management of severe hip OA is guided by high-quality evidence including the effectiveness, benefits and harms between THA and exercise, which may be used to facilitate and influence shared-decision making in the discussion of treatment approach in clinical practice.

Therefore, the primary aim of this trial is to investigate whether THA followed by standard care is superior to 12 weeks of supervised PRT followed by 12 weeks of optional unsupervised PRT for improving hip pain and function in patients with severe hip OA after 6 months. We hypothesise that patients randomised to THA followed by standard care will improve significantly more in hip function and pain 6 months after initiating the treatment than those randomised to PRT.

METHODS AND ANALYSIS
Study design
The trial is a multicentre (four sites), stratified (by site), randomised (allocation 1:1), controlled, parallel-group superiority trial. Eligible patients will be randomised to THA followed by standard care or 12 weeks of supervised PRT followed by 12 weeks of optional unsupervised PRT. The primary outcome will be change in patient-reported hip pain and function, measured using the Oxford Hip Score (OHS), from baseline to 6 months after initiating the treatment (THA/PRT). Secondary outcome assessments will be performed at 3, 12, 24 and 60 months.

The study protocol is reported in accordance with the ‘Standard Protocol Items: Recommendations for Interventional Trials’ (SPIRIT) (online supplemental file 1), while reporting of the trial will follow the ‘Consolidated Standards of Reporting Trials’ (CONSORT) statement. The description of the PRT treatment adheres to the ‘Consensus on Exercise Reporting Template’ (CERT) (online supplemental file 2), and muscle strength descriptors suggested by Toigo and Boutellier.

Patient enrolment started at the first hospital in September 2019 and at the last hospital in February 2020. Patient recruitment is expected to be completed in June 2021.

Participants
Patients will be recruited from the orthopaedic departments at University Hospital of Southern Denmark, Vejle Hospital and Odense University Hospital (OUH) in the Region of Southern Denmark, Aarhus University Hospital (AUH) in the Central Denmark Region and Næstved Hospital in Region Zealand.

Inclusion criteria
(1) Patients aged ≥50 years; (2) Clinical history and symptoms consistent with primary hip OA (including hip OA due to mild hip dysplasia that may be treated with standard components) and radiographic verified hip OA defined as joint space narrowing <2 mm; (3) Considered eligible for THA by an orthopaedic surgeon (ie, hip-related pain, symptom duration >3 months, functional impairment or decreased range-of-motion, and attempted treatment with analgesics).

Exclusion criteria
(1) Severe walking deficits (dependency of two crutches or walker); (2) Body mass index (BMI) >35 kg/m²; (3) Lower extremity fractures within previous 12 months; (4) Planned other lower extremity surgery within 6 months; (5) Cancer diagnosis and current chemotherapy, immunotherapy or radiotherapy; (6) Neurological diseases (eg, previous stroke, multiple sclerosis, Parkinson’s, Alzheimer’s); (7) Other reasons for exclusion (ie, inadequacy in written and spoken Danish, mentally unable to participate, physically unable to comply with the PRT protocol due to comorbidity (eg, severe heart disease, previous major lower extremity surgery within previous 6 months)).

Recruitment procedure
All patients referred from general practice to the orthopaedic departments for evaluation for THA will be assessed for eligibility during the standard clinical examination conducted by orthopaedic surgeons specialised in treatment of patients with hip OA. Eligible patients will be informed briefly about the trial by the orthopaedic surgeon using generic guidance focusing on the following topics: current evidence of treatment effects (THA/PRT), trial objective and procedures, randomisation process, content of baseline and follow-up sessions, risks and harms, cross-over and withdrawal procedures, clinical implications and funding. Each orthopaedic surgeon and project coordinator involved in the trial will be trained and instructed in performing standardised verbal information about the trial to reduce disclosures of opinions and imbalances in treatment presentation to facilitate communication of equipoise to patients during the recruitment procedure. Prior to deciding on participation in the trial, eligible patients will be recommended to consider and/or discuss participation with a relative for at least 24 hours. For those eligible and willing to
participate, written informed consent will be obtained by the local project coordinator prior to baseline assessment.

**Randomisation and allocation concealment**

Patients will be randomised after baseline assessment to either THA or PRT with a 1:1 allocation as per a computer-generated randomisation schedule, stratified by recruitment site using permuted blocks of random sizes (2–6). An independent data manager will develop a computer-generated list of random numbers using the randomisation tool in Research Electronic Data Capture (REDCap). Administrators of the randomisation procedure will be blinded to block sizes and randomisation sequence at all times during the trial period. The randomisation code will be stored in REDCap with no access from the project group. In practice, after recruitment and baseline measurements, a project coordinator from each hospital will administer the online allocation procedure by entering patient data into REDCap, which will enable the randomisation tool and the group allocation will be revealed to the patient. After randomisation, the project coordinator will refer to THA or PRT by booking a surgery date, or inform the municipal rehabilitation centre who provides an appointment for the first training session. A flowchart of patient allocation is illustrated in figure 1.

**Blinding**

Outcome assessors will conduct baseline and follow-up assessment blinded to group allocation. Prior to the 6 months follow-up assessment, patients will be instructed not to disclose the allocated treatment and to cover the index hip to conceal a potential surgical scar after THA to ensure blinding of outcome assessors. The patients, and orthopaedic surgeons and physiotherapists involved the treatments will not be blinded to group allocation after baseline assessment. A statistician blinded to group allocation will perform the statistical analyses. Finally, blinded results from the data analyses (group A compared with group B) will be presented to the author group followed by development of two written interpretations. The author group will sign a consensus statement comprising both interpretations prior to the unsealing of the randomisation code.

**Observational cohort**

Patients declining participation in the trial will be invited into a parallel prospective observational cohort using identical endpoints and patient-reported outcomes. Written informed consent will be obtained for all patients willing to participate in the observational cohort.

**Interventions**

**Total hip arthroplasty**

All patients allocated to the THA group will follow a standard fast-track multimodal surgical programme including patient information, optimised pain management, and early mobilisation. One to three weeks preoperatively, patients will receive detailed information from orthopaedic surgeons, physiotherapists and nurses about the surgical procedure, hospitalisation and postoperative home-based rehabilitation. On the day of the surgery, patients will be hospitalised and THA will be performed by experienced orthopaedic surgeons in accordance with the standard posterior surgical approach. A few hours after surgery, patients will be mobilised to a sitting or standing position, and receive physiotherapy once or twice per day. Patients will be discharged within 0–4 days after surgery, when conforming to the hospital-specific discharge criterion (table 1). After discharge, all patients will receive a standard hospital-specific home-based exercise programme aiming at increasing hip muscle strength and range-of-motion (online supplemental file 3). If considered necessary by a physiotherapist, a referral to supervised postoperative rehabilitation will be performed in accordance with the Danish National clinical guideline on hip OA. Patients will follow hospital-specific procedures after discharge ranging from no postsurgical control to postsurgical assessment of the hip at 6 weeks or 3 months.

**Progressive resistance training**

Patients allocated to the PRT group will attend 12 weeks of supervised PRT with two weekly training sessions a week (60 min per session) at one of 12 municipal rehabilitation centres. All training sessions will be conducted with one-to-one supervision by a physiotherapist and ≥48 hours of rest in between sessions. The standardised PRT protocol comprises 10 min warm-up on a stationary bicycle followed by four exercises for the lower extremities performed unilaterally in machines or cable pulleys with as full range-of-motion as possible in three sets separated by 60 sec of rest in the following order: leg press, hip extension, hip flexion and hip abduction. Patients will be instructed to complete the concentric phase of each repetition ‘as fast as possible’, maintain full extension for 1 s, and perform the eccentric phase in 2–3 s. The physiotherapist will provide verbal encouragement and motivation during training sessions. Progression of training load will follow a linear model of periodisation with an initial relative load of 12 repetition maximum (RM) in week 1–2, 10 RM in week 3–6 and 8 RM in week 7–12. The absolute training load will be increased if patients are able to perform two or more repetitions than intended, and decreased if less than eight repetitions are completed. For all patients, the absolute training load will be recorded and adjusted on set-by-set basis using muscular contraction to volitional failure. Patient-reported hip pain during and after training sessions will be assessed using a Numerical Rating Scale graded from 0 (no pain) to 10 (worst pain imaginable). Pain levels from 0–2 will be considered as ‘safe’, 3–5 as ‘acceptable’ and >5 as ‘high risk’. The day after a training session hip pain should subside to pain ‘as usual’ otherwise training load will be decreased during the following session. Following completion of 12 weeks of supervised PRT, patients will be provided the option of 12 weeks of
Patients referred to the orthopaedic departments at University Hospital of Southern Denmark, Vejle Hospital, Odense University Hospital, Aarhus University Hospital, and Næstved Hospital for evaluation for THA

Assessed for eligibility (n)

Enrolment

Randomised (n=120)

Allocation

Allocated to THA (n=60)
- Received allocated intervention (n)
- Did not receive allocated intervention (n)

Allocated to PRT (n=60)
- Received allocated intervention (n)
- Did not receive allocated intervention (n)

Lost to follow-up (n)
Discontinued intervention (n)

Analysis

Analysed (n)
- Excluded from analysis (n)

6 months
Primary endpoint

Lost to follow-up (n)
Discontinued intervention (n)

Analysed (n)
- Excluded from analysis (n)

12 months
Follow-up

Lost to follow-up (n)
Discontinued intervention (n)

Analysed (n)
- Excluded from analysis (n)

24 months
Follow-up

Lost to follow-up (n)
Discontinued intervention (n)

Analysed (n)
- Excluded from analysis (n)

60 months
Follow-up

Lost to follow-up (n)
Discontinued intervention (n)

Analysed (n)
- Excluded from analysis (n)

Figure 1  CONSORT flow chart. Expected enrolment, randomisation and follow-up. CONSORT, Consolidated Standards of Reporting Trials; PRT, progressive resistance training; THA, total hip arthroplasty.
unsupervised PRT at a public fitness centre or private physiotherapy clinic. The physiotherapist will instruct the patients in the principles of the PRT. All physiotherapists will attend a 2-hour group-based training session and receive a detailed training protocol describing each exercise, progression principles and pain management. Furthermore, a project worker with experience in using PRT in patients groups and not otherwise affiliated with trial will audit the training session twice one month apart at selected municipal rehabilitation centres. The muscle strength descriptors of the PRT protocol are presented in table 2 and full details are described in online supplemental file 4.

Crossover and withdrawal

The physiotherapists will be instructed to encourage patients in the PRT group to continue and complete the 12 weeks of supervised PRT and continue to exercise until the 6 months follow-up to reduce crossover and withdrawals from the trial. Patients in the PRT group experiencing unsatisfactory outcomes or deterioration of their symptoms may contact the orthopaedic departments for a reassessment for THA. Crossover to THA may be performed at any time during the trial period and each reason for crossover or withdrawal will be registered. Patients in the THA group declining surgery after randomisation will be attained in the trial and asked to participate in the follow-up assessments.

Outcome measures

Patient characteristics

The following data will be obtained at baseline: sex, age, height, weight, BMI, educational level, employment status, marital status, smoking status, alcohol consumption, index hip, hip symptom duration, previous THA/total knee arthroplasty (TKA), previous treatment due to hip symptoms, medicine consumption and comorbidities.

Primary outcome

The primary outcome measure will be the between-group difference in change from baseline to 6 months follow-up in the OHS. The OHS is a 12-item patient-reported questionnaire developed to assess hip pain and function in a

| Table 1 | Discharge criteria and postoperative procedures at Vejle Hospital, Odense University Hospital (OUH), Aarhus University Hospital (AUH) and Næstved Hospital |
|---------|----------------------------------------------------------------------------------|
| Outcome | Vejle Hospital | OUH | AUH | Næstved hospital |
| In-and-out of bed | Independent | Independent | Independent | Independent |
| Sit-to-stand | Not described | Independent | Not described | Independent |
| Walking with assistive devices | Independent | Independent | Independent | Independent |
| Stair-walking | Independent | Independent | Independent | Independent |
| Basic activities of daily living | Independent | Independent | Independent | Independent |
| Understanding of the home-based postoperative exercise programme | Sufficient | Independent | Independent | Independent |
| Referral to supervised postoperative rehabilitation | If necessary | If necessary | If necessary | Always |
| Postoperative control at hospital | After 6 weeks at the physiotherapy department if the patient has performed home-based postoperative rehabilitation | None | After 3 months at the orthopaedic department if requested by the patient | None |

| Table 2 | Muscle strength descriptors of the PRT protocol |
|---------|-----------------------------------------------|
| Variable | Week 1–2 | Week 3–6 | Week 7–12 |
| Load magnitude | 12 RM | 10 RM | 8 RM |
| No of repetitions | 12 | 10 | 8 |
| No of sets | 3 | 3 | 3 |
| Rest in-between sets | 60 s | 60 s | 60 s |
| Sessions per week | 2 | 2 | 2 |
| Duration of training period | 2 weeks | 4 weeks | 6 weeks |
| Contraction modes per repetition | | | |
| Concentric | As fast as possible | As fast as possible | As fast as possible |
| Isometric | 1 s | 1 s | 1 s |
| Eccentric | 2–3 s | 2–3 s | 2–3 s |
| Rest between repetitions | 0 s | 0 s | 0 s |
| Time under tension per repetition | 5–6 s | 5–6 s | 5–6 s |
| Volitional muscular fatigue | Yes | Yes | Yes |
| Range-of-movement | Maximum possible | Maximum possible | Maximum possible |
| Rest between sessions | ≥48 hours | ≥48 hours | ≥48 hours |
| Anatomical definition of exercise | Yes | Yes | Yes |

PRT, progressive resistance training; RM, repetition maximum.
composite score ranging from 0 (worst) to 48 (best).51.52 The OHS has been validated in hip OA patients undergoing THA, displaying excellent validity, reliability and responsiveness.53–55

**Key secondary outcomes**

**Hip disability and Osteoarthritis Outcome Score**
The Hip disability and Osteoarthritis Outcome Score (HOOS) is a 40-item patient-reported questionnaire consisting of five subscales covering symptoms, pain, activities of daily living (ADL) function, sport/recreation and hip-related quality of life with each subscale score ranging from 0 (worst) to 100 (best).56 The HOOS is reliable, valid and responsive in patients with hip OA undergoing non-surgical treatment and THA.56–59

**University of California Los Angeles Activity Score**
The University of California Los Angeles (UCLA) Activity Score will be used to measure patient-reported physical activity level ranging from 1 (inactive) to 10 (regular participation in impact sport or heavy labour).60 The UCLA is reliable, valid and responsive in patients with hip OA undergoing THA.61.62

**Functional performance**
The 40 m fast-paced walk test (40 m-FPWT) measures the total time to walk 4×10 m (m/s).63 Patients will be instructed in walking as quickly and safely as possible to a visible mark 10 m away, return and repeat for a total of 40m.63 Usage of assistive walking devices will be recorded and one practice trial will be provided to check understanding.64 The 40 m-FWT is a valid and responsive measure for assessing short distance maximum walking speed with excellent inter-rater reliability.63 The 30 s chair stand test (30 s-CST) measures the number of sit-to-stand repetitions completed within 30 s.65.66.67 Two to three slow-paced practice repetitions will be performed to check understanding followed by one test trial.64 The 30 s-CST is a valid and responsive measure of lower-extremity muscle strength evaluating sit-to-stand function with good to excellent intrarater and inter-rater reliability.63–66 The tests are recommended by the Osteoarthritis Research Society International (OARSI) as components of the minimal core set to assess functional performance in patients with hip OA.64

**Serious adverse events**
Serious adverse events (SAEs) will be defined in accordance to the ‘International Conference on Harmonisation-Good Clinical Practice’ guidelines.67 Crossover to THA will not be classified as an SAE. An auditing committee will evaluate SAEs for seriousness independent of whether there is a causal relationship with the trial treatments or outcome assessments. SAEs will be collected from The Danish National Patient Registry and through medical record reviews conducted at the primary endpoint. Furthermore, a short patient-reported questionnaire will be administered at the 3 and 6 months follow-up.

**Exploratory outcomes**

**Visual Analogue Scale**
Pain intensity in the index hip at rest and during activities within the previous 24 hours will be assessed using a unidimensional Visual Analogue Scale (VAS) ranging from 0 (no pain) to 100 (worst pain imaginable), which is a reliable, valid and responsive measure of pain in patients with hip OA.49

**EuroQol Group 5-dimension 5 Levels**
Health-related quality of life will be assessed using the reliable and valid EuroQol Group 5-dimension 5 Level (EQ-5D-5L) including the summary index ranging from −0.624 (worst) to 1.000 (best) (Danish value set) and EQ-VAS ranging 0 (worst imaginable health) to 100 (best imaginable health).68–72

**Global perceived effect, patient acceptable symptom state and treatment failure**
Global perceived effect (GPE) will be assessed for seven domains (overall hip problems, hip pain, hip symptoms, ADL function, sports and recreation, hip-related quality of life and physical activity) rated on a 15-point Likert scale ranging from ‘a very great deal worse’ (worst) to ‘a very great deal better’ (best).73–77 The GPE is a reliable and valid measure to assess effect of the treatment recommended by OARSI.73.74.75.76 Patient acceptable symptom state and treatment failure will be rated on a dichotomous scale (yes/no).77.78

**Muscle strength**
Isometric hip muscle strength of the index hip will be measured with a handheld dynamometer (Commander Echo Wireless Console and Muscle Tester, JTech Medical, Salt Lake City, Utah, USA) using a reliable procedure79 in the following fixed order: hip extension (prone-position), hip flexion (seated-position), and hip abduction (supine-position). The outcome assessor will apply resistance 5 cm proximal to the proximal border of the lateral malleolus at the posterior calf-complex for hip extension and hip abduction, and 5 cm proximal to the border of the patella for hip flexion.79 During all tests, the patients will perform a 5 sec maximal voluntary isometric contraction against the dynamometer.79 Four trials of each test will be conducted separated by 30 s of rest to avoid muscle fatigue.79 The highest value of the four measurements will be used in the analysis. Strength values will be weight-adjusted and reported as Newton meters per kilogram of the bodyweight (Nm/kg).79

**Physical activity**
Habitual physical activity will be recorded with a tri-axial accelerometer (AX3, Axivity, Newcastle, UK) mounted on...
the lateral side of the right thigh for 7 days consecutive days. Data will be postprocessed using a custom designed algorithm (MATLAB, Mathworks, Natick, Massachusetts, USA) validated for patients after THA. Parameters of physical activity such as number of steps, cadence, time spent sedentary, standing, walking, bicycling and number of sit-to-stand transfers will be measured. Moreover, the algorithm constructs an intensity parameter where each 10 s data window is classified into one of the following four categories: very low intensity activity (eg, sitting or standing, 0–0.05 g), low intensity activity (eg, standing or shuffling, 0.05–0.1 g), moderate intensity activity (eg, slow or normal walking, 0.1–0.2 g), and high intensity activity (eg, fast walking, running or jumping, >0.2 g).

Other measures
Medicine consumption due to the index hip or other reasons (yes/no; type; frequency), participation in optional unsupervised PRT (no/yes; content; duration; frequency), participation in postoperative supervised exercise (no/yes; content; duration; frequency) and other treatments related to the index hip received during the trial period (no/yes; type of treatment; duration; frequency) will be recorded using a patient-reported questionnaire. The supervising physiotherapists will register adherence with the PRT sessions and progression of each exercise. High adherence is defined as participation in ≥75% of the sessions (ie, 18 out of 24 sessions); moderate adherence as participation in 50%–74% of the sessions; and poor adherence as participation in <50% of the sessions. Finally, THA surgeries performed in the PRT group will be registered through patients’ medical records.

Data collection procedure
Outcome assessors will conduct all baseline and 6 months follow-up assessments at the hospital. Before starting the data collection, the assessors will attend a 3-hour training session to attain equal performance of test protocol procedures and interpretation of tests. Baseline characteristics and patient-reported outcomes will be collected using electronic online questionnaires. At baseline and 6 months follow-up, patients will complete the patient-reported questionnaires in an undisturbed examination room at the hospitals. At the secondary follow-ups, an email containing a link to the online questionnaires will be sent to the patients. A reminder email will be sent to the patients, if no reply is received within three days. In case of no reply to the reminder email, patients will be contacted by telephone. An overview of the data collection is presented in table 3.

Data management
Patient-reported outcome data will be entered directly in REDCap by the patients with the ‘required fields’ option activated to ensure no missing items from completed questionnaires. Functional performance and muscle strength data will be entered in REDCap by the outcome assessors using double data entry and answer validation to ensure data quality. Patient data will be pseudonymised by assigning study numbers to each patient. Personal data about the patients will be located separately from the main dataset to protect confidentiality during each phase of the trial. All electronic data will be entered or uploaded encrypted to a password-secured server (Region of Southern Denmark) conforming to current data protection standards. The raw data set will be maintained in storage for 5 years after completion of the trial, with indefinite restricted access due to sensitive data. After publication of the trial an anonymised patient-level dataset and corresponding statistical code will be made publicly available if required by the scientific journal, in which the results are published. In contrary, if this is not required access to the completely anonymised patient-level dataset will be available from the corresponding author on reasonable request.

Data monitoring
No formal data monitoring committee will be composed, as SAEs of both treatments are well known. The author group will discuss any SAE occurring during baseline to the 6 months follow-up, and monitor recruitment, treatment and attrition rates including any concerns related to the trial. No interim analysis will be performed.

Auditing committee
An auditing committee will be formed, consisting of members with prior adjudication experience, to assess and classify all SAEs occurring in the trial. After the final patient has completed the 6 months follow-up, each member will be provided with the SAE data in raw format. The members will independently assess all SAEs followed by classification into subcategories. Any disagreements will be resolved by consensus or by requesting additional information from the hospitals if disagreements persist.

Sample size and power calculation
The sample size and power calculation was based on the expected between-group difference in the OHS mean change score from baseline to the 6 months follow-up. Based on previous studies on patients with hip OA undergoing THA, the predicted OHS mean baseline value will be between 14 and 20 points. For the OHS from baseline to 6 months after THA, the minimal clinically important difference of the change score between two groups has been estimated to be 5 points and the standard deviation (SD) of the change score has been found to be approximately 8 points. Both groups are expected to experience clinically relevant improvements corresponding to a 20-point mean improvement in the THA group as reported in previous studies, and a 10 (up to 15) point mean improvement in the PRT group comparable with effects of previous interventions.

For a two-sample pooled t-test of a normal mean difference with a two-sided significance level of 0.05 (p<0.05), assuming a common SD change of 8, a sample size of 60
### Table 3  Overview of the data to be collected in the trial

| Enrolment | Baseline | Allocation | 3 months follow-up | 6 months follow-up‡ | 12 months follow-up | 24 months follow-up | 60 months follow-up |
|-----------|----------|------------|-------------------|---------------------|---------------------|---------------------|---------------------|
| Eligibility screen | X | | | | | | |
| Informed consent | X | | | | | | |
| Baseline measurements | | | | | | | X |
| Allocation | | X | | | | | |

#### Primary outcome

**OHS**

| Time point of outcome assessment | X | X | X | X | X | X | X |

#### Key secondary outcomes

**HOOS symptoms**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**HOOS pain**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**HOOS ADL**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**HOOS sport and recreation**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**HOOS QoL**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**UCLA activity score**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**30 s chair stand test**

| Time point of outcome assessment | X | | |

**40 m fast-paced walk test**

| Time point of outcome assessment | X | | |

**Serious adverse events**

| Time point of outcome assessment | X | X | |

#### Exploratory outcomes

**VAS Pain**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**EQ-5D-5L**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**Medication**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**GPE**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**PASS**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**Treatment failure**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**Physical activity (triaxial)**

| Time point of outcome assessment | X | | |

**Isometric hip muscle strength**

| Time point of outcome assessment | X | | |

#### Other measurements

**Patient characteristics**

| Time point of outcome assessment | X | |

**Crossover**

| Time point of outcome assessment | X | X | X | X | X | X | X |

**PRT adherence and progression**

| Time point of outcome assessment | X | |

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*Continued*
per group has a power of 0.92 for the primary outcome to detect a mean change difference of 5 OHS points after 6 months between the THA and PRT group.

The final deadline for patient recruitment was a priori set 18 months (ie, February 2021) after the inclusion of patients was started. This was prolonged 4 months (ie, June 2021) due to the COVID-19 lockdown in Denmark in 2020. To obtain at least 80% power to detect a between-group difference in mean change of 5 OHS points with a SD change of 8 OHS points, a sample size of 42 per group will be required. The anticipated changes in OHS in the THA and PRT group are illustrated in figure 2.

**Statistical methods**

All descriptive statistics and tests will be reported in accordance with the recommendations of the ‘Enhancing the QUAlity and Transparency Of health Research’ network and the CONSORT statement. Visual inspection (QQ-plot, histograms and scatterplots) of the standardised residuals from the statistical model will be used to assess the assumption of normality and homogeneity of variances.

The primary analysis will be based on the between-group difference in change in the primary and key secondary outcomes from baseline to the 6 months follow-up, according to the intention-to-treat (ITT) principle (ie, all patients as randomised regardless of departures from allocation treatment, adherence, withdrawals and/or treatment crossover). Between-group differences of continuous outcomes will be estimated using repeated-measures analysis of covariance applied in mixed effects linear models. Data will be analysed with each outcome variable ($Y_i$) at baseline ($Y_{0,i}$) as a covariate, using a multilevel repeated measures random effects model with patients as the random effects factor based on a restricted maximum likelihood (REML) model. Change from baseline to the 6 months follow-up will be the dependent variable, and baseline value (one for each patient), treatment group (two levels: THA and PRT) and time point (three levels: baseline, 3 and 6 months), hospital (four levels: Vejle, OUH, AUH and Næstved) will be included as covariates, as well as the interaction between treatment group and time. This statistical model include all between-group comparisons at all outcome assessment time points, which also allows for evaluation of the average effect (ie, group as a main effect), as well as the trajectory over time from baseline to 6 months follow-up (ie, group×time interaction). Categorical outcomes will be analysed with logistic regression using identical fixed effect factors and covariates as the mixed linear model (ie, REML model).
Missing data will be handled indirectly and statistically modelled using repeated-measures linear mixed models. These models are valid if data are ‘Missing at Random’ (ie, any systematic difference between the missing values and the observed values can be explained by differences in observed data). The following four point framework for rigorous interpretation of the impact of missing data will be applied in the ITT analysis: (1) attempt to follow up all randomised patients, even if they withdrew from allocated treatment, (2) perform a main analysis of all observed data that are valid under a plausible assumption about the missing data, (3) perform sensitivity analyses to explore the effect of departures from the assumption made in the main analysis and (4) account for all randomised patients, at least in the sensitivity analyses.

Sensitivity and exploratory analyses will be performed with the purpose to test the robustness of the ITT analysis, including a per-protocol (ie, surgery performed in the THA group and participation in ≥75% of the training sessions in the PRT group) and as-treated analysis, in which patients will be analysed based on their adherence to the randomised treatment expecting four groups: (1) patients randomised to THA, (2) patients randomised to PRT without undergoing THA in the follow-up period, (3) patients randomised to THA but declined surgery post randomisation and (4) patients randomised to PRT undergoing THA during the follow-up period.

Subgroup analyses will be performed to examine whether the observed treatment effect varies across patient subgroups, to explore whether the overall treatment effect is modified by the value of a variable assessed at baseline: analysed by sex, median age, obesity (BMI ≥30 kg/m^2), median duration of hip symptoms, previous THA, median OHS, median UCLA Activity Score, median walking speed in the 40 m-FPWT and median sit-to-stand repetitions in the 30 s-CST. The statistical approach for this evaluation of potential effect modifiers will be a test for statistical interaction to evaluate whether the treatment effect varies across levels of the effect modifier.

In addition, an explorative causal mediation analysis will be conducted to evaluate walking speed, sit-to-stand repetitions and hip muscle strength (extension, flexion and abduction) as potential mediators of effects using univariate and multivariate linear regression, in which the total effect of the treatment (THA/PRT) on hip pain and function (primary outcome) is decomposed into direct and indirect effects. The direct effect refers to the causal pathway by which THA or PRT has an effect on hip pain and function not through the mediator. The indirect effect refers to the effect of THA or PRT that operates entirely through the mediator of interest. As this approach allows decomposition into direct and indirect effects, the proportion mediated by the potential mediator(s) will be calculated as an estimation of their importance.

All results will be presented with 95% CIs and associated p values. A two-sided p<0.05 will be considered as statistically significant. A 95% CI excluding a difference greater than 5 OHS points between groups will be interpreted as indicating absence of a minimal clinically important difference. The analyses of the key secondary outcomes will be performed in prioritised order until one of the analyses fails to show a statistically significant difference, or until all analyses have been completed at a statistical significance level of p<0.05. Data analyses will be conducted according to a pre-specified statistical analysis plan made publicly available prior to inclusion of the final patient or the final deadline for patient recruitment and performed using SAS software V.9.4 (SAS Institute, Cary, North Carolina, USA).

**Patient and public involvement**

A qualitative patient and public involvement (PPI) study preceded the initiation of this trial to explore context-relevant input from patients with hip OA scheduled for THA, clinicians and political stakeholders. In summary, six focus group interviews were conducted according to group status using open-ended, semistructured interview guides. Interviews were recorded, transcribed verbatim and subsequently thematic analysed. The results from the analysis markedly improved trial design, recruitment procedures, selection of meaningful outcomes, patient material and PRT protocol. The detailed findings from the PPI study will be published separately.

**ETHICS AND DISSEMINATION**

The trial has been approved by The Regional Committees on Health Research Ethics for Southern Denmark (Project-ID: S-20180158) and the Danish Data Protection Agency (Journal No 19/20337). All results from the trial will be published in international peer-reviewed scientific journals (open access) regardless of the results being considered positive, negative or inconclusive. Authorship eligibility will be based on the recommendations from The International Committee of Medical Journal Editors. Any important protocol amendments will be registered at ClinicalTrial.gov, reported to The Regional Committees on Health Research Ethics for Southern Denmark and addressed in the primary trial manuscript.

**DISCUSSION**

This is the first RCT to investigate the effectiveness of THA as superiority compared with exercise in patients with severe hip OA. The results of the current trial are expected to enable evidence-based recommendations, which may be used to facilitate the shared decision-making process in the discussion of treatment strategy for the individual patient with severe hip OA. A recent similar RCT in patients with severe knee OA showed that TKA followed by exercise resulted in superior pain relief and functional improvement compared with exercise. Additionally, one out of three patients allocated to the exercise group underwent TKA within 2 years of follow-up.
The current trial has some limitations. First, the orthopaedic surgeons and physiotherapists involved in the treatments as well as the patients will not be blinded to group allocation. This is considered an inherent limitation due to the nature of the compared treatments. Second, low recruitment is a major limitation in trials randomising patients to surgery or non-surgical treatment ranging from 7% to 22%, which may decrease the generalisability of the findings. Therefore, eligible patients declining participation in the current trial will be invited into a prospective observational cohort study in order to evaluate the external validity. Furthermore, treatment crossovers are common in these type of trials ranging from 26% to 45%, at 12 and 24 months of follow-up, which may bias the results. Thus, the primary endpoint will be set 6 months after initiating the treatment (THA/PRT) as previous studies have shown minor improvements from 6 to 12 months after THA, which might reduce crossovers in the current trial. Third, there are differences in the discharge criterion (table 1), postoperative rehabilitation protocols (online supplemental file 3), and procedures after THA between the hospitals in the current trial, which may affect the number of patients receiving supervised postoperative rehabilitation from each site. However, this reflects current clinical practice in Denmark and a recent meta-analysis found no differences between supervised or home-based postoperative rehabilitation after THA, and thus, it is considered unlikely to influence the results of the current trial.

Fourth, previous studies have investigated the preoperative and/or postoperative effect of exercise in patients with hip OA undergoing THA and the current evidence is inconclusive in relation to optimal exercise type and intensity. PRT performed with a high-velocity concentric phase (explosive-type) may increase muscle power more than PRT using a slow-to-moderate velocity, and this is considered important for improving physical function in healthy older adults. In support, PRT has shown clinically relevant improvements in patient-reported physical function and leg extension muscle power compared with standard care in patients with hip OA scheduled for THA.

The strengths of the trial are the multicentre, assessor-blinded, randomised controlled design with a priori registration, protocol publication, and blinded analysis and interpretation ensuring the foundation of a high-quality trial. Also, the current trial will enrol typical patients with hip OA eligible for THA, and the surgical procedures will be conducted at four hospitals with highly specialised and experienced orthopaedic departments performing between 175 and 781 primary THA annually. Furthermore, the PRT protocol applied in the current trial has been developed on available evidence on patients with severe hip OA and designed in accordance with the ACSM recommendations for progression models in resistance training for healthy adults suggesting a training frequency two times per week using a training load of 8–12RM performed in sets of three with high-velocity concentric contractions to be effective for increasing muscle strength and power. Lastly, a comprehensive PPI process preceded the current trial and all outcome measures are considered reliable and valid comprising patient-reported and functional performance measurements.

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