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Protocol Article

Prosthesis versus exercise for rotator cuff tear arthropathy – protocol of a randomised controlled trial

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ABSTRACT

INTRODUCTION. Reverse total shoulder arthroplasty is a well-established treatment for patients with rotator cuff tear arthropathy. The outcome after reverse total shoulder arthroplasty has been investigated in several studies and national registries. However, the treatment has not been compared to non-surgical treatment. The primary aim of this trial is to investigate whether reverse total shoulder arthroplasty is superior to exercise in patients with rotator cuff tear arthropathy who are eligible for reverse total shoulder arthroplasty.

METHODS. In this Nordic multicentre, randomised, controlled clinical trial, 102 patients with rotator cuff tear arthropathy who are eligible for reverse total shoulder arthroplasty will be allocated (1:1) to either reverse total shoulder arthroplasty followed by usual care or to an exercise intervention. The exercise intervention comprises 12 weeks of exercise with one weekly physiotherapist-supervised session and two home-based exercises. The primary outcome is the total Western Ontario Osteoarthritis of the Shoulder index score at a 12-month follow-up.

CONCLUSIONS. The ongoing randomised controlled trial will provide insights into treatment decisions for patients with rotator cuff tear arthropathy.

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Rotator cuff tear arthropathy is characterised by rotator cuff insufficiency, progressive arthritic changes of the glenohumeral joint and superior migration of the humeral head. Clinically, it presents with joint effusion, pain and loss of motion. For patients with severe rotator cuff tear arthropathy, persistent pain and unresponsive to nonoperative management, the standard treatment is reverse total shoulder arthroplasty [1]. The use of this procedure has been increasing, and [2, 3] rotator cuff tear arthropathy is now the third most common indication for shoulder arthroplasty in Denmark [2].

A systematic review of observational studies on clinical practice revealed that less than 40% of patients with

osteoarthritis are referred to or advised to exercise interventions [4]. The proportion of patients with rotator cuff tear arthropathy who have undergone a qualified exercise intervention before surgery remains unknown.

Recently, the surgical management of several shoulder conditions, including proximal humerus fractures, subacromial pain syndrome and degenerative large to massive rotator cuff tears (mean patient age 66.7 years), has not proven to be superior to non-surgical treatments, including exercises [5-7]. A recent Cochrane review summarised the existing evidence for shoulder replacement in the treatment of glenohumeral osteoarthritis and rotator cuff tear arthropathy [8]. However, none of the studies included in the review compared shoulder replacement surgery to non-surgical treatment and the authors were therefore unable to determine whether shoulder replacement is a more effective treatment than other non-surgical treatments [8]. Reverse total shoulder arthroplasty yields favourable outcomes in terms of pain relief and functional outcome in patients with rotator cuff tear arthropathy [9, 10]. However, it is unknown whether reverse total shoulder arthroplasty is superior to an exercise intervention, which is likely to be less expensive and have fewer complications.

The primary aim of this trial is to assess the comparative effectiveness of reverse total shoulder arthroplasty and a 12-week exercise programme on patient-reported pain and shoulder function, measured with the Western Ontario Osteoarthritis of the Shoulder index (WOOS) at 12-month. We hypothesise that surgical treatment with reverse total shoulder arthroplasty leads to a clinically relevant improvement in the total WOOS score compared to the exercise programme.

Methods

Study design

The trial is designed as a Nordic multicentre, randomised, investigator-blinded, controlled trial. The study protocol is reported following the 'Standard Protocol Items: Recommendations for Interventional Trials' (SPIRIT) [11]. Reporting the RCT will follow the Consolidated Standards of Reporting Trials (CONSORT) guidelines [12].

Setting and location

Patients will be recruited from the departments of orthopaedic surgery at Aarhus University Hospital, Aalborg University Hospital, Viborg Regional Hospital, Silkeborg Regional Hospital and Esbjerg Hospital, Denmark, Oslo University Hospital, Norway, and Tampere University Hospital, Finland.

Study patients and recruitment procedure

Orthopaedic surgeons in the treating hospitals will screen patients for eligibility. Patients aged 60-85 years with rotator cuff tear arthropathy who are eligible for surgery with a reverse total shoulder arthroplasty and meet the inclusion and exclusion criteria can be included (**Table 1**) [13]. They will receive oral and written information about the trial, and all participants who accept will give their written informed consent. Recruitment commenced in April 2021 and is expected to conclude by March 2026. If delays occur, the project group may contact additional centres for possible expansion of the study and extension of the study period.

TABLE 1 Inclusion and exclusion criteria.

Inclusion criteria
Patients 60-85 yrs
Rotator cuff tear arthropathy of the glenohumeral joint: Hamada grade 3, 4 and 5 [11]
Eligible for surgery with reverse total shoulder arthroplasty
Exclusion criteria
Previous shoulder fracture: fracture of the proximal humerus or glenoid fracture
Other planned upper extremity surgery within 6 mos.
Rheumatoid arthritis or other types of systemic arthritis
Cancer diagnosis and actively receiving chemo-, immuno- or radiotherapy
Neurological diseases affecting shoulder mobility, e.g., disability after previous stroke, multiple sclerosis, Parkinson's, Alzheimer's disease
Other reasons for exclusion include being mentally unable to participate or planned absence for > 14 days in the first 3 mos. after the baseline test
Unable to communicate in the respective languages of the participating countries

Interventions

Surgical group

Patients randomised to the surgical group will undergo treatment with reverse total shoulder arthroplasty performed by experienced shoulder surgeons, using the approach and implant preferred by the surgeon. Most patients will be discharged the day after surgery. After discharge, all patients will receive postsurgical exercises, a written rehabilitation plan and follow-up by physiotherapists. Sling use is recommended for a minimum of two weeks. Immediately after surgery, patients will be allowed to move their shoulder passively within 0 degrees of external rotation and 90 degrees of flexion. Two weeks after surgery, patients will be allowed to perform active flexion and can use their arm with the elbow fixed to their side. Six weeks after surgery, active movement of their shoulder is allowed within their comfort zone, while slowly increasing exercise load. Patients in the surgical group who decline surgery after randomisation will remain in the trial and participate in the follow-up assessments.

Exercise group

The exercise programme, tested in a previous feasibility study, was deemed safe and feasible [14]. It consists of 12 weeks of exercise, with one physiotherapist-supervised session and two home-based sessions per week. Detailed descriptions of the exercise intervention can be found in the PROACT trial protocol [15]. The programme includes two warm-up exercises and five exercises targeting shoulder mobility, rotator cuff strength and postural improvement.

Patients will maintain an exercise log to track adherence. At three months, patients may consult a shoulder surgeon, and those with unsatisfactory results may crossover to surgery, with the reason for crossover being recorded. Patients remaining in the exercise group will receive four individual physiotherapist-supervised booster sessions, at four, six, eight and ten months after the first exercise session.

Outcomes

Patient-reported outcome measures (PROMs) and accelerometer-based activity will be collected at baseline

before randomisation as detailed in **Table 2.** PROMs will be collected at a three-month follow-up after initial treatment. At 12-month follow-up, both PROMs and accelerometer-based physical activity will be collected. Furthermore, PROMs will be collected at two, five and ten years after the initial treatment. An overview of study activities is presented in **Table 3.**

TABLE 2 Outcomes in the REACT trial.

Type	Outcome	Measurement, follow-up, mos.
Primary	WOOS	12
Secondary	WOOS	3, 24, 60, 120
	DASH	3, 12, 24, 60, 120
	VAS pain at rest	3, 12, 24, 60, 120
	VAS pain during activity	3, 12, 24, 60, 120
	VAS pain at night	3, 12, 24, 60, 120
	Use of analgesics during the past week: paracetamol, NSAID, opioids	3, 12, 24, 60, 120
	Serious adverse events	3, 12, 24, 60, 120
	Adverse events	3, 12, 24, 60, 120
Other	Upper extremity activity	12
	NRS pain before exercise: exercise group only	During exercise intervention
	NRS pain after exercise: exercise group only	During exercise intervention
	EQ-5D-5L	3, 12, 24, 60, 120
	iPCQ: Danish patients only	3, 12
	PASS	3, 12, 24, 60, 120
	Number of reverse total shoulder arthroplasties: exercise group	24, 60, 120
	Adherence to supervise sessions: exercise group	B-3
	Adherence to unsupervised sessions: exercise group	B-3, 3-12

B = baseline; DASH = Disabilities of the Arm, Shoulder and Hand; EQ-5D-5L = European Quality of Life - 5 Dimensions - 5 Levels; iPCQ = Productivity Costs Questionnaire; NRS = numeric rating scale; PASS = Patient Acceptable Symptom State; VAS = visual analogue scale; WOOS = Western Ontario Osteoarthritis of the Shoulder index.

TABLE 3 Study activities.

	Visit 1	Online/letter	Visit 2	Online/letter
Time	Baseline	3 mos.	12 mos.	2, 5 and 10 yrs
Informed consent	√			
Demography	√[a]			
Inclusion/exclusion criteria	√			
Randomisation	√			
Patient-reported outcome data	√[b]	√[c]	√[c]	√[b]
Accelerometer measurements	√		√	
Surgical information	√[d]			
Radiological measurements	√[e]	√[e]	√[e]	
Treatment-related variables		√[f]	√[f]	√[f]

DASH = Disabilities of the Arm, Shoulder and Hand; EQ-5D-5L = European Quality of Life - 5 Dimensions - 5 Levels; iPCQ = Productivity Costs Questionnaire; NRS = numeric rating scale; VAS = visual analogue scale; WOOS = Western Ontario Osteoarthritis of the Shoulder index.
a) The demography includes questions regarding age, sex, height, weight, hand dominance, duration of shoulder symptoms, civil status, educational level, employment status, alcohol intake, smoking behaviours and comorbidities.
b) Patient-reported outcomes include VAS at rest, during activity and at night, analgesic consumption in the last week, WOOS, DASH and EQ-5D-5L.
c) At the 3- and 12-month follow-up, the Danish patients will also complete the iPQC.
d) Surgical information is collected for patients in the surgical group, including the duration of the surgery and the type of prosthesis.
e) Radiological information includes radiography and CT for all patients before surgery and radiography for surgical patients at 3 and 12 months. Surgeons will also complete a report for the surgical patients.
f) Treatment-related variables include adverse and serious adverse events, compliance with the exercise intervention and pain before and after supervised exercise sessions using NRS and crossovers.

Primary outcome

The primary outcome is the WOOS score at the 12-month follow-up. WOOS measures shoulder-related quality-of-life across four domains: 1) physical symptoms; 2) sport, recreation and work; 3) lifestyle; and 4) emotions [16]. WOOS consists of 19 items answered using a visual analogue scale (VAS) ranging from 0 to 100, leading to a total score of 0-1,900, with 0 being the best possible score. Raw scores can be converted to a percentage (0-100, 100= best). The Danish version of WOOS has been translated and validated in patients with glenohumeral osteoarthritis [16].

Secondary outcomes

In addition to WOOS, the patients will report other PROMs, namely the Disabilities of the Arm, Shoulder and Hand (DASH) [17]; patient-reported pain intensity at rest, during activity and nightly pain using the 100 mm VAS; the use of analgesics during the last week (paracetamol, non-steroidal anti-inflammatory drug (NSAID), opioids). Furthermore, surgeons and physiotherapists will report serious adverse events and adverse events.

Serious adverse events and adverse events

Serious adverse events are defined as events requiring hospitalisation or causing death. Patients in the surgical group will be monitored for serious adverse events during the first four weeks after discharge.

Adverse events, defined as any unintended and unfavourable sign, symptom or disease resulting in healthcare contact, will be [18] reported according to the Consort Group Guidelines (**Table 4**).

TABLE 4 Adverse events for the surgical group and the exercise group.

Surgical group
Post-operative infections
Instability
Periprosthetic fracture
Loosening of ≥ 1 of the arthroplasty components
Exercise group [18]
Focus will be on exercise-related injuries:
Persistent pain
Fatigue
Bursitis
Low-back pain
Oedema

When 50% of patients are recruited, an independent steering committee will review complication rates and correlate them to expected rates from the literature. An unexpectedly high complication rate will be reported to the project group, which will decide whether to discontinue randomisation or continue the study.

Other outcomes

Other outcomes are described in Table 2 [19]. Upper extremity physical activity is measured over three consecutive days on both arms using tri-axial (Axivity, Newcastle upon Tyne, UK) accelerometers [20], the censors are mounted on the upper arms and measure activity 24/7 in three planes.

Sample size

The sample size calculation is based on WOOS data from the Danish Shoulder Arthroplasty Register and end scores obtained from the feasibility study [14]. The mean WOOS was 81.3 points from the Danish Shoulder Arthroplasty Register [2]. The assumed standard deviation (SD) was ± 22. The mean WOOS was 67 (SD: ± 22) in the feasibility study [14]. With a 5% level of significance and a sample size of 78 patients. The drop-out rate was set to 30%, the total number of patients needed is 102.

Randomisation

After baseline assessment, patients are randomised (1:1) to either reverse total shoulder arthroplasty or exercise (Supplementary Figure 1), stratified by site with random block sizes. The Research Electronic Data Capture

(REDCap) randomisation system is used for data storage and randomisation. A project coordinator will refer the patient to either surgery or exercise.

Data sharing plan

Individual de-identified data that underlie the results reported in the main article can be made available to researchers who provide a methodologically sound proposal. Additional documents such as the Study Protocol, Statistical Analysis Plan and Analytic Code will also be provided. Data will be accessible immediately following publication and retained for five years after the ten-year follow-up publication. Requests should be directed to the principal investigator. Researchers seeking data access must submit a proposal for review and sign a data access agreement.

Blinding

Outcomes collected at baseline will be assessed blinded to the treatment. During follow-ups, patients will complete questionnaires from home, either online or by mail. At 12 months, patients will visit the hospital to collect data on upper extremity physical activity. To minimise interpretation bias, the blinded results from the primary data analyses will be presented to the project group (JBL, TMT, APL, AR and IM), followed by the development of two written interpretations, which will be signed before unsealing the results.

Observational cohort

To evaluate the external validity, patients declining to participate in the RCT will be invited to join a prospective observational cohort using identical endpoints and outcomes. Cohort patients sign a written informed consent and follow standard surgical treatment with reverse total shoulder arthroplasty.

Statistical methods

The primary analysis will be based on the total WOOS at 12 months on an intention-to-treat basis, i.e., all patients will be analysed in the intervention group in which they were randomly allocated, irrespective of their actual treatment. The comparison between groups will be analysed using a linear mixed-effects model. Fixed effects include intervention group and time (three and 12 months), and the patient will be included as a random effect. Age, sex, study site and baseline WOOS will be included as fixed covariates. Interaction between the study groups and time will be included in the model to estimate the treatment effect at each time point. Confidence intervals are estimated for each time point. Due to the repeated mixed model analyses, no missing data will be imputed.

Details of the statistical analysis plan will be made publicly available before the inclusion of the final patient.

Ethics

The trial was approved by the Central Denmark Region Committee on Biomedical Research Ethics (Journal No. 1-10-72-29-21) and by the Danish Data Protection Agency (Journal No. 1-16-02-200-21). The study will be conducted in accordance with the Declaration of Helsinki II. The trial is registered with clinicaltrials.gov NCT04864158. At the conclusion of the trial, any protocol deviations will be determined and reported. The funders had no role in the planning or implementation of the trial and only provided financial support.

Trial registration: ClinicalTrials.gov ID: NCT04864158.

Discussion

To our knowledge, the REACT trial is the first to compare the effectiveness of surgical versus non-surgical treatment for rotator cuff tear arthropathy. The results of this trial are anticipated to provide evidence-based recommendations aiding in the shared decision-making process in determining treatment strategies for patients with rotator cuff tear arthropathy.

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