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Exercise and analgesia for rehabilitation following hip fracture surgery

Submission date
05/02/2025

Recruitment status
Recruiting

Registration date
05/03/2025

Overall study status
Ongoing

Last Edited
02/07/2025

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aim
As we age, the strength of our bones and muscles can decrease, making hip fractures more likely. A simple fall or trip from standing can result in a broken hip, requiring admission to hospital and likely an operation to fix or replace the damaged bone. In the elderly, a broken hip represents a significant life event, and may affect their ability to walk, live independently, or enjoy the same actives they were able to participate in prior to their injury. As such, understanding how muscles recover following surgery for a broken hip, and identifying ways of improving strength and function, is of vital importance. This research study is looking at the way muscle functions by studying which genes are expressed in muscle cells following hip fractures. The pattern of gene expression will provide an insight into how the muscle cells are functioning and how quickly they are recovering. This will be compared to other measures of muscle size and function: in particular, the size of muscles on a whole-body MRI scan and clinical measurements (for example, questionnaire answers, grip strength, and walking ability). We aim to explore the effect of exercise training on muscle recovery following hip fracture, comparing the injured, exercised leg to the non-injured, unexercised leg. Additionally, we aim to look at the effects of common painkillers (NSAIDs) on muscle function. We plan to recruit forty patients to take part in this research study. The study's findings should help to improve our understanding of muscle recovery at the cellular level and identify potential opportunities to improve clinical recovery following hip fracture.

Who can participate?
Adults aged over 60 years of age, who have who have been admitted to hospital with a broken hip which is being treated with surgery.

What does the study involve?
Participants are asked to join the study shortly after admission to hospital with a broken hip. Participants must meet the eligibility criteria in order to take part. Four weeks after surgery, all participants will be asked to complete a resistance exercise physiotherapy plan, requiring twice-weekly gym sessions for 12 weeks. Additionally, participants will be randomised to receive one of two standardised painkiller regimens: either containing or omitting NSAIDs. Participants will undergo a whole-body MRI scan before and after the exercise plan, to assess changes in muscle size. Additionally, participants will undergo four small muscle biopsies (microbiopsy) from their

thigh muscles at various points during these physiotherapy sessions. At five time points, participants will have blood samples taken. One stool sample will be collected in the first two weeks post-operation. If participants undergo hip replacement surgery necessitating removal of a portion of the broken hip bone, the bone removed will be collected for analysis. Additionally, we will complete four questionnaires, three hand strength and walking assessments, and two glucose tolerance tests.

What are the possible benefits and risks of participating?
There will be no immediate direct benefit to those taking part, but the information we get from this study may help patients rehabilitate from hip fracture more effectively in future. Some studies have shown that resistance exercise increases muscle size and strength, and this study will involve regular, supervised physiotherapy sessions, additional to those normally offered by the NHS. The information we get from this research will improve our understanding of what happens to muscles as we get older and may help us to develop new treatments to help older people recover after a fall.

Muscle micro-biopsies might cause some minor discomfort, bruising, or tenderness around the site of the biopsy, and muscle soreness for 1-2 days after the procedure. Any pain or discomfort experienced will be managed as part of your post-operative pain relief and is expected to be much lower than the discomfort that is associated with having hip surgery itself.

In this study, participants will be randomly assigned to one of two analgesic regimens: either including or excluding the use of NSAIDs. NSAIDs have been used for many years, and their side-effects are well known. Although rare, the main serious risks of taking NSAID medications include damage to the stomach lining (peptic ulceration) that may cause bleeding, and kidney damage. Participants will be carefully screened to ensure the risk of these side-effects is as low as possible, and blood tests will be monitored carefully throughout the study duration.

Where is the study run from?
Participants will be recruited from Queen’s Medical Centre, Nottingham (UK). Follow-up visits will take place in the University of Nottingham (David Greenfield Human Physiology Unit, and Sir Peter Mansfield Imaging Centre).

When is the study starting and how long is it expected to run for?
January 2025 to October 2026

Who is funding the study?
The study is funded by the National Institute of Health and Care Research Biomedical Research Centre, Nottingham (NIHR BRC, Nottingham, UK)

Who is the main contact?
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Contact information

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
353208

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Protocol number 25006

Study information

Scientific Title
Standardised clinical analgesic regimen and exercise therapy after hip fracture

Acronym
CLARET-HIP

Study objectives
The hypothesis of this study is that the administration of a structured resistance exercise programme will upregulate genes associated with muscle protein synthesis and anabolic cellular pathways.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 14/04/2025, London Riverside REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; riverside.rec@hra.nhs.uk), ref: 25/LO/0276

Study design
Single-centre prospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Quality of life, Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Acute fragility fracture of the hip requiring surgical management

Interventions
All participants will attend the DGHPU twice weekly for 12 weeks, for a supervised rehabilitation exercise intervention, with isolated, unilateral injured-leg exercises alone. The uninjured, unexercised leg will therefore act as a control. They will additionally be offered routine inpatient post-hip fracture physiotherapy advice and leaflet, as per routine practice in our department. During visits to the DGHPU, participants will undergo isokinetic resistance exercise training intervention focused on the injured leg knee extensors. All exercises will be performed using a Humac NORM isokinetic dynamometer (CSMi inc., Stoughton, MA, USA). Participants will undergo 5 sets of 30 repetitions of maximal voluntary isokinetic knee extension at 60°/s. Training will be fully supervised by unit staff and physiotherapists.

Intervention Type
Other

Primary outcome measure

Muscle mRNA gene expression measured using a custom TaqMan array at 5-, 9-, 13-, and 17-weeks post-operation.

Secondary outcome measures
1. Isometric knee extension strength and isokinetic knee extension power and fatigability measured fortnightly using a Humac NORM dynamometer, at weeks 5, 7, 9, 11, 13, 15 and 17 post-operation.
2. Whole body and bilateral leg muscle volumes measured using whole-body MRI at weeks 4 and 17 post-operation
3. Muscle protein synthesis measured using D2O incorporation into skeletal muscle micro-biopsy specimens at 5-, 9-, 13-, and 17-weeks post-operation.
4. Muscle satellite cell number measured on microscopy of muscle micro-biopsy specimens at 5-, 9-, 13-, and 17-weeks post-operation.
5. Glucose disposal, measured via oral glucose tolerance test performed at weeks 5 and 17 post-operation
6. Handgrip strength measured using a Jamar handgrip dynamometer at weeks 0-2, 5, 11, and 17 post-operation.
7. Mobility and walking speed, measured using a 4-metre walk test at weeks 0-2, 5, 11 and 17 post-operation.
8. General patient-reported quality of life measured using the EQ5D-5L questionnaire at weeks 0 (baseline), 5, 17, and 26 post-operation.
9. Hip-specific pain and function measured using the Oxford Hip Score at weeks 0 (baseline), 5, 17, and 26 post-operation.
10. General disability level measured using the Disability Rating Index at weeks 0 (baseline), 5, 17, and 26 post-operation.
11. Level of cognitive impairment, using the Montreal Cognitive Assessment at baseline, and repeated at weeks 5 and 17 post-operation.
12. Serum concentration of inflammatory cytokines measured using proteomic analysis, at day 0 (pre-operative baseline), day 1-3, and week 17 post-operation.
13. Safety monitoring blood tests measured using FBC, U&E and LFT analyses of venous blood at baseline, and weeks 5, 8, 11, 14, and 17 post-operation.
14. Femoral head bone structure and density measured using micro-CT analysis of resected bone specimen, taken intraoperatively.
15. Gut microbiome composition measured using microbiome analyses of faecal specimen, collected on one occasion during the first two weeks post-surgery.
16. Clinical outcomes (such as peri-operative complications, adverse events, length of stay, and discharge location) measured via audit of the medical notes relating to the hip fracture admission.

Overall study start date
17/01/2025

Completion date
01/10/2026

Eligibility

Key inclusion criteria
1. Acute isolated hip fracture requiring operative intervention
2. Age ≥60 years old

3. Understands English
4. Able to give informed consent
5. Hip replacement surgery a criterion for collection of bone sample

Participant type(s)
Patient

Age group
Senior

Lower age limit
60 Years

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Ipsilateral knee replacement, tendon rupture, or patella fracture
2. History of neurological pathology, or stroke with motor function impairment
3. Evidence of impaired renal function (eGFR <30ml/min/1.73m²)
4. Diagnosis of Type 1 Diabetes Miletus
5. Rockwood Clinical Frailty Scale ≥5
6. BMI ≥40 kg/m²
7. Contraindication to NSAID therapy:
i. History of hypersensitivity or allergy to ibuprofen (e.g., asthma, rhinitis, angioedema, urticaria)
ii. History of asthma or hay fever with previous NSAID-associated exacerbation
iii. History of Crohn's disease or ulcerative colitis
iv. History of haemorrhagic stroke
v. Active or history of recurrent peptic ulcer/haemorrhage
vi. History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
vii. Severe heart failure (NYHA Class IV), severe renal failure or severe hepatic failure
viii. Concomitant regular prescription of aspirin with a daily dose above 75 mg, or other non-steroidal anti-inflammatory medicine
ix. Concomitant anticoagulant or antiplatelet prescription during study follow-up period (weeks 5-17 post-surgery)

Date of first enrolment
01/07/2025

Date of final enrolment
01/07/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen's Medical Centre
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Sponsor type
University/education

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
NIHR Nottingham Biomedical Research Centre

Alternative Name(s)
Nottingham Biomedical Research Centre, Nottingham Biomedical Research Centre - NIHR, NIHR Nottingham BRC, BRC, NIHR NBRC

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The results from the study will be presented at medical conferences and in scientific or clinical journals to allow findings to be shared with other researchers. Results will also be used by Mr. Christopher Deacon as part of his PhD thesis and may be used to design future research aimed at improving recovery after surgery.

Your coded (anonymised) data may be shared with journals, experts, or other scientists to verify the quality of results. However, you will not be identified in any report or publication.

Intention to publish date
01/10/2027

Individual participant data (IPD) sharing plan
The datasets generated and analysed during the current study will be available on request from christopher.deacon@nottingham.ac.uk

IPD sharing plan summary
Available on request