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Surgery for knee articular cartilage injuries

Submission date
05/03/2020

Recruitment status
Stopped

Registration date
06/03/2020

Overall study status
Stopped

Last Edited
18/01/2024

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Knee injuries are common and can lead to pain and disability. Injuries to the smooth cartilage that lines the ends of the bone in joints can cause ongoing problems as the cartilage does not have a blood supply and rarely heals once injured. 10,000 people a year in the UK have a severe articular cartilage injury that warrants surgical treatment. There are two main ways in which these injuries can be treated surgically, the first is to try to address the symptoms without trying to restore the cartilage; such as cleaning (debriding) the area or replacing the damaged area with an implant. The other way is to try to repair or restore the cartilage in the damaged area. Cartilage does not grow back on its own, so an operation known as “microfracture” can be performed to encourage the cartilage to grow. A surgical tool is used to make perforations in the bone in the damaged area which allows blood and bone marrow to seep out of the holes, encouraging healing. A “scaffold”, which is usually made of the same material that makes up most of the cartilage (collagen), can be added, termed Autologous Matrix-Induced Chondrogenesis (AMIC). The scaffold is secured in place and acts as a template for new cartilage to form on. It is not clear if using a scaffold improves the outcome for patients. Using scaffold makes the operation more complex (approximately 20 minutes longer) and the cost of the scaffold is approximately £900, so it is important to establish if adding a scaffold results in a better outcome for patients and is cost-effective for the NHS. The study will find out whether adding the scaffold is worthwhile or not for patients with knee articular cartilage injuries.

Who can participate?
Patients aged 18 and over with a symptomatic chondral or osteochondral defect of the knee

What does the study involve?
Participants are randomly allocated into one of two groups. Those in the first group will have microfracture surgery with the insertion of a scaffold. Those in the second group will have microfracture surgery alone. Patients will be asked to attend the hospital for clinical follow-up at 3 months, 6 months, 1 year and 2 years after their surgery. The first three visits are part of routine care for patients following this surgery. The appointment at 2 years is outside of routine care and reasonable travel expenses will be covered. The researchers will ask patients to complete a questionnaire at baseline and then at each follow-up visit. This will provide information about the patient's general health and work status; for example, how they are feeling, what activities they are able to perform and how much pain they are feeling. Patients will also be asked some questions about any visits to hospital they have had, other healthcare

they have received in the community, or any expenses and burdens they may have incurred because of their injury.

What are the possible benefits and risks of participating?
The researchers cannot promise that the study will help the participants, but it is hoped that the results from this study may help benefit the NHS and improve the management of future patients.

Where is the study run from?
North Bristol NHS Trust and the University of Bristol (UK)

When is the study starting and how long is it expected to run for?
September 2019 to October 2022

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?
Michael Whitehouse (Chief Investigator) or Lucy Dabner (Trial Manager)
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Contact information

Type(s)
Public

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
270719

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
HTA - NIHR127849, IRAS 270719

Study information

Scientific Title
A randomised controlled trial of scaffold insertion and microfracture compared to microfracture alone for the treatment of chondral or osteochondral defects of the knee

Acronym
SISMIC

Study objectives
It is hypothesised that in patients with symptomatic chondral or osteochondral defects of the knee requiring treatment, microfracture with microstructural scaffold leads to a Knee Injury and Osteoarthritis Outcome Score superior outcome at 2-years compared with microfracture alone. The overall aim of this study is to evaluate the clinical and cost-effectiveness of microstructural scaffold in patients undergoing microfracture for a chondral or osteochondral defect of the knee.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/06/2021, West Midlands - Black Country Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)207 104 8010; blackcountry.rec@hra.nhs.uk), ref: 21/WM/0110

Study design

Multicentre parallel-group superiority randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Symptomatic chondral or osteochondral defect of the knee

Interventions
Randomisation will be performed using a secure internet-based randomisation system ensuring allocation concealment. Trial participants will be randomised in a 1:1 ratio to receive either microfracture of the chondral/osteochondral lesion with insertion of a bilayer collagen matrix microstructural scaffold or microfracture alone. Participants and clinical care teams (except for staff involved in the surgery) and members of the research team responsible for data collection will be blinded to allocation.

Both groups will be followed for 2 years by clinical review to collect information about quality of life, symptoms and pain in the knee, complications of surgery, need for further surgery and costs to the NHS and patients.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Articular cartilage repair outcome assessed using participant-reported Knee injury and Osteoarthritis Outcome Score (KOOS) collected using a questionnaire at baseline, 3, 6, 12 and 24 months

Key secondary outcome(s))
Data will be collected to characterise the following secondary outcomes over the 2-year follow up period:
1. Knee function assessed using International Knee Documentation Committee (IKDC) subjective knee evaluation score at 2 years (range 0-100 with 100 representing the best level of symptoms, function and activity). Domains include symptoms experienced over the last 1-4 weeks and when undertaking particular activities, including sporting activities and activities of daily living. It is reliable and validated with a minimal clinically important difference (MCID) of 9 points. This is collected using a questionnaire at baseline, 3, 6, 12 and 24 months.
2. Activity assessed using Tegner-Lysholm activity grading scale (range 0-100 with 100 representing the best level of function/activity). There are 8 questions based on ability or symptoms including limp, support, pain, instability, locking, swelling, stair-climbing and squatting. This is collected using a questionnaire at baseline, 3, 6, 12 and 24 months.
3. Health-related quality of life (HRQoL) assessed using EQ-5D-5L, a validated, generalised and standardised instrument comprising a visual analogue scale measuring self-rated health and a health status instrument of 5 domains related to daily activities. This instrument will be used to derived 2-year quality-adjusted life years (QALYs), by attaching UK preference-based utility indices to the EQ-5D-5L health states and weighting them with survival over time. This is collected using a questionnaire at baseline, 3, 6, 12 and 24 months.
4. Productivity assessed using Work Productivity and Activity Impairment (WPAI), a validated

instrument which measures the impact of health and symptom severity on work productivity and non-work activities. Absenteeism and presenteeism will be valued using the human capital approach and estimates of average weekly earnings to estimate productivity losses for the economic evaluation. This is collected using a questionnaire at baseline, 3, 6, 12 and 24 months.
5. Complications, including bleeding, infection, deep vein thrombosis or pulmonary embolism, need for further surgery (non-joint replacement and joint replacement), collected on study case report forms by the research nurse.
6. Resources required to i) deliver the two treatments, ii) treat short- and long-term complications; iii) follow-up care in hospital, including rehabilitation, outpatient appointments, A&E, and re-admissions. Other health and social care resources required in the community and patient expenditures with their care will be collected from the participant using questionnaires at baseline, 3, 6, 12 and 24 months. Resources will be valued using Department of Health and Social Care reference costs, and national unit costs for health and social care, where available, or local sources otherwise.

Completion date
25/10/2022

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. 18 years of age or older
2. Symptomatic chondral or osteochondral defect of the knee sited on the medial or lateral femoral condyles, trochlea or patella as confirmed by standard clinical practice
3. Chondral or osteochondral lesion measuring no more than 4 cm2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
10

Key exclusion criteria
Current participant exclusion criteria as of 12/08/2021:
1. Unstable, ligamentous injury to the knee that will not be treated

2. Unstable, meniscal tear that will not be treated
3. Less than 50% of native meniscal volume remaining in the knee following previous meniscal surgery
4. Knee alignment that in the opinion of the surgeon requires realignment surgery/osteotomy
5. Chondral or osteochondral lesion measuring >4 cm^2 following operative debridement of the lesion to a stable chondral rim
6. Chondral or osteochondral lesion that is being treated has been treated previously with one of the study interventions
7. Defects occurring on the tibial chondral surface
8. Patient unable/unwilling to adhere to trial procedures
9. Unable to provide written informed consent
10. Prisoners
11. Enrolled in another clinical trial and:
11.1. Co-enrolment is not permitted by the other trial
11.2. Co-enrolment would be burdensome for the patient
11.3. The intervention of the other trial could interfere with the SISMIC primary outcome

Previous participant exclusion criteria:
1. Unstable, untreated ligamentous injury to the knee
2. Unstable, untreated meniscal tear
3. Less than 50% of native meniscal volume remaining in the knee following previous meniscal surgery
4. Knee alignment that in the opinion of the surgeon requires realignment surgery/osteotomy
5. Chondral or osteochondral lesion measuring >4 cm2 following operative debridement of the lesion to a stable chondral rim
6. The chondral or osteochondral lesion that is being treated has previously been treated with either of the study interventions
7. Defects occurring on the tibial chondral surface
8. Patient unable/unwilling to adhere to trial procedures
9. Unable to provide written informed consent
10. Prisoners
11. Enrolled in another clinical trial and: a) co-enrolment is not permitted by the other trial; or b) co-enrolment would be burdensome for the patient

Date of first enrolment
28/10/2021

Date of final enrolment
25/10/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-Trym
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BS10 5NB

Sponsor information

Organisation
North Bristol NHS Trust

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Data will not be made available for sharing until after publication of the main results of the study. Thereafter, anonymised individual patient data will be made available for secondary research, conditional on assurance from the secondary researcher that the proposed use of the

data is compliant with the MRC Policy on Data Sharing regarding scientific quality, ethical requirements and value for money. A minimum requirement with respect to scientific quality will be a publicly available pre-specified protocol describing the purpose, methods and analysis of the secondary research, e.g. a protocol for a Cochrane systematic review. Please contact Michael Whitehouse using the following email: sismic-study@bristol.ac.uk.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol (other)			19/01/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes