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The ASSERT (Acute Sacral inSufficiEncy fractuRe augmenTation) study

Submission date
30/07/2018

Recruitment status
No longer recruiting

Registration date
10/08/2018

Overall study status
Completed

Last Edited
08/06/2022

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The pelvis is the sturdy ring of bones located at the base of the spine. Breaking the pelvis is common in older people, often caused by a fall from a standing height or less. These fractures are usually treated without an operation, but are associated with considerable risk of dying, significant disability, and enormous healthcare costs. Keyhole spinal surgery involves fixing the pelvis (with bone cement and screws if required) and has been shown to be safe and clinical effective. Whether this should now become the standard treatment for this type of injury requires further research. However, before a large scale study is conducted, we will assess whether such a study is feasible. The aim of this study is to undertake a small study to help design a future trial to evaluate the benefits and cost savings of treating older people with broken bones in the pelvis using keyhole spinal surgery.

Who can participate?
Patients aged 70 and over going to hospital with a broken pelvis (broken at the front and the back of the pelvis)

What does the study involve?
Participants are randomly allocated to either keyhole surgery or no operation (the current treatment for these type of fractures). The study assesses whether there are enough patients to take part; whether patients are willing to be randomly allocated; if the doctors are willing to keep to the random decisions. Measurements are collected over 12 weeks to find out whether a future study is practical. The main outcome of a future study will be a measure of mobility, of which two different scales will be tested, together with measuring: pain scores, pain medication taken; quality of life; interaction with health services and healthcare costs. Safety follow-up outcome measures are collected at 12 months. There are also interviews with participants and clinicians to explore their experiences and recommendations for improving a future trial.

What are the possible benefits and risks of participating?
Participants receive additional assessments at various time points to see how well they are recovering from their injury. In those allocated to surgery, it is expected that surgery will result in early and better pain control which may aid early mobilisation. Patients may understandably be very anxious when admitted to hospital with a pelvic fracture and the thought of taking part

in a study may be the least of their priorities. Therefore, patients are given 24 hours to decide, which also allows them to ask further questions. Participants will require an x-ray at the time of the surgery and after the procedure. This exposes the participant to radiation, but the amount is very small, and the risks of long-term problems are small compared to the potential benefits of the treatment.

Where is the study run from?
Queens Medical Centre (UK)

When is the study starting and how long is it expected to run for?
October 2018 to March 2021

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
38895

Study information

Scientific Title
The ASSERT (Acute Sacral inSufficiEncy fractuRe augmenTation) randomised controlled, feasibility in older people trial

Acronym
ASSERT

Study objectives

The trialists hypothesise that keyhole spinal sacral fixation (cement augmentation +/ screw fixation) is a clinical and cost-effective intervention compared to current standard practice, non-surgical management in older people presenting to hospital with a Lateral Compression Pelvic Fragility Fracture and therefore should become first line treatment for the management of these fractures. Prior to a comprehensive clinical trial, the trialists will undertake a feasibility study to understand how such a future trial can be successfully delivered.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East - Newcastle & North Tyneside 2 Research Ethics Committee, 05/07/2018, ref: 18/NE /0212

Study design
Randomised; Interventional; Design type: Treatment, Process of Care, Management of Care, Surgery

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Fragility fracture of the pelvis

Interventions
TRIAL DESIGN
Parallel, two-arm randomised controlled trial with participants individually allocated on a 1:1 ratio to either surgical intervention (keyhole surgical intervention) or non-surgical conservative care. Embedded within the feasibility study will be a health economic analysis to understand resource utilisation and implication of such an intervention; and a qualitative study which will focus on the experiences of participants and clinicians involved in the study, their insights and further recommendations for improving trial acceptability and processes.

TRIAL SETTING
The study will be conducted in a single site, Queens Medical Centre, Nottingham University Hospitals NHS Trust (acute trust catchment population 700,000; tertiary spinal surgical unit catchment population 3.5 million). Participants will be recruited from the Queens Medical Centre, Nottingham University Hospitals NHS Trust with follow up conducted in either the acute hospital, rehabilitation facility or participant's place of residence depending on where there will be at the time of the respective follow up schedule. The study will be delivered in collaboration with the Leicester Clinical Trials Unit (LCTU). The LCTU will be responsible for site set-up and training, randomisation, database development and maintenance, data management, trial management, statistical analysis and monitoring of data quality and trial conduct. A trial manager appointed by the LCTU will oversee the day-to-day running of the trial.
Participants will be randomly allocated to either surgical intervention or conservative non-surgical care on the day they consent via a secure web based system maintained by the LCTU. This will be undertaken using computer generated permuted balanced blocks of randomly varying size. The research assistant (RA) will electronically contact the web based system and

each participant will receive a randomisation number. Participants and their GPs will be notified of allocation to either surgical or non-surgical arm of the study. Their participation will also be recorded in their medical notes.

Due to the nature of the study, it will not be possible to blind the participant to surgical or non-surgical intervention, however all further analysis will be undertaken blinded to the allocation of treatment intervention. Allocation to groups will be concealed until after the participant baseline enrolment data has been entered into the trial randomisation system.

DATA COLLECTION
This will include data collected from the medical and nursing notes and where appropriate the participant and/or carer by the RA.
• Sociodemographic data (age, sex, deprivation, fracture) details;
• Cognitive Assessment as measured by the 30 point Montreal Cognitive Assessment (MoCA) tool. The MoCA assesses several cognitive domains: the short-term memory recall task (5 points) involves two learning trials of five nouns and delayed recall after approximately five minutes; visuospatial abilities are assessed using a clock-drawing task (3 points) and a three-dimensional cube copy (1 point); multiple aspects of executive functions are assessed using an alternation task adapted from the trail-making B task (1 point), a phonemic fluency task (1 point), and a two-item verbal abstraction task (2 points); attention, concentration, and working memory are evaluated using a sustained attention task (target detection using tapping; 1 point), a serial subtraction task (3 points), and digits forward and backward (1 point each); language is assessed using a three-item confrontation naming task with low-familiarity animals (lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points), and the aforementioned fluency task; orientation to time and place is evaluated by asking the subject for the date and the city in which the test is occurring (6 points);
• Charlson Co-morbidity Index. The Charlson comorbidity index predicts the one-year mortality for a patient who may have a range of comorbid conditions, such as heart disease, AIDS, or cancer (a total of 22 conditions). Each condition is assigned a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one. Scores are summed to provide a total score to predict mortality.
• Timed Up and Go Test (TUG) which assesses a person's mobility requiring both static and dynamic balance. It uses the time that a person takes to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down. During the test, the person is expected to wear their regular footwear and use any mobility aids that they would normally require. The TUG is used frequently in the elderly population, as it is easy to administer and can generally be completed by most older adults.
• Roland Morris Disability Questionnaire (RMDQ) designed to assess self-rated physical disability caused by low back pain.
• Numeric Pain Rating Scale. This is an eleven-point unidimensional measure of pain intensity, which has been widely used in diverse adult populations, ranging from 0-no pain to 10-worst imaginable pain. Participants will be asked to give their average pain score on mobilising.
• Quality of Life as measured by the EQ-5D-3L, a generic quality of life measure used for health economic analysis. Scores range 0 to 1, with 1 indicating perfect health and it also includes a 0 to 100 VAS to assess general health.
• Activities of daily living (ADL) as measured by the Barthel Index. This is an ordinal scale used to measure performance in ADL. Each performance item is rated on this scale with a given number of points assigned to each level or ranking. A higher number is indicative of a greater degree of independence following discharge from hospital .
• Pain medication prescribed*
*Pain medication prescribed: Analgesic consumption will be recorded at each time point. This will include the daily dose of each analgesic. Each medication will be classified as “strong opioid”,

“mild opioid” or “non-narcotic analgesic”. The opioids classified as “strong” include oxycodone, morphine, fentanyl, pethidine, hydromorphone, buprenorphine and tramadol. The opioids classified as “mild” include medications containing codeine or dextropropoxyphene. The non-opioid medications include paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs). The participant will be given a score of 0, 1 or 2 in each of these three analgesic medication categories depending on the number of concurrent different medications being taken within each category. If the participant is taking two different “strong” opioid preparations, for example one prolonged release and another for breakthrough pain, then the score in the strong narcotic category will be 2. If the participant is using one strong opioid medication the score in this category will be 1. If the participant is taking no “mild” narcotics the score in that category is zero. If the participant is taking either paracetamol or an NSAID, then the score in that category will be 1 and if taking both it will be 2. The scores obtained in each of these three categories will be compared between the two groups. In addition the daily opiate dose will be converted into a morphine dose equivalent using the Opioid Dose Equivalence, calculation of oral Morphine Equivalent Daily Dose. The morphine equivalent daily dose at each data point will be compared between the two groups.

TRIAL ASSESSMENT TIME POINTS
Follow up timings will be counted from the time of randomisation. Participants will be followed up face to face at: week 1 (±3 day) and week 12 (±7 days); and with a telephone interview: at week 4(±7 days).
Follow up assessments at each time point will include:
• Participant still living (established by the hospital’s NHS spine portal enquiry).
• Hospital length-of-stay (ascertained by the hospital electronic database, supplemented by review of medical notes by a different member of staff to maintain blinding, if necessary)
• Unplanned hospital re-admission within 28 and 91 days post discharge (ascertained by the hospital electronic database, supplemented by review of medical notes if necessary).

Participant assessments will include:
Face to Face: TUG, RMDQ, Numeric Pain Rating Scale, EQ-5D-3L, Barthel ADL, Pain Medication Prescribed-Telephone visit: RMDQ, Numeric Pain Rating Scale, EQ-5D-3L, Barthel ADL, Pain Medication Prescribed
In addition, at week 12, to inform the definitive economic analysis, the trialists will assess resource use between surgical and non-surgical treatments; the ease of access to information about resource use from routine database systems; and the feasibility of collecting such data.

Surgical resource use will be collected by the RA from the medical notes. The cost associated with the surgery will be based on the recorded resource use for the surgery (e.g. consumables, equipment, grade and number of nursing staff present during the operation). Further health resource information will be extracted by the RA from the hospital electronic system (NotIS) and the GP electronic systems. This will include any outpatient appointment, outpatient procedures, emergency department visits, inpatient admissions related to the study or GP visits during the 12-week follow up period. The unit costs of these resources will be based on information from the following sources: national databases such as the NHS Healthcare Resource Group (HRG) Tariff, the Personal Social Services Research Unit (PSSRU) Costs of Health, the Office of National Statistics (ONS) Bulletin Annual Survey of Hours and Earnings, and NHS Reference Costs (https://www.gov.uk/government/collections/nhs-reference-costs). Any unit cost that is not available will be estimated in consultation with the hospital finance department. Social care costs will be difficult to collect but will be discussed with the participant at the 12-week visit.

A 12 month (±28 days) safety follow up telephone call will also be undertaken for all participants. Complemented by hospital and GP records, this will include:

• Participant still living (established by the hospital's NHS spine portal enquiry).
• Unplanned hospital re-admissions within the last 9 months
• Surgical complications

QUALITATIVE ASSESSMENTS
The study will be complemented by a nested interview study to provide essential insights into the feasibility, design and conduct of a definitive large-scale trial. This will focus on the experiences of participants and clinicians in the study, their insights and their recommendations for improving trial acceptability and processes.
Semi-structured interviews will be undertaken with a purposeful sample of up to 10 participants to explore their views on the trial and recruitment process, the presentation of study information, study documentation and reasons for accepting randomisation. A maximum variation sampling strategy will be employed to ensure we capture a broad range of patients. An interview topic guide will be used to ensure similar areas are covered in each interview and will essential cover questions around: how have they found the study, the good things about the study, the not so good things and what could be done to improve the study.
Interviews will be undertaken face-to-face, in a private space on the hospital ward between day 7 and day 10 following randomisation. It is expected that by this time, the participants will still be in hospital and will have had their surgery (if in the intervention arm or symptoms well controlled if in the non-operative arm). Interviews will last no more than thirty minutes (to minimise disruption to routines) and all interviews will be audio recorded, transcribed in full and anonymised.
These interviews will be followed up by another, but shorter interview, with participants who complete the study, combined with their week 12 data collection follow up visit. The questions will be similar as above.

The trialists will also interview a small number of clinicians (n=5) to explore their experiences of the study. These semi-structured interviews will consider their thoughts about participant recruitment (eligibility and randomisation) as well as reflect upon the process of integrating the research with the clinical team. Interviews will be undertaken face-to-face, in a private office, lasting 15-20 mins. Interviews will be recorded and transcribed in full. All clinicians will be asked to give written, informed consent, using a dedicated clinician interview consent form. The interviews will be audio taped and transcribed.

TRIAL INTERVENTION
Participants will be listed on the rolling trauma list and the surgical procedure will be carried out by an experienced spinal surgeon. The choice of the surgical intervention will be dependent on the participant's general condition, the morphology of the fracture and the surgeon's preference /experience. The intervention will be based on the MRI morphology of the fracture. Additional screw fixation will be offered to participants with extensive fractures.
After appropriate anaesthesia / sedation and antibiotics, the participant will be laid prone on the procedure table. Local anaesthetic (where necessary) will be injected into the skin and subcutaneous tissue down to bone. Based on the planned procedure, unilateral or bilateral 5 mm stab incisions will be created to allow the introduction of the percutaneous needle. An 11-gauge or 13-gauge percutaneous needle will be introduced into back of the pelvis using a short axis technique under fluoroscopic image guidance. Bone cement will then be injected under continuous xray fluoroscopic screening. The objective will be to achieve a maximal fill of the fracture. The injection will be terminated when there is satisfactory distribution of the cement or if there is any cement leak into an adjacent structure. After completing cementation, the percutaneous needles will be retracted, a final antero-posterior X-rays undertaken and the total volume of injected cement documented. Skin sutures will be used to seal the skin incisions and a dressing applied. Where screws are inserted, these will be inserted used a similar technique.

Usual post-operative care and monitoring will follow after the surgery. Participants will be encouraged to mobilise as pain allows and be prescribed analgesia as required.

In the non-surgical group, participants will be commenced on appropriate analgesia, titrated accordingly, as per hospital policy and based on the WHO analgesic ladder (http://www.paineurope.com/tools/who-analgesic-ladder). Participants will be re-assessed daily by the medical team and worsening of initial injury may result in the participant being offered surgery. This will be recorded (reasons for surgical indication) in each case. Participant data will be collected up until the point the decision is made for surgical intervention.
All other standard NHS care – medical, nursing and allied health input, rehabilitation and bone health management will be provided to both groups, including daily assessment by the ward physiotherapist.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Feasibility study primary outcomes:
1. Number of eligible patients
2. Number of patients and doctors willing to be randomised/randomise and adherence to randomisation
Timepoint(s): 12 weeks

Key secondary outcome(s))
1. Rate of participant recruitment and retention
2. Clinician adherence to randomisation
3. Data on the completeness and variability of outcome measures
4. Adverse events and failure of non-operative conservative treatment

Outcomes for the subsequent definitive trial to be tested:

Primary outcome measures:
1. Mobility is measured using the Timed Up and Go Test (TUG) at Week 1
2. Disability is measured using the Roland Morris Disability Questionnaire (RMDQ) at Weeks 1, 4, 12

Secondary outcome measures:
1. Fracture information based on clinical assessment of fracture type (bilateral or unilateral) and suitability for surgery at baseline
2. Surgery details, including information on staffing, length of procedure, intraoperative complications, x-ray usage, per-operative cover, anaesthetic, intervention performed and any adverse events captured in the CRFs and medical notes at Week 0, Day of Surgery
3. Mental capacity is measured using the MoCA at baseline
4. Health status and predictions of mortality are assessed using the Charlson CoMorbidity Assessment at baseline
5. Pain is measured using the Numeric Pain Rating Scale at baseline and Weeks 1, 4, 12
6. Quality of life is measured using the EQ-5D-3L at Week 12
7. Activity level is measured using the Barthel Activities of Daily Living Index at baseline and Weeks 1, 12
8. Analgesia use is measured using information from medical notes during surgery and postoperatively at baseline and Weeks 1, 4, 12

9. Health and social care resource use, measured using health economics questionnaires and qualitative interviews at Week 12

Completion date
01/03/2021

Eligibility

Key inclusion criteria
1. Participants presenting to the Nottingham University Hospital NHS Trust with a Pelvic Fragility Fracture involving fractures at both the front and back of the pelvis
2. Aged 70 years and over
3. Ambulatory with/without walking aids before the injury
4. Injury sustained within 5 days of presenting to hospital

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
9

Key exclusion criteria
1. Complex pelvic fractures (e.g. fractures involving/or close to the hip joint) requiring urgent surgery or progressive weight bearing exercises
2. Pathological fracture in the context of known or unknown malignancy
3. Previous surgery of the pelvis with metal obstructing the planned paths of the iliosacral screws
4. Condition that precludes surgery or general/spinal anaesthesia
5. Bedbound prior injury
6. Receiving palliative care
7. Moribund on admission

Date of first enrolment
01/10/2018

Date of final enrolment
01/08/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queens Medical Centre
Nottingham University Hospitals NHS Trust
HCOP research office, F Floor West Block
Queen's Medical Centre Campus
Derby Road
Nottingham
United Kingdom
NG7 2UH

Sponsor information

Organisation
Nottingham University Hospitals NHS Trust

ROR
https://ror.org/05y3qh794

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-0816-20002

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from:
1. Chief Investigator Prof Opinder Sahota (Opinder.Sahota@nuh.nhs.uk)
2. Leicester Clinical Trials Unit Study Statistician Nishal Bhupendra Jaicim (nbj4@leicester.ac.uk)
3. Leicester Clinical Trials Unit Trial Manager Sarah Edwards (sarah.edwards@leicester.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/05/2022	04/05/2022	Yes	No
Protocol article	protocol	10/07/2019	07/08/2020	Yes	No
Basic results	version 2	03/05/2022	08/06/2022	No	No
HRA research summary			28/06/2023	No	No
Other publications	baseline screening data	25/01/2021	27/04/2022	Yes	No
Other publications	prospective screening results	20/03/2020	27/04/2022	Yes	No
Other publications	qualitative study results	09/07/2021	27/04/2022	Yes	No