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TRAUMA

The Warwick Hip Trauma Evaluation Two – an abridged protocol for the WHiTE Two Study

AN EMBEDDED RANDOMISED TRIAL COMPARING THE DUAL-MOBILITY WITH POLYETHYLENE CUPS IN HIP ARTHROPLASTY FOR FRACTURE

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Fractures of the proximal femur are one of the greatest challenges facing the medical community, constituting a heavy socioeconomic burden worldwide. Controversy exists regarding the optimal treatment for independent patients with displaced intracapsular fractures of the proximal femur. The recognised alternatives are hemiarthroplasty and total hip replacement. At present there is no established standard of care, with both types of arthroplasty being used in many centres. The principal advantages of total hip replacement are a functional benefit over hemiarthroplasty and a reduced risk of revision surgery. The principal criticism is the increased risk of dislocation. We believe that an alternative acetabular component may reduce the risk of dislocation but still provide the functional benefit of total hip replacement in these patients. We therefore propose to investigate the dislocation risk of a dual-mobility acetabular component compared with standard polyethylene component in total hip replacement for independent patients with displaced intracapsular fractures of the proximal femur within the framework of the larger WHiTE (Warwick Hip Trauma Evaluation) Comprehensive Cohort Study.

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Introduction

Fracture of the proximal femur is one of the greatest challenges facing the medical community. In 1990, a global incidence of 1.31 million was reported, associated with 740 000 deaths.[1] Proximal femoral fractures constitute a heavy socioeconomic burden worldwide. The cost of this clinical problem is estimated at 1.75 million disability adjusted life years lost, and 1.4% of the total healthcare burden in established market economies.[1]

The accepted treatment of a displaced intracapsular fracture is an arthroplasty.[2] This includes both hemiarthroplasty (HA), in which the proximal femur is replaced, and total hip replacement (THR), through which both the femur and acetabulum are replaced. Recently, an increasing body of evidence has demonstrated that for selected, comparatively healthy and independent patients, THR offers functional benefit and a reduced risk of revision surgery over HA.[3]

The principal clinical concern with THR is the risk of dislocation. Dislocation often requires inpatient admission for closed reduction and may require revision surgery with its consequent risks. Alternative acetabular components are available with dual-mobility bearing surfaces (THR-DM) that may reduce the risk of dislocation, yet provide the functional benefit of standard THR.[4]

The aim of this trial is to investigate the dislocation risk of a dual-mobility acetabular component compared with a standard polyethylene component in THR for independent patients with displaced intracapsular fractures of the proximal femur.

Patients and Methods

Study design. This will be a single-centre, multi-surgeon, parallel, two-arm, standard-of-care randomised controlled pilot study. It will be embedded within the WHiTE Comprehensive Cohort Study.[5] The study will include a two-way superiority comparison between standard THR and THR-DM.

Ethical approval. This study has been reviewed by the National Research Ethics Service Committee – West Midlands & Coventry (13/WM/0110). The study was given ethical approval on 1 May 2013. The research will be carried out in compliance with the Helsinki Declaration.

Study registration. This study has been registered with the International Standard Randomised Controlled Trial Number Register (ISRCTN90544391).

Study participants. All patients aged ≥ 60 years with an AO/OTA type B3 fracture[6] of the proximal femur are eligible for inclusion in this study. Patients will be excluded if they have chronic cognitive impairment, or in the opinion of the consultant trauma surgeon the patient will not benefit from THR, or are medically unfit for an operation and are treated non-operatively.

Recruitment. Pre-enrolment eligibility checks will be carried out to ensure that participants are not enrolled in error, and informed written consent will be obtained prior to enrolment. Confirmation of these checks will be carried out by the Chief Investigator, or persons designated by the Chief Investigator, before enrolment. Inclusion of the participant in the study will be flagged on their clinical notes by means of a study sticker. An annotation will be made in the participant's medical notes to reflect that the patient has consented to take part in the trial. A copy of the patient information material as well as a copy of the signed consent form will be filed in the patient's notes.

Timeline. Recruitment is planned to commence in May 2013 and last for one year in the first instance.

Consent. The large majority of patients with fracture of the proximal femur are a clinical priority for urgent operative care. They will undergo surgery on the next available trauma operating list. All patients with a fracture of the proximal femur are in pain and have received opiate analgesia. It is therefore understandable that patients find the initial period of their treatment in hospital confusing and disorientating. Similarly, patients' next of kin, carers and friends are anxious at this time and may also have difficulty in weighing the large amounts of information that they are given about the injury and plan for treatment.

In this emergency situation the focus is on obtaining consent for surgery (where possible) and informing the patient and any next of kin about immediate clinical care. It is not possible for the patient/consultee to review trial documentation, weigh the information and communicate an informed decision about whether they would wish to participate.

Conducting research in this 'emergency setting' is regulated by the Mental Capacity Act 2005 (MCA).[7] As patients are likely to lack capacity as described above, and because of the urgent nature of the treatment limiting access to and appropriate discussion with personal consultees, we propose to act in accordance with section 32, subsection 9b of the MCA following a process approved by the relevant research ethics committee. Those patients who have surgery on the next available trauma operating list enter the study under presumed consent; we will not obtain consent prior to surgery but will endeavour to inform an appropriate consultee. Where a Personal Consultee is available, they will be provided with the study information. The Personal Consultee will be given the opportunity to ask questions and discuss the study after which their oral agreement will be recorded.

Due to the urgent nature of the treatment limiting access to and appropriate discussion with Personal Consultees, we will act in accordance with section 32 subsection 9b of the MCA. Where a Personal Consultee is not available then a Nominated Consultee will be identified to advise the research team. The Nominated Consultee will be the patient's treating Trauma and Orthopaedic Surgeon. If that surgeon is a member of the research team, another independent surgeon will be identified.

At the first appropriate time when the patient has regained capacity (this will usually be on the first day after surgery) the research associate will provide the participant with all of the study information. The participant will be given the opportunity to ask questions and discuss the study with their family and carers. They will then be asked to provide written consent for continuation in the study.

Rarely, some patients may be able to consent before their operation, namely those whose surgery has been delayed for clinical reasons. These patients will be approached by the research team before their operation for consent to participate in the study. Some patients, whose surgery has been delayed, may still not have capacity, e.g. those who are acutely confused. If the clinical team in charge of that patients care do not think that the patient is able to provide clinical consent for their operation, then the research team will approach a consultee for agreement that the patient participate in the study. The patient themselves will be approached for consent as soon as the clinical team deem that they have regained capacity following their operation.

For participants who do not regain capacity or lack capacity, reasonable efforts will be made to identify a Personal Consultee as described in the Mental Capacity Act 2005. If no Personal Consultee can be identified then a Nominated Consultee will be identified to advise the research team.

At all times the Chief Investigator will act in accordance with the patients' best interests.

Best efforts will be made to involve participants who, temporarily or permanently, lack capacity in the decision to be involved in the study. The clinical team will make a judgement about the amount and complexity of the information that the participant is able to understand and retain on an individual basis. Appropriate information will be communicated to the participant and updated as their understanding changes.

Any new information that arises during the trial that may affect participants' willingness to take part will be reviewed by the Trial Steering Committee; if necessary this will be communicated to all participants. A revised consent form will be completed if necessary.

Responsibility for recording and dating both oral and written informed consent or agreement will be with the investigator, or persons designated by the investigator, who conducted the informed consent discussion.

Post-recruitment withdrawals and exclusions. Participants may withdraw from the study at any time without prejudice. The General Practitioners of those participants who are 'lost to follow-up' will be contacted in order to attempt to complete the follow-up. Participants may be withdrawn from the study at the discretion of the Chief Investigator due to safety concerns.

Treatment allocation

Sequence generation. The allocation sequence will be generated randomly to achieve a 1:1 ratio using blocks of variable sizes.

Allocation concealment. The allocation will be determined using secure, online randomisation via a distant computer generated system administered by University of York (York, United Kingdom).

Allocation implementation. Participants will be enrolled by the trial research associates. Participants will be assigned to their treatment allocation prior to the time of surgery by accessing the online randomisation programme. This will allow for treatment allocation to be implemented outside of working hours.

Blinding. Participants will be blinded to the treatment allocation. The operating surgeon will not be blinded to the allocation. All clinical outcomes will be assessed by blinded assessors. Patients will be kept blinded until the completion of the trial when the blinding is broken. There will be no formal analysis of the success of the blinding.

Study treatments. Pre-operative assessment, anaesthetic technique and post-operative rehabililtation will be identical to all other participants recruited into the larger WHiTE Comprehensive Cohort Study.[5]

Surgical intervention

Participants who can tolerate penicillins will receive 1 g flucloxacillin and 3 mg/kg to 5 mg/kg gentamicin at induction as an intravenous (IV) infusion over 15 to 30 minutes. Penicillin-sensitive participants will receive teicoplanin 600 mg, or 800 mg if body mass exceeds 80 kg, as an IV bolus and 3 mg/kg to 5 mg/kg gentamicin as an IV infusion over 15 to 30 minutes. Those who have a positive screen for methicillin-resistant *Staphylococcus aureus* (MRSA) will be given the same prophylaxis as those who are penicillin-sensitive.

Participants will be positioned in the lateral position. The operating surgeon will perform their preferred approach. The hip will be dislocated and the head excised. Participants will be randomly allocated to one of two groups: 1) standard bearing THR; or 2) dual-bearing THR.

Group 1: Standard bearing THR. The approach, implant and operative technique employed will be at the discretion of the operating surgeon.

Group 2: Dual-bearing THR. The approach, femoral implant and operative technique employed will be at the discretion of the operating surgeon. An uncemented Novae dual-mobility acetabular component (SERF Dedienne Sante, Lyon, France) will be implanted in accordance with the manufacturer's operative guide.

Follow-up

Schedule. Participant outcomes will be assessed at baseline (pre-injury status recorded upon admission to hospital) and at four, 16 and 52 weeks.

Measures of clinical effectiveness. The primary outcome will be the rate of dislocation. Secondary outcomes will include the EuroQol 5-Dimension (EQ-5D)[8] measure of general health, the ICEpop CAPability measure for Older people (ICECAP(O)),[9] the Oxford hip score (OHS),[10] mortality risk, revision risk and cause, and length of hospital stay.

Health economic measures. The patient-recorded outcome data will be combined with mortality data extracted from the National Hip Fracture Database (NHFD) to estimate a quality-adjusted life year (QALY) profile for each patient. This will allow us to estimate the production of health associated with surgical procedures and treatment pathways for each participant.

Power and sample size

The data to adequately inform a sample size calculation for this study are not available. The limited available evidence suggests a likely dislocation risk of between 5% and 7% in the standard THR group[3] and 1% in the DM-THR group.[4] Based upon the NHFD report,[11] approximately 100 independent patients with AO/OTA B3[6] fractures of the proximal femur are treated operatively per year at University Hospitals Coventry and Warwickshire NHS Trust. The mortality of these patients was 1% at 120 days following the index fracture. Given these likely event risks, a pragmatic sample recruited over one year should provide adequate data to inform a subsequent sample size calculation for a definitive trial.

Statistical analysis

Analysis of clinical effectiveness. The primary outcome measure, the proportion of patients sustaining a dislocation of their arthroplasty within one year of the index fracture, will be analysed using a chi-squared test for differences between standard THR (control) and THR-DM (test) on an intention-to-treat basis. Treatments will be considered to differ significantly if p-values are < 0.05 (5% level). Similarly, chi-squared tests will be used to assess the significance of observed differences for the secondary proportional outcome measures. If the numbers in the contingency tables are small (cells with values < 10) then Fisher's exact test will be used in preference to the chi-squared test. In addition to the main analysis, that will report treatment group effects for the primary outcome measure, a subsidiary analysis will use a multiple linear regression model to investigate the relationship between each patient's EQ-5D score at 12 months and the treatment arm, age, gender and dementia for each patient.

Estimates, and 95% confidence intervals, from the regression model, and unadjusted results from *t*-tests will be reported and inferences made on the significance of the treatment effect. All analyses will be based upon an intention-to-treat analysis so missing data due to protocol violations will not be relevant. The primary outcome measure in this study has been chosen in order to limit the possibility of losing data from failed participant follow-up. The primary measure can be sourced from the patient, relative, General Practitioner or NHFD.

Analysis of cost effectiveness. The economic evaluation will estimate the incremental cost effectiveness of THR-DM and standard THR. The primary outcome will be the quality adjusted life year gained. Health-related quality of life will be estimated using the EQ-5D score. These data will be collected at baseline (pre-injury status), four, 12 and 52 weeks post-injury. Hospital based resource use will be extracted form participants' clinical record. Unit cost data will be obtained from University Hospitals Coventry and Warwickshire NHS Trust. A within trial evaluation will compare the outcomes and cost up to one year post-injury using trial data and index hospital episode data.

Analysis of adverse events. The number and temporal pattern of adverse events will be investigated to assess if these differ between treatment groups.

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- X. L. Griffin: Inception, Design, Writing of the protocol, Guarrantor
- J. McArthur: Preparation of protocol
- J. Achten: Preparation of protocol
- N. Parsons: Writing the paper
- M. L. Costa: Inception

ICMJE Conflict of Interest:

- None declared