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A comparison of patient reported outcome measures following total knee replacement with either the Depuy Synthes Attune™ or Depuy Synthes PFC™ total knee replacement systems: A single blinded randomised controlled trial study protocol

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Abstract

Introduction: Total knee arthroplasty is a successful procedure with excellent clinical outcomes although a 15 % dissatisfaction rate remains. Design differences between knee prostheses continue to be developed in an effort to improve these outcomes. We aimed to design a study to evaluate the effect of these design features on the functional and clinical outcomes following total knee arthroplasty.

Methods: We have designed a single blinded randomised controlled trial to evaluate outcomes comparing two different knee replacement prostheses. We will randomise 150 patients to undergo a total knee replacement with either the DePuy Synthes AttuneTM or the DePuy Synthes PFC SigmaTM cruciate retaining systems. There will be 75 patients in each arm. Preoperative and postoperative patient reported outcome measures (PROMS) data will be recorded together with clinical outcomes including range of movement and complication rates. The primary end point will be functional and clinical outcomes at one year post surgery.

All analyses shall be carried out on an intention to treat basis, retaining patients in their initial treatment groups irrespective of any protocol violations. Missing data are anticipated to be small and primary analysis will be carried out on a complete case basis. All analyses shall be evaluated using a two-sided hypothesis test, assessing all P-value at the 0.05 level with associated 95% confidence intervals.

Ethical approval for the study has been sought and obtained from the NRES Committee North West – Greater Manchester South, UK, Reference 14/NW/1330.

Discussion: This trial will provide a robust assessment of the clinical and functional differences between two types of knee replacement prostheses by utilising a blinded randomised controlled trial with multiple functional and generic outcome measures and close follow up of the patient cohort.

Introduction

Total knee arthroplasty (TKA) is a successful orthopaedic procedure with excellent clinical outcomes and survivorship [1]. There are many different types of knee prostheses utilised in the UK and certain design features vary among implants. For primary TKA, design features vary from cruciate retaining or posterior stabilised, fixed or rotating tibial platforms and in terms of the sagittal radius of curvature of the femoral components.

There are concerns regarding patient satisfaction within the reported literature with some Patient Reported Outcome Measures (PROMS) reporting a dissatisfaction rate of 15% - 30% following TKA [2]. Nam *et al.,* using a new outcomes assessment for TKA, showed whilst 90% of patients were 'satisfied' with the overall function of the knee, only 66% of patients reported their knee to feel 'normal', the incidence of residual pain remained high at 33% and only 47% of patients reported the complete absence of a limp [3]. In attempting to improve outcome following TKA, there is currently a drive from implant manufacturers to change implant design to improve patient outcomes and satisfaction.

The Depuy Synthes PFC Sigma™ Total Knee Replacement system, (Warsaw, Indiana, US), has been used worldwide and has shown to have excellent outcomes and survival [4]. In the 11th Annual report in 2014, the National Joint Registry revealed it was the most widely used TKA system in the UK with excellent 10 year survivorship [5]. This system is a bicondylar total knee replacement system. In it's cruciate retaining system, which is the most widely used design, the femoral component comprises a dual radius design which changes at the transition from the distal portion of component to the posterior condyles.

More recently in 2013, Depuy Synthes launched the Attune™ prosthesis. The most notable difference in the femoral component of this system is a multi-radius transition at the distal component to posterior condyle region. This has been attributed to conferring greater

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mid flexion stability as the implanted knee moves from extension to flexion as a result of the more gradual change in the femoral component radius of curvature [6]. This design feature has also been proposed to offer greater functional benefits and a greater range of movement as compared to other implants.

The objective of this study is to assess for functional differences and clinical outcomes in patients undergoing a Total Knee Arthroplasty with either the PFC Sigma™ or the Attune™ cemented cruciate retaining fixed bearing knee prosthesis with the null hypothesis that there is no difference between the outcomes of either system. The primary outcome measure will be Patient Reported Outcome Measures reported at one year following surgery.

Ethical approval

Ethical approval for the study has been sought and obtained from the NRES Committee North West – Greater Manchester South, UK, Reference 14/NW/1330.

Methods and trial design

The study is designed as a single blinded randomised controlled trial with patients blinded to their treatment arm. Subjects will remain blinded as to their treatment arm for the duration of the trial period which will be 1 year for each subject. The patient population will comprise patients being referred to or currently under review for symptomatic knee osteoarthritis at Wrightington Hospital, United Kingdom.

Patient inclusion and exclusion criteria

The following inclusion criteria have been set to standardise enrolment into the trial and to minimise variability in patient selection which may confound the outcomes of TKA which are being assessed.

Inclusion criteria

1) Male or female sex between 22 and 90 years inclusive

2) A diagnosis of non-inflammatory osteoarthritis of the knee

3) Primary Varus Osteoarthritic deformity

4) Stable Collateral Ligaments at time of pre-operative clinical examination

5) Patient is a candidate for routine primary knee arthroplasty (cruciate retaining) in line with manufacturer guidelines

6) Subject is able to give consent to procedure

Exclusion criteria

1) A patient with a diagnosis of inflammatory Osteoarthritis

2) Severe bone defects or deformity which will require augmentation with bone graft or augmented prosthesis or a constrained device

3) Valgus Osteoarthritis

4) Previous Patellectomy

5) Patient has a contralateral TKR which is a PFC™ or Attune™ implant

6) Patient has a poorly functioning or symptomatic contra-or ipsilateral Total Hip Replacement

7) Previous lower limb amputation on either limb

8) Previous fractures, osteotomy or surgery to the knee which required metal implantation and/or ligament reconstruction.

8) Neurogenic cause for arthritis in knee or associated neurological symptoms in lower limb referred from spine

Patients will be primarily recruited and consented during the clinic consultation. Enrolment and consent to the trial will only be performed by researchers with Good Clinical Practice (GCP) certification. Consent forms and patient information sheets have been devised using departmental guidance and protocols.

Data collection

Both demographic and clinical data will be recorded throughout the trial period. Demographic data will include age, sex, height, weight, body mass index as well as co-morbidities. Clinical data will include implant sizes, wound closure methods, tourniquet time, ASA grade, Hospital Length of Stay, Pre and post operative Haemoglobin and complications including but not limited to infection, deep vein thrombosis and further surgery to the operated or non operated limb within the trial period for any reason will be recorded.

Clinical and functional outcome measures

The outcomes of interest comprise general and disease specific patient reported outcome measures (PROMs). Disease specific scores include the Oxford Knee Score (OKS) [7], the Oxford Knee Score Activity and Participation Questionnaire (OKS-APQ) [8] and the Patient Knee Implant Performance score (PKIP) [9]. The SF-36 [10] and EQ5D – 5L [11] will also be completed as generic health measures.

The pre- and post operative range of movement (ROM) as measured with a goniometer will also be assessed together with Visual Analogue Pain Scores (VAS). Radiological assessment using the Centricity Enterprise™ (GE Healthcare) picture archive and communication system (PACS) will also be utilised to document implant positioning.

Trial packs comprising a pre-operative pack, a 6 week post-operative pack, a 12 week post-operative pack and a 52 week post-operative pack will be devised comprising the relevant outcome measures to allow ease of completion for the subjects (Table 1).

Statistical analysis

Randomisation

Patients will be randomised using sealed envelopes based on lists prepared in advance of the first patient being randomised. Randomisation lists shall be produced by the trial statistician via randomly permuted blocks using the `ralloc' command within the statistical package Stata (Statacorp LP, Texas). No stratification factors are to be included in the study.

Sample size calculation and safety monitoring

The primary endpoint is the difference between pre surgery and 6 week, 3 months and 1 year measurements of the Oxford Knee Score. Previous data give an estimated standard deviation of the change in OKS of 10 points. It is anticipated that a reduction under the control prosthesis will result in a 10 point reduction. A reduction of 5 points is considered a minimum clinically relevant difference.

Based on a two-sided alpha level of 0.05, a total sample size of 150 patients (75 in each treatment arm) are sufficient to obtain a statistical power of 80%. This is inclusive of a 10% patient dropout rate.

Table 1. Illustrates the time periods at which these assessment will be made.

Time point in trial	Assessments recorded
Pre-operative	OKS, OKS-APQ, PKIP, SF-36, EQ5D – 5L, VAS, Pre-operative ROM
Week 6 post-operative	OKS, OKS-APQ, PKIP, EQ5D – 5L, VAS, Post-operative ROM
Week 12 post operative	OKS, OKS-APQ, PKIP, EQ5D – 5L, VAS, Post-operative ROM
Week 52 post operative	OKS, OKS-APQ, PKIP, SF-36, EQ5D – 5L, VAS, Radiological assessment, Post-operative ROM

All analyses shall be carried out on an intention to treat basis, retaining patients in their initial treatment groups irrespective of any protocol violations. Missing data are anticipated to be small and primary analysis will be carried out on a complete case basis. All analyses shall be evaluated using a two-sided hypothesis test, assessing all P-value at the 0.05 level with associated 95% confidence intervals.

The primary endpoint is the difference in the OKS between pre surgery and 6 weeks, 3 months and 1 year following surgery. The primary analysis will be carried out using a t-test to compare the difference in means between the two groups at 3 months. For the binary endpoint of complication rate, the primary analysis shall be carried out using a Chi-Square/Fishers test as appropriate. Further analyses shall be carried out using linear regression techniques adjusting for any key covariates of interest and considering performing surgeon as a random effect.

It is estimated that under standard therapy, 2% of patients will experience some sort of postoperative complication such as ongoing pain, swelling, deep vein thrombosis or superficial or deep infection. Due to the small probabilities, it is difficult to set any formal design criteria based on complication rate. As there is no expected increase in complication a safety analysis shall be carried out on the first 22 patients to be enrolled in the study and have at least 3 months follow up. If 3 or more patients experience an implant related adverse event toxicity, then the trial will be stopped due to an unacceptable complication rate. If the true complication rate is 2% there is a less than 1% chance that 2 of the first 12 patients will observe a complication.

Given the short duration of the trial and the formal stopping rules in terms of complication, it is considered that an independent data and monitoring committee is not required. The progress of the trial will be evaluated by a trial management group who will monitor trial issues such as recruitment, adherence to protocol and complication rate at regular time-points during the trial duration.

Discussion

With rapidly advancing knowledge on the outcomes of TKA and with engineering improvements in the design of implants, many new prostheses continue to be developed and introduced into the orthopaedic community. As a result, surgeons must carefully choose appropriate implants to utilise in patients based on sound clinical trials to not only improve patient care but also to maintain patient safety. Randomised controlled trials (RCT) are considered to be the best form of evidence-based medicine however there is a paucity of these within the orthopaedic literature relating to knee replacement designs and conducting these trials are challenging [12]. One significant barrier to undertaking such trials is the fact that once a new prosthesis is approved by the appropriate regulatory body; either by CE marking in Europe or by the US Food and Drug Administration (Rockville, Maryland); surgeons are then free to use the implant as they see fit with relatively few restrictions [13]. The manufacturers have normally invested significant sums in the development of the implant and are potentially then more likely to want to market the potential advantages rather than risk undermining their own investment with a well designed RCT which could potentially report negative results. This system differs significantly from the pharmaceutical industry whereby new drugs must first undergo safety trials followed by efficacy trials before being launched.

In an effort to tackle the dissatisfaction rate following TKA, a number of implants with design differences have been introduced into the orthopaedic community with only laboratory data being presented to the clinician as to the implants potential success and not clinical/PROMS data obtained through performing clinical trials.

There have been several instances within the orthopaedic community where implants have been introduced and used as part of orthopaedic surgical procedures with detrimental consequences. The recall of the 3M Capital Cemented Hip System (3M Healthcare) due to an high early failure rate of the femoral component lead to a number of hip replacements being revised and was a strong factor behind the development and introduction of the National Joint Registry [14]. In 2010, the Depuy ASR™ Hip Resurfacing and Acetabular XL™ systems were recalled again secondary to an unacceptable high early failure rate [15]. Prior to the introduction of these implant systems there were no clinical trials performed to examine their longer term safety and efficacy.

With the orthopaedic community and implant companies striving to improve outcomes following arthroplasty surgery by introducing new implants and adjusting design features of current implants, clinical trials are of increasing importance to not only ensure the safety of patients but also to provide accurate and longer term data on the longevity and function of the implants. The current study aims to assess for potential functional benefits in total knee arthroplasty using a robust randomised controlled trial and by utilising multiple functional and generic outcome measures with close follow up of the patient cohort.

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Conflict of interest

The authors declare that there is no conflict of interests.

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