

Total versus partial knee replacement in patients with medial compartment knee osteoarthritis: the TOPKAT RCT

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Scientific summary

The TOPKAT RCT

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Scientific summary

Background

Knee replacement for treatment of osteoarthritis of the knee is an effective and common procedure, with > 700,000 procedures performed each year in the USA and 1,076,778 procedures performed in the UK between 2003 and 2017. There are two main surgical options to replace the diseased areas of late-stage medial compartment osteoarthritis of the knee. Some surgeons consider the treatment of choice to be a total knee replacement, whereas others feel that it is best to replace just the damaged component of the knee with a partial or unicompartmental knee replacement. Such variation in decision-making for patients who have similar pathology is well recognised, with high levels of disagreement between surgeons for implant choice. The best treatment option remains uncertain, with little evidence to date to prove the clinical effectiveness and cost-effectiveness of either treatment management option.

The literature to date has consisted of individual cohort studies, indirect comparisons and retrospective studies, which often examine very specific aspects of knee replacement surgery (e.g. complications and the ability to kneel). To our knowledge, no large, well-powered, multicentre randomised controlled trial has been undertaken to directly compare partial knee replacement with total knee replacement. Joint registry data have shown a trend towards total knee replacement having better implant survival, but other studies are characterised by low-level evidence, consensus and peer influence. To provide robust and unbiased estimates of the relative benefits and harms of the procedures and assess cost-effectiveness, a large randomised controlled trial was required.

The trial was required to evaluate clinical effectiveness at the 5-year follow-up, a time point that is considered the minimum for arthroplasty evaluation; however, early reoperation and complications were also considered key to this comparison. Evaluation of 5-year revision was an important aspect of the trial, as it has been implied that partial knee replacement is more technically demanding than total knee replacement, a feature that may contribute to the increased incidence of complications/failure seen in the larger national registry data.

Objectives

The main objective for TOPKAT (Total or Partial Knee Arthroplasty Trial) was to assess the clinical effectiveness and cost-effectiveness of total knee replacement compared with partial (unicompartmental) knee replacement in patients with medial compartment osteoarthritis of the knee in a formal randomised comparison. The primary outcome measure was a patient-reported outcome measure, the Oxford Knee Score. A second research question involved failure of each type of operation in terms of reoperation, revision and a composite outcome measure of the Oxford Knee Score and reoperation. Other objectives included investigation and comparison of post-operation activity levels, complications and patient satisfaction. The findings are intended to guide surgical decision-making for patients, surgeons and health-care providers.

Methods

The study was a multicentre randomised controlled trial of patients who were randomised to either partial knee replacement or total knee replacement. The target sample size was 500 patients. The trial had a combined equipoise/expertise-based approach to randomisation. The expertise-based randomisation enabled surgeons not in equipoise to participate in the trial by working in pairs, each

providing the operation type that they felt was appropriate (as 'experts'). Patients were randomised to the partial knee replacement or the total knee replacement surgeon in the pair. The 'in equipoise'-based randomisation involved surgeons who had sufficient experience of both operation types and who were willing to perform either operation. Minimum levels of expertise were ensured, with all surgeons having had appropriate training in both operations and having performed a minimum of 10 partial knee replacement and 10 total knee replacement procedures. Patients were not blinded to their intervention.

Outcome measures

The trial was designed and powered to examine both self-reported outcome (at 5 years) and complication/reoperation differences between the groups at 5 years. The primary outcome measure was the Oxford Knee Score, a well-validated patient-reported outcome questionnaire that is specifically developed to assess function and pain after knee replacement surgery.

Of the secondary outcome measures recorded, the frequency of complications and failure of operation were considered particularly important to assess differences between the two interventions. Complications were assessed by distinguishing those that required re-admission and reoperation (revision or other related procedure). Failure of intervention was assessed using a prespecified composite outcome assessment (combination of reoperation and poor outcome as defined by Oxford Knee Score); poor outcome was ascribed if the Oxford Knee Score did not improve by > 4 points.

Other secondary measures were:

- The American Knee Society Score at 2 months and 1 year post surgery and 5 years post randomisation. Both clinical assessment and function were recorded.
- The University of California Los Angeles Activity Score at 2 months post surgery and 1–5 years post randomisation.
- The High Activity Arthroplasty Score at 2 months post surgery and 1–5 years post randomisation.
- The EuroQol-5 Dimensions at 2 months (post surgery) and 1–5 years post randomisation.
- Self-reported anchor-type questions about satisfaction, transition in relation to problems, overall health, transition in relation to overall health and reflection on whether or not they would still have the operation again.
- Surgical (intra- and post-operative) complications.
- Health-care and patient resource use (e.g. length of hospital stay at time of operation, 2 months post surgery and 1–5 years post randomisation).
- Reoperation rate following knee replacement surgery, including revision.
- Composite outcome assessment – failure of intervention defined as reoperation (including revision) and/or poor outcome indicated by Oxford Knee Score.
- Oxford Knee Score-Activity and Participation Questionnaire adjunct score to the Oxford Knee Score at years 4 and 5 post randomisation.
- Radiographic imaging of the knee preoperatively, immediately postoperatively and at 5 years post randomisation.

Participants and setting

A total of 528 patients were recruited from 27 UK NHS sites (68 surgeons) from January 2010 to September 2013. Participants had to have osteoarthritis of the medial compartment of the knee and satisfy general requirements for a medial partial knee replacement. Potential participants were identified in outpatient and at pre-assessment clinics by participating surgeons, or were identified from local databases. Participants signed a consent form during their screening visit and were free to withdraw from the study at any time.

Study interventions

The trial was pragmatic and compared partial knee replacement with total knee replacement using any brand or model of implant in common use. For this reason, surgeons were free to use the implant

of their own or their institution's choice. A total knee replacement involved all surfaces of the knee being replaced. The procedure involved excising both diseased and normal femoral condyles, the tibial plateau and often the patella, as well as removing or releasing some of the ligaments. The artificial implant could be cemented in position if desired. A partial knee replacement involved only the diseased area of the joint being replaced. The healthy compartments of the knee and ligaments were retained and artificial implants were inserted in place of the diseased area.

Recruitment and consent

The preoperative (baseline) assessment included the Oxford Knee Score, activity level, health-care resource use and the American Knee Society Score. Routine preoperative X-rays were also performed. Randomisation (which utilised minimisation) used a web-based randomisation service at the Centre for Healthcare Randomised Trials, Health Services Research Unit, University of Aberdeen. The minimisation algorithm incorporated sex, age (< 50, 50–70 or > 70 years) and baseline Oxford Knee Score band (≤ 14 , 15–21 or ≥ 22) and 'delivery unit'. A delivery unit was either an 'equipoise surgeon' or a pair of 'expertise surgeons' who had complementary expertise.

Operative details were recorded in theatre and routine post-operative X-rays were conducted. Patients then attended a clinic for the American Knee Society Score assessment at 2 months, 1 year and 5 years post operation. All other outcomes were collected using postal questionnaires. In cases where there was > 12 weeks between randomisation and the operation date (owing to the waiting list), an additional Oxford Knee Score was administered at the clinical assessment 1 year post surgery.

Statistics and analysis

The sample size was calculated on the Oxford Knee Score and the reoperation rate. Detection of a change in reoperation rate of 7% between groups (from 5% to 12%) at 80% power and using a significance level of $p < 0.05$ (two-sided) required a sample size of 250 patients per group. A total of 250 patients per group also provided 90% power to detect a reoperation increase to 14% (difference of 9%). For the primary end point at 5 years, a sample size of 500 patients (250 in each group) was also required to identify clinically significant differences in Oxford Knee Score. This sample size provided 90% (and 80%) power to detect a mean difference of 3.0 (and 2.0) Oxford Knee Score points at 5% (two-sided) significance level using a standard deviation of 10.0 points.

Statistical analysis was primarily on an 'intention-to-treat' basis and participants were analysed according to their allocated group using all available participant data. Low frequency event data, such as reoperation and revision, were also analysed on an 'as-treated' basis to avoid misrepresentation because of lack of compliance to the allocated intervention (crossover). The Oxford Knee Scores for total knee replacement and partial knee replacement were compared using multiple linear regression analysis adjusted for minimisation factors and baseline Oxford Knee Score and using robust cluster variance to account for surgery delivery unit. Any differential impact of expertise versus equipoise delivery of the intervention on treatment effect was explored using an interaction effect. Prespecified subgroup analyses of sex, Oxford Knee Score band and age were explored using treatment-by-subgroup interactions. Secondary outcomes were analysed using the same approach as the primary outcome within a generalised linear models framework. Binary variables (including complications and reoperations at 5 years) and length of hospital stay (counted in full days) were compared using a Poisson regression to estimate risk ratios adjusted for minimisation covariates with robust cluster variance to account for surgery delivery unit. Statistical significance was judged at the two-sided 5% level and treatment effect estimates are presented with corresponding 95% confidence intervals. Missing effectiveness data were not imputed in the principal analysis. For Oxford Knee Score and EuroQol-5 Dimensions, three-level version, at 1 and 5 years, sensitivity analyses explored the impact of imputing worse case (0 and -0.594, respectively) across both groups and each of the randomised groups in turn.

For the health economics analysis, the total costs and quality-adjusted life-years for all 528 participants were estimated from the date of recruitment until the earliest of death, withdrawal from study or the

end of follow-up at 5 years. Both costs and quality-adjusted life-years were discounted at 3.5% per year. Mean total health-care costs and quality-adjusted life-years were estimated using separate linear regression models controlling for treatment allocation, age group, sex and baseline Oxford Knee Score band, following the main clinical analysis. For quality-adjusted life-years, we also controlled for EuroQol-5 Dimensions score at baseline. Incremental cost-effectiveness ratios were calculated by dividing the mean cost difference between partial knee replacement and total knee replacement by the mean quality-adjusted life-year difference. The joint uncertainty around incremental total costs and quality-adjusted life-years (i.e. the difference between partial knee replacement and total knee replacement) was also investigated. Sensitivity analyses, using a complete-case analysis, were also provided.

Results

In total, 528 patients were randomised and baseline variables between groups were well balanced. A representative range of implants was used in the trial when compared with UK National Joint Registry data. The follow-up primary outcome response rate was 88%. At 5-year follow-up, both operations had good outcomes. Patients in both groups had superior outcome to their preoperative baseline status. The changes in Oxford Knee Score following partial knee replacement and total knee replacement intervention were substantial (mean Oxford Knee Score change greater than 18 points for both procedures).

There was no evidence of difference between groups in the primary outcome of mean Oxford Knee Score at the 5-year time point (difference 1.04, 95% confidence interval -0.42 to 2.50). Although there was no evidence of difference in the primary outcome between groups at the 5-year time point in a cross-sectional and marginal analysis, a post hoc area under the curve analysis of the Oxford Knee Score for the duration of the study did show significant benefit in favour of partial knee replacement over total knee replacement. More patients achieved higher outcome scores after partial knee replacement than other total knee replacement. It should be noted that this difference across operation types was similar and smaller than the minimal clinically important difference of the score [mean 36.6 (standard deviation 8.3), mean 35.1 (standard deviation 9.1), respectively].

Secondary outcome measures showed consistent patterns of benefit for partial knee replacement, although some differences were small and non-significant: Oxford Knee Score-Activity and Participation Questionnaire difference 1.00 (95% confidence interval -3.50 to 5.50), University of California Los Angeles difference 0.17 (95% confidence interval -0.009 to 0.43), EuroQol-5 Dimensions visual analogue score difference 4.0 (95% confidence interval 1.36 to 6.67) and patient satisfaction (82% for partial knee replacement and 77% for total knee replacement). The EuroQol-5 Dimensions visual analogue scale global health instrument revealed significant differences in favour of partial knee replacement. Both transition (problems better now than before operation: partial knee replacement 95% and total knee replacement 90%) and reflection (Would you have the operation again?: partial knee replacement 91% and total knee replacement 84%) were significantly better for partial knee replacement, although both of these variables are potentially susceptible to bias owing to the lack of blinding.

The frequency of reoperation (including revision) by the treatment received was similar in both groups: 22 out of 245 partial knee replacement patients and 28 out of 269 total knee replacement patients. Revision rates at 5 years were 10 out of 245 for partial knee replacement and 8 out of 269 for total knee replacement. There were 28 'failures' of partial knee replacement, as defined by the composite outcome, and 38 'failures' of total knee replacement.

The health economic evaluation found partial knee replacement to be more effective (0.240 quality-adjusted life-years, 95% confidence interval 0.046 to 0.434 quality-adjusted life-years) and to cost less than total knee replacement (£910, 95% confidence interval £317 to £1503) over the 5 years of follow-up. This finding was a result of slightly better outcome (as measured by the EuroQol-5 Dimensions), lower partial knee replacement surgery costs and lower follow-up health-care costs. If cost of the implant devices

is assumed to be equal partial knee replacement remains less costly and more effective than total knee replacement.

Trials are susceptible to interpretation bias, especially if differences are small and investigators have prior preference for a particular intervention. A summary set of blinded results was sent to a group of entirely independent and unconnected assessors (trial experts and surgeons) to help interpret the results and impact of the trial in an unbiased manner.

There are many strengths of this study. To our knowledge, it is the largest randomised controlled trial to date in the world with the longest and most comprehensive follow-up. The study was well powered and the follow-up rates were very high (88%). The pragmatic design, the large number of sites and surgeons and the wide variety of implants used provided high external validity. The inclusion of an expertise component allowed high surgeon participation, regardless of their personal equipoise. Employment of independent assessors to interpret the results helped to neutralise personal and institutional bias.

Limitations included lack of patient blinding and some non-compliance with allocated interventions, although this had little effect on the overall results. Surgeons providing partial knee replacement were all experienced with this procedure.

Conclusions

Both total knee replacement and partial knee replacement are effective, offer similar clinical outcomes and have similar reoperation and complication rates. The revision rates for partial knee replacement in this trial were, however, substantially lower than those found in other studies and in non-randomised cohort data. The reasons require further investigation, one being that TOPKAT involved surgeons who were already experienced at implanting partial knee replacement, leading to a lower revision rate. Several secondary patient-reported measures were significantly higher for partial knee replacement, and partial knee replacement was more cost-effective than total knee replacement at 5 years. Although total knee replacement is safe and adequate, on the basis of the combined clinical and cost-effectiveness results, partial knee replacement shows some advantages over total knee replacement for patients with late-stage medial compartment osteoarthritis.

Clinical impact

Both total knee replacement and partial knee replacement remain treatment options for medial compartment arthritis of the knee. This study has shown that partial knee replacement offers some advantages over total knee replacement. However, the operation should be carried out by those with sufficient experience and expertise, and surgical training programmes should address any unmet need identified by this study.

Future work

Further follow-up is required to assess the longer-term stability of these findings over time (10-year follow-up started in March 2020 and will be completed by October 2023). Further research is also required into the effect of experience and the disparity between trial and cohort data.

Trial registration

This trial is registered as ISRCTN03013488 and ClinicalTrials.gov NCT01352247.

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This report

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