A matched comparison of long term outcomes of total and unicompartmental knee replacements in different ages based on national databases: analysis of data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

Hasan R Mohammad, Alexander D Liddle, Andrew Judge, David W Murray

Qualifications, appointments and roles of the authors

[1, 2] Mr Hasan R Mohammad - MRCS, MRes (Dist), DPhil (Oxon).
Clinical Research Fellow in Orthopaedics.
[3]Mr Alexander D Liddle – DPhil FRCS(Orth). Clinical Senior Lecturer and Consultant Orthopaedic Surgeon.
[1, 2] Professor Andrew Judge – BSc, MSc, PhD. Professor of Translational Statistics.
[1] Professor David W Murray – MD, FRCS. Consultant Orthopaedic Surgeon and Professor of Orthopaedic Surgery.

Institutional address

1. Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences University of Oxford, Nuffield Orthopaedic Centre, Oxford, OX3 7LD, United Kingdom.
2. Musculoskeletal Research Unit, Bristol Medical School, University of Bristol, Level 1 Learning and Research Building, Southmead Hospital, Westbury-on-Trym, Bristol, BS10 5NB, United Kingdom.
3. MSk Lab, Imperial College London, Sir Michael Uren Building, 80 Wood Lane, London W12 0BZ, United Kingdom.

Corresponding author:

Name: Mr Hasan Raza Mohammad

Email: hasanmohammad@doctors.org.uk

Tel: +44 (0) 7841 873 244

Corresponding Author Address: The Botnar Research Centre, Old Road, Oxford, OX3 7LD.

A matched comparison of long term outcomes of total and unicompartmental knee replacements in different ages based on national databases: analysis of data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man

ABSTRACT

Background: The two main treatment options for end stage single compartment knee arthritis are unicompartmental (UKR) or total knee replacement (TKR). We compared the long term outcomes in different age groups.

Methods: 54,215 UKRs and 54,215 TKRs from the National Joint Registry and Hospital Episode Statistics database were propensity score matched and Kaplan-Meier and regression analysis used to compare revision, reoperation, mortality and three month complications.

Results: UKR had higher 10 year (yr) revision rates (12% versus 5%, Hazard Ratio (HR) 2.31, p<0.001) and 10 yr re-operation rates (25% versus 21%, HR 1.12, p<0.001). UKR had lower 10 yr mortality rates (13.6% versus 15.5%, HR of 0.86, p<0.001). UKR had lower rates of medical (p<0.001) and procedure related (p<0.001) complications and deaths (HR 0.61, p=0.02). If 100 patients had a UKR instead of a TKR then over 10 yrs, if they were <55 yr old there would be 7 more re-operations and 1 less death, 55-64 yr 6 more reoperations and 2 more deaths; 65-74 yr 4 more re-operations and 2 less deaths, and ≥75 yr 2 more re-operations and 4 less deaths.

Conclusions: UKR have higher revision and slightly higher re-operation rates but lower mortality rates than matched TKR. The decision to do a UKR should, in part, be based on the balance of these risks, which are influenced by patient age. In the elderly group (>75 yr) the data suggests that UKR compared to TKR have a greater absolute reduction in mortality than the increase in re-operation rate.

Keywords: Age, Revision, Reoperation, Total knee replacement, Unicompartmental knee replacement

Levels of evidence: III

Abstract word count: 246 words

INTRODUCTION

The two main types of knee replacement are total (TKR) and unicompartmental (UKR) [1]. In TKR the whole tibiofemoral articular surface is replaced, whereas in UKR only the affected compartment is replaced. About half of knees needing replacement are appropriate for UKR, yet currently only 10% of knee replacements performed are UKRs [2, 3]. Although there is evidence of UKR having lower levels of early complications, improved function and better cost effectiveness, the long term outcomes have not been compared in different age groups [4-6].

National Registers are one of the best sources of data to assess the risks as they have data on large numbers of cases. National Registers are informed by surgeons every time a knee replacement component is implanted. If new components are implanted in a knee that has previously been replaced Registers define this as a revision and consider it to be a failure. [3, 7, 8]. When assessing risk of surgery, patients need to know all the potential adverse events. These include mortality, medical and implant related complications and all re-operations, not just those defined as revisions such as amputations, internal fixation for fracture, debridement for infection, manipulation under anaesthetic etc,

The aim of this study was to compare the adverse outcomes (revision, reoperation, complications and mortality) of matched TKR and UKR using data from three national datasets: National Joint Registry for England, Wales and Northern Ireland (NJR); Hospital Episodes Statistics Admitted Patient Care records (HES-APC) and Office of National Statistics (ONS).

MATERIAL AND METHODS

Data sources

The NJR was established in April 2003 and is the world's largest arthroplasty register [3]. HES-APC is a database of all admission episodes for patients being admitted to an NHS hospital in England and contains detailed information for every admission (including comorbidities, deprivation indices, ethnicity), and every surgical procedure (including medical complications, reoperations) [9]. Mortality data were provided from the ONS through NHS Digital. Datasets were linked using pseudo anonymised identification numbers with full details presented in the results section. Exclusion criteria included patients under 18 years, incomplete data for matching, patellofemoral replacements, bilateral knee replacements and knee replacements which could not be linked between databases (Figure 1).

Outcomes of interest

Outcomes of interest were: (1) revision rate, (2) reoperation rate, (3) three month HES reported complication rate and (4) mortality rate. Subgroup analyses were performed on patients stratified by age into four groups as per the joint registries; (1) <55 yrs, (2) 55-64 yrs, (3) 65-74 yrs and (4) ≥75 yrs.

Complications were divided into medical complications and procedure complications. Medical complications were defined as a stroke, myocardial infarction (MI), respiratory tract infection (RTI), deep vein thrombosis/pulmonary embolism (DVT/PE), urinary tract infection (UTI), acute renal failure (ARF) or blood transfusion. Procedure complications were defined as wound dehiscence, surgical site infection, fracture, mechanical prosthesis complications and neurovascular injury.

<u>Statistical analysis</u>

There were significant differences in baseline characteristics between TKR and UKR groups (Table 1). To address the problem of confounding [4, 10] we a priori matched the TKR and UKR groups. Logistic regression was used to generate propensity scores, representing the probability that a patient received a UKR. Factors within the model included patient demographics and surgical factors (including surgeon caseload defined as the mean number of cases performed per year, calculated as described previously) [11, 12]. All patient and surgical factors in Table 1 were used for matching, apart from body mass index (BMI), which had a large proportion of missing data. This is a well-recognised approach for comparing implant types [10, 11, 13, 14]. The algorithm used matched 1:1 on the logit of the propensity score with a 0.02- standard deviation (SD) caliper width. We used greedy matching without replacement which has been shown to have superior performance for estimating treatment effects [15]. Standardized mean differences (SMDs) were examined both before and after matching to assess for any covariate imbalance, with SMDs >10% suggestive of covariate imbalance [16]. After matching, 108,430 knee replacements (54,215 TKRs and 54,215 UKRs) were included for analysis.

Cumulative survival was determined using the Kaplan–Meier method. Separate calculations were made for the two ‘implant survival’ endpoints - revision surgery (any implant component removed, exchanged, or added) and reoperation surgery (any additional surgery to the knee joint including revision). The endpoint for patient survival was all-cause mortality. Survival rates were compared, using Cox regression models. If the proportional hazards assumption was violated, survival hazards were analysed in sections, with breaks being placed at the points of divergence from proportionality. To account for clustering within the matched cohort, a robust variance estimator was tested in regression models. A multi-level frailty model sensitivity analysis was performed to control for patient clustering within surgeons, but this did not influence the results. The proportional chi-square test with Yates' correction was used to compare the frequency of revisions for specific indications and three month medical complications.

Risk reduction can be presented in various ways such as relative or absolute risk reduction, or numbers needed to treat [17]. Absolute risk reduction is particularly useful as it is easily understood by patients and clinicians and does not tend to exaggerate differences. We present the absolute risk reduction between comparative groups.

All statistical analyses were performed using Stata (Version 15.1; StataCorp, College Station, TX, USA). P values of <0.05 were considered statistically significant and 95% confidence intervals (CIs) are reported.

RESULTS

Between 1st January 2004 and 31st December 2018 1,186,514 knee replacements were performed. From these 858,725 were linked to the HES admitted patient care records. After removing patellofemoral replacements and missing implant types there were 850,383 knee replacements for analysis. From these 687,910 TKR and 55,248 UKRs had complete sets of data for all patient, surgical and implant confounding factors and were included (Figure 1). There were significant differences in baseline characteristics between the TKR and UKR groups (Table 1). After 1:1 propensity score matching, the study group consisted of 54,215 TKRs and 54,215 UKRs (Table 1). The mean follow-up for both groups were 7 yrs (SD 3.7).

Revision endpoint

In the TKR group there were 1,842 revisions at mean of 3.7 yrs (SD 3.0) postoperatively and in the UKR group there were 4,034 revisions at a mean of 4.1 yrs (SD 3.2). 10 yr survival for TKR and UKR at 10 yrs were 95.1% (CI 94.8-95.4) and 87.9% (CI 87.5-88.3) respectively. The absolute difference in revision rate at ten yrs was 7.2%. The Hazard Ratio (HR) for revision from 0-10 yrs was 2.31 (CI 2.19-2.45, $p<0{\cdot}001$). The HR changed with time (Figure 2A) but the rate of survival of TKR was superior at all time points. Between 0-2 yrs the HR was 1.99 (CI 1.82-2.18, $p<0.001$) and between 2-10 yrs was 2.54 (CI 2.36-2.73, $p<0.001$). The revision indications are summarised in Table 2.

Reoperation endpoint

In the TKR group there were 8,491 reoperations at a mean of 2.6 yrs (SD 2.9) postoperatively. In the UKR group there 9,277 reoperations at a mean of 3.2 yrs (SD 3.0) postoperatively. 10 yr survival was 79.3% (CI 78.9-79.8) for TKR and 74.6% (CI 74.1-75.1) for UKR. The absolute difference in the rate of reoperation ten yrs was 4.7%. The overall HR for reoperation from 0-10 yrs was 1.12 (CI 1.08 to 1.15, p<0.001). The HR for reoperation varied with time (Figure 2B). In the first two UKR was superior with a HR of 0.90 (CI 0.86-0.94, p<0.001). From 2 to 10 yrs TKR was superior with a HR of 1.47 (CI 1.40-1.53, p<0.001).

<u>Three month complications</u>

Complication risk following surgery were significantly (p<0.001) lower for UKR (2.97% n=1,611) than for TKR (4.77%, n=2,587). The absolute difference was 1.8%. Medical complications were significantly lower following UKR (3.08% vs 1.86%, p<0·001). The rates of RTI, DVT/PE, UTI, ARF and blood transfusion were significantly lower for UKR (Table 3). Procedure-related complications were significantly lower following UKR (1.83% vs 1.16%, p<0.001). The rates of wound dehiscence, surgical site infection and mechanical prosthesis complication were all significantly lower for UKR. The rate of fracture was significantly higher for UKR.

<u>Mortality</u>

In the TKR group there were 5,808 deaths at a mean of 6.6 yrs (SD 3.5) postoperatively and in the UKR group there were 4,859 deaths at a mean of 6.7 yrs (SD 3.6). At all-time points postoperatively the HR was below one showing that the death rates following UKR were less than following TKR. However over time the effect size decreased reflecting the decreasing influence of the surgery over time (Table 4). The 30 day mortality was 0.07% and 0.03% in the TKR and UKR groups, respectively giving a HR of 0.38 (p=0.002, Figure 2C). The 90 day mortality was 0.12% and 0.07% with a HR of 0.61 (p=0.02, Figure 2C). At 1 yr the mortality was 0.44% and 0.33% with a HR of 0.77 (p=0.007). The 5 yr mortality rates were 4.7% and 4.0% with a HR of 0.84 (p<0.001). At 10 yrs the mortality rates were 15.5% and

13.6% with a HR of 0.86 ($p<0.001$). The 10 yr patient survival following TKR was 84.5% (CI 84.1 to 85.0) and following UKR was 86.4% (CI 86.0 to 86.8) (Figure 2D). The absolute difference in 10 yr patient survival was 1.9%.

<u>Effect of age on revision, reoperation, non-revision reoperation and mortality</u>

For both TKR and UKR the 10 yr implant survival (revision and reoperation endpoint) improved with increasing age. The numbers in each age group are summarised in Table 5. There was a significant interaction between age and risk of revision ($p<0.02$). With increasing age groups the relative risk of revision surgery for UKR increased compared to TKR as evidenced by the increased HRs (Table 6). In contrast with increasing age the absolute difference in risk of revision surgery for UKR compared to TKR progressively decreased from 9.8% for <55 yrs to 4.6% for ≥75 yrs. There was no significant interaction between age and reoperation (p=0·10). However with increasing age, as the overall re-operation rate decreased (Table 6), the absolute difference in risk of reoperation for UKR compared to TKR progressively decreased from 6.6% for <55 yrs to 2.4% for ≥75 yrs.

Patient survival worsened with increasing age. There was a significant interaction between age and mortality risk ($p<0.001$). In all age groups the mortality risk was significantly lower following UKR. However with increasing age groups the magnitude of this reduction decreased evidenced by the decreasing effect size (Table 6). In contrast with increasing age the absolute difference in mortality for TKR compared to UKR progressively increased from 1.2% for <55 yrs to 3.9% for ≥75 yrs

Complication rate increased with increasing age. For TKR it increased from 4.3% for <55 yrs to 7.4% for ≥75 yrs. For UKR it increased from 2.3% for <55 yrs to 5.3% for ≥75 yrs. In all age groups the overall complication rate was significantly lower for UKR than TKR. The absolute difference in rates in each age group were similar and ranged from 1.7% to 2.1%. The rate of medical complications was significantly lower for UKR in all age groups. The rate of implant complications was also significantly lower for UKR in all groups except the ≥75 yrs group where no difference was observed (Table 7).

Figure 3 summarises the absolute difference in risks in different age groups. With increasing age, over the ten yr period, the absolute number of excess revisions and re-operations related to the change from TKR to UKR decreased, whereas the absolute number of deaths avoided increased. The decreased rate of 3 month complications associated with UKR increased slightly with increasing age.

DISCUSSION

This study shows at 10 yrs UKR has a significantly higher risk of revision and re-operation than matched TKR. However the increase in risk of re-operation was small (1.1 times) was much less than the increased risk of revision (2.3 times). Whilst revision is important, reoperations are a more patient relevant outcome. In contrast the rate of mortality and complication rate following UKR is lower than that of TKR. The benefits and risks of both procedures change profoundly with age.

Most surgeons feel that in the elderly, the most reliable solution for severe knee arthritis is TKR as, due to the patients limited life expectancy, they will not need a revision. As a result almost all elderly patients are treated with TKR and only 4.2% of knee replacements in patients older than 75 yrs being a UKR [3] which may be misguided (Figure 3). In patients over 75 yrs at 10 yrs although the TKR revision rate is low (2.2%) but the reoperation rate is appreciably higher (13%). In the elderly (>75 yr) the analysis suggests that the UKR compared to TKR have a greater absolute reduction in mortality (3.9%) than the increase in re-operation rate (2.4%). Furthermore the incidence of early complications was 2% lower with UKR compared to TKR. These findings, if generalisable, would suggest that in elderly patients UKR should be used whenever the indications are satisfied. In this age group approximately 36% of knee replacements are appropriate for UKR [18] so approximately ten times as many UKRs could be done.

The situation is different in younger patients. As the overall death rate is so much lower in the young than the old, the difference between the death rate following UKR and TKR was also much smaller. At ten years the absolute death rate of the UKR group was 1.2% less than that of the TKR group. A difference of this magnitude may still be of importance to young patients and might outweigh the 6.6% increased absolute risk of re-operation (Figure 3). In these young patients, whether they have had a TKR or a UKR, the chance of having a reoperation (31% or 37% respectively) or revision (9% or 20%) is high. However re-operations and particularly the revisions are likely to be more major operations after TKR than UKR. In particular most UKR revisions tend to be conversions to TKR so UKR are delaying the need for a TKR [4].

In making the decision whether to have a UKR or TKR patients in intermediate age groups, 55-64 and 65-74 yrs old, need to balance the risks. The UKR group, compared to the TKR group, had an increased absolute risk at ten years of having a re-operation (5.7% and 3.6%) a decreased absolute risk of dying (1.7% and 2.2%), and a decreased absolute risk of having an early complication (1.71% and 1.79%).

The death rate following TKR during the first month after the operation is 2.6 times higher than after UKR and during the first three months is 1.6 times higher. These findings are supported by previous studies [4, 19] and may be explained by the higher risk of early medical complications. TKR is a bigger operation with larger incisions with more tissue damage and removal. During the first 10 yrs the death rate after TKR is 1.2 times higher than after UKR. The difference decreases with time and by 8 to 10 yrs it is no longer significant. This suggests that the operation has an effect on mortality for an extended period. This may be because post-operative medical complications can cause permanent damage and result in longer term mortality. Another possible explanation is that as the function following UKR is better than after TKR [20], UKR patients do more exercise which will improve general health and decrease mortality.

The strengths of this study are that it is an unselected registry sample recruited over an extended period. By linking the NJR and HES-APC datasets various clinical outcomes were assessed with adequate power and follow up. Additionally the propensity matching allowed for a fair comparison of cohorts and helped address risks of confounding factors.

The main study limitations are those of all matched studies based on National data sets. Firstly as, it is retrospective and is based on observational data, any associations found do not imply causation. Secondly propensity matching only helps to control for identified predictors and does not help reduce the risk of confounding from unmeasured variables. For example uncaptured patient variables, such as frailty, nutrition, baseline activity levels, compliance may at least partly explain the observed differences in mortality, revision, re-operation and complications.

Other limitations are that matching can reduce the generalisability of findings, however as we were able to match almost all the UKRs to TKRs this is unlikely to be an issue. The only way to achieve balance with respect to both known and unknown confounders is with a randomised trial but this would require impractically large numbers and follow up. Another limitation is the lack of radiographic data, so we do not know if knees treated with TKR could have been treated with a UKR. There was a significant proportion of missing BMI data preventing matching on this variable, however the BMI was well balanced between groups. However the missing BMI remains a limitation.

CONCLUSIONS

In conclusion at ten years, UKR had higher overall revision rates and slightly higher reoperation rates but lower mortality and complication rates than matched TKR. These rates varied in different age groups. About half of knees needing replacement could potentially be treated by UKR. If 100 knees due to have a TKR had a UKR instead then the analysis suggests that over ten years, for <55 years old there would be 7 more re-operations and 1 fewer death, 55-64 years 6 more reoperations and 2 fewer deaths; 65-74 years 4 more re-operations and 2 fewer deaths, ≥ 75 years 2 more re-operations and 4 fewer deaths. However like all matched studies based on national datasets there is the limitation that associations do not imply causation and residual unmeasured confounders may have influenced the results.

LIST OF FIGURES

Figure 1. Data flowchart of dataset cleaning and merging

Figure 2. Kaplan Meier graph comparing TKR and UKR survival: (A) revision endpoint, (B) reoperation endpoint, (C) mortality endpoint to 1 year and (D) mortality endpoint to 10 years.

Figure 3. Bar chart showing the absolute increase or decrease in 10 year re-operations, 10 year mortality and 3 month complications if 100 patients in each age group had a UKR instead of a TKR

LIST OF TABLES

ACKNOWLEDGEMENTS

We thank the patients and staff of all the hospitals in England, Wales, Northern Ireland and Isle of Man who have contributed data to the National Joint Registry. We are grateful to the Healthcare Quality Improvement Partnership (HQIP), the NJR Research Sub-committee and staff at the NJR Centre for facilitating this work. The authors have conformed to the NJR's standard protocol for data access and publication. The views expressed represent those of the authors and do not necessarily reflect those of the National Joint Registry Steering Committee or the Healthcare Quality Improvement Partnership (HQIP) who do not vouch for how the information is presented. During the conduct of the study HRM was supported by the Henni Mester scholarship from the University of Oxford and research fellowship from the Royal College of Surgeons of England.

REFERENCES

1. Price AJ, Alvand A, Troelsen A, Katz JN, Hooper G, Gray A, Carr A, Beard D. Knee replacement. Lancet 392(10158): 1672, 2018
2. Willis-Owen CA, Brust K, Alsop H, Miraldo M, Cobb J. Unicondylar knee arthroplasty in the UK National Health Service: an analysis of candidacy, outcome and cost efficacy. Knee 16(6): 473, 2009
3. National Joint Registry. National Joint Registry 15th Annual Report. National joint registry for England, Wales, Northern Ireland and Isle of Man. 2018
4. Liddle AD, Judge A, Pandit H, Murray DW. Adverse outcomes after total and unicompartmental knee replacement in 101 330 matched patients: a study of data from the National Joint Registry for England and Wales. Lancet 384(9952): 1437, 2014
5. Liddle A, Pandit H, Judge A, Murray D. Patient-reported outcomes after total and unicompartmental knee arthroplasty: a study of 14 076 matched patients from the National Joint Registry for England and Wales. Bone Joint J 97(6): 793, 2015
6. Burn E, Liddle AD, Hamilton TW, Judge A, Pandit HG, Murray DW, Pinedo-Villanueva R. Cost-effectiveness of unicompartmental compared with total knee replacement: a population-based study using data from the National Joint Registry for England and Wales. BMJ Open 8(4): e020977, 2018
7. Australian Orthopaedic Association. Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR). Hip, Knee & Shoulder Arthroplasty. 2019
8. The New Zealand Joint Registry. Twenty Year Report January 1999 to December 2018. New Zealand Joint Registry 2019
9. NHS Digital. Hospital Admitted Patient Care Activity 2019-20. In.: NHS Digital Accessed [4/10/2020]. 2020
10. Mohammad HR, Matharu GS, Judge A, Murray DW. Comparison of the 10-year outcomes of cemented and cementless unicompartmental knee replacements: data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. Acta Orthop 91(1): 76, 2020
11. Mohammad HR, Matharu GS, Judge A, Murray DW. The Effect of Surgeon Caseload on the Relative Revision Rate of Cemented and Cementless Unicompartmental Knee Replacements: An Analysis from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man. J Bone Joint Surg Am, 2020
12. Liddle AD, Pandit H, Judge A, Murray DW. Effect of surgical caseload on revision rate following total and unicompartmental knee replacement. J Bone Surg Am 98(1): 1, 2016
13. Matharu GS, Judge A, Murray DW, Pandit HG. Trabecular metal acetabular components reduce the risk of revision following primary total hip arthroplasty: A propensity score matched study from the National Joint Registry for England and Wales. J Arthroplasty, 2017
14. Matharu GS, Judge A, Murray DW, Pandit HG. Outcomes after metal-on-metal hip revision surgery depend on the reason for failure: a propensity score-matched study. Clin Orthop Relat Res 476(2): 245, 2018
15. Austin PC. Some methods of propensity-score matching had superior performance to others: results of an empirical investigation and Monte Carlo simulations. Biom J 51(1): 171, 2009
16. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 28(25): 3083, 2009
17. Ahmed H, Naik G, Willoughby H, Edwards AG. Communicating risk. BMJ 344, 2012

18. Kennedy JA, Mellon SJ, Lombardi AV, Berend KR, Hamilton TW, Murray DW. Candidacy for medial unicompartmental knee replacement declines with age. Orthop Traumatol Res 2020
19. Hunt LP, Blom AW, Matharu GS, Kunutsor SK, Beswick AD, Wilkinson JM, Whitehouse MR. Patients Receiving a Primary Unicompartmental Knee Replacement Have a Higher Risk of Revision but a Lower Risk of Mortality Than Predicted Had They Received a Total Knee Replacement: Data From the National Joint Registry for England, Wales, Northern Ireland, and the Isle of Man. J Arthroplasty, 2020
20. Wilson HA, Middleton R, Abram SG, Smith S, Alvand A, Jackson WF, Bottomley N, Hopewell S, Price AJ. Patient relevant outcomes of unicompartmental versus total knee replacement: systematic review and meta-analysis. BMJ 364, 2019