■ KNEE

Predictors of mortality after total knee replacement

A TEN-YEAR SURVIVORSHIP ANALYSIS

N. D. Clement,
P. J. Jenkins,
I. J. Brenkel,
P. Walmsley

From Queen Margaret Hospital, Dunfermline, United Kingdom

We report the general mortality rate after total knee replacement and identify independent predictors of survival. We studied 2428 patients: there were 1127 men (46%) and 1301 (54%) women with a mean age of 69.3 years (28 to 94). Patients were allocated a predicted life expectancy based on their age and gender.

There were 223 deaths during the study period. This represented an overall survivorship of 99% (95% confidence interval (CI) 98 to 99) at one year, 90% (95% CI 89 to 92) at five years, and 84% (95% CI 82 to 86) at ten years. There was no difference in survival by gender. A greater mortality rate was associated with increasing age ($p < 0.001$), American Society of Anesthesiologists (ASA) grade ($p < 0.001$), smoking ($p < 0.001$), body mass index (BMI) < 20 kg/m^2 ($p < 0.001$) and rheumatoid arthritis ($p < 0.001$). Multivariate modelling confirmed the independent effect of age, ASA grade, BMI, and rheumatoid disease on mortality. Based on the predicted average mortality, 114 patients were predicted to have died, whereas 217 actually died. This resulted in an overall excess standardised mortality ratio of 1.90. Patient mortality after TKR is predicted by their demographics: these could be used to assign an individual mortality risk after surgery.

More than 55 000 total knee replacements (TKRs) are performed each year in the United Kingdom.[1] However, there are life-threatening risks associated with TKR, including infection, pulmonary embolism, and myocardial infarction.[2]

The reported mortality rate after TKR ranges from 0.21% at 30 days[3] to 35.6% at nine years.[4] The 90-day mortality is reported as being between 0.38% and 0.64%.[5,6] Parry, Smith and Blom[6] recently showed that this early mortality represents an increased risk of death when compared with a matched population (odds ratio (OR) 2.1). The medium-term survival of patients after TKR, however, is better than that of the general population.[7]

Increasing age has been shown to be associated with an increased early mortality rate after TKR when compared to that of the general population[7]: however, no difference in mortality rate was seen when patients who had undergone TKR were compared with a matched cohort awaiting TKR for osteoarthritis.[6]

The long-term mortality after TKR is unclear. A single study has reported an increased mortality for patients with rheumatoid disease when compared with those with osteoarthritis, however other confounding factors were not considered.[4] We are not aware of any study which has assessed other confounding variables, either modifiable or non-modifiable, to predict survival after TKR.

This prospective study establishes the overall mortality rate from TKR up to ten years post-operatively and identifies independent predictors of survival. We discuss the clinical implications of these predictors and potential strategies for avoiding adverse outcomes.

Patients and Methods

All patients from a district general hospital with a catchment population of 360 000[8] who underwent a primary TKR between January 1998 and September 2010 were prospectively entered into a database. A dedicated research nurse collected their demographic details, which included: age at time of replacement, gender, American Society of Anesthesiologists (ASA) grade,[9] body mass index (BMI), smoking status, and type of arthritis. The patients were followed up at 18 months, five years, and ten years with clinical and radiological assessment. If a patient underwent a revision within the study period it was recorded in the database.

A cemented Press-Fit Condylar Sigma TKR (PFC-Sigma; DePuy International Ltd, Leeds, United Kingdom) was used in each case.

■ N. D. Clement, MRCSEd, SORT-IT Research Fellow
■ P. J. Jenkins, MRCSEd, Speciality Registrar
Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA, UK.

■ I. J. Brenkel, FRCSEd , Consultant Orthopaedic Surgeon
■ P. Walmsley, FRCSEd(Tr & Orth), Consultant Orthopaedic Surgeon
Queen Margaret Hospital, Department of Orthopaedics and Trauma, Whitefield Road, Dunfermline KY12 0SU, UK.

Correspondence should be sent to Mr N. D. Clement; e-mail: nickclement@doctors.org.uk

doi:10.1302/0301-620X.94B2.28114 $2.00

J Bone Joint Surg Br 2012;94-B:200–4.
Received 7 August 2011; Accepted after revision 19 October 2011

Table I. Cumulative survival proportions at five years and ten years (Kaplan-Meier) with p-value for log-rank comparison of survival curves (CI, confidence interval)

	Kaplan-Meier survival (95% CI)		p-value (log-rank)
	Five-year	Ten-year	
Overall	90 (89 to 92)	84 (86 to 92)	
Gender			
Male (n = 1127)	91 (89 to 93)	84 (87 to 91)	0.765
Female (n = 1301)	90 (88 to 92)	84 (81 to 87)	
Age group (yrs)			
< 60 (n = 354)	98 (96 to 99)	95 (91 to 98)	< 0.001
60 to 69 (n = 788)	94 (92 to 96)	89 (86 to 92)	
70 to 79 (n = 961)	89 (87 to 91)	82 (79 to 86)	
80 to 89 (n = 297)	76 (70 to 82)	57 (44 to 70)	
≥ 90 (n = 9)	61 (17 to 100)	61 (17 to 100)	
N/A* (n = 19)			
ASA† grade			
1 (n = 163)	96 (93 to 99)	96 (93 to 99)	< 0.001
2 (n = 1113)	93 (91 to 94)	90 (88 to 93)	
3 (n = 436)	85 (81 to 89)	78 (73 to 83)	
4 (n = 5)	75 (33 to 100)	75 (33 to 100)	
N/A* (n = 717)			
BMI‡ group (kg/m^2)			
< 20 (n = 26)	72 (55 to 90)	72 (55 to 90)	< 0.001
20 to 35 (n = 1917)	90 (88 to 92)	83 (80 to 85)	
> 35 (n = 445)	95 (92 to 97)	92 (87 to 96)	
N/A* (n = 40)			
Smoking			
No (n = 2060)	96 (94 to 98)	95 (91 to 98)	< 0.001
Yes (n = 366)	90 (82 to 98)	82 (71 to 93)	
N/A* (n = 2)			
Diagnosis			
Rheumatoid arthritis (n = 100)	79 (71 to 87)	75 (65 to 85)	0.009
Other (n = 2328)	91 (89 to 93)	86 (84 to 88)	

* N/A, information not available
† ASA, American Society of Anesthesiologists
‡ BMI, body mass index

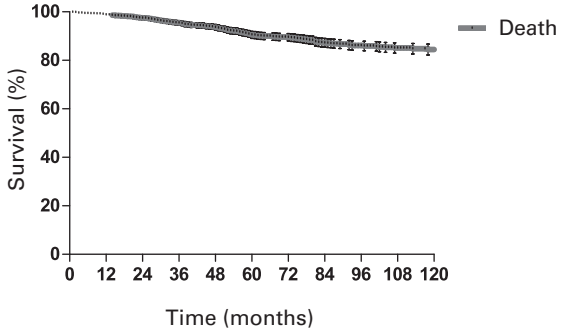

Fig. 1
Kaplan-Meier survival curve for all patients.

Patellar resurfacing was not routinely performed. Each procedure was performed by, or under the supervision of, a consultant surgeon. Prophylactic intravenous antibiotics were administered before the application of the tourniquet and, in all routine cases, low-molecular-weight heparin was given as prophylaxis for deep-vein thrombosis. From 2004 onwards, Fondaparinux (GlaxoSmithKline PLC, Brentford, United Kingdom) was used in high-risk patients.

During the study period, 2428 patients underwent a TKR of whom 571 had bilateral procedures. There were 1127 men (46%) and 1301 (54%) women with a mean age of 69.3 years (28 to 94) and a mean BMI of 30.4 kg/m^2 (15.7 to 60.8). In the bilateral group, 424 patients had a staged procedure and 147 had the procedures performed simultaneously.

Statistical analysis. Patients were allocated a predicted life expectancy based on their age (rounded to the nearest five-year group) and gender.[10] The time from their TKR was calculated. If this exceeded their predicted life expectancy the patient was marked as an expected death. Expected death compared with actual death was compared with the construction of a two-by-two table and chi-squared test.

Kaplan-Meier methodology was used to investigate survival.[11] Patients reaching the end of their period of follow-up were censored, and deaths were recorded as the primary endpoint. When a patient was censored the total number of patients at risk fell by one. When a patient died, the mortality proportion of those at risk was calculated as a simple proportion and added to the cumulative mortality proportion (hazard proportion). Survival curves were plotted with (1 – cumulative mortality) against time. Censored patients were recorded on the graph with a black symbol, while a death was represented by a stepwise fall in the survival curve. Survival curves were compared for the variables gender, ASA score, BMI, age group, rheumatoid or osteoarthritis and smoking status, and tested for significance using the log-rank test. A p-value < 0.05 was accepted as showing a significant difference between comparison groups. A Cox proportional hazards model was used to examine the independent effects of these variables on mortality over time while controlling for age and gender. An 'enter' methodology was used and no variable selection algorithms were used. Age and BMI were entered as continuous variables: dummy variables were created for ASA grades 2, 3 and 4 to determine the relative odds of death in each group when compared with ASA grade 1. The odds ratio for each categorical variable is reported relative to a base value (ASA 1, absence of disease). Where a continuous variable is assessed, the OR represents the change based on a one unit change in the underlying variable.

Results

There were 223 deaths during the study period. Of the 2205 patients who survived, 274 were available for follow-up after ten years. This represents an overall survivorship

Table II. Cox proportional hazard model for death following total knee replacement showing higher age, lower body mass index, smoking status, rheumatoid arthritis and American Society of Anesthesiologists (ASA) grade 3 were independent predictors of death

Variable	Odds ratio (95% confidence interval)	p-value
Gender		
Male	1.00	
Female	0.82 (0.63 to 1.06)	0.131
Age	1.08 (1.06 to 1.10)	< 0.001
Body mass index	0.97 (0.94 to 1.00)	0.023
Smoking status		
Never smoked	1.00	
Current or ex-smoker	3.08 (2.21 to 4.29)	< 0.001
Pathology		
Any other pathology	1.00	
Rheumatoid arthritis	2.02 (1.24 to 3.29)	0.005
ASA grade		
1	1.00	
2	0.93 (0.64 to 1.36)	0.702
3	2.15 (1.47 to 3.16)	< 0.001
4	1.26 (0.17 to 9.20)	0.817

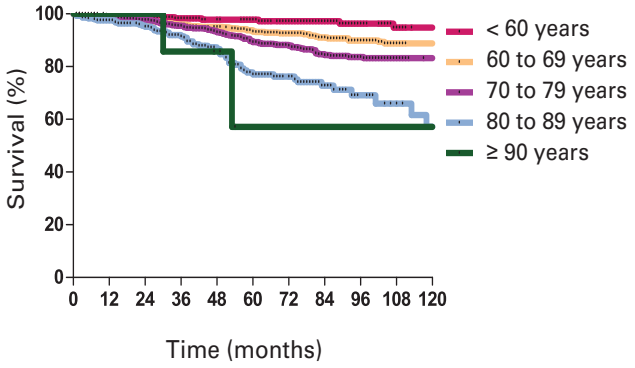

Fig. 2

Kaplan-Meier survival curve by age group.

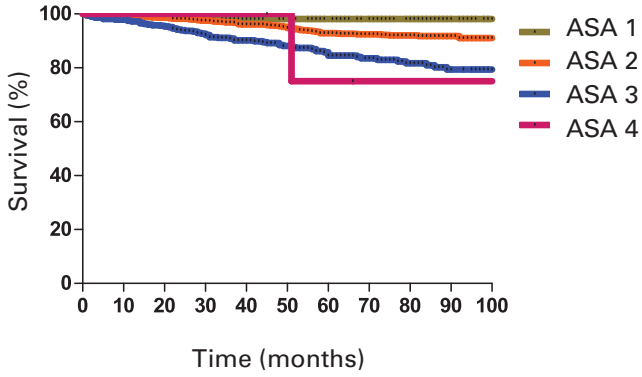

Fig. 3

Kaplan-Meier survival curve by American Society of Anesthesiologists (ASA) grade.

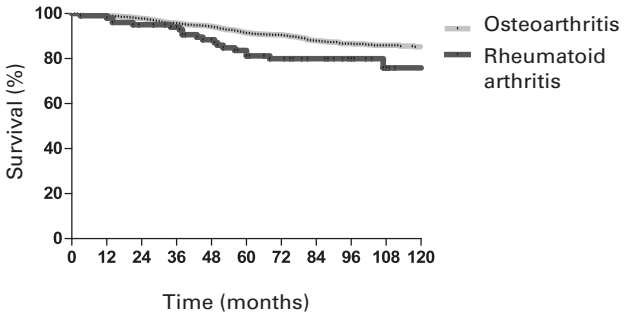

Fig. 4

Kaplan-Meier survival curve by osteoarthritis and rheumatoid arthritis.

of 99% (95% confidence interval (CI) 98 to 99) at one year, 90% (95% CI 89 to 92) at five years, and 84% (95% CI 82 to 86) at ten years (Fig. 1).

Table I illustrates the five and ten-year survivorship by patient demographics. There was no difference in survival by gender (log-rank test, p = 0.765) and survival was not related to whether patients had undergone simultaneous bilateral (p = 0.112) or sequential bilateral TKR (p = 0.077). There was a difference in survival based on age (p < 0.001) and ASA grade (log-rank, p < 0.001): increasing age and ASA grade were associated with poorer survival (Figs 2 and 3). Those patients with a history of smoking were at an increased risk of dying (90% *versus* 75% at ten years; log-rank, p < 0.001). A higher mortality rate was observed in those patients with a BMI of < 20 kg/m^2 (log-rank, p < 0.001). Patients with rheumatoid arthritis were more likely to die post-operatively than those with osteoarthritis (log-rank, p < 0.001) (Fig. 4). Multivariate modelling confirmed the independent effect of age, ASA grade, BMI, and rheumatoid disease on mortality (Table II).

On the basis of the mean predicted mortality, 114 patients were predicted to have died, whereas 217 actually died, although some deaths were not included as there are no predicted life expectancies for patients > 85 years of age (n = 28). In the expected death group, 41 (36%) of 114 patients died, compared with 176 (7.7%) in the group not expected to die. This resulted in an overall increased standardised mortality ratio of 1.90, with an excess mortality rate for the TKR patients compared with their predicted mortality rate (4.8% *versus* 9.0%; OR 2.0, p < 0.0001).

Discussion

This study has identified isolated predictors of mortality after TKR. Our observed unadjusted mortality rate after TKR is comparable to that cited in other survivorship

studies.[7,12] We have also demonstrated that smoking, a diagnosis of rheumatoid arthritis, increasing age, BMI and ASA grade are isolated predictors of mortality. Using these variables it should be statistically possible to predict the mortality rate of patients after TKR in the short, medium and long term. Unlike previous studies we have also demonstrated an excess mortality for those patients undergoing a TKR, which was nearly double the predicted rate.

The short- and medium-term survival of our group of patients were similar to that of other published studies.[4,7,12] However, the long-term survival rate we observed at ten years was greater than that predicted by previous studies.[4,7,12] This may be explained by the variation in case-mix between the patients in previous studies and those in our cohort. Ohzawa et al[4] observed a 64.4% survival rate at nine years, but this substantially poorer survival was because 60% of their patients had rheumatoid arthritis. They identified a 57.2% mortality rate at nine years for rheumatoid patients as opposed to 96% for patients with osteoarthritis. Our study supports this finding, as we have shown that rheumatoid arthritis is an independent predictor of mortality. Robertsson et al[12] showed a 68% survival rate, ten years after TKR, using data from the Swedish arthroplasty register. They noted that younger patients (< 55 years) were at an increased risk of dying and that older patients (> 70 years) were at a lesser risk of dying, than the standard population. They identified a 68% ten-year survivorship, 16% lower than our ten-year survival rate (84%) despite the similar mean age of both cohorts. In their study, however, only age was analysed as a predictor of mortality. It may be that other confounding factors, which we have identified in this study, affected their mortality rate. This may also explain why they observed a higher standardised mortality rate in younger patients, as age may not be the only individual factor that led to their death.

The unique feature of our study was the identification of isolated predictors of death after TKR. These predictors could be used to improve patient survival after TKR. The potentially modifiable factors: BMI, smoking and ASA grade, could improve survival if addressed pre-operatively. A high BMI is associated with an increased rate of revision,[13,14] but has not previously been linked to an increased mortality rate after TKR. A recent systematic review showed that smoking was associated with a significantly higher risk of post-operative complications and early death after TKR.[15] A higher ASA grade is associated with an increased mortality rate after hip fracture surgery,[16] and with a higher Charlson comorbidity index after total hip replacement.[17] However, no study has determined whether medical interventions that address these modifiable risk factors improve survival. The non-modifiable risk factors, age and rheumatoid disease, could still be of value during the consent process when informing patients of their risk of dying after surgery. These predictors should be also addressed when comparing differing cohorts for audit or study purposes to ensure that an accurate comparison is made once case-mix variables have been acknowledged.

The independent risk factors associated with mortality after TKR could be used as a tool to predict an individual's mortality after surgery. As part of fully informed patient consent prior to TKR, a patient should be made aware of the risks associated with their surgery.[18] Death is a significant risk and should be discussed. The exact rate quoted to each patient will depend on the figures from each individual centre, but a rate of 1% for the first 90 days would seem a reasonable estimate.[2] However, using the isolated individual risk factors we have identified, each patient could have an individual mortality risk assigned and documented during the consent process. We acknowledge that this figure is based on a cohort and not an individual, but it would serve as a reference point. Furthermore this information could be used to demonstrate the benefits of modifying specific risk factors to patients, and give them an insight into their risk behaviour, in an attempt to improve their post-operative survival.

The reason for the excess standardised mortality rate in our cohort, relative to the general population, is not apparent. A single study previously found a similar increase in the standardised mortality ratio after TKR but this was only apparent after fifteen years of follow-up.[12] They hypothesised that this was a reflection of a younger patient population with an increased level of comorbidity, resulting in a higher mortality rate in their old age. Our comparison population was only matched for age and gender, not for comorbidity. It may be that our cohort had an increased level of comorbidity, which resulted in an increased mortality rate. In addition, a recent population-based cohort study of 1163 patients identified osteoarthritis of the hip or knee to be associated with an excess all-cause mortality rate, with a standardised mortality ratio of 1.55.[19] This figure supports our own excess mortality ratio of 1.9, and may be even closer once corrected for other case-mix variables.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

1. **Culliford DJ, Maskell J, Beard DJ, et al.** Temporal trends in hip and knee replacement in the United Kingdom: 1991 to 2006. *J Bone Joint Surg [Br]* 2010;92-B:130–135.
2. **Ellams D, Forsyth O, Mistry A, et al.** National Joint Registry for England and Wales: 7th Annual Report, 2010. http://www.njrcentre.org.uk/NjrCentre/Portals/0/NJR%207th%20Annual%20Report%202010.pdf (date last accessed 19 October 2011).
3. **Parvizi J, Sullivan TA, Trousdale RT, Lewallen DG.** Thirty-day mortality after total knee arthroplasty. *J Bone Joint Surg [Am]* 2001;83-A:1157–1161.
4. **Ohzawa S, Takahara Y, Furumatsu T, Inoue H.** Patient survival after total knee arthroplasty. *Acta Med Okayama* 2001;55:295–299.
5. **Khan A, Emberson J, Dowd GS.** Standardized mortality ratios and fatal pulmonary embolism rates following total knee replacement: a cohort of 936 consecutive cases. *J Knee Surg* 2002;15:219–222.
6. **Parry MC, Smith AJ, Blom AW.** Early death following primary total knee arthroplasty. *J Bone Joint Surg [Am]* 2011;93-A:948–953.
7. **Schroder HM, Kristensen PW, Petersen MB, Nielsen PT.** Patient survival after total knee arthroplasty: 5-year data in 926 patients. *Acta Orthop Scand* 1998;69:35–38.

8. **No authors listed.** General Register Office for Scotland: mid-2008 population estimates Scotland population estimates by sex, age and administrative area, 2009. http://www.gro-scotland.gov.uk/files2/stats/gros-mid-2008-population-estimates-scotland-population-estimates-by-sex-age-and-administrative-area/j1075008.htm (date last accessed 19 October 2011).
9. **No authors listed.** American Society of Anesthesiologists: ASA physical status classification system. http://www.asahq.org/clinical/physicalstatus.htm (date last accessed 19 October 2011).
10. **No authors listed.** General Register Office for Scotland: abridged life table, by sex, age and NHS board area, Scotland 2007-09, 2010. http://www.gro-scotland.gov.uk/files2/stats/life-expectancy-admin-areas/07-09/0709le-table5.pdf (date last accessed 19 October 2011).
11. **Kaplan EL, Meier P.** Nonparametric estimation from incomplete observation. *J Am Statist Assn* 1958;53:457–481.
12. **Robertsson O, Stefansdottir A, Lidgren L, Ranstam J.** Increased long-term mortality in patients less than 55 years old who have undergone knee replacement for osteoarthritis: results from the Swedish Knee Arthroplasty Register. *J Bone Joint Surg [Br]* 2007;89-B:599–603.
13. **Spicer DD, Pomeroy DL, Badenhausen WE, et al.** Body mass index as a predictor of outcome in total knee replacement. *Int Orthop* 2001;25:246–249.
14. **Amin AK, Clayton RA, Patton JT, et al.** Total knee replacement in morbidly obese patients: results of a prospective, matched study. *J Bone Joint Surg [Br]* 2006;88-B:1321–1326.
15. **Singh JA.** Smoking and outcomes after knee and hip arthroplasty: a systematic review. *J Rheumatol* 2011;38:1824–1834.
16. **Holt G, Smith R, Duncan K, Finlayson DF, Gregori A.** Early mortality after surgical fixation of hip fractures in the elderly: an analysis of data from the scottish hip fracture audit. *J Bone Joint Surg [Br]* 2008;90-B:1357–1363.
17. **Pedersen AB, Baron JA, Overgaard S, Johnsen SP.** Short- and long-term mortality following primary total hip replacement for osteoarthritis: a Danish nationwide epidemiological study. *J Bone Joint Surg [Br]* 2011;93-B:172–177.
18. **No authors listed.** Department of Health: reference guide to consent for examination or treatment. Second ed. 2009. http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_103653.pdf (date last accessed 19 October 2011).
19. **Nuesch E, Dieppe P, Reichenbach S, et al.** All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ* 2011;342:d1165.