



# Long-term mortality and causes of death among patients with a total knee prosthesis in primary osteoarthritis



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## ABSTRACT

**Background:** Short and midterm mortality of patients with osteoarthritis (OA) who have undergone total knee arthroplasty (TKA) is generally lower than that of the general population. Due to an increasing number of young patients who undergo TKA the expected lifetime of these patients is increasing. The purpose of this study was to assess the causes of death and long-term mortality among Finnish TKA patients.

**Methods:** Standardized mortality ratios (SMRs) for total and site specific causes of death were calculated for 9443 TKA patients operated on in 1980 to 1996 for OA and followed until 2012.

**Results:** The mean follow-up time was 14 years (maximum 33 years). During follow-up, 77% of the patients had died. The all-cause SMR was 1.00. It was significantly lower than in the reference population (SMR 0.73) during the first 10 years after operation, but higher during the next 10 years (SMR 1.23), and even more after 20 years (SMR 1.95). The SMR for cardiovascular mortality was 1.03 and accounted for 52% of all deaths. Significant excess mortality was observed in diseases of the digestive tract (SMR 1.29). Deaths due to cardiovascular diseases, Alzheimer's disease and dementia comprised 68% of all deaths that took place 10 years or later after TKA.

**Conclusions:** The mortality of TKA patients with OA is significantly reduced during the first 10 postoperative years but exceeds the mortality of the general population after that. This trend should be taken into account when young patients undergo a TKA.

**Level of evidence:** Observational study, III.

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## 1. Introduction

Mid-term mortality of patients with total knee arthroplasty (TKA) for primary osteoarthritis (OA) in previous single and multicenter studies has been reported to be the same [1], lower [2–4] or even higher [5] than that of the general population. In a large US Medicare cohort the hazard ratio for mortality of TKA patients at seven years compared with matched knee OA patients who have not undergone a TKA was significantly reduced [6].

Results from the Swedish Knee Arthroplasty Register show that the OA TKA patients have a reduced overall mortality during the first 12 post-operative years, after which it increases and become significantly higher than in the general population. This increase was especially strongly associated with patients younger than 55 years. Cardiovascular, gastrointestinal, and urogenital diseases were largely responsible for the higher mortality. The authors proposed that there may be a link between early onset of knee OA and increased mortality [7].

There is growing evidence that OA is associated with cardiovascular diseases (CVDs) [8–10] which may relate to the long-term mortality of TKA patients. Patients with radiologically verified OA of the hip or knee have an increased risk of all cause mortality when followed up for a median of 13 to 14 years [10,11].

TKA is essential for the treatment of severe pain and for the restitution of walking ability. The mortality of patients with OA of the knee undergoing TKA may not exceed that of the general population, but this consideration is hampered by the fact that the long-term impact of TKA on all cause and disease specific mortality is not well known. The purpose of this study of a Register was to assess how all disease and main disease group specific late mortality deviates from those of the general population over a long period of time.

## 2. Patients, materials and methods

The patient data were obtained from the Finnish Arthroplasty Register covering the years 1980 to 1996. The dates and causes of death of the cohort subjects were retrieved from Statistics Finland by record linkage using the individual's personal identity code as the key. The coverage of the cause-of-death statistics is virtually complete.

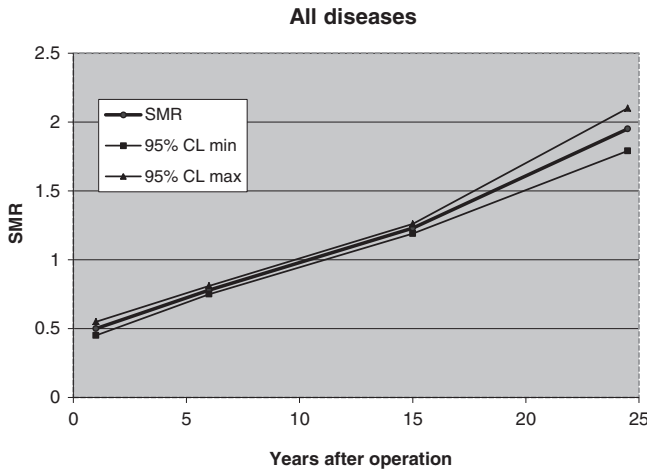
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**Table 1**

Numbers of patients (n) with total knee arthroplasty by sex and age at operation and number of person-years at risk up to the end of 2012.

Age (years)	Men		Women		All	
	n	Person-years	n	Person-years	n	Person years
30 to 39	6	22	6	14	12	36
40 to 49	37	177	47	226	84	403
50 to 59	221	1134	528	2307	749	3441
60 to 69	787	5405	2801	16,613	3589	22,018
70 to 79	821	11,100	3572	46,173	4393	57,273
≥80	129	7242	488	41,294	617	48,536
Total	2001	25,080	7443	106,628	9443	131,708



**Fig. 1.** Standardized mortality ratios (SMRs) with 95% confidence limits for all diseases during 25 years of follow-up among 9443 patients with a total knee arthroplasty for osteoarthritis.

Only patients who had undergone primary TKA and who were operated on for OA were included in the final analysis. The follow-up of the patients started from the first primary TKA. Mortality risk related to later revisions were not studied separately. The patient data have been described in detail previously [12]. All patients had received an unconstrained TKA, 79% had cobalt chromium molybdenum and 21% titanium aluminium vanadium alloy parts. The percentage of cemented component fixation on the femoral side was 46 and on the tibial side 57.

The standardized mortality ratio (SMR) was expressed as the ratio of observed and expected number of cases. The expected numbers of deaths were calculated by multiplying the number of person-years in each stratum by the corresponding average mortality rate throughout Finland during the period of observation. The number of observed cases for each cause of death and person-year during the follow-up was stratified by gender, calendar period, five year age group, and the

**Table 2**

Observed number of total deaths (Obs), standardized mortality ratio (SMR) 95% confidence interval (95% CI) among 9443 patients with total knee arthroplasty for osteoarthritis by gender and number of postoperative years.

Time since TKA surgery (completed years)	Men		Women		All patients	
	Obs	SMR (95% CI)	Obs	SMR (95% CI)	Obs	SMR (95% CI)
0–1	96	0.50 (0.41–0.61***)	218	0.50 (0.44–0.56***)	314	0.50 (0.45–0.55***)
2–9	680	0.84 (0.78–0.90***)	1822	0.77 (0.73–0.80***)	2502	0.78 (0.75–0.81***)
10–19	758	1.22 (1.13–1.30***)	3098	1.23 (1.19–1.27***)	3856	1.23 (1.19–1.26***)
20+	79	1.65 (1.31–2.05***)	503	2.00 (1.83–2.17***)	582	1.95 (1.79–2.11***)
Total	1613	0.97 (0.92–1.01)	5641	1.01 (0.98–1.03)	7254	1.00 (0.98–1.02)

\*\*\* p < 0.001.

follow-up time since the TKA operation. The calendar periods were 1980 to 1985, 1986 to 1991, 1992 to 1997, 1998 to 2002, 2003 to 2007, and 2008 to 2012. The closing date was December 31, 2012. The follow-up categories were <1, 1 to 9.99, 10 to 19.99, and ≥20 years since the operation. The 95% confidence intervals (95% CIs) were defined assuming that the number of observed cases followed a Poisson distribution.

The list of causes of death based on International Classification of Diseases (ICD) versions: ICD-8, ICD-9, and ICD-10. Of the main categories cancer, cardiovascular disease (CVD), respiratory, genitourinary, digestive system, dementia, Alzheimer's disease, and accidental deaths were analyzed. This study was approved by the National Institute for Health and Welfare, decision THL/1615/5.05.00/2013. The study subjects were not contacted and therefore no informed consents were required according to the Finnish regulations.

**3. Results**

Total number of person-years was 131,708 and 79% of the patients were females (Table 1). A total of 7254 (77%) of the TKA patients had died by the closing date. The mean follow-up time was 14 years (Table 1).

All-cause mortality was significantly reduced during the first 10-year follow-up period, but it was significantly increased during the second follow-up decade and reached the level of mortality of the normal population by 11 years. After 20 years of follow-up, the mortality of the study group exceeded significantly the mortality of the normal population (Fig. 1, Table 5). There were 1020 fewer deaths than expected during the first decade of follow-up, and an excess of 1005 cases after that period (Table 3). Females and males had similar SMRs throughout the follow-up period (Table 2).

Overall cancer mortality was significantly reduced but showed an increasing trend over time and reached the mortality of the normal population by the 17th postoperative year (Fig. 2, Table 3). Cancer deaths were reduced by 16.3% during the first 10 year period and by 1.0% after that (Table 3).

Respiratory tract cancer mortality was especially low: the SMR of all patients was 0.68 (95% CI 0.57 to 0.81); 0.61 (95% CI 0.46 to 0.78) for males and 0.78 (95% CI 0.59 to 0.99) for females. Mortalities from colon, breast and cervical and uterine cancer were significantly decreased as well. Late mortality in prostate and hematopoietic cancers was similar with that of the average population.

Cardiovascular disease was the most common cause of death and mortality increased linearly during the whole follow-up time. It reached the level of the normal population by the 10th postoperative year and remained higher than for the general population during the remaining follow-up time (Fig. 3, Table 5). Cardiovascular disease accounted for 52% of all causes of death. During the first 10 years there was a 40.2% reduction from the expected value, but after that cardiovascular deaths comprised 631 numerical excess deaths, which is 62.8% of all numerical excess deaths (Table 3). Men and women presented with a similar trend of CVD mortality: the SMRs during the first postoperative year were 0.61 and 0.52, from two to nine years 0.86 and 0.76, from 10 to 19 years 1.37 and 1.30, and after 20 years 1.68 and 2.06, respectively.

Mortality in respiratory diseases was lower during the first 10 years (Tables 4 to 5), after which it was in accordance with the general population both for males and females.

Mortality from Alzheimer's disease and dementia was also significantly lower during the first 10 years after surgery, after which it showed a steep increase (Tables 4 to 5). There was a significant excess of deaths in these diseases among females (SMR 1.56, 95% CI 1.27 to 1.87) but not among males (SMR 0.96, 95% CI 0.79 to 1.14). This group of diseases was the second highest cause of death with 18.7% after 10 years with a numerical excess of 43.5 deaths (Table 3).

A similar trend was observed concerning the mortality due to genitourinary and digestive tract diseases. The mortality in digestive tract diseases was significantly increased (SMR 1.29) (Tables 4 to 5). The incidence of accidental deaths was in line with the normal population (Tables 4 to 5). There was, however, a numerical excess of 16.6 deaths after the 20th postoperative year (Table 3).

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