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Cause-Specific Mortality Trends Following Total Hip and Knee Arthroplasty

CJ Michet III^a, CD Schleck^b, DR Larson, MS^b, H Maradit-Kremers, MD^b, DJ Berry, MD^a, and DG Lewallen, MD^a

^aDepartments of Orthopedic Surgery, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905

^bDepartments of Health Sciences Research, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905

Abstract

Background—While studies have demonstrated that mortality after total hip (THA) and total knee (TKA) arthroplasty is better than the general population, the causes of death are not well established. We evaluated cause-specific mortality after THA and TKA.

Methods—The study included population-based cohorts of patients who underwent THA (N=2019) and TKA (N=2259) between 1969 and 2008. Causes of death were classified using the International Classification Diseases 9th and 10th editions. Cause-specific standardized mortality ratios (SMR) and 95% confidence intervals (CI) were calculated by comparing observed and expected mortality. Expected mortality was derived from mortality rates in the United States white population of similar calendar-year, age and sex characteristics.

Results—All-cause mortality was lower than expected following both THA and TKA. However, there was excess mortality due to mental diseases such as dementia following both THA (SMR 1.40, 95% CI: 1.08, 1.80) and TKA (SMR 1.49, 95% CI: 1.19, 1.85). There was also excess mortality from inflammatory musculoskeletal diseases in THA (SMR 3.50, 95% CI: 2.11, 5.46) and TKA (SMR 4.85, 95% CI: 3.29, 6.88). When the cohorts were restricted to patients with osteoarthritis as the surgical indication, the excess risk of death from mental diseases still persisted in THA (SMR 1.36, 95% CI: 1.02, 1.78) and TKA (SMR 1.52, 95% CI: 1.20, 1.91).

Conclusion—THA and TKA patients experience a higher risk of death from mental and inflammatory musculoskeletal diseases. These findings warrant further research to identify drivers of mortality and prevention strategies in arthroplasty patients.

Keywords

Total knee arthroplasty; total hip arthroplasty; mortality; standardized mortality ratio; cause-specific mortality; dementia

Please address all correspondence to: Hilal Maradit Kremers, MD MSc, Mayo Clinic, 200 First Street SW, Rochester, MN, 55905, Tel: (507) 266-3169, Fax: (507) 284-1516, maradit@mayo.edu.

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Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are increasingly common procedures for the management of advanced osteoarthritis.[1] Life expectancy following these procedures, however, is not fully understood. So far, the majority of the mortality studies following THA and TKA are limited to early postoperative mortality.[2-4] The small number of studies on long-term mortality patterns demonstrates that mortality among patients undergoing THA and TKA is better than the general population for about eight to ten years following surgery, but then levels off, and in some cases surpasses expected mortality after ten years.[5-10] Early mortality advantage is largely attributed to selection of healthier patients for surgery. Yet, it is unknown why the early mortality advantage disappears over time. One possibility is that the comorbid conditions are responsible for the increased risk of death after ten years. For example, in a cohort of 57,979 Swedish TKA patients, the risk of death was increased from cardiovascular, gastrointestinal and urogenital diseases after twelve years following surgery.[7] This finding is mainly confined to younger TKA patients. These comorbid conditions, however, are also common causes of death in the general population, and thereby confound our understanding of mortality following these procedures. There is limited understanding of the causes of death in the rapidly growing arthroplasty population. In order to address this issue further, we examined cause-specific mortality patterns following THA and TKA.

Methods

We conducted a retrospective cohort study in Olmsted County, Minnesota using the resources of the Rochester Epidemiology Project (REP), a comprehensive medical records linkage system.[11, 12] Olmsted County (2010 population: 144,248) is particularly well suited for a study of this nature due to its relative geographic isolation and small number of medical providers. The REP collects data from all healthcare providers in the area, and thereby creates a population-based infrastructure with effectively complete ascertainment and follow-up of patients who had undergone THA or TKA.

The study population included previously described cohorts of all Olmsted County residents who underwent primary THA (n=2019) or TKA (n=2259) between January 1, 1969 and December 31, 2008.[13] Patients were followed up longitudinally until death or August 31, 2014. Only 2.4% of the cohort was lost-to-follow-up. For individuals who were deceased, causes of death were ascertained through review of medical records and death certificates and classified using the International Classification of Diseases, 9th edition (ICD-9) and 10th edition (ICD-10). ICD-9 categories were converted to ICD-10 categories prior to analysis. . The causes of death could not be determined in 36 (1.8%) of the deaths in the THA cohort and 34 (1.5%) of the deaths in the TKA cohort.

At the time of surgery, the median age of the 2019 THA patients was 68 years (minimum 15, maximum 97) and 1181 (58%) were female. The median age of the 2259 TKA patients was 69 years (minimum 14, maximum 93) and 1420 (63%) were female. The underlying surgical indication was osteoarthritis in 1611 (80%) of the THA and 1938 (86%) of the TKA patients.

Statistical Analyses

Statistical analyses were performed separately for the THA and TKA cohorts. All calculations were repeated by limiting the cohort to 1611 THA and 1938 TKA patients with osteoarthritis as the underlying surgical indication. Death rates following THA and TKA were evaluated using a person-years approach, in which the observed number of deaths in each cohort was compared to the expected number of deaths over the follow-up period. Expected survival was generated using the life tables for the United States white population. The results were reported as standardized mortality ratios (SMRs) with corresponding 95% confidence intervals (CI). The confidence intervals were calculated assuming that the expected rates were fixed and the observed deaths followed a Poisson distribution. The SMRs were calculated separately for men, women and combined. There was no evidence to suggest that the SMR differed between men and women, and therefore, the combined results were reported. The person-years analysis included follow-up time so that separate calculations could be made for the first year after arthroplasty, 1-10 years following surgery, and beyond 10 years after surgery. In the calculations of the SMRs for these temporal subsets, only events and person-years of exposure during the follow-up time window of interest were considered.

Results

Over a mean follow-up of 11.9 (± 7.4) years, 1079 of the 2019 THA patients died as compared with 1173 expected deaths (SMR 0.92, 95% CI: 0.87, 0.98). THA patients had a significantly reduced risk of death from circulatory and endocrine diseases, as indicated by the confidence intervals less than 1.00 (Figure 1). However, the observed number of deaths were significantly higher than the expected number of deaths for mental and behavioral diseases (SMR 1.40, 95% CI: 1.08, 1.80), musculoskeletal and connective tissue diseases (SMR 3.50, 95% CI: 2.11, 5.46) and injuries, poisoning and certain other consequences of external causes (SMR 2.36, 95% CI: 1.57, 3.41). A similar pattern was observed in the TKA cohort (Figure 2). Over a mean follow-up of 11.2 (± 5.8) years, 1012 of the 2259 TKA patients died as compared with 1245 expected deaths (SMR 0.81, 95% CI: 0.76, 0.86). Despite a significantly reduced risk of death from several common causes, TKA patients experienced a significantly higher risk of death from mental and behavioral diseases (SMR 1.49, 95% CI: 1.19, 1.85) and musculoskeletal and connective tissue diseases (SMR 4.85, 95% CI: 3.29, 6.88) (Figure 2). The excess musculoskeletal mortality was due to patients with inflammatory arthritis where the cause of death was rheumatoid arthritis or other inflammatory arthritis in 9 of the 19 musculoskeletal deaths in THA patients, and 22 of the 31 musculoskeletal deaths in TKA patients. The remaining musculoskeletal deaths were osteomyelitis or infective arthritis cases. The excess mortality due to mental and behavioral diseases was almost entirely due a high number of deaths from dementia; the cause of death was dementia in 55 of the 62 mental disorders-related deaths in THA patients and 73 of the 83 mental disorders-related deaths in TKA patients.

We then examined the observed and expected number of deaths according to the time since THA (Table I) and TKA (Table II) surgery. There were a total of 91 deaths during the first year after THA surgery (Table I), and with 93.5 expected deaths, the risk of death during the

first year after THA was similar to the general population (SMR 0.97, 95% CI: 0.78, 1.20). The risk of death was significantly lower than the general population during the 1-10 year time period after THA surgery. A total of 647 deaths occurred between 1-10 years after THA surgery and this was lower than the 758.6 expected deaths (SMR 0.85, 95% CI: 0.79, 0.92, Table I). During the 1-10 year time period after THA, the risk of death was similar or lower than the general population for the majority of the causes of death except for musculoskeletal diseases and injuries, poisoning and certain other consequences of external causes after THA (Table I). Beyond 10 years, the risk of death was similar to the general population in THA (SMR 1.06, 95% CI: 0.95, 1.18), but we observed a significantly higher risk of death from mental disorders (SMR 1.70, 95% CI: 1.12, 2.47) and musculoskeletal diseases (SMR 6.56, 95% CI: 3.00, 12.46).

Table II shows the observed and expected number of deaths according to the time since TKA surgery. There were a total of 60 deaths during the first year after TKA surgery, and with 103 expected deaths, the risk of death during the first year after TKA was significantly lower than the general population (SMR 0.58, 95% CI: 0.44, 0.75). The risk of death was also lower than the general population during the 1-10 year time period after TKA surgery (SMR 0.72, 95% CI: 0.67, 0.78). Patient selection was evident with significantly reduced risk of death from several common causes of death, i.e. neoplasms and diseases of the circulatory system. Beyond 10 years after TKA, the risk of death was higher than the general population (SMR 1.19, 95% CI: 1.06, 1.32). This was largely due to higher risk of death from mental disorders (SMR 2.03, 95% CI: 1.43, 2.78), diseases of the circulatory system (SMR 1.22, 95% CI: 1.02, 1.44), musculoskeletal system (SMR 9.04, 95% CI: 4.67, 15.79) and injury/external causes of death (SMR 3.85, 95% CI: 1.41, 8.38).

When the cohorts were restricted to 1611 THA (Figure 3) and 1938 TKA (Figure 4) patients with osteoarthritis as the underlying surgical indication, the overall SMR was lower in both THA (SMR 0.81, 95% CI: 0.76, 0.87) and TKA (SMR 0.77, 95% CI: 0.72, 0.83). The excess musculoskeletal mortality was no longer significant after excluding patients with inflammatory arthritis (THA SMR 1.95, 95% CI: 0.89, 3.70; TKA SMR 1.44, 95% CI: 0.62, 2.83). However, the excess mortality due to mental diseases persisted with SMR of 1.36 (95% CI: 1.02, 1.78) in THA and 1.52 (95% CI: 1.20, 1.91) in TKA.

Discussion

In this population-based study spanning almost forty years and including over 5000 patients with an average of 12 years of follow-up, long-term mortality following THA and TKA was better than the general population with significantly reduced risk of death from several common diseases, including neoplasms and diseases of the circulatory and respiratory systems. Yet, the risk of death was elevated for mental and musculoskeletal diseases. The excess musculoskeletal mortality is confined to patients with inflammatory arthritis, whereas the reasons for the excess deaths due to dementia are unknown.

To our knowledge, this is one of the few studies examining cause-specific mortality in THA and TKA. Long-term mortality studies are scarce in arthroplasty, and published studies mostly focus on relative mortality trends by age, sex and calendar year.[5-8, 13] Our

findings are largely consistent with these earlier studies demonstrating; (a) low relative mortality that is in part attributed to patient selection, and (c) high mortality among patients who underwent surgery for inflammatory arthritis. The magnitude of the relative mortality estimates in our cohort is consistent with earlier studies with about 20-25% lower mortality risk as compared to the general population.[7, 8] Finally, rheumatoid arthritis and other forms of inflammatory arthritis are associated with excess mortality, especially due to cardiovascular disease.[14-16] This is evidenced in our overall cohort with a higher risk of death due to musculoskeletal diseases following both THA and TKA. The remaining musculoskeletal deaths were mostly joint infections and osteomyelitis, rare but devastating arthroplasty complications.

An unexpected finding of our study is the increased risk of death from mental diseases, in particular dementia, in both the THA and TKA patients. Although this finding is in contrast to two previous cause-specific mortality studies from Finland and Sweden [5, 7] it is consistent with a recent TKA study from Finland.[17] The Finnish TKA cohort included 9443 TKA patients with an average 14 years of follow-up during which 77% of the cohort were deceased. Similar to our study, dementia-related mortality was significantly lower than the general population during the initial 10 years after surgery, but showed a steep increase after 10 years with a significant excess number of dementia deaths among female TKA patients (SMR 1.56). The reasons for the discrepant findings across studies may include differences in duration of follow-up, differences in analysis methodology or temporal changes in coding/recording of the causes of death. Dementia is typically under-coded in death certificates, and it is possible that the coding of dementia in our community is more complete than the rest of the country.[18] Elevated mortality from dementia was recently reported in the osteoarthritis literature in a cohort of 1163 osteoarthritis patients from United Kingdom and a large study from Taiwan.[19, 20] The reasons for this finding are unknown, but we speculate that this may potentially be driven by the concomitant risk factors for dementia patients with arthritis treated with arthroplasty, such as obesity, low physical activity, or low grade systemic inflammation associated with advanced osteoarthritis. Another intriguing possibility is increased serum metal ion levels from corrosion or wear of certain hip and knee implants. Further research is warranted in this area. These results may have important implications for patient and implant selection, and clinical follow-up of arthroplasty patients.

This study should be interpreted in light of some potential limitations. First, the study population was predominantly white and findings may not be generalizable to more racially and ethnically diverse populations. The local source population is socioeconomically comparable to other largely white populations in the United States, and previous cause-specific mortality studies were generalizable to the rest of the rest of the country.[21, 22] Second, despite the long and complete follow-up, the THA and TKA cohorts are relatively small, and therefore, limit power for analyses of less common causes of death, e.g. infections and diseases of the endocrine and nervous systems. Finally, the study did not include surgeries after 2008, although follow-up continued through August 2014. Cause-specific mortality patterns in later years may be different due to secular trends with more complex patients undergoing surgery.[23]

In conclusion, long-term mortality following THA and TKA is better than the general population; however, the risk of death is elevated for inflammatory musculoskeletal and mental diseases. Further research is warranted to understand the reasons for excess mortality from dementia in arthroplasty patients.

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Figure 1. Observed Versus Expected Underlying Causes of Death Following Total Hip Arthroplasty (THA)

Figure 2. Observed Versus Expected Underlying Causes of Death Following Total Knee Arthroplasty (TKA)

Figure 3. Observed Versus Expected Underlying Causes of Death Following Total Hip Arthroplasty (THA) in Patients with Osteoarthritis

Figure 4. Observed Versus Expected Underlying Causes of Death Following Total Hip Arthroplasty (TKA) in Patients with Osteoarthritis

Observed (O) Versus Expected (E) Deaths and Standardized Mortality Ratios (SMR) by Time Interval Since Total Hip (THA) Arthroplasty

Table 1

ICD-10 Chapter Cause of death	O/E	0-1 year SMR (95% CI)	O/E	1-10 years SMR (95% CI)	O/E	>10 years SMR (95% CI)	O/E	All follow-up SMR (95% CI)
Certain Infections and Parasitic Diseases	0/1.4	0.00 (0.00, 2.55)	12/12.8	0.94 (0.49, 1.64)	5/5.4	0.93 (0.30, 2.17)	17/19.6	0.87 (0.51, 1.39)
Neoplasms	21/20.6	1.02 (0.63, 1.56)	147/154.8	0.95 (0.80, 1.12)	46/55.4	0.83 (0.61, 1.11)	214/230.8	0.93 (0.81, 1.06)
Diseases of the Blood and Blood-Forming Organs	0/0.3	0.00 (0.00, 11.22)	3/2.8	1.08 (0.22, 3.16)	0/1.3	0.00 (0.00, 2.86)	3/4.4	0.68 (0.14, 2.00)
Endocrine, Nutritional, and Metabolic Diseases	0/3.1	0.00 (0.00, 1.19)	15/24.9	0.60 (0.34, 0.99)	5/9.9	0.50 (0.16, 1.18)	20/37.9	0.53 (0.32, 0.81)
Mental and Behavioral Disorders	1/1.9	0.52 (0.01, 2.91)	34/26.4	1.29 (0.89, 1.80)	27/15.9	1.70 (1.12, 2.47)	62/44.2	1.40 (1.08, 1.80)
Diseases of the Nervous System	3/3.3	0.91 (0.19, 2.65)	31/34.7	0.89 (0.61, 1.27)	7/15.1	0.46 (0.19, 0.96)	41/53.1	0.77 (0.55, 1.05)
Diseases of the Circulatory System	40/44.0	0.91 (0.65, 1.24)	261/344.0	0.76 (0.67, 0.86)	160/149.5	1.07 (0.91, 1.25)	461/537.5	0.86 (0.78, 0.94)
Diseases of the Respiratory System	11/9.6	1.15 (0.57, 2.06)	59/81.4	0.73 (0.55, 0.94)	44/36.0	1.22 (0.89, 1.64)	114/127.0	0.90 (0.74, 1.08)
Diseases of the Digestive System	2/3.0	0.66 (0.08, 2.38)	17/23.8	0.71 (0.42, 1.14)	10/9.5	1.05 (0.50, 1.93)	29/36.4	0.80 (0.53, 1.14)
Diseases of the Musculoskeletal System	1/0.4	2.24 (0.06, 12.45)	9/3.6	2.49 (1.14, 4.73)	9/1.4	6.56 (3.00, 12.46)	19/5.4	3.50 (2.11, 5.46)
Diseases of the Genitourinary System	2/2.1	0.96 (0.12, 3.47)	16/18.8	0.85 (0.49, 1.38)	7/8.3	0.84 (0.34, 1.73)	25/29.2	0.86 (0.55, 1.26)
Injury, Poisoning and Certain Other Consequences of External Causes	7/1.0	7.13 (2.87, 14.70)	15/7.1	2.12 (1.19, 3.50)	6/3.8	1.58 (0.58, 3.43)	28/11.9	2.36 (1.57, 3.41)
All causes	91/93.5	0.97 (0.78, 1.20)	647/758.6	0.85 (0.79, 0.92)	341/320.7	1.06 (0.95, 1.18)	1079/1173	0.92 (0.87, 0.98)

The following ICD-10 categories not shown due to low numbers: deaths due to diseases of the eye and adnexa; diseases of the ear and mastoid process; diseases of the skin and subcutaneous tissue; pregnancy, childbirth, and the puerperium; certain conditions originating in the perinatal period; congenital malformations, deformations, and chromosomal abnormalities; and symptoms, signs, and abnormal clinical and laboratory findings; external causes of morbidity and mortality.

Table II
Observed (O) Versus Expected (E) Deaths and Standardized Mortality Ratios (SMR) by Time Interval Since Total Knee (TKA) Arthroplasty

ICD-10 Chapter Cause of death	O/E	0-1 year SMR (95% CI)	O/E	1-10 years SMR (95% CI)	O/E	>10 years SMR (95% CI)	O/E	All follow-up SMR (95% CI)
Certain Infections and Parasitic Diseases	0/1.7	0.00 (0.00, 2.14)	7/15.9	0.44 (0.18, 0.90)	7/5.2	1.35 (0.54, 2.79)	14/22.8	0.61 (0.34, 1.03)
Neoplasms	13/24.5	0.53 (0.28, 0.91)	129/183.7	0.70 (0.59, 0.83)	38/46.9	0.81 (0.57, 1.11)	180/255.1	0.71 (0.61, 0.82)
Diseases of the Blood and Blood-Forming Organs	0/0.4	0.00 (0.00, 9.99)	2/3.2	0.62 (0.08, 2.24)	1/1.0	0.97 (0.02, 5.39)	3/4.6	0.65 (0.13, 1.89)
Endocrine, Nutritional, and Metabolic Diseases	0/3.6	0.00 (0.00, 1.01)	12/30.4	0.39 (0.20, 0.69)	6/8.9	0.67 (0.25, 1.46)	18/42.9	0.42 (0.25, 0.66)
Mental and Behavioral Disorders	4/2.1	1.89 (0.51, 4.84)	41/34.8	1.18 (0.85, 1.60)	38/18.7	2.03 (1.43, 2.78)	83/55.7	1.49 (1.19, 1.85)
Diseases of the Nervous System	1/3.9	0.25 (0.01, 1.42)	31/45.5	0.68 (0.46, 0.97)	17/17.4	0.98 (0.57, 1.57)	49/66.8	0.73 (0.54, 0.97)
Diseases of the Circulatory System	24/45.4	0.53 (0.34, 0.79)	236/370.2	0.64 (0.56, 0.72)	37/112.7	1.22 (1.02, 1.44)	397/528.3	0.75 (0.68, 0.83)
Diseases of the Respiratory System	5/11.3	0.44 (0.14, 1.03)	81/99.0	0.82 (0.65, 1.02)	30/31.0	0.97 (0.65, 1.38)	116/141.3	0.82 (0.68, 0.98)
Diseases of the Digestive System	4/3.4	1.19 (0.32, 3.05)	17/27.2	0.63 (0.36, 1.00)	11/7.7	1.42 (0.71, 2.54)	32/38.3	0.84 (0.57, 1.18)
Diseases of the Musculoskeletal System	1/0.5	1.89 (0.05, 10.52)	18/4.5	3.97 (2.35, 6.27)	12/1.3	9.04 (4.67, 15.79)	31/6.3	4.85 (3.29, 6.88)
Diseases of the Genitourinary System	2/2.4	0.84 (0.10, 3.05)	17/22.7	0.75 (0.44, 1.20)	7/7.5	0.93 (0.38, 1.92)	26/32.6	0.80 (0.52, 1.17)
Injury, Poisoning and Certain Other Consequences of External Causes	1/0.8	1.19 (0.03, 6.62)	6/5.7	1.06 (0.39, 2.30)	6/1.6	3.85 (1.41, 8.38)	13/8.1	1.61 (0.86, 2.75)
All causes	60/103	0.58 (0.44, 0.75)	631/872	0.72 (0.67, 0.78)	321/270	1.19 (1.06, 1.32)	1012/1245	0.81 (0.76, 0.86)

The following ICD-10 categories not shown due to low numbers: deaths due to diseases of the eye and adnexa; diseases of the ear and mastoid process; diseases of the skin and subcutaneous tissue; pregnancy, childbirth, and the puerperium; certain conditions originating in the perinatal period; congenital malformations, deformations, and chromosomal abnormalities; and symptoms, signs, and abnormal clinical and laboratory findings; external causes of morbidity and mortality.