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# Total Knee Arthroplasty: Is It Safe? A Single-Center Study of 4,124 Patients in South Korea

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**Background:** Although total knee arthroplasty (TKA) is considered an effective treatment for knee osteoarthritis, it carries risks of complications. With a growing number of TKAs performed on older patients, understanding the cause of mortality is crucial to enhance the safety of TKA. This study aimed to identify the major causes of short- and long-term mortality after TKA and report mortality trends for major causes of death.

**Methods:** A total of 4,124 patients who underwent TKA were analyzed. The average age at surgery was 70.7 years. The average follow-up time was 73.5 months. The causes of death were retrospectively collected through Korean Statistical Information Service and classified into 13 subgroups based on the International Classification of Diseases-10 code. The short- and long-term causes of death were identified within the time-to-death intervals of 30, 60, 90, 180, 180 days, and > 180 days. Standard mortality ratios (SMRs) and cumulative incidence of deaths were computed to examine mortality trends after TKA.

**Results:** The short-term mortality rate was 0.07% for 30 days, 0.1% for 60 days, 0.2% for 90 days, and 0.2% for 180 days. Malignant neoplasm and cardiovascular disease were the main short-term causes of death. The long-term (> 180 days) mortality rate was 6.2%. Malignant neoplasm (35%), others (11.7%), and respiratory disease (10.1%) were the major long-term causes of death. Men had a higher cumulative risk of death for respiratory, metabolic, and cardiovascular diseases. Age-adjusted mortality was significantly higher in TKA patients aged 70 years (SMR, 4.3; 95% confidence interval [CI], 3.3–5.4) and between 70 and 79 years (SMR 2.9; 95% CI, 2.5–3.5) than that in the general population.

**Conclusions:** The short-term mortality rate after TKA was low, and most of the causes were unrelated to TKA. The major causes of long-term death were consistent with previous findings. Our findings can be used as counseling data to understand the survival and mortality of TKA patients.

**Keywords:** *Total knee arthroplasty, Knee osteoarthritis, Mortality, Death*

Total knee arthroplasty (TKA) is one of the most popular and effective surgical procedures for end-stage osteoarthritis. The replacement of the damaged knee with an artificial joint has been reported to alleviate the pain substantially and improve the knee's functional aspect.[1] In 2014, over 680,000 TKAs were performed in the United States, and the frequency of such practice is expected to grow more than 1.68 million times annually by 2030.[2,3]

Recently, there has been an increasing effort to reduce the risks of complications of TKA, which contribute to short-term mortality and morbidity. Preoperative screening excludes high-risk patients, such as those with diabetes mellitus, who are most likely to experience major

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complications and infections, thereby reducing the overall complication rate of patients undergoing TKA.[4-8] Tranexamic acid has been implemented to minimize blood loss and the risk of transfusion during the operation.[9,10] After spinal anesthesia was found to lower rates of deep infection, unplanned readmissions, and blood transfusion of TKA patients, spinal anesthesia has been preferred to general anesthesia.[11,12] Furthermore, continuous efforts have been made to understand how new drugs, such as rivaroxaban and thromboprophylaxis, lower the incidence of venous thromboembolism and pulmonary embolism.[13,14]

However, the risks of major complications and mortality related to TKA still exist and there is a lack of publication that addresses the uncommon causes of mortality after TKA.[15] With the aging of the population and the growing number of TKAs performed on both much younger and older patients, understanding the latest causes and the underlying factors of mortality for the larger population are crucial for reducing the incidence of major complications and enhancing the safety of the surgical procedure. Having such a comprehensive list of mortality causes can be informative for single centers during the preoperative risk assessment of patients.

Therefore, the purpose of the study was to identify the major causes of short- and long-term mortality after TKA and to report age-, sex-, and cause-specific long-term mortality trends for major causes of death over time.

## METHODS

This study was approved by the Institutional Review Board of Seoul National University Hospital (No. 2006-199-1137), and written informed consent was waived for all patients.

### Study Population

This retrospective cohort study consisted of a study population comprising patients who underwent TKA at a tertiary referral hospital from September 2005 to December 2018 (n = 4,124). Patients who had undergone either unilateral or bilateral primary TKA were enrolled. The study was based on 4,124 patients, including 3,408 women (88%) and 449 men (12%) (Table 1). There were 219 female deaths (82%) and 48 male deaths (18%). In total, 267 patients (6.5%) died after TKA within the given study period.

The date and the cause of the patients' death based on the International Classification of Diseases Tenth Revision (ICD-10) code were retrospectively collected through Korean Statistical Information Service (KOSIS), a one-stop service that contains key records of domestic, international, and North Korean statistics. Additional follow-up progress of TKA patients both in and out of our institution was acquired by matching the resident registration number inputted in our electronic health record system with the KOSIS database. Additional medical information previously unavailable at our institution level, such as the death or cause of death of a patient lost to follow-up, was accessible. Despite the lack of documentation and dispersed information of patients often being a problem in analyzing the patients retrospectively, this study was able to secure a robust dataset with minimal missing data. All patients were longitudinally followed until July 21, 2020.

A total of 13 subgroups were classified based on the International Statistical Classification of Diseases and Related Health Problems (ICD) by the World Health Organization to analyze the leading causes of death. A total

**Table 1.** Demographic Characteristics

| Characteristics | No death (n = 3,857) | Death (n = 267) | *p*-value |
|---|---|---|---|
| Age (yr) | 70.5 ± 6.9 | 73.4 ± 6.4 | < 0.001 |
| Survival time (mo) | 73.4 ± 51.4 | 75.0 ± 42.0 | 0.5 |
| Sex | | | 0.003 |
| Female | 3,408 (88) | 219 (82) | |
| Male | 449 (12) | 48 (18) | |

Values are presented as mean ± standard deviation or number (%).

**Table 2.** Short-Term Cause of Death after TKA in Individual Case

| Case no. | Postoperation day until death | Cause of death |
|---|---|---|
| 1 | 7 | Hemorrhagic stroke |
| 2 | 19 | Unknown |
| 3 | 30 | Lung cancer |
| 4 | 37 | GI bleeding |
| 5 | 51 | Aplastic anemia |
| 6 | 75 | Unknown |
| 7 | 107 | HCC with brain metastasis |
| 8 | 108 | Malignant neoplasm |
| 9 | 155 | Cardiovascular disease |
| 10 | 163 | Cerebrovascular disease |

TKA: total knee arthroplasty, GI: gastrointestinal, HCC: hepatocellular carcinoma.

of 4 subgroups were formed based on the first letter of the ICD-10 Code: malignant neoplasm (C), metabolic disease (E), respiratory system (J), and digestive system (K). The remaining 9 subgroups were formed with a more specified classification: certain infectious and parasitic diseases (A00-B99), Parkinson disease (G12, G20), Alzheimer disease (G30), hypertensive diseases (I10-I12), cardiovascular disease (I20, I21, I25, I26, I42, I46, I49, I50), cerebrovascular disease (I60, I61, I63, I64, I69), chronic kidney disease (N18), and injury, poisoning, and certain other consequences of external causes (S00-T98).

### Statistical Analysis

Univariate analysis of all variables was conducted through Pearson's chi-square tests for categorical variables and *t*-tests for continuous variables to identify factors that have a significant difference between death and no-death groups. Differences were considered significant if a *p*-value was < 0.05. The proportion (frequency) was measured for each corresponding cause of death to identify the cause of death for the study population. The short-term cause of death was identified by dividing the time to death intervals into 30, 60, 90, and 180-day mortality and observing the causes within the specified time frame. The long-term cause of death was identified in the same way, but for ≥ 180 days.

Age-specific mortality causes were evaluated in three age groups: below 70 years, 70 to 79 years, and ≥ 80 years. The five leading causes of death of TKA patients were compared to the five leading causes of death in the general population provided by Statistics Korea (KOSTAT), a central governmental organization for statistics in Korea.

Mortality rates after TKA were reported as standard mortality ratios (SMRs) with the associated 95% confidence intervals (CI). The SMR was calculated by dividing the observed number of deaths by the expected number of deaths. The expected number of deaths was computed by referring to the age-specific mortality rate of the general population provided by KOSTAT. Cumulative incidence curves using competing risk analysis were generated to identify the long-term mortality trends of the main causes of death. The relative frequency of deaths was estimated to correspond to the specified follow-up time. It was adjusted by sex to show how the trends differed for the male and female populations.

## RESULTS

Among the 4,124 patients, 267 deaths (6.5%) occurred after TKA within the study period. The average time to death from the operation was approximately 75 months. The average follow-up time of surviving patients was 73.5 months, with a minimum of 1 year and a maximum of 16.7 years. The average age at death was 73.4 years.

### Short-Term Cause of Death

Among the total 4,124 patients, the short-term mortality rate was 0.07% (n = 3) for 30 days, 0.1% (n = 5) for 60 days, 0.1% (n = 6) for 90 days, and 0.2% (n = 10) for 180 days. Malignant neoplasm and cerebrovascular disease were the main short-term causes of death (Table 2). Of the total enrolled patients, 10 patients died within the 180-day mortality period (0.2%): 3 patients (30%) died of malignant neoplasm that had been recognized prior to the operation, and 3 patients (30%) died of cerebrovascular disease. The third-highest short-term cause of death was unknown death (n = 2, 20%). The records did not reveal any significant changes in patients that led to specified causes of death. Cardiovascular disease (n = 1, 10%) and

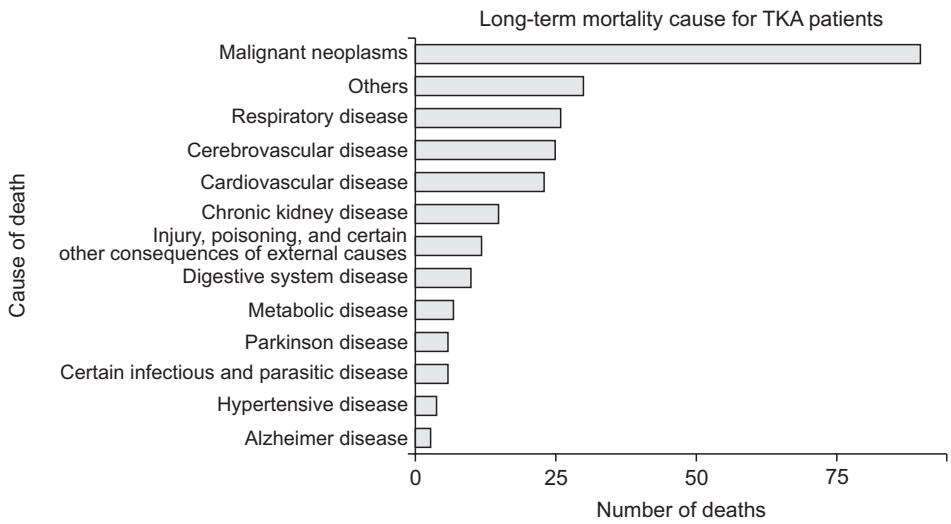


**Fig. 1.** The graph shows the frequency of long-term causes of death of total knee arthroplasty (TKA) patients in descending order.

certain infectious and parasitic diseases (n = 1, 10%) followed next.

### Long-Term Cause of Death

Among the total 4,124 patients, the long-term (> 180 days) mortality rate was 6.2% (n = 257). Of the 257 long-term mortality cases, malignant neoplasm was the major cause of death (n = 90, 35%), followed by others (n = 30, 11.7%), respiratory disease (n = 26, 10.1%), cerebrovascular disease (n = 25, 9.7%), cardiovascular disease (n = 23, 9%), chronic kidney disease, (n = 15, 5.8%), injury, poisoning, and certain other consequences of external causes (n = 12 cases, 4.7%), digestive system disease (n = 10, 3.9%), metabolic disease (n = 7, 2.7%), certain infectious and parasitic diseases (n = 6, 2.3%), Parkinson disease (n = 6, 2.3%), hypertensive disease (n = 4, 1.6%), and Alzheimer disease (n = 3, 1.2%) (Fig. 1).

### Age-Specific Cause of Death

The five leading causes of death among the 73 TKA patients aged below 70 years were malignant neoplasm (n = 30, 41%), chronic kidney disease (n = 9, 12.3%), respiratory disease (n = 8, 11%), cardiovascular disease (n = 7, 9.6%), and cerebrovascular disease (n = 4, 5.5%). The five leading causes of death for the general population aged below 70 years include malignant neoplasm, cardiovascular disease, cerebrovascular disease, chronic kidney disease, and respiratory disease.[15] Compared to the general population, TKA patients in our study showed increased mortality for chronic kidney and respiratory-related diseases.

For TKA patients aged between 70 to 79 years, the five leading causes were malignant neoplasm (n = 53, 33.5%), others (n = 21, 13.3%), cerebrovascular disease (n = 17, 10.8%), cardiovascular disease (n = 15, 9.5%), and respiratory disease (n = 15, 9.5%). The five leading causes of death for the general population aged between 70 to 79 years include malignant neoplasm, cardiovascular disease, cerebrovascular disease, respiratory disease, and metabolic disease.[15] The leading causes of death in our TKA patients and the general population showed no significant differences.

For TKA patients aged ≥ 80 years, the five leading causes of death were malignant neoplasm (n = 10, 27.8%), others (n = 9, 25%), cerebrovascular disease (n = 6, 16.7%), metabolic disease (n = 3, 8.3%), and respiratory disease (n = 3, 8.3%). The five leading causes of death for the general population aged ≥ 80 years include malignant neoplasm, cardiovascular disease, respiratory disease, cerebrovascular disease, and Alzheimer disease.[15] Compared to the general population, TKA patients in our study showed higher mortality related to metabolic disease.

**Table 3.** SMRs after TKA

| Age at surgery | Observed | Expected | SMR (95% CI) | *p*-value |
|---|---|---|---|---|
| < 70 yr | 73 | 17 | 4.3 (3.3–5.4) | < 0.001 |
| 70–79 yr | 158 | 53 | 2.9 (2.5–3.5) | < 0.001 |
| ≥ 80 yr | 36 | 30 | 1.2 (0.8–1.7) | 0.2 |

SMR: standard mortality ratio, TKA: total knee arthroplasty, CI: confidence interval.

### Age-Specific Mortality Rate

The SMR for TKA patients aged below 80 years was statistically significantly different from that in the general population (Table 3). TKA patients aged below 70 years (SMR, 4.3; 95% CI, 3.3–5.4) and between 70 and 79 years (SMR, 2.9; 95% CI, 2.5–3.5) both showed an increase in mortality compared to that in the general population. TKA patients aged ≥ 80 years did not show a statistically significant difference in mortality from that of the general population. Overall, the mortality rate of TKA patients exhibited a downward trend as age increased.

### Sex- and Cause-Specific Long-Term Mortality Trends

The cumulative incidences of competing risk of cause-specific death by sex depict the probability of death after TKA for both male and female populations. The cumulative risk of mortality significantly differed between the male and female populations for respiratory ($p = 0.029$), metabolic ($p = 0.004$), and cardiovascular diseases ($p = 0.021$). For all three causes, men had a higher cumulative risk of death. The risk of mortality in men significantly increased approximately 6 years postoperatively for respiratory disease and 9 years postoperatively for metabolic disease (Fig. 2A and B). For cardiovascular disease, men had a higher cumulative risk of death immediately after operation; however, approximately 13 years postoperatively, the cumulative risk of mortality in the female population showed a sudden increase, which was comparable to that in the male population (Fig. 2C). The cumulative risk of mortality did not differ statistically significantly for the remaining causes of death between the male and female populations.

## DISCUSSION

In this retrospective cohort study of 4,124 TKA patients with an average of 6 years of follow-up, we found our results were consistent with those of previous studies in that TKA patients had low short-term mortality. In addition, our findings suggest that the causes of death for patients

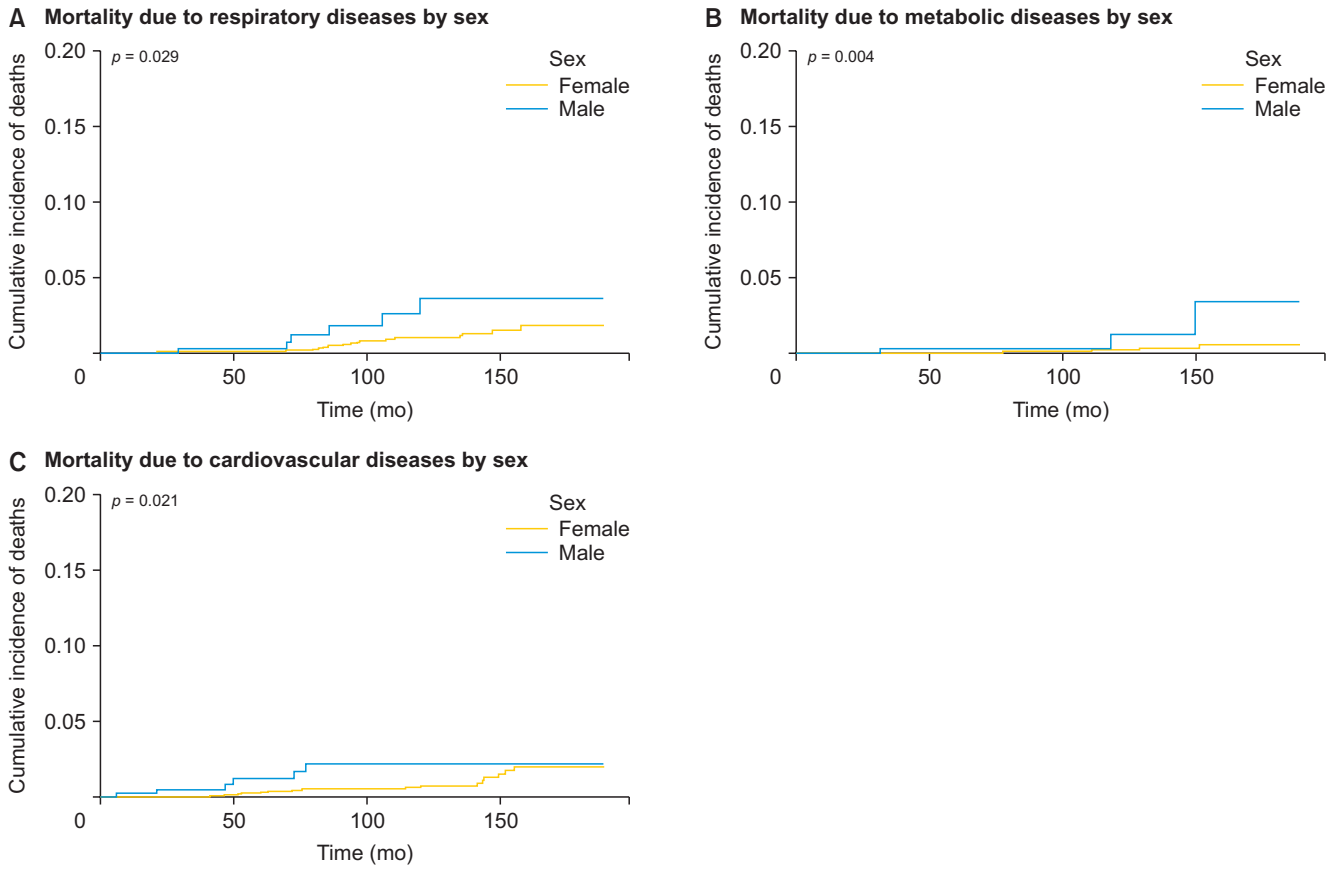


**Fig. 2.** Graphs showing the cumulative incidence rates of deaths from respiratory disease (A), metabolic disease (B), and cardiovascular disease (C) for male and female patients up to 15 years after total knee arthroplasty.

experiencing mortality within the postoperative period of 180 days show minimal to no association with the surgery. A closer chart review of those patients showed that most patients and their causes of death did not show signs of any major complications caused after TKA. Most deaths were sudden and had unidentified causes, with a few deaths caused by the unanticipated worsening of underlying diseases. Furthermore, although the leading causes of death for the TKA patients were similar to those of the general population, the findings showed that TKA patients aged below 80 years were more likely to experience death compared to those in the general population, with men having a higher cumulative risk of death than women for three of the leading causes, including respiratory, metabolic, and cardiovascular disease.

While most remain unassociated, short-term deaths caused by massive gastrointestinal bleeding and postoperative stroke have been found to be associated with TKA. Previous studies have identified massive gastrointestinal bleeding and postoperative stroke as potential complications after TKA.[16,17] The risk of gastrointestinal bleeding is reported to be higher within the first 2 weeks of operation, and the use of clopidogrel during the acute perioperative period has been found to increase the risk of postoperative gastrointestinal bleeding.[17,18] Preoperative anticoagulants have also been found to be associated with postoperative stroke.[19] Although we cannot directly associate the two deaths with TKA, we suggest monitoring patients after TKA for gastrointestinal bleeding and postoperative stroke even if they do not have any history or underlying disease related to these complications.

The long-term causes of death after TKA at our institution followed similar rankings in previous studies, with malignant neoplasm being the major cause of death after TKA.[20,21] The proportion of patients who died due to malignant neoplasm (35.0%) was consistent with that in previous studies, which was within the 30% to 35% range.[20,21] Our findings also suggest that mortality due to malignant neoplasm is significantly higher than mortality due to other causes. We believe that malignant neoplasm accounts for approximately 20% more death than other causes due to our institution being a tertiary referral hos-

pital. As our institution is a tertiary hospital that admits patients with referrals from providers in primary and secondary care, it has a higher chance of operating TKA on patients with higher risk, which leads to a higher number of deaths due to malignant neoplasm after TKA.

Our findings showed a high mortality rate due to circulatory disease (cerebrovascular disease, cardiovascular disease, and hypertensive disease combined) and respiratory disease, which also parallels previous studies that have identified circulatory and respiratory diseases as leading causes of death.[20,21] The proportion of patients who died due to circulatory disease (20.2%) was consistent with the proportion (22.9%) reported by Choi et al.,[20] a South Korean national cohort longitudinal study conducted to identify the mortality rate and causes of deaths of TKA patients in South Korea. However, the proportion of death due to circulatory disease remained comparatively lower than that reported based on the American population, while they shared similar rankings in general.[20] For respiratory disease, the proportion of deaths due to respiratory disease (10.1%) was higher than the proportion of death (6.8%) reported by Choi et al.[20]

The long-term mortality due to metabolic disease and injury, poisoning, and certain other consequences of external causes was comparatively lower than that in previous studies. Choi et al.[20] listed trauma (10.6%), which can also be referred to as certain other consequences of external causes, as the second leading cause of death in TKA patients. In our study, only 6 patients (2.3%) died due to trauma, which is significantly lower than that reported by Choi et al.[20] The overall rank and the proportion of deaths due to metabolic disease were also higher in the study by Choi et al.[20] compared to our findings (7.2% vs. 2.7%). Chronic kidney disease was also one of the leading causes of long-term mortality after TKA. This was one of the unexpected findings, as there is a lack of studies that have reported high mortality rates due to chronic kidney disease after TKA. The other causes of death included sudden and unknown deaths (R96, R98, R99) or those that could not be categorized by an ICD-code.

There are limitations to this study. First, our retrospective cohort study is a single-center study. The results reflect the local population with similar patient and hospital characteristics. Without a comparison group included in our study, the results may not be generalized to the larger population that does not share similar characteristics as our patients and institution. However, single-center studies can still provide meaningful results as the data encompasses even the initial stages of the patient data and allows for a more detailed and accurate analysis of individual patients. Second, our data did have unknown causes of death. Although most of our patients had been accurately tracked through KOSIS, a few patients did not have documentation on their exact cause of death. These unknown causes of death could have affected the ranking of long-term causes of mortality, but there is no way of identifying the unknown mortality causes.

In conclusion, the short-term mortality rate after TKA was low and mostly unrelated to TKA itself. The long-term mortality rate was high for patients below 80 years of age, with men having a higher cumulative risk of death than women for respiratory, metabolic, and cardiovascular disease. The above findings can be used as counseling data to better understand the survival and mortality of TKA patients.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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