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Bilateral Total Knee Arthroplasty: Risk Factors for Major Morbidity and Mortality

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DISCLOSURES

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Abstract

Background—Bilateral total knee arthroplasties (BTKA) performed during the same hospitalization carry increased risk for morbidity and mortality as compared to the unilateral approach. However, no evidence-based stratifications to identify patients at risk for major morbidity and mortality are available. Our objective was to determine the incidence and patient-related risk factors for major morbidity and mortality among patients undergoing BTKA.

Methods—Nationwide Inpatient Survey data collected for the years 1998–2007 were analyzed and cases of elective BTKA procedures were included. Patient demographics, including comorbidities, were analyzed and frequencies of mortality and major complications were computed. Subsequently, a multivariate analysis was conducted to determine independent risk factors for major morbidity and mortality.

Results—Included were 42,003 database entries, representing an estimated 206,573 elective BTKA. The incidence of major in-hospital complications and mortality was 9.5%. Risk factors for adverse outcome included advanced age [odds ratios (OR) for age groups 65–74 and >75 years were 1.88 (Confidence Interval (CI) 1.72; 2.05) and 2.66 (CI 2.42; 2.92), respectively, compared to the 45–65 year group], male gender [OR 1.54 (CI 1.44; 1.66)], and a number of comorbidities. The presence of congestive heart failure (OR 5.55 (CI 4.81; 6.39)) and pulmonary hypertension [OR 4.10 (CI 2.72; 6.10)] were the most significant risk factors associated with increased odds for adverse outcome.

Conclusions—We identified patient-related risk factors for major morbidity and mortality in patients undergoing BTKA. Our data can be used to aid in the selection of patients for this procedure.

Introduction

Despite advantages in cost savings, the performance of bilateral total knee arthroplasties (BTKA) during the same hospitalization remains controversial,^{1–5} because it may be associated with increased risk of morbidity and mortality compared with a unilateral (UTKA) or staged approach.^{1–3}

In an attempt to decrease patient risk, clinicians have adopted more conservative selection patterns when considering patients for BTKA. This is evidenced by nationwide trends suggesting a decrease in the use of BTKA in patients with cardiopulmonary disease and advanced age.⁶ In the absence of evidence-based guidelines, however, some hospitals have created advisories to aid in the selection of patients who are deemed appropriate candidates.⁵ Unfortunately, these advisories are rare and based on expert opinion only. Recommendations are extrapolated from data evaluating outcomes after knee arthroplasties in general, because available institutional series of BTKA are inadequate and underpowered to appropriately determine risk factors for major complications and mortality in this patient population. Furthermore, because bilateral procedures are a pathophysiologically different entity from unilateral approaches, as the increased thromboembolic load of debris and cement results in far greater effects on the cardiovascular and pulmonary system,^{7, 8} these recommendations may be biased. It is therefore not surprising that despite the preselection of younger and overall healthier BTKA patients than those undergoing UTKA, increased morbidity and mortality persists.^{2,3}

In order to overcome the stated limitations, we analyzed data from a nationally representative database to specifically determine patient-related risk factors for major complications among patients undergoing BTKA. We have previously used this database to show an increased risk of adverse perioperative events of BTKA compared to UTKA when evaluating a cohort comprised of all primary total knee arthroplasty recipients³. For this

investigation we have restricted our cohort to BTKA recipients, excluded nonelective procedures, and included the most recently available data for analysis as to allow for the determination of risk factors and evaluated the outcome of major complications in this particular group of patients. The goal of this study was to provide an evidence-based background for future recommendations and guidelines that can be used by primary care providers, internists, orthopedists, anesthesiologists and other perioperative physicians to risk-stratify patients in need of BTKA.

We hypothesized that patients of advanced age and those with preexisting comorbidities would be at increased risk for adverse events.

Materials and Methods

Annual data files for the Nationwide Inpatient Survey (NIS) are sponsored by the Agency for Healthcare Research and Quality and were commercially obtained from the Hospital Cost and Utilization Project. In-depth information on the NIS design can be obtained electronically.^{9, 10} The NIS is the largest all-payer database in the United States. It contains information from approximately 8 million hospital admissions yearly and is a 20% stratified sample (i.e., designed to representatively include hospitals of different size, location, teaching status, geographic area, and ownership) of approximately 1000 hospitals in 38 states. NIS contains more than 100 clinical and nonclinical data elements, including those regarding diagnoses, procedures, admission and discharge status, as well as patient and hospital characteristics. The NIS offers weighting procedures that allow for the generation of nationally representative estimates. Many investigations on various topics across the field of medical specialties have used this database.¹¹ As data used in this study are sufficiently deidentified, this study was exempt from review by our IRB.

Selection of Study Sample and Statistical Methods

Our study sample includes NIS data for each year between 1998 and 2007. Discharges with an International Classification of Diseases- 9th revision-Clinical Modification (ICD-9-CM) procedure code for BTKA were identified. This was achieved by inclusion of entries, which listed a code for primary TKA (81.54) twice, as reported previously.^{2, 3, 6} Support for the assumption that admissions with two occurrences of this code are bilateral procedures and not mistakes in coding, is provided by two observations: 1) The NIS supplies dates on which various procedures took place, which differ in cases in which the two knee replacements were performed on different days during the same hospitalization; and 2) The characteristics of the unilateral procedure group (identified by the procedure code appearing once) differed significantly from that of the bilateral procedure group (i.e. shorter length of stay, etc).³

Only entries indicating routine, elective admissions were included (see flowchart in appendix). The study goal was to determine risk factors for major complications and mortality after BTKA. Frequencies of major complications were analyzed by determining cases that listed ICD-9-CM diagnosis codes consistent with either postoperative cerebral infarction, pulmonary compromise, sepsis, shock/cardiorespiratory arrest, acute myocardial infarction, cardiac complications (except myocardial infarction), pneumonia, and thrombosis/pulmonary embolism based on modified definitions provided in the Complication Screening Package designed for use with administrative data.¹² Comorbidity profiles were analyzed by determining the prevalence of a number of disease states as defined in the Comorbidity Software provided by the Agency for Healthcare Research and Quality based on the Elixhauser method.^{13,14} As pulmonary hypertension was previously identified as a risk factor for morbidity and mortality in orthopedic patients,¹⁵ we included

this disease complex in our analysis instead of the less well defined entity of “pulmonary circulatory disease” provided in the method by Elixhauser et al.¹⁴

Patient characteristics were reported for the groups with and without the outcome of mortality/morbidity (table 1). These included: age (continuous as well as categorized as 0–44, 45–64, 65–74, and >75 years), gender, and race (White, Black, Hispanic, Other, missing). Two-year time periods (1998–1999, 2000–2001, 2002–2003, 2004–2005, 2006–2007) were considered in all analyses to account for any potential temporal changes in practice or coding. Weighted means and percentages were shown for continuous and categorical variables. Approximately 30% of entries in the race category were not available and were imputed as “white”. This step was based on an approach previously described, and the observation that institutions with increased rates of unavailable data for race served populations with higher than average white to black patient ratios.^{3, 16} In order to account for a potential impact of this approach, we also created a separate category for the missing values. Both approaches were used for analysis in this study.

The incidence of major complications and mortality is shown in Figure 1 using bar graphs. Table 2 contains information on comorbidities by outcome status. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC). To facilitate analysis of data collected in a complex survey design and to obtain consistent estimates of mean and variance parameters taking into account the complex survey data setting, SAS procedures SURVEYMEANS, SURVEYFREQ, and SURVEYLOGISTIC were utilized for descriptive analyses and final modeling efforts.

For the purpose of building a parsimonious model restricted to strong predictive covariates only, the following steps were taken:¹⁷ First, clinical judgment and significance at a p-value of 15% level in the univariate analyses (as in Tables 1 and 2) were used to identify variables for the process of multivariable modeling. Second, additional variable selection and internal validation of the predictive performance of the model was achieved through a two-step, nonparametric bootstrapping process.¹⁸ In the bootstrap procedure, the original set of data of size N becomes a parent population from which samples of size N are randomly drawn with replacement. In the first step of internal validation the bootstrapping technique was used for variable selection. One hundred bootstrap samples were created, and a stepwise procedure was applied to each sample utilizing a forward selection method (with a selection entry level = 0.20).

From this analysis, we calculated the percentage of samples for which each variable was included in the model from the 100 samples. Percent inclusion (80% cutoff decided a priori) was used to determine the prognostic importance of a variable, because it was expected that a prognostically important variable would be included in the model for a majority of the bootstrap samples. For variables which were not included, if the frequency of pair wise combinations included in the model was greater than 90%, then include the one with the largest frequency in the final model. In the second internal validation step, optimism-corrected Area Under the Receiver Operating Characteristic (ROC) Curve (AUC) (also referred to as the C-statistic) was computed utilizing %BVAL macro from SAS.¹⁹ Models with C-statistics greater than 0.7 are deemed to have good discriminatory/predictive power. Third, the model finalized at the second stage was processed one more time utilizing the SURVEYLOGISTIC procedure instead of the LOGISTIC procedure to be able to obtain appropriate estimates of the variance for the weighted survey data. This step was necessary, because the SURVEYLOGISTIC does not allow for forward selection procedure. This methodology has previously been described by Hosmer et al. as appropriate.²⁰

Results

We identified 42,003 entries fitting selection criteria, representing an estimated 206,573 elective BTKA procedures performed between 1998 and 2007 in the US. Of those 9.5% developed major complications or mortality during their hospitalization. Patients of older age, male gender and white race were disproportionately more affected by major morbidity and mortality (Table 1). Cardiac complications made up the majority of adverse occurrences postoperatively (Figure 1).

Patients who suffered a major complication or mortality had a higher prevalence of comorbidities, including chronic lung diseases, congestive heart failure and pulmonary hypertension (Table 2).

Age, sex, race, chronic lung disease, congestive heart failure, coagulopathy, neurologic disorders, peripheral vascular disease, renal disease, cardiac valvular disorders, electrolyte/fluid abnormalities, pulmonary hypertension and obesity were selected for multivariate model building. Race, peripheral vascular disease and obesity were excluded from the model, as they did not meet the cut-off for inclusion. In the final model, increasing age emerged as an independent risk factor for major morbidity and mortality. Compared to patients in the age group between 45–64 years, those below the age of 45 were half as likely to have a major complication or mortality [OR 0.49 (CI 0.30; 0.81)]. Patients aged 65–74 and >75 years were 1.81 (CI 1.67; 2.30) and 2.52 (CI 2.30; 2.77), respectively, more likely to suffer a major adverse outcome compared to their 45–65 year old peers. Male gender was associated with increased odds for adverse outcome [OR 1.50 (CI 1.40; 1.61)]. A number of comorbidities were identified as independent risk factors for major complications and mortality (Figure 2). The presence of congestive heart failure and pulmonary hypertension were the most significant comorbidities associated with increased odds for adverse outcome. The optimism-corrected C-statistics from the final model was 0.7.

Discussion

We were able to characterize the incidence of major complications and mortality in patients undergoing BTKA and identify risk factors. Independent risk factors included advanced age, male sex and a number of comorbidities, with congestive heart failure and pulmonary hypertension carrying the highest odds for major adverse outcome. Our data can be used to help guide the selection of individuals who are considered candidates for this procedure.

Understanding the pathophysiology leading to increased morbidity and mortality in patients undergoing joint arthroplasty and especially bilateral procedures is important when interpreting our findings. Previous research suggests that complications after joint arthroplasty can be related to overall intraoperative embolic debris and cement load that gains access to the vascular system during surgery, on one hand, and the end-organ reserve, on the other.^{7,8,15, 21} Embolic material entering the lung causes lung injury and increases pulmonary vascular resistance,^{7,8} which in turn may lead to right ventricular and atrial strain promoting arrhythmias, hypotension and venostasis.²² These events may be responsible for the increased rates of ARDS and thromboembolic events seen in patients undergoing bilateral versus unilateral TKA.² Similarly, increased exposure of the CNS and other organs, such as the kidney, to embolic material may explain higher rates of delirium and renal complications in BTKA versus UTKA patients.^{2, 3}

In this study we identified advanced age to be a risk factor for increased morbidity and mortality. This finding is consistent with previous research^{3, 21} and could be explained by the known phenomenon of age-related physiologic decline in end-organ reserve.²³ Thus, it is possible that while embolic load associated with surgery remains unchanged in the

elderly, the capacity of organs to withstand the insult is decreased, resulting in worse outcome.

Male sex was found to be associated with increased odds of major morbidity and mortality. While previously described in the arthroplasty population,²¹ the reasons for this finding have to remain speculative at this point, but potential reasons may include hormonal differences that may offer some degree of protection for female patients.²⁴

A number of comorbidities independently increased the risk for major morbidity and mortality, with congestive heart failure and pulmonary hypertension being associated with the highest odds. Preexisting decreased vascular reserve of the lung is a likely factor associated with this finding. Indeed, the load-dependent response and capacity of the lung to absorb the embolic insult was shown in healthy patients undergoing bilateral hip arthroplasty.⁸ While no significant changes in pulmonary vascular resistance were seen after the first joint implantation, an increase in pulmonary vascular parameters was measured after the second implantation, suggesting that the ability of the pulmonary vascular bed to compensate may be overwhelmed by the larger embolic load of two joints. Interestingly, these derangements continued to be present on postoperative day one, suggesting that the stresses are prolonged and not short-lived, as commonly assumed. While these pulmonary hemodynamic changes may be of limited clinical consequence in otherwise healthy individuals,⁸ significantly increased rates of morbidity and mortality among patients with pulmonary hypertension undergoing even unilateral hip and knee replacement have been found¹⁵. It is therefore not surprising that pulmonary hypertension was one of the two most significant risk factors for morbidity and mortality in this study.

Given these findings, it seems prudent to screen patients who are suspected of having increased pulmonary pressure or right heart dysfunction, including patients with sleep apnea²⁵ and those with a history of pulmonary embolism,²⁶ and consider them at high risk. Attempting the estimation of pulmonary pressures by echocardiography in patients at risk for pulmonary hypertension during preoperative testing may therefore be of benefit. Although no data are available to judge what level of pulmonary hypertension should be considered significant in this setting, taking a conservative approach in judgment when assessing suitability for BTKA may be advisable until more research is available. If preoperative pharmacologic treatment of abnormal parameters is of benefit has to remain speculative at this point and would warrant detailed investigations.

Equally important risk factors identified included a number of comorbidities suggesting decreased end-organ reserve, i.e., renal disease, neurologic disease, congestive heart failure and chronic pulmonary disease. It has to be mentioned that these comorbidities are not uniquely associated with adverse outcomes among BTKA patients,²¹ as many surgical procedures are defined by significant metabolic injury, fluid shifts and other insults exposing various organ systems to a number of stresses. However, when considering the likely pathophysiology (i.e., intraoperative debris embolization) of morbidity and mortality in the BTKA population, physicians should be cautioned against worsening of organ function in this particular setting. While many clinicians are well aware of the impact of cardiac and pulmonary disease on the outcome in surgical patients, our results serve to alert about the negative impact of diseases with low prevalence on perioperative morbidity and mortality. This in turn, underlines the advantages of large database research, which allows for the study of low incidence scenarios.

Our study is limited by a number of factors inherent to secondary data analysis of large administrative databases. As such, clinical information (i.e., type of anesthesia, amount of blood loss, length of surgery etc.) available in the NIS is limited, and our analysis must be

interpreted in this context. Because of the nature of the NIS, only in-patient data are available and thus complications and events after discharge are not captured. Furthermore, the need for readmission cannot be accounted for in this database. Thus, conclusions should be limited to the acute perioperative setting with the notion that mortality and complications are likely underestimated.

In this context, we are also unable to compare the outcomes of patients who have two TKAs performed during different hospitalizations. While we have previously shown that staging procedures a few days apart during the same hospitalization offers no benefit in the risk for mortality and even may increase the risk for perioperative complications,³ Ritter et al. suggest that 30-day mortality rates of the BTKA performed 3 to 12 months apart was between 0.29% and 0.36%, compared to significantly increased rates for simultaneously performed BTKA (0.99%) and those scheduled 6 weeks apart (0.48%).²⁷

It must also be mentioned that the identification of co-morbidities in this study was based on the validated method of Elixhauser et al, that is based on the bundling of ICD-9 codes to define various co-morbidities in administrative databases.¹⁴ However, it is often not possible to determine from ICD-9 codes to if a co-morbidity is preexisting or acquired during the hospitalization. It should be kept in mind though, that this does not diminish the value of the co-morbidities identified as risk factors as studied in this analysis, as they should alert clinicians of increased risk if they are encountered before surgery.

Furthermore, our modeling approaches are also somewhat limited by software availability and a gap in research in the arena of application of stepwise procedure in logistic regression analyses of survey data that take the survey design (stratification and clustering) and strata weights into account. We followed the latest recommendations published by Hosmer et al.²⁰ on how to deal with this situation, but it is clear that further simulation-based research is needed for delineating the scenarios in which there might be deviation in the models fitted through 'design-based' and 'model-based' approaches. Software development incorporating procedures for fitting logistic regression in a stepwise manner for complex survey data is also necessary for easy implementation.

An additional limiting factor is the bias associated with the retrospective nature of our study. Nevertheless, because of the availability of data from a large, nationally representative sample, this type of analysis may provide a more accurate estimate of events surrounding BTKA than various prospective studies that are limited in sample size and thus lack the ability to capture low-incidence outcomes.

In conclusion, we were able to identify a number of risk factors for major morbidity and mortality in patients undergoing BTKA. These data can be utilized to aid in the selection of patients for this procedure, that otherwise may be associated with increased morbidity and mortality as compared to a unilateral approach.

While it is beyond the scope of this article to provide final and specific guidelines, we would urge institutions to engage in discussions in order to establish criteria to restrict BTKA procedures to patients with decreased reserve of the cardiopulmonary, vascular, renal and central nervous system and contemplate exclusion of patients of advanced age and those with evidence of significant end-organ disease. Until detailed evaluation guidelines can be agreed on, it seems prudent to exclude the elderly and patients with American Society of Anesthesiologists Class of 3 and higher. Patients at risk for occult derangements of pulmonary hemodynamics and right heart dysfunction (i.e., the obese, those with sleep apnea, chronic obstructive pulmonary disease, and with previous pulmonary embolism) should undergo cardiopulmonary evaluation with echocardiography to rule out significant

preexisting increases in pulmonary artery pressures, which may predispose patients to increased morbidity and mortality.

Given the controversy surrounding this issue and the fact that a number of studies have been published in recent years on this subject, it may be time for the establishment of national guidelines to aid physicians and patients with the decision of whether to proceed with BTKA.

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References

1. Restrepo C, Parvizi J, Dietrich T, Einhorn TA. Safety of simultaneous bilateral total knee arthroplasty: A meta-analysis. *J Bone Joint Surg Am.* 2007; 89:1220–6. [PubMed: 17545424]
2. Memsoudis SG, González Della Valle A, Besculides MC, Gaber L, Sculco TP. In-hospital complications and mortality of unilateral, bilateral, and revision TKA: Based on an estimate of 4,159,661 discharges. *Clin Orthop Relat Res.* 2008; 466:2617–27. [PubMed: 18704616]
3. Memsoudis SG, Ma Y, González Della Valle A, Mazumdar M, Gaber-Baylis LK, MacKenzie CR, Sculco TP. Perioperative outcomes after unilateral and bilateral total knee arthroplasty. *Anesthesiology.* 2009; 111:1206–16. [PubMed: 19934863]
4. Hooper GJ, Hooper NM, Rothwell AG, Hobbs T. Bilateral Total Joint Arthroplasty: The Early Results from the New Zealand National Joint Registry. *J Arthroplasty.* 2009; 24:1174–7. [PubMed: 19056233]
5. Urban MK, Chisholm M, Wukovits B. Are Postoperative Complications More Common with Single-Stage Bilateral (SBTKR) Than with Unilateral Knee Arthroplasty: Guidelines for Patients Scheduled for SBTKR. *HSS J.* 2006; 2:78–82. [PubMed: 18751852]
6. Memsoudis SG, Besculides MC, Reid S, Gaber-Baylis LK, González Della Valle A. Trends in Bilateral Total Knee Arthroplasties: 153,259 Discharges between 1990 and 2004. *Clin Orthop Relat Res.* 2009; 467:1568–76. [PubMed: 19002540]
7. Memsoudis SG, Starcher B, González Della Valle A, Ma Y, Jules-Elysee K, Sculco TP. Urine desmosine as a marker of lung injury following total knee arthroplasty. A pilot study. *HSS J.* 2009; 5:154–8. [PubMed: 19521737]
8. Memsoudis SG, Salvati SA, Go G, Ma Y, Sharrock NE. Perioperative Pulmonary Circulatory Changes during Bilateral Total Hip Arthroplasty Under Regional Anesthesia. *Reg Anesth Pain Med.* 2010; 35:417–21. [PubMed: 20814281]
9. HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality; Rockville, MD: 2008. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp
10. Introduction to the HCUP National Inpatient Sample (NIS) 2006. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP); Rockville, MD: 2008. Available at: http://www.hcup-us.ahrq.gov/db/nation/nis/2006NIS_INTRODUCTION.pdf
11. Publications from the Healthcare Cost and Utilization Project Databases. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project (HCUP); Rockville, MD: 2009. Available at: <http://www.ahrq.gov/data/hcup/hcupref.htm>
12. Iezzoni LI, Daley J, Heeren T, Foley SM, Fisher ES, Duncan C, Hughes JS, Coffman. Identifying complications of care using administrative data. *Medical Care.* 1994; 32:700–15. [PubMed: 8028405]

13. HCUP Comorbidity Software. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality; Rockville, MD: 2009. Available at: www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp
14. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998; 36:8–27. [PubMed: 9431328]
15. Memtsoudis SG, Ma Y, Chiu YL, Walz JM, Voswinckel R, Mazumdar M. Perioperative mortality in patients with pulmonary hypertension undergoing major joint replacement. *Anesth Analg*. 2010; 111:1110–6. [PubMed: 20841415]
16. Kozak LJ. Underreporting of race in the National Hospital Discharge Survey. *Adv Data*. 1995; 265:1–12. [PubMed: 10154340]
17. Harrell, FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*. 1. New York, NY: Springer-Verlag; 2001. p. 215-265.
18. Sauerbrei W, Schimacher M. A bootstrap resampling procedure for model building: application to the cox regression model. *Statistics in Medicine*. 1992; 11:2093–109. [PubMed: 1293671]
19. Gonen, M. *Analyzing Receiver Operating Characteristic Curves With SAS*. 1. Cary, North Carolina: SAS Institute Inc; 2007.
20. Hosmer, DW.; Lemeshow, S. *Applied logistic regression*. 2. New York, NY: Wiley; 2000.
21. Memtsoudis SG, González Della Valle A, Besculides MC, Esposito M, Koulouvaris P, Salvati EA. Risk Factors for Perioperative Mortality after Lower Extremity Arthroplasty: A Population-Based Study of 6 901 324 Patient Discharges. *J Arthroplasty*. 2010; 25:19–26. [PubMed: 19106028]
22. Urban MK, Sheppard R, Gordon MA, Urquhart BL. Right ventricular function during revision total hip arthroplasty. *Anesth Analg*. 1996; 82:1225–9. [PubMed: 8638795]
23. Loran DB, Hyde BR, Zwischenberger JB. Perioperative management of special populations: the geriatric patient. *Surg Clin North Am*. 2005; 85:1259–66. [PubMed: 16326206]
24. Choi BG, McLaughlin MA. Why men's hearts break: effects of sex steroids. *Endocrinol Metab Clin North Am*. 2007; 36:365–77. [PubMed: 17543724]
25. Bradley TD. Right and left ventricular functional impairment and sleep apnea. *Clin Chest Med*. 1992; 13:459–79. [PubMed: 1521413]
26. Kline JA, Steuerwald MT, Marchick MR, Hernandez-Nino J, Rose GA. Prospective evaluation of right ventricular function and functional status 6 months after acute submassive pulmonary embolism: frequency of persistent or subsequent elevation in estimated pulmonary artery pressure. *Chest*. 2009; 136:1202–10. [PubMed: 19542256]
27. Ritter M, Mamlin LA, Melfi CA, Katz BP, Freund DA, Arthur DS. Outcome implications for the timing of bilateral total knee arthroplasties. *Clin Orthop Relat Res*. 1997; 345:99–105. [PubMed: 9418626]

Appendix

The flowchart illustrates the sample selection process and the incidence of cases with and without major complications and mortality.

Figure 1. Depicted is the incidence of major complications and mortality among cases of bilateral total knee arthroplasty.

Figure 2.

Shown are the adjusted odds ratios for major complications/mortality associated with a number of comorbidities. The reference group is the cohort of patients without the specific disease. All presented risk factors are significant as the confidence intervals do not overlap with 1. Odds ratios were calculated from PROC SURVEYLOGISTIC after adjusting for age, sex and two-year time period.

Table 1
Patient demographics of cases with and without major complications/mortality

Shown are the total number and percent of cases with and without major complications and mortality. The weighted N represents the national estimated number of procedures derived from the actual number of entries in the Nationwide Inpatient Survey (unweighted N).

Demographics				
	Major Complication/Mortality			
Group	Yes	No	p-value [*]	Total
Unweighted N=	3986	38017	<0.001	42003
Weighted N=	19662	186911		206573
(%)	9.52	90.48		100
Average age (years)	70.1	65.47		65.11
Age groups (%)				
0–44	0.42	1.59	<0.001	1.48
45–64	24.43	43.21		41.42
65–74	41.31	36.44		36.9
≥75	33.84	18.76		20.2
Gender (%)				
Male	49.95	40.03	<0.001	40.98
Female	50.05	59.97		59.02
Race (%)				
White	65.96	63.4	0.002	63.64
Black	2.98	3.74		3.66
Hispanic	1.27	1.72		1.67
Other	1.79	2.25		2.2
Missing	28	28.9		28.82

* P-values were calculated using Chi-square test from PROC SURVEYFREQ.

Table 2
Prevalence of comorbidities in cases with and without major complications/mortality

Shown are the weighted N and percent of cases with and without major complications and mortality.

Prevalence of Comorbidities				
Comorbidity	Complications Weighted N (%)	No Complications Weighted N (%)	p-value*	Total
Alcohol abuse	143(0.73%)	985(0.53%)	0.11	1128(0.55%)
Chronic lung disease	2832(14.41%)	19711(10.55%)	<0.001	22543(10.91%)
Congestive heart failure	2317(11.78%)	2943(1.57%)	<0.001	5259(2.55%)
Uncomplicated diabetes mellitus	2882(14.66%)	25817(13.81%)	0.15	28699(0.17%)
Complicated diabetes mellitus	229(1.16%)	1689(0.90%)	0.11	1918(0.93%)
Liver dysfunction	127(0.65%)	814(0.44%)	0.07	940(0.46%)
Coagulopathy	881(4.48%)	2772(1.48%)	<0.001	3653(1.77%)
Neurologic disorders	517(2.63%)	3039(1.63%)	<0.001	3556(1.72%)
Obesity	2397(12.19%)	25135(13.45%)	0.03	27532(13.33%)
Peripheral vascular disease	449(2.28%)	2176(1.16%)	<0.001	2625(1.27%)
Renal disease	505(2.57%)	1305(0.70%)	<0.001	1810(0.88%)
Pulmonary hypertension	335(1.70%)	462(0.25%)	<0.001	797(0.39%)
Cardiac valvular disorders	1777(9.04%)	6464(3.46%)	<0.001	8241(0.10%)
Electrolyte/fluid abnormalities	3709(18.87%)	14276(7.64%)	<0.001	17986(8.71%)
Metastatic cancer	17(0.09%)	79(0.04%)	0.25	96(0.05%)
Cancer	100(0.51%)	858(0.46%)	0.65	959(0.46%)

* P-value was calculated from Chi-Square tests from PROC SURVEYFREQ.