

Perioperative Outcomes after Unilateral and Bilateral Total Knee Arthroplasty

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Background: **The safety of bilateral total knee arthroplasties (BTKAs) during the same hospitalization remains controversial. The authors sought to study differences in perioperative outcomes between unilateral and BTKA and to further compare BTKAs performed during the same *versus* different operations during the same hospitalization.**

Methods: **Nationwide Inpatient Sample data from 1998 to 2006 were analyzed. Entries for unilateral and BTKA procedures performed on the same day (simultaneous) and separate days (staged) during the same hospitalization were identified. Patient and healthcare system–related demographics were determined. The incidences of in-hospital mortality and procedure-related complications were estimated and compared between groups. Multivariate regression was used to identify independent risk factors for morbidity and mortality.**

Results: **Despite younger average age and lower comorbidity burden, procedure-related complications and in-hospital mortality were more frequent after BTKA than after unilateral procedures (9.45% *vs.* 7.07% and 0.30% *vs.* 0.14%; $P < 0.0001$ each). An increased rate of complications was associated with a staged *versus* simultaneous approach with no difference in mortality (10.30% *vs.* 9.15%; $P < 0.0001$ and 0.29% *vs.* 0.26%; $P = 0.2875$). Independent predictors for in-hospital mortality included BTKA (simultaneous: odds ratio, 2.23 [95% confidence interval, 1.69–2.95]; $P < 0.0001$; staged: odds ratio, 2.01 [confidence interval, 1.28–3.41]; $P = 0.0031$), male sex (odds ratio, 2.02 [confidence interval, 1.75–2.34]; $P < 0.0001$), age older than 75 yr (odds ratio, 3.96 [confidence interval, 2.77–5.66]; $P < 0.0001$), and the presence of a number of comorbidities and complications.**

Conclusion: **BTKAs carry increased risk of perioperative morbidity and mortality compared with unilateral procedures. Staging BTKA procedures during the same hospitalization offers no mortality benefit and may even expose patients to increased morbidity.**

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TOTAL knee arthroplasty (TKA) remains the most effective treatment of end-stage osteoarthritis. When both joints are affected, bilateral TKA (BTKA) reduces the overall cost of care by 18–36% and duration of hospital stay by approximately 4–6 days. Furthermore, this approach may reduce overall use of pain medication and recovery time.[1–3] Despite these advantages, the safety of BTKA remains controversial.[4–7] Recent publications that use large patient samples have concluded that BTKA surgery is associated with an increase in morbidity and mortality when compared with staged and unilateral procedures. These studies include a meta-analysis of randomized trials,[6] a review from the Swedish Knee Arthroplasty Register,[4] and an analysis of data from the National Hospital Discharge Survey.[7]

Conversely, a number of researchers and clinicians maintain that the bilateral approach carries little to no additional risk in carefully selected patients.[8,9] The studies supportive of BTKA, however, tend to represent outcomes from restricted, small patient samples from specialized, high-volume institutions and surgeons, who may have fewer complications but whose experience may not allow for generalizability. The small sample sizes in these studies also prohibit adequate representation of low-incidence outcomes.[10] In view of these conflicting results, nationally representative trend data suggest that clinicians have adopted a more conservative approach when selecting patients as candidates for BTKA, as evidenced by a decrease in the prevalence of cardiopulmonary disease and advanced age among BTKA recipients.[11] In the absence of official guidelines, some hospitals have adopted advisories against the performance of BTKA procedures in patients who are deemed to be at increased risk for adverse outcomes. These include patients older than 75 yr, those with an American Society of Anesthesiologists physical status classification of III or greater, and those with significant cardiopulmonary comorbidities.[9] However, these criteria are often questioned because the information on risk factors for adverse outcomes are derived from studies that are burdened by limitations of small sample size and inclusion of restricted patient population (*e.g.*, single institution, academic centers, or Medicare recipients).[12–15]

In a further attempt to reduce unfavorable outcomes associated with this elective procedure and in addition to selecting suitable candidates, some physicians perform procedures on different days during the same hospitalization

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to strike a balance between the benefits of BTKA and the related clinical risk.[9,16] However, this strategy is largely based on very limited information. Only two single-institution studies[16,17] have attempted to evaluate the comparative effectiveness of staging procedures during the same hospitalization with an interval of 2–7 days apart. While no effect in one[17] and a negative effect associated with staging was found in the other,[16] both studies were burdened by the inclusion of a small number of subjects, thus restricting their ability to adequately capture low-incidence outcomes. In general, population-based data on this topic remain rare, because most studies addressing this problem are limited by factors mentioned previously. Furthermore, they insufficiently address outcomes in the immediate perioperative setting.[12–15]

To overcome some of these limitations, we used data from the Nationwide Inpatient Sample (NIS), the largest annual all-payer database in the United States, and sought to study (1) whether differences in perioperative outcomes between unilateral TKA (UTKA) and BTKA exist, (2) whether procedures performed on the same day (simultaneously) *versus* at different operations (staged) during the same hospitalization were associated with different outcomes, and (3) whether risk factors for perioperative morbidity and mortality after TKA procedures could be identified.

Materials and Methods

Nationwide Inpatient Sample annual data files are sponsored by the Agency for Healthcare Research and Quality and are commercially obtained from the Hospital Cost and Utilization Project. Detailed information on the NIS design can be found on the Internet.†‡‡ The NIS represents the largest all-payer inpatient discharge database in the United States and contains information from approximately 8 million hospital admissions per year. Having grown since its inception in 1988 when it included data from eight states, the most recent data files represent a 20% stratified sample (*i.e.*, designed to representatively include hospitals of different size, location, teaching status, geographic area, and ownership) of approximately 1,000 hospitals in 38 states. It includes more than 100 clinical and nonclinical data elements, such as diagnoses, procedures, admission and discharge status, patient demographics (*e.g.*, sex, age, race, payment source, duration of stay), and hospital characteristics (*e.g.*, size, location, teaching status). The NIS provides weights that allow for nationally representative estimates. A large number of studies addressing various questions across the spectrum of medical specialties,§§ including anesthesiology,[18–20] have used the NIS database. The use of this study was exempt from review by the institutional review board because the data used in this study are sufficiently deidentified.

Study Sample and Statistical Analysis

Our study sample consists of all data in NIS for each year between 1998 and 2006. To improve the sample representativeness of NIS, the sampling and weighting strategy was modified beginning with the 1998 data. To avoid any bias introduced by this change, we chose to include data collected only after 1998 in our study. At the time of analysis, the 2006 data set was the latest available. Discharges with an *International Classification of Diseases, 9th Revision, Clinical Modification* procedure code for primary TKA (81.54) were identified and included in the sample. Two procedure type groups were created: UTKA and BTKA. UTKAs were identified by the occurrence of the procedure code 81.54 once, and those with BTKA had this procedure code listed twice, as reported previously.[7,11,12] The prevalence of procedure subtypes and respective demographics (age, sex, race, disposition status, primary source of payment, distribution of procedures by hospital size, teaching status, location, and duration of care) were estimated. For a large number of cases (approximately 40%), the race category was not available. We imputed the missing discharges as white. This was the largest group in our study, and this approach has been previously described by Bateman *et al.*[18] Frequencies of procedure-related complications were analyzed by determining cases that listed *International Classification of Diseases, 9th Revision, Clinical Modification* diagnosis codes specifying complications of surgical and medical care (diagnosis codes 996.X–999.X; appendix). In addition, we studied the prevalence of selected adverse diagnoses, including pulmonary embolism, venous thrombosis, respiratory insufficiency after trauma or surgery/adult respiratory distress syndrome, and acute posthemorrhagic anemia, using the *International Classification of Diseases, 9th Revision, Clinical Modification* diagnosis code system (appendix). 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.‖‖ To determine the overall comorbidity burden, comorbidity indices were calculated as described by Charlson *et al.*[21] and were adjusted for use with administrative data as recommended by Deyo *et al.*[22] Differences in in-hospital mortality between procedure subtypes were as-

†† HCUP Databases. Healthcare Cost and Utilization Project. July 2008. Agency for Healthcare Research and Quality, Rockville, Maryland. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Last modified July 11, 2008. Accessed May 14, 2009.

‡‡ Introduction to the HCUP National Inpatient Sample (NIS) 2006. May 2008. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project. Available at: http://www.hcup-us.ahrq.gov/db/nation/nis/2006NIS_INTRODUCTION.pdf. Last modified May 14, 2008. Accessed May 14, 2009.

§§ Publications from the Healthcare Cost and Utilization Project Databases. Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project. Available at: http://www.ahrq.gov/data/hcup/hcupref.htm. Accessed May 14, 2009.

‖‖ HCUP Comorbidity Software. Healthcare Cost and Utilization Project. April 2009. Agency for Healthcare Research and Quality, Rockville, Maryland. Available at: www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp. Last modified April 24, 2009. Accessed May 14, 2009.

Table 1. Demographics of Unilateral and Bilateral Total Knee Arthroplasty Discharges

	Unilateral (n = 626,439 Unweighted, 3,055,368 Weighted)			Bilateral (n = 43,350 Unweighted, 212,994 Weighted)			
	F	WF	%	F	WF	%	*P* Value
Age group							< 0.0001
0–44 yr	13,030	63,458	2.08	673	3,273	1.54	
45–64 yr	215,570	1,050,251	34.37	17,452	85,590	40.18	
65–75 yr	222,142	1,082,807	35.44	16,123	79,178	37.17	
≥ 75 yr	175,697	858,851	28.11	9,102	44,953	21.11	
Sex							< 0.0001
Male	222,537	1,084,672	35.56	17,947	88,008	41.35	
Female	402,856	1,965,684	64.44	25,367	124,813	58.65	
Race							< 0.0001
White	559,020	2,730,731	89.31	39,663	195,102	91.54	
Black	31,037	150,296	4.92	1,617	7,856	3.69	
Hispanic	23,371	111,047	3.63	993	4,759	2.23	
Other	13,489	65,589	2.15	1,105	5,407	2.54	
Insurance							< 0.0001
Medicare	38,188	1,863,334	61.06	23,670	116,331	54.71	
Medicaid	16,116	78,918	2.59	708	3,500	1.65	
Private/HMO	204,848	998,328	32.71	17,719	87,024	40.93	
Other	22,855	111,056	3.64	1,185	5,781	2.72	
Discharge status							< 0.0001
Routine	168,005	822,165	27.04	6,304	31,038	14.66	
Short-term hospital	4,891	24,136	0.79	495	2,442	1.15	
Other transfers	276,517	1,352,432	44.48	30,699	151,025	71.33	
Home health care	172,743	836,380	27.51	5,432	26,481	12.51	
Against medical advice	175	864	0.03	15	75	0.04	
Died in hospital	845	4,121	0.14	131	636	0.3	
Alive, destination unknown	112	528	0.02	3	16	0.01	
Hospital size							< 0.0001
Small	91,796	429,435	14.05	6,006	28,268	13.26	
Medium	162,036	779,629	25.51	10,612	51,272	24.06	
Large	372,752	1,847,002	60.44	26,761	133,589	62.68	
Hospital location							< 0.0001
Rural	87,411	443,945	14.53	5,349	27,425	12.87	
Urban	539,173	2,612,121	85.47	38,030	185,704	87.13	
Teaching status							< 0.0001
Nonteaching	374,122	1,804,006	59.03	21,294	106,439	49.94	
Teaching	252,462	1,252,060	40.97	22,085	106,690	50.06	

Tabulated are patient and healthcare system–related demographics for discharges after unilateral and bilateral total knee arthroplasty. Presented are unweighted and weighted frequencies as well as proportions in percent for either procedure type.

F = frequency; HMO = healthcare maintenance organization; WF = weighted frequency.

sessed. We further compared in-hospital mortality and complications among BTKA recipients whose procedures were performed on the same day (simultaneously) *versus* a different day (staged) of their hospitalization. Unweighted frequencies representing the actual number of entries in the NIS as well as weighted frequencies calculated to provide national estimates are presented in this study.

All statistical analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC). To facilitate analysis of data collected in a complex survey design (including stratification, clustering, replication, and unequal probabilities of selection) and to obtain consistent estimates of mean and variance parameters taking into account the complex survey data setting, we used SAS procedures SURVERYMEANS, SURVEYFREQ, and SURVEYLOGISTIC for descriptive, comparative (tables 1–3), and logistic regression analysis (tables 4–7). Continuous variables are presented as means and 95% confidence intervals (CIs), and categorical variables are described as percentages. Although the conventional threshold of statistical significance (*i.e.*, $P < 0.05$) was used to guide model development, we also reported full *P* values and 95% CIs to let readers interpret the significance of the findings in light of the potential undue effect that very large sample size might have on the *P* values.

The data-splitting approach[23] was used for model development and validation by dividing the entire data set into a training data set (80%) on which the model was developed and the other 20% of data, which was used for validation. Univariate analysis for differences between procedure types was conducted by *t* test for continuous variables and chi-square test for categori-

Table 2. Procedure-related Complications among Unilateral and Bilateral Total Knee Arthroplasty Discharges

	Unilateral			Bilateral			
	F	WF	%	F	WF	%	*P* Value
Device-related complications							
Device related	5,420	26411	0.86	228	1115	0.52	< 0.0001
Organ-specific complications							
CNS	763	3,764	0.12	107	531	0.25	< 0.0001
Cardiac	5,849	28,700	0.94	720	3,562	1.67	< 0.0001
Peripheral vascular	1,501	7,374	0.24	159	809	0.38	< 0.0001
Respiratory	5,680	27,827	0.91	550	2,700	1.27	< 0.0001
Gastrointestinal	4,603	22,510	0.74	631	3,098	1.45	< 0.0001
Genitourinary	4,839	23,747	0.78	497	2,453	1.15	< 0.0001
Other complications of procedure							
Shock	97	467	0.02	33	161	0.08	< 0.0001
Hematoma/seroma	5,934	28,731	0.94	601	2,915	1.37	< 0.0001
Punctured vessel/nerve	426	2,090	0.07	39	192	0.09	0.0003
Wound dehiscence	297	1,443	0.05	28	134	0.06	0.0013
Infection	1,393	6,800	0.22	66	327	0.15	< 0.0001
Other	10,468	50,955	1.67	891	4,387	2.06	< 0.0001
Medical complication	789	3,876	0.13	106	257	0.25	< 0.0001

The incidences of complications coded as procedure related for unilateral and bilateral total knee arthroplasties are shown.
CNS = central nervous system; F = frequency; WF = weighted frequency.

cal variables. Four multivariate logistic regression models were constructed, and odds ratios (ORs) and 95% CIs were estimated to determine independent predictors for in-hospital morbidity and mortality (table 4). Models 1–3 were fitted to identify (1) the effect of demographic variables and overall comorbidity burden, (2) the effect of individual comorbidities, and (3) the effect of perioperative complications on in-hospital mortality (outcome variable), respectively. Model 4 was constructed to determine the impact of individual comorbidities on the occurrence of any procedure-related complications as defined above and detailed in the appendix. Procedure subtypes (UTKA, simultaneous BTKA, and staged BTKA), patient demographic variables (age, sex, and race), and healthcare system–related variables (primary source of payment, discharge status, hospital bed size, location, and teaching status) were retained in all four models as covariates to reduce potential background bias. In model 1, overall comorbidity was summarized by the Deyo comorbidity index.[22] Individual comorbidities, including alcohol abuse, chronic lung disease, and others (see full list in table 5), were substituted for the Deyo comorbidity index in model 2. In model 3, complications including those affecting the central nervous system, cardiac, and others (see full list in table 6) were

Table 3. Procedure-related Complications among Simultaneous and Staged Bilateral Total Knee Arthroplasty Discharges

	Simultaneous			Staged			
	F	WF	%	F	WF	%	*P* Value
Device-related complications							
Device related	130	633	0.51	41	204	0.49	0.6249
Organ-specific complications							
CNS	53	261	0.21	23	118	0.28	0.0092
Cardiac	427	2105	1.69	133	671	1.61	0.2364
Peripheral vascular	115	591	0.47	27	138	0.33	0.0002
Respiratory	282	1371	1.1	116	584	1.4	< 0.0001
Gastrointestinal	344	1,681	1.35	149	760	1.82	< 0.0001
Genitourinary	270	1,329	1.07	106	544	1.3	0.0001
Other complications of procedure							
Shock	16	76	0.06	3	18	0.04	0.1916
Hematoma/seroma	354	1,709	1.37	119	585	1.4	0.6913
Punctured vessel/nerve	21	103	0.08	7	34	0.08	0.927
Wound dehiscence	15	70	0.06	3	15	0.04	0.1194
Infection	37	183	0.15	17	85	0.2	0.013
Other	486	2,412	1.94	219	1,084	2.59	< 0.0001
Medical complication	59	297	0.24	25	124	0.3	0.0391

The incidence of complications coded as procedure related for simultaneous and staged bilateral total knee arthroplasties are shown.
CNS = central nervous system; F = frequency; WF = weighted frequency.

Table 4. Multivariate Logistic Regression Models—Model Selection and Validation

	Model 1	Model 2	Model 3	Model 4
Outcomes	Mortality outcome (dead/alive)	Mortality outcome (dead/alive)	Mortality outcome (dead/alive)	Any procedure-related complication (yes/no)
Predictors	Comorbidity index	Individual comorbidities	Perioperative procedure-related complications	Individual comorbidities
Covariates	Procedure types, patient demographic and healthcare system–related variables	Procedure types, patient demographic and healthcare system–related variables	Procedure types, comorbidity index, patient demographic and healthcare system–related variables	Procedure types, patient demographic and healthcare system–related variables
C statistic on the training data set (80%)	0.72	0.77	0.80	0.77
C statistic on the validation data set (20%)	0.71	0.79	0.79	0.75
Hosmer–Lemeshow test (*P* value) on the training data set (80%)	0.57	0.04	0.03	0.03
Hosmer–Lemeshow test (*P* value) on the validation data set (20%)	0.85	0.13	0.11	0.14

Presented is information regarding the four logistic regression models used to determine risk factors for morbidity and mortality associated with total knee arthroplasty. Results of the validation studies are also reported.

considered as predictors while controlling for overall comorbidity burden using the Deyo comorbidity index.[22] A dichotomous outcome variable showing whether a procedure-related complication occurred during the hospitalization was created for model 4, and individual comorbidities (see full list in table 7) were included as predictors. For each individual predictor, the OR, 95% CI, and *P* value were computed.

Table 5. Risk Factors for Perioperative Mortality after Total Knee Arthroplasty—Comorbidities (Model 2)

Comorbidity	Regression Coefficient Estimate	Odds Ratio	95% CI	*P* Value
Alcohol abuse	0.25	1.28	0.57–2.88	0.552
Chronic lung disease	0.18	1.2	0.98–1.47	0.0844
Congestive heart failure*	1.62	5.03	4.14–6.11	< 0.0001
Uncomplicated diabetes mellitus	0.12	1.13	0.92–1.39	0.2475
Complicated diabetes mellitus	0.13	1.13	0.67–1.92	0.643
Liver dysfunction	0.28	1.32	0.55–3.17	0.5381
Coagulopathy*	0.96	2.62	1.88–3.67	< 0.0001
Neurologic disorders*	1.03	2.8	1.06–3.81	< 0.0001
Obesity	−0.26	0.77	0.57–1.03	0.08
Peripheral vascular disease*	0.4	1.5	1.01–2.22	0.0422
Renal disease*	1.25	3.49	2.52–4.84	< 0.0001
Pulmonary circulatory disease*	2.46	11.75	9.05–15.25	< 0.0001
Cardiac valvular disorders	0.12	1.12	0.84–1.49	0.4278
Electrolyte/fluid abnormalities*	1.3	3.67	3.06–4.4	< 0.0001
Metastatic cancer*	1.33	3.76	1.09–13.02	0.0364
Cancer	0.18	1.2	0.54–2.68	0.6535

Listed are the results of logistic regression model 2 detailing the odds ratios and 95% confidence intervals (CIs) associated with various comorbidities for the outcome of mortality.

* Risk factor with $P < 0.05$.

Multicollinearity was judged by checking the value inflation factor and the condition index. The conventional criterion of considering multicollinearity to be absent if the value inflation factor is less than 10 and the condition index is greater than 30 was used. Full multivariate logistic regression models were reduced by excluding any predictors with *P* values greater than 0.05.

Table 6. Risk Factors for Perioperative Mortality after Total Knee Arthroplasty—Procedure-related Complications (Model 3)

Complication	Regression Coefficient Estimate	Odds Ratio	95% CI	*P* Value
Device-related complications				
Device related*	0.76	2.13	1.19–3.8	0.0104
Organ-specific complications				
CNS*	3.13	22.77	14.28–36.31	< 0.0001
Cardiac*	2.65	14.19	11.25–17.91	< 0.0001
Peripheral vascular	1.69	5.42	0.81–36.06	0.0807
Respiratory*	0.76	2.13	1.39–3.26	0.0005
Gastrointestinal*	1.36	3.9	2.64–5.77	< 0.0001
Genitourinary*	0.4	1.5	0.89–2.52	0.1291
Other complications of procedure				
Shock*	2.71	15.1	3.88–58.81	< 0.0001
Hematoma/seroma	0.29	1.33	0.75–2.37	0.3338
Punctured vessel/ nerve	−1.02	0.36	0.01–64.53	0.7006
Wound dehiscence*	1.88	6.56	2.13–20.2	0.001
Infection	0.51	1.67	0.6–4.65	0.3245
Other	0.27	1.31	0.71–2.42	0.3905
Medical complication	−1.4	0.25	0.01–4.74	0.3527

Listed are the results of logistic regression model 3 detailing the odds ratios and 95% confidence intervals (CIs) associated with various procedure-related complications for the outcome of mortality.

* Risk factor with $P < 0.05$.

CNS = central nervous system.

Table 7. Risk Factors for Any Procedure-related Complications after Total Knee Arthroplasty—Comorbidities (Model 4)

Comorbidity	Regression Coefficient Estimate	Odds Ratio	95% CI	*P* Value
Alcohol abuse*	0.33	1.4	1.22–1.6	< 0.0001
Chronic lung disease*	0.11	1.12	1.08–1.16	< 0.0001
Congestive heart failure*	0.7	2.01	1.91–2.11	< 0.0001
Uncomplicated diabetes mellitus	0.02	1.02	0.99–1.06	0.1367
Complicated diabetes mellitus*	0.29	1.34	1.22–1.47	< 0.0001
Liver dysfunction	0.08	1.09	0.93–1.26	0.287
Coagulopathy*	0.63	1.88	1.74–2.04	< 0.0001
Neurologic disorders*	0.15	1.16	1.08–1.25	< 0.0001
Obesity	0.02	1.02	0.98–1.06	0.382
Peripheral vascular disease*	0.22	1.24	1.15–1.34	< 0.0001
Renal Disease*	0.31	1.36	1.23–1.5	< 0.0001
Pulmonary circulatory disease*	1.06	2.88	2.64–3.14	< 0.0001
Cardiac valvular disorders*	0.19	1.21	1.15–1.28	< 0.0001
Electrolyte/fluid abnormalities*	0.89	2.43	2.35–2.52	< 0.0001
Metastatic cancer*	0.35	1.42	1.01–1.98	0.0423
Cancer	0.04	1.04	0.89–1.21	0.6356

Listed are the results of logistic regression model 4 detailing the odds ratios and 95% confidence intervals (CIs) associated with various comorbidities for the outcome of the occurrence of any procedure-related complication.

* Risk factors with $P < 0.05$.

The Akaike information criterion was implemented to compare full models with reduced models for model selection. Lower Akaike information criterion scores were considered indicative of a better fit. The four final models were validated on both the training and the validation data set by a test of model discrimination using the c statistic and a test of model calibration using the Hosmer–Lemeshow (H-L) test.[24] The c statistic is the same as the area under the receiver operating characteristic curve[25] and is used to measure how well the model discriminates between observed data at different levels of the outcome. A c statistic value between 0.7 and 0.8 is considered indicative of acceptable discrimination.[26] The H-L test evaluates whether a logistic regression model is well calibrated so that the probability predictions from the model reflect the true occurrence of events in the data. Nonsignificant *P* values for this test are considered indicative of a well-calibrated model. However, it is important to keep in mind that caution needs to be taken for interpreting significant *P* values for the H-L in the setting of a large-sample-size study.[27]

To further test the validity of the NIS as a data source for our study context, we compared the rate of our primary outcome of in-hospital mortality with that previously reported in the literature over a similar time frame in the clinical setting, as described by Bateman *et al.*[18] Similar reported mortality rates in the literature would therefore underline confidence in the robustness of our data source.

Results

Demographics of UTKA and BTKA Discharges

We identified a total of 670,305 admissions between 1998 and 2006 during which a TKA procedure was performed. This represented a weighted national estimate of 3,270,836 hospitalizations. Of those, 6.52% had bilaterally performed procedures. The average age was 67.46 (CI, 67.43–67.49) yr for admissions undergoing UTKA and 66.14 (CI, 66.05–66.23) yr for BTKA procedures ($P < 0.0001$).

Table 1 contains information on patient and healthcare system–related demographic variables. Duration of hospital stay was significantly longer for BTKA compared with UTKA recipients (4.71 [CI, 4.68–4.74] *vs.* 3.99 [CI, 3.98–4.00] days; $P < 0.0001$). Comorbidities under study tended to be more prevalent among UTKA than BTKA recipients, except for obesity, cardiac valvular disease, and pulmonary circulatory disease (fig. 1). The

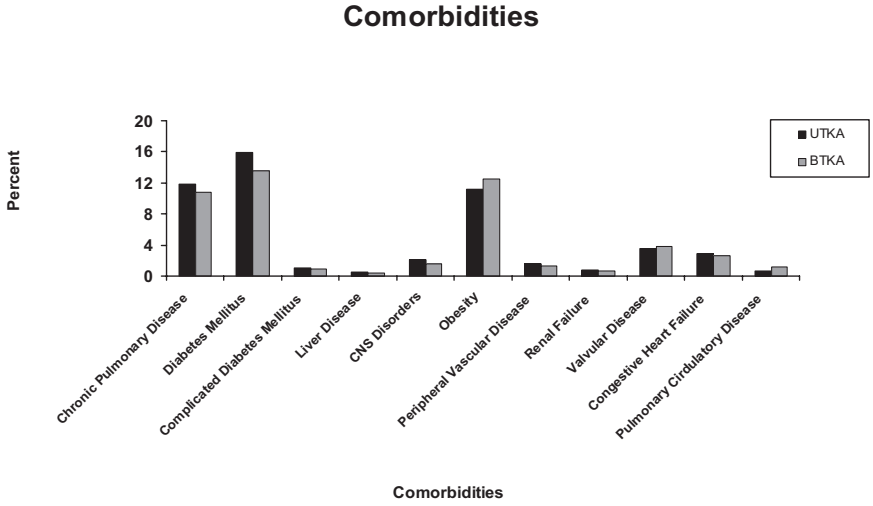

Fig. 1. Prevalence of selected comorbidities among unilateral and bilateral total knee arthroplasty discharges. BTKA = bilateral total knee arthroplasty; CNS = central nervous system; UTKA = unilateral total knee arthroplasty.

average comorbidity index among admissions for BTKA recipients was significantly lower compared with those for UTKA (0.48 [CI, 0.47–0.49] *vs.* 0.55 [CI, 0.54–0.56]; $P < 0.0001$).

Outcomes after UTKA and BTKA

Complications considered procedure related were more frequent among BTKA *versus* UTKA recipients (9.45% *vs.* 7.07%; $P < 0.0001$; table 2). The incidences of pulmonary embolism (0.82% *vs.* 0.39%), venous thrombosis (1.21% *vs.* 0.72%), and adult respiratory distress syndrome (0.48% *vs.* 0.25%) were also increased among BTKA compared with UTKA recipients ($P < 0.0001$). Acute posthemorrhagic anemia was coded at approximately double the rate among BTKA *versus* UTKA procedures (27.02% *vs.* 14.52%; $P < 0.0001$). In-hospital mortality was higher among BTKA compared with UTKA recipients (0.30% *vs.* 0.14%; $P < 0.0001$). The average ages of fatalities after UTKA and BTKA were similar (74.37 [CI, 73.74–75.01] *vs.* 73.07 [CI, 71.54–74.60] yr; $P = 0.1144$). Mortalities after BTKA occurred sooner after admission to the hospital than after UTKA procedures (6.86 [CI, 5.20–8.53] *vs.* 8.41 [CI, 7.55–9.27] days), but this difference was not significant ($P = 0.1184$).

Staged versus *Simultaneous BTKAs during the Same Hospitalization*

Of all entries for BTKA, 22.33% (9,688) did not allow for determination of timing of one or both procedures and were therefore excluded from the subgroup analysis. To make sure that the observed data could sufficiently represent the target patient population, we conducted a sensitivity analysis and found that our results are reliable and robust insofar as (1) the observed BTKA and the missing BTKA followed similar distributions in patient demographics, and (2) in the extreme case when all missing BTKAs were considered as simultaneous BTKAs or staged BTKAs, the risk factors for mortality and any procedure-related complications found by logistic regression retained their significance.

Of the BTKA discharges included, 74.8% were performed simultaneously, whereas the remainder were performed on separate days of the hospital admission. The average time between staged procedures was 3.59 (CI, 3.39–3.79) days. The average age of discharges associated with staged procedures was 66.18 (CI, 65.96–66.39) yr and 66.00 (CI, 65.88–66.12) with simultaneous BTKA ($P = 0.1567$). There was no difference in the overall comorbidity severity between the simultaneous *versus* staged group (comorbidity index 0.48 [CI, 0.47–0.49] for simultaneous and 0.49 [CI, 0.48–0.51] for staged BTKA; $P = 0.3332$). Duration of stay was longer after staged BTKA compared with simultaneous procedures (5.37 [CI, 5.30–5.43] *vs.* 4.52 [CI, 4.48–4.56] days, respectively; $P < 0.0001$).

Generally, procedure-related complications were more frequently encountered in discharges associated with staged compared with simultaneous BTKA (10.30% *vs.* 9.15%, respectively; $P < 0.0001$). Table 3 details the incidence of specific procedure-related complications. For all categories, staged procedures had either a higher or a similar incidence of complications.

Adverse events such as adult respiratory distress syndrome and posthemorrhagic anemia occurred at higher rates after staged procedures compared with simultaneous BTKA (0.62% *vs.* 0.40%; $P < 0.0001$ and 29.61% *vs.* 25.17%; $P < 0.0001$, respectively). Venous thrombosis and pulmonary embolism occurred more frequently among simultaneous procedure recipients (1.48% *vs.* 1.22%; $P = 0.0002$ and 0.89% *vs.* 0.77%; $P = 0.0218$, respectively).

No statistical difference in the rates of in-hospital mortality was seen between either BTKA approach (0.29% for simultaneous and 0.26% for staged BTKA, respectively; $P = 0.2875$).

Risk Factors for Perioperative Morbidity and Mortality after TKA

An overproportional number of deaths occurred among BTKA recipients (13.42% of total mortalities) compared with the prevalence of BTKA (6.51%) among the study sample. Multivariate regression revealed a number of independent risk factors for mortality after TKA. Patient-related factors that significantly increased the risk for perioperative mortality were male sex (OR, 2.02 [CI, 1.75–2.34]; $P < 0.0001$) and age (age > 75 yr: OR, 3.96 [CI, 2.77–5.66]; $P < 0.0001$; age between 65 and 75 yr: OR, 1.69 [CI, 1.19–2.40]; $P = 0.0032$ when compared with those aged 45–65 yr). Entries for simultaneous (OR, 2.23 [CI, 1.69–2.94]; $P < 0.0001$) and staged (OR, 2.09 [CI, 1.28–3.41]; $P = 0.0031$) BTKAs had a significantly increased odds of perioperative mortality when compared with UTKAs. Healthcare system–related factors associated with increased risk for mortality included only hospital size. Surgeries undertaken in large and medium-sized hospitals were associated with higher odds of perioperative mortality (large: OR, 1.48 [CI, 1.16–1.89]; $P = 0.0015$; medium: OR, 1.44 [CI, 1.10–1.87]; $P = 0.0075$ when compared with small hospital size). No other patient demographic and healthcare system–related factors (hospital location, hospital teaching status, type of insurance, and race) were significantly associated with altered risk of mortality.

The estimate of the impact of overall comorbidity burden on mortality was obtained by logistic regression model 1 (table 4). We found that for every unit increase in comorbidity index, the odds of perioperative mortality increased by 13.6% (OR, 1.136 [CI, 1.055–1.223]; $P = 0.0007$). A number of comorbidities detected by logistic regression model 2 (table 4) increased the risk of a fatal outcome (table 5), among which pulmonary circulatory

disease was associated with the highest increase in the risk for perioperative mortality (OR, 11.75 [CI, 9.05–15.25]; $P < 0.0001$). Interestingly, after controlling for covariates, the presence of obesity was not revealed to alter the odds of mortality after TKA.

When controlling for comorbidity severity and other patient and healthcare system–related demographics, a number of procedure-related complications and adverse events (logistic regression model 3; table 4) were associated with an increased risk for perioperative mortality (table 6). Among admissions with the highest risk for mortality were those whose perioperative course was significant for complications affecting the central nervous system (OR, 22.77 [CI, 14.28–36.31]; $P < 0.0001$), cardiac (OR, 14.19 [CI, 11.25–17.91]; $P < 0.0001$), and those experiencing shock (OR, 15.10 [CI, 3.88–58.81]; $P < 0.0001$). Further, the occurrence of pulmonary embolism and adult respiratory distress syndrome increased the risk for mortality by 18- and 15-fold, respectively (OR, 17.54 [CI, 12.69–24.22]; $P < 0.0001$ and OR, 14.61 [CI, 10.35–20.63]; $P \leq 0.0001$, respectively). The incidence of venous thrombotic events was not associated with a risk-adjusted increase in perioperative mortality after TKA (OR, 0.93 [CI, 0.49–1.79]; $P = 0.8372$).

Patient-related factors that increased the risk for perioperative procedure-related complications included male sex (OR, 1.41 [CI, 1.38–1.44]; $P < 0.0001$), older age (age > 75 yr *vs.* age 45–64 yr: OR, 1.40 [CI, 1.34–1.46]; $P < 0.0001$), and minority race (black *vs.* white: OR, 1.29 [CI, 1.26–1.39]; $P < 0.0001$; other (excluding black and Hispanic) *vs.* white: OR, 1.23 [CI, 1.15–1.32]; $P < 0.0001$). Entries for simultaneous (OR, 1.40 [CI, 1.33–1.47]; $P < 0.0001$) and staged (OR, 1.66 [CI, 1.52–1.79]; $P < 0.0001$) BTKAs had a significantly increased odds of perioperative morbidity when compared with UTKAs; staged BTKAs had a significantly increased odds of perioperative morbidity compared with simultaneously performed BTKAs (OR, 1.18 [CI, 1.07–1.30]; $P = 0.0008$).

Through logistic regression model 4 (table 4), a set of comorbidities were determined that were associated with increased risk of procedure-related complications (table 7), among which congestive heart failure (OR, 2.01 [CI, 1.91–2.11]; $P < 0.0001$), pulmonary circulatory disease (OR, 2.88 [CI, 2.64–3.14]; $P < 0.0001$), and electrolyte/fluid abnormalities (OR, 2.43 [CI, 2.35–2.52]; $P < 0.0001$) were associated with the highest odds.

Model Diagnostics

Multicollinearity was found absent for all variables (value inflation factor in the range of 1.01–1.76 and condition index in the range of 21.09). Lower Akaike information criterion scores were found for all full models (table 4). The c statistic values on both the training data set and the validation data set were estimated to be in the range 0.7–0.8, indicating acceptable discrimination. No significant differences were found between the predicted and observed probabilities of death through model 1 in both data sets and models 2–4 in the validation data set for the H-L test. The low *P* values for the H-L test for models 2–4 on the training data set might have indicated that these two models are not well calibrated. However, the H-L test is known to not perform well with large sample sizes such as ours, and thus we are not deeming our model suspect of bad calibration.

Discussion

In this study of nationally representative data collected for the NIS between the years 1998 and 2006, we found an increased incidence of perioperative complications (9.45% *vs.* 7.07%; $P < 0.0001$) and in-hospital mortality (0.30% *vs.* 0.14%; $P < 0.0001$) among hospital admissions undergoing BTKA when compared with UTKA procedures. Procedures performed in a staged approach during the same hospitalization were associated with an increased incidence of most studied in-hospital complications when compared with simultaneous surgeries, and offered no mortality benefit (0.29% for simultaneous and 0.26% for staged BTKA; $P = 0.2875$). Risk factors for in-hospital mortality included a bilateral procedure, advanced age, male sex, and the presence of a number of comorbidities and perioperative complications. In view of the increasing use of TKA, and in particular of BTKA among the United States population,[11,28] these findings are of importance to the perioperative physician for better assessment of the chance of morbidity and mortality and better identification of patients at risk. These data can help to inform patients adequately of related risks before embarking on this by and large elective procedure.

A number of studies published in recent years have concluded that BTKAs are associated with increased rates of mortality and complications when compared with unilateral or procedures staged at different hospitalizations.[4,6] We recently studied data from the National Hospital Discharge Survey from the years 1990–2004 and found an in-hospital mortality rate of 0.5% among BTKA recipients *versus* 0.3% among UTKA recipients. Risk-adjusted mortality among patients undergoing BTKA was three times higher compared with those receiving a UTKA. Despite younger average age and lower comorbidity burden, rates and risks of procedure-related complications compared with those undergoing UTKA were also increased.[7] However, data available in the National Hospital Discharge Survey did not allow for comparison between outcomes of BTKAs performed in one *versus* different surgical sessions, a limitation also described by Barrett *et al.*[12] when using Medicare data. Further, our previous analysis was limited because of the inherent characteristics and operation of the National Hospital Discharge Survey. Among the constraints were

a limited amount of available variables (*i.e.*, limited number of diagnosis codes, patient characteristics, and hospital characteristics) and an estimated sample based on only 1% of the actual national in-hospital population (compared with the 20% sample used in the NIS), thus limiting statistical power when studying low-incidence outcomes.

While providing extremely valuable information, previous studies addressing the issue of mortality after BTKA are limited by relatively small sample sizes, use of single-institution data, and observation periods that far exceed the perioperative period, thus introducing variables that are beyond the control of perioperative physicians.[13,14] The combination of the facts that BTKAs are undoubtedly a more invasive procedure and that most fatal and near fatal outcomes occur early after surgery[14,29,30] suggests that focusing on the immediate perioperative period may be appropriate to study procedure related mortality in this setting and has been advocated by others.[13]

A number of authors have addressed the question of mortality and complications after BTKA during one hospitalization *versus* staged during different hospitalizations, but a paucity of studies exists on the issue of simultaneous *versus* staged procedures during the same hospitalization. Therefore, the practice of performing staged procedures during the same hospitalization in the desire to reduce the risk of mortality and morbidity[4,6] while maintaining the advantages of a bilateral procedure[1,2] remains largely based on anecdote. In a study including 267 patients who underwent BTKA during the same hospitalization, Sliva *et al.*[16] found that bilateral procedures performed 4–7 days apart were associated with higher risk of mortality and morbidity when compared with simultaneously performed procedures. However, only four patients experienced a complication in these two groups, pointing out the difficulties of studying low incidence events with institutional data. When further examining the time interval between BTKAs performed during the same hospitalization, Wu *et al.*[17] recently found no difference in outcomes when procedures were performed 2 or 7 days apart, but the authors pointed out that the lack of power secondary to their small sample size of 79 patients was a major limitation.

The availability of nationally representative data and a relatively large sample population allowed us to overcome this particular limitation. When examining the incidence of perioperative complications, we were able to confirm the results of previous studies that found an increased rate of adverse events after BTKA *versus* UTKA. Further, staged procedures were associated with higher rates of most complications than simultaneously performed surgeries. However, no difference in in-hospital mortality was found between the two approaches. Reasons for this discrepancy have to remain speculative, and causal relations cannot be studied with data available in the NIS. One explanation may be the coincidence of the second procedure with the peak of metabolic injury and the incidence of most in-hospital complications, including myocardial infarctions, arrhythmias, venous thrombotic events, and so forth, on the first few postoperative days,[29,30] suggesting a double-hit phenomenon.

Having determined that a staged *versus* simultaneous approach during the same hospitalization may not offer any mortality benefit and may even lead to increased morbidity, the question remains about the optimal timing of the second TKA. Unfortunately, our data source did not allow us to study this issue, because patients cannot be followed up during different hospitalizations using data available in the NIS. It must be noted that Ritter *et al.*[31] showed a mortality benefit for a staged *versus* simultaneous procedure when waiting as little as 6 weeks between surgeries (0.99% *vs.* 0.48%) with a rate compared with UTKAs after 3 months (approximately 0.3%).

We identified a number of risk factors for in-hospital mortality after TKA. In addition to male sex and advanced age, which have been reported as risk factors for mortality after TKA in the past,[7,14] increasing overall comorbidity burden and the presence of a number of specific comorbidities were associated with an independently increased risk of perioperative mortality in this study. Increased comorbidity burden and mortality among joint arthroplasty patients has been correlated by Rauh *et al.*[32] in the past. The diseases linked with the highest risk for a fatal outcome were pulmonary circulatory disease, metastatic cancer, renal disease, and congestive heart failure. Our results would suggest that patients with these diseases should therefore not be considered candidates for BTKA. Although medical treatment before surgery may yield optimization of the patient's condition, it cannot be concluded from this study whether this intervention would modify risk for these overwhelmingly difficult-to-treat conditions.

As expected, a number of perioperative complications were independently associated with postoperative morbidity and mortality. In addition to perioperative shock, complications affecting the central nervous system and pulmonary embolism increased the risk for fatal outcome the most. Pulmonary embolism has long been recognized as a major problem after lower extremity arthroplasty,[7,22] and much effort has been devoted to preventing it.[17,32]

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, duration of surgery, and so forth) 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, readmissions cannot be discerned from this database. Therefore, conclusions should be limited to the acute perioperative setting with the notion that mortality and complications are likely underestimated. Although it cannot be excluded that the entry of complications or comorbidities may be subject to some form of coding or reporting bias, there is no reason to believe that reporting should differ between procedure types, thus exposing both BTKA and UTKA procedures to the same bias within the same data collection construct. Comparative analysis should therefore be less likely affected by such bias. Further, it is not likely that a "hard" outcome such as mortality should be subject to this form of bias, and this is one of the reasons why it was chosen as an endpoint in this study. In an additional validation step of our data source, we were able to find an in-hospital mortality rate in our study (0.15%) concordant with that recently reported by Pulido *et al.*[33] in 5,173 primary total knee arthroplasty patients (0.12%) between 2000 and 2006, thus allowing for a comparative capture time frame and years of observation.

Identification of the timing of BTKA procedures was not possible in approximately one fourth of entries. The reason for this is that approximately one third of states contributing to NIS do not provide information on the procedure dates of multiple procedures; therefore, it was not possible to include all BTKA procedures in our analysis of staged *versus* simultaneous surgeries. However, the conclusions from the regression models did not change when treating the missing entries as either staged or simultaneous. Further, the demographics of the missing entries followed those of the general BTKA group, thus offering assurance of the robustness of our data.

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 TKA than various prospective studies that are limited in sample size and thus lack the ability to capture low-incidence outcomes.

In conclusion, using a nationally representative database, we determined that BTKA carried an increased adjusted risk of in-hospital mortality and greater incidence of in-hospital complications when compared with UTKA procedures. Staging of BTKA during the same hospitalization does not offer any mortality benefit and may be associated with an increase in complications. More studies are needed to answer whether there are conditions (center selection, patient subpopulations) under which this procedure can be performed without increased risk. Until such data exist, the performance of BTKA during one hospitalization (staged or simultaneous) cannot be recommended based on our findings. If performed, however, careful patient selection for BTKA and in-depth discussion about risks and alternatives with the patient cannot be overemphasized. Risk factors identified in this analysis may be used to gauge the perioperative mortality risk for individual patients, and the presence of significant diseases should lead to exclusion of patients as candidates for BTKA.

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Appendix: List of *International Classification of Diseases, 9th Revision, Clinical Modification*, Diagnosis Codes Included to Identify Comorbidities, Adverse Diagnosis, and Complications among Discharges

Procedure-related complications	
Device related	996
Central nervous system	9970
Cardiac	9971
Peripheral vascular	9972
Respiratory	9973
Gastrointestinal	9974
Genitourinary	9975
Other organ specific	9976–9979
Postoperative shock	9980
Hematoma/seroma	9981
Accidental puncture/laceration	9982
Disruption operative wound	9983
Postoperative infection	9985
Other complications of procedure	9986–9989
Complications of medical care	999
Other adverse events	
Acute posthemorrhagic anemia	2851
Pulmonary embolism	4151
Pulmonary insufficiency after trauma and surgery/adult respiratory distress syndrome	5185
Venous thrombotic events	4511, 4512, 4518, 4519, 4532, 4538, 4539

Four- and five-digit codes are included under the respective three- and four-digit codes.