Biological sex has No impact on postoperative complications following simultaneous bilateral total knee arthroplasty

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ARTICLE INFO

Keywords:

Biological sex
Simultaneous TKA
Total knee arthroplasty
Bilateral

ABSTRACT

Introduction: Simultaneous bilateral total knee arthroplasty (bTKA) is a viable option for treatment of bilateral knee osteoarthritis. The aim of this study is to identify the impact of biological sex on postoperative outcomes. **Methods:** A retrospective cohort study was conducted utilizing the ACS-NSQIP database. bTKA patients were identified and stratified into groups based upon biological sex. Adverse events after surgery was evaluated with univariate and multivariate analysis.

Results: Biological sex is not an independent risk factor for development of postoperative complications.

Conclusion: When determining patient qualification of simultaneous or staged bTKA, biological sex should not be taken into consideration.

1. Introduction

The number of total knee arthroplasties (TKA) performed per year in the United States is rising steadily and a total of 4 million Americans are estimated to be living with knee replacements.^{1,2} Women more commonly receive total knee replacements than men, with the estimated prevalence at 4.8% and 3.4% over the age of fifty, respectively.² Due to these statistics and the inherent anatomical differences that exist in the knee joint between males and females, biological sex has been explored as a factor affecting postoperative outcomes in patients undergoing TKA.³ To date, the literature examining the role that biological sex plays on postoperative outcomes in TKA, such as pain, pulmonary and cardiac abnormalities, and mortality has been inconclusive.^{4,5,6} In addition to these contradictory findings, these studies predominantly focus on unilateral TKA.

Conditions such as severe osteoarthritis and rheumatoid arthritis affect both knee joints in approximately one third of knee replacement cases.^{7,8} Surgical interventions in these cases include a bilateral simultaneous procedure, in which both knees are operated on at a single time under a single anesthetic, or a bilateral staged procedure, in which the knees are operated on at separate times.⁹ Advantages of the simultaneous bilateral procedure over the staged bilateral and unilateral

procedures include the use of a single anesthetic, and a decreased length of hospital stay, which leads to lower hospital costs.^{8,9,10} Despite these advantages, critics question the simultaneous bilateral procedure due to inconclusive data regarding its safety.⁸

While some studies demonstrate a low rate of medical complications, others argue that simultaneous bilateral TKA carries a higher rate of serious cardiac and pulmonary complications, and mortality compared to unilateral TKA, and higher rates of mortality following surgery compared to staged, bilateral TKA.^{8,9,11} In one of the largest studies to date, the complication rate and mortality for patients undergoing bilateral TKA was found to be 1.6 times higher than patients undergoing unilateral TKA.¹² Thus, the purpose of this study is to use a national database to expand on the biological sex-related research involving total knee arthroplasties. We use a more comprehensive set of outcome criteria, including infection, death, and complications involving the cardiac, pulmonary, and renal systems to determine whether biological sex plays a role in postoperative outcomes of simultaneous bilateral TKA. Specifically, we aim to determine (1) if there are differences in patient demographics and comorbidities in patients undergoing simultaneous bilateral TKA, and (2) if biological sex is an independent risk factor for development of postoperative complications.

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<https://doi.org/10.1016/j.jor.2019.06.013>

Received 24 April 2019; Accepted 6 June 2019

Available online 06 June 2019

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2. Materials and methods

Data were collected using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database for all revision total knee arthroplasties between 2007 and 2016. The American College of Surgeons NSQIP database is a national database with over 600 hospitals participating that focuses on risk-adjusted outcomes and measures to improve the quality of surgical care. Current Procedural Terminology (CPT) codes were used to identify appropriate patients who underwent bilateral total knee arthroplasty (TKA) using CPT code 27447 for primary and concurrent surgeries. If a patient had 27447 listed for both, then the procedure was deemed to be a bilateral TKA. Patients were then stratified into two groups based upon biological sex (male or female). Demographic information, comorbidities, and postoperative complications within 30 days of surgery were collected. Demographic information included race and age. Previously identified risk factors for complications were identified including smoking status, diabetic status, body mass index (BMI), dyspnea status, American Society of Anesthesiologists (ASA) class, type of anesthesia used, and preoperative functional status. Medical comorbidity data collected included chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), renal failure, dialysis patients, steroid use, weight loss, bleeding disorders, and transfusions.

Thirty-day postoperative complications to be studied included surgical site wound infection, deep wound infection, organ or space infections, wound dehiscence, pneumonia, reintubation, pulmonary embolism, failure to wean off ventilator for greater than 48 h, renal failure, renal insufficiency, urinary tract infection, stroke, cardiac arrest, myocardial infarction, deep vein thrombosis, sepsis and septic shock, and all-cause death. Complications were also added for each cohort and labeled as all-cause postoperative complications. Postoperative outcomes within 30 days that were also analyzed included extended length of stay and unplanned return to the operating room. Extended length of stay was determined to be an inpatient hospital stay of greater than 7 days, a number deemed to be appropriate based on previous literature.¹³

Statistical Package for the Social Sciences (SPSS; version 22; Armonk, NY) software was used to conduct univariate and multivariate analyses on demographic data, comorbidities, and postoperative complications. Chi-square test, and one-way analysis of variance (ANOVA) were used to perform univariate testing where appropriate. Although age and BMI were analyzed by chi-square test, and one-way ANOVA, the continuous variable was chosen for multivariate analysis over the categorical variable if both the categorical analysis and one-way ANOVA tests resulted in statistical significance. Risk factors with $P < 0.2$ in univariate analyses were selected for multivariate analyses to determine independent risk factors for returning back to the operating room (OR) and extended length of stay. Biological sex was included as a risk factor in the multivariate analysis along with the risk factors that met criteria for multivariate selection. Multivariate analysis was performed using binary logistic regression analysis on postoperative complications, retuning back to the OR, and extended length of stay within 30 days using forward stepwise. The results of the multivariate analyses were reported with P values and odds ratios with 95% confidence intervals. A P value of < 0.05 was deemed the cutoff value for statistical significance.

3. Results

3.1. Demographics

A total of 6132 patients who underwent simultaneous bilateral TKA were included in this study, of which 2630 were male and 3502 were female. After stratifying by biological sex, there were statistically significant differences in race ($p < 0.001$), diabetes mellitus status ($p = 0.042$), age ($p > 0.001$), and BMI ($p < 0.001$) among males and

Table 1

Demographics and clinical characteristics of patients undergoing simultaneous BTKA

	Male		Female		P-value
	2630		3502		
	N	%	N	%	Male vs Female
Race					< 0.001
White	2175	82.7%	2782	79.4%	
Black or African American	122	4.6%	288	8.2%	
Hispanic	87	3.3%	116	3.3%	
American Indian or Alaska Native	8	0.3%	12	0.3%	
Asian	69	2.6%	116	3.3%	
Native Hawaiian or Pacific Islander	12	0.5%	19	0.5%	
Anesthesia Type					0.193
General	1534	58.3%	2091	59.7%	
Regional	879	33.4%	1098	31.4%	
MAC/IV Sedation	214	8.1%	309	8.8%	
ASA					0.557
1 or 2	2492	94.8%	3384	96.6%	
3 or 4	29	1.1%	30	0.9%	
Diabetes Mellitus Status					0.042
No DM	2196	83.5%	3000	85.7%	
NIDDM	347	13.2%	410	11.7%	
IDDM	87	3.3%	92	2.6%	
Smoking Status					0.121
Yes	223	8.5%	249	7.1%	
No	2407	91.5%	3253	92.9%	
Dyspnea Status					0.181
No dyspnea	2521	60.0%	3323	94.9%	
Moderate exertion	108	4.1%	171	4.9%	
At rest	1	0.0%	8	0.2%	
Functional Status Pre-op					0.485
Independent	2598	98.8%	3440	98.2%	
Partially Dependent	14	0.5%	36	1.0%	
Totally Dependent	0	0.0%	1	0.0%	
Age					< 0.001
18-40	99	3.8%	158	4.5%	
31-40	655	24.9%	918	26.2%	
41-50	1175	44.7%	1464	41.8%	
51-60	609	23.2%	828	23.6%	
> 60	92	3.5%	134	3.8%	
BMI					< 0.001
Nonobese (BMI 18.5–25)	1060	40.3%	1128	32.2%	
Overweight(BMI 25-30	830	31.6%	959	27.4%	
Obese I (BMI 30–35)	467	17.8%	789	22.5%	
Obese II (BMI > 35)	267	10.2%	619	17.7%	

females. A higher percentage of male patients were white, non-insulin dependent diabetics (Type 2), between the ages of 41–50, and nonobese or overweight as determined by BMI. There were no biological sex differences in the type of anesthesia used ($p = 0.193$), ASA class ($p = 0.557$), smoking status ($p = 0.121$), dyspnea status ($p = 0.181$), and functional status pre-operation ($p = 0.485$). These data are shown in [Table 1](#).

3.2. Comorbidities

In total, 1734 of the male patients (65.9%) included in the study had comorbidities, while 2334 of the female patients (66.6%) had comorbidities. Female patients were more likely to use steroids ($p = 0.005$) than male patients. There were no statistically significant differences between biological sex with regards to COPD ($p = 0.623$), CHF ($p = 0.317$), Hypertension ($p = 0.608$), Renal Failure ($p = 0.513$), Dialysis ($p = 0.988$), Weight Loss ($p = 0.351$), and Preoperative Transfusion ($p = 0.768$) in our cohort of patients. Notably, the most common comorbidity in both biological sexes was hypertension, which was present in 61.1% of males and 60.4% of females ([Table 2](#)).

Table 2
Comorbidities of patients undergoing simultaneous BTKA.

	Male		Female		Male vs Female
	2630		3502		
	N	%	N	%	
COPD	55	2.1%	85	2.4%	0.623
CHF	7	0.3%	2	0.1%	0.317
Hypertension	1606	61.1%	2114	60.4%	0.608
Renal Failure	1	0.0%	0	0.0%	0.513
Dialysis	2	0.1%	3	0.1%	0.988
Steroid Use	56	2.1%	124	3.5%	0.005
Weight Loss	6	0.2%	3	0.1%	0.351
Preop Transfusion	1	0.0%	3	0.1%	0.768

3.3. Complications

A total of 1736 patients had complications following simultaneous bilateral TKA, including 635 male patients and 1101 female patients. There were no statistically significant differences in occurrence of total complications with regards to biological sex ($p = 0.078$). Using a univariate analysis, females were found to more likely require a postoperative transfusion ($p < 0.001$) than males. However, multivariate analysis did not show that biological sex was an independent risk factor for requiring postoperative transfusion (CI: 0.066–1.217; $p = 0.09$). Lastly, there was no statistically significant difference in the occurrence of all other complication types using a univariate analysis (Table 3).

4. Discussion

Biological sex plays an important role in total knee arthroplasties (TKA). Women both undergo a higher number of procedures than men and have a higher prevalence of total knee replacements in the general population over the age of 50.^{2,14} In our study of 6132 simultaneous bilateral TKAs between 2007 and 2016, 57.1% of procedures were

Table 3
Postoperative complications following simultaneous BTKA.

Complications	Male		Female		Male versus Female p
	2630		3502		
	N	%	N	%	
Any complication	635	24.1%	1101	31.4%	0.078
Superficial surgical site wound	13	0.5%	18	0.5%	0.974
Deep surgical site infection	5	0.2%	6	0.2%	0.978
Organ/Space Infection	7	0.3%	5	0.1%	0.552
Wound Dehiscence	6	0.2%	3	0.1%	0.351
Pneumonia	13	0.5%	14	0.4%	0.843
Reintubate	9	0.3%	10	0.3%	0.913
Pulmonary Embolism	30	1.1%	52	1.5%	0.482
Fail to wean > 48hr	5	0.2%	4	0.1%	0.740
Renal Insufficiency	10	0.4%	6	0.2%	0.280
Renal Failure	4	0.2%	3	0.1%	0.744
Urinary tract Infection	25	1.0%	58	1.7%	0.057
Stroke	3	0.1%	4	0.1%	0.995
Cardiac arrest	6	0.2%	4	0.1%	0.546
Myocardial Infarction	11	0.4%	7	0.2%	0.290
Postoperative Transfusion	427	16.2%	832	23.8%	< 0.001
Deep Vein Thrombosis	44	1.7%	54	1.5%	0.863
Sepsis	9	0.3%	13	0.4%	0.968
Septic Shock	4	0.2%	4	0.1%	0.916
Death	4	0.2%	4	0.1%	0.916
Other Outcomes					
Extended LOS (> 7 days)	79	3.0%	110	3.1%	0.840
Return to OR	39	1.5%	56	1.6%	0.879

performed on women. Reasons for this discrepancy have been proposed, such as the higher incidence of osteoarthritis in the female population and the intrinsic anatomic differences in the knee joint, such as the femoral-condylar height-width relationship.^{3,14}

As a result of these differences, recent literature has attempted to determine the role that biological sex plays in the outcome of total knee arthroplasties. Thus far, contradictory data has been shown regarding biological sex on postoperative outcomes of TKA. Using postoperative pain as an outcome criterion, some studies have found that there are no biological sex specific differences in postoperative pain in patients receiving TKA at 6 months or 12 months.^{15,16} On the other hand, other studies have found that women display a higher degree of postoperative pain at 1 and 2 years.^{5,14} Expanding past just postoperative pain as an outcome, Memtsoudis et al. demonstrated that the male sex was associated with an increased risk for respiratory and cardiac complications, but not pulmonary embolism following TKA.¹² On the other hand, Singh et al. argue that female sex is associated with higher rates of thromboembolic events within 90 days following TKA.⁶

The literature surrounding the role that biological sex plays in the outcomes of simultaneous bilateral total knee arthroplasties is limited. Males have been linked to an increased risk of mortality following simultaneous bilateral TKA.¹⁴ Ritter et al. demonstrate in a study of 2050 simultaneous bilateral TKAs that males have nearly twice the death rate as females following the procedure with an average follow-up of 5 years.¹⁴ However, our study, which was of larger scope at 6132 simultaneous bilateral TKAs, found no association between sex and mortality. Further, we include a more comprehensive list of complications, such as cardiac, pulmonary, and renal dysfunction, sepsis, and death, and found that there is no association between sex and total complications. Notably, biological sex specific differences existing in the population undergoing bilateral TKA, such as steroid usage, race, diabetes mellitus status, age, and BMI, did not appear to affect overall complication rate. The only specific complication that had an association with sex was postoperative transfusion ($p < 0.001$). While univariate analysis revealed that females who had undergone bilateral TKA were more likely to require a postoperative transfusion than males, multivariate analysis demonstrated that biological sex was not an independent risk factor for requiring postoperative transfusion.

There were a variety of limitations for this study. First, this study was only able to assess.

Complication rates up to one-month post-operatively. This is due to the limitation of the NSQIP.

Database, as data beyond one-month post-operatively is not collected. In addition, NSQIP lacks orthopedic-specific complications such as aseptic loosening, instability and peri-prosthetic fracture. The 30-day window for short-term complication reporting is likely to contribute to underreporting of the influence of biological sex on post-operative complications. Revisions and infectious diagnoses such as deep and superficial SSI may present outside of the immediate post-operative timeframe, leading NSQIP to miss potential postoperative complications. Despite these limitations, the results of our study allowed for significant conclusions due to the large sample size.

5. Conclusion

The literature surrounding the role of biological sex on the outcome of total knee arthroscopies is inconclusive. Using a national database of 6132 simultaneous bilateral TKAs performed between 2007 and 2016, we examine the role that sex plays in the occurrence of postoperative complications. We determine that there is no association between biological sex and total postoperative complications following simultaneous bilateral TKA. Thus, when considering simultaneous bilateral knee replacement, sex does not need to be considered when counseling patients on the risks of surgery.

Financial disclosures

No financial salaries or benefits were received for this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jor.2019.06.013>.

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