Journal of Clinical Orthopaedics and Trauma 11 (2020) 147–153

Contents lists available at ScienceDirect

Journal of Clinical Orthopaedics and Trauma

journal homepage: www.elsevier.com/locate/jcot

The impact of chronic kidney disease on postoperative complications in patients undergoing revision total knee arthroplasty: A propensity matched analysis

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ARTICLE INFO

Article history:
Received 27 January 2019
Received in revised form
1 June 2019
Accepted 3 June 2019
Available online 4 June 2019

Keywords:
Revision total knee arthroplasty
Chronic kidney disease
Complications
Surgical outcomes
NSQIP
Mortality

ABSTRACT

Objectives: Though the role of chronic kidney disease (CKD) has been studied previously in primary arthroplasty procedures of the hips and knees, there is a paucity of literature analyzing CKD's impact on surgical outcomes in revision total knee arthroplasty (rTKA) patients. As the number of patients with CKD requiring revision surgery increases, more vigilant pre-operative and post-operative measures can be taken to ensure successful outcomes. This retrospective study sought to 1) determine differences in demographics and preoperative comorbidities of patients with normal or mild CKD and those with moderate/severe CKD and 2) establish moderate/severe CKD as an independent risk factor for complications in the 30-day postoperative period in patients undergoing rTKA.

Methods: The ACS-NSQIP database was queried for patients who had undergone rTKA from 2005 to 2016. Patient were assigned to one of five CKD severity classes after eGFR calculation and were further stratified into two cohorts: stages 1/2 vs. stages 3/4/5. After propensity matching to generate a matched normal/mild CKD cohort of rTKA patients, univariate and multivariate analyses were used to assess differences and the impact of severe CKD on the risk for complications.

Results: There were significant differences in several demographic features, comorbidities, and complications between the two cohorts upon univariate analyses. Upon multivariate analyses, CKD of moderate/severe/failure status was found to be a significant independent risk factor for acute renal failure (OR 18.097, 95% CI 4.970–65.902, $p < 0.001$), blood transfusions (OR 1.697, 95% CI 1.500–1.919, $p < 0.001$), return to the operating room (OR 1.257, 95% CI 1.009–1.566, $p = 0.041$), extended length of stay (OR 1.707, 95% CI 1.292–2.255, $p < 0.001$), and mortality (OR 2.165, 95% CI 1.116–4.200, $p = 0.022$) in the 30-day postoperative period.

Conclusion: This current study found moderate/severe CKD to be an independent risk factor for several complications and should guide healthcare professionals for better patient-optimization. Orthopaedic surgeons should factor in CKD severity in the management of patients undergoing rTKA to effectively mitigate the effects of adverse events.

1. Introduction

Osteoarthritis (OA) of the knee is one of the most common causes of chronic disability in the Western world, with a particularly high burden of disease in elderly populations.[1,2] Increasing numbers of Americans are also undergoing total knee arthroplasty (TKA) for the treatment of OA.[3,4] An aging population and an increasing rate of obesity are examples of factors that not only contribute to increased TKA, but also simultaneously contribute to

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https://doi.org/10.1016/j.jcot.2019.06.002
0976-5662/

increasing chronic kidney disease (CKD).[5–7] The negative effects of CKD have been linked to an increase in morbidity and mortality – with more severe stages of the disease being directly linked to a shorter lifespan.[8] The rising prevalence represents a problem for orthopaedic surgeons who may wish to treat OA with TKA in patients with CKD. Multiple studies have established increased complication rates in CKD patients undergoing total joint arthroplasties (TJA).[9–11] Although CKD has been established as an independent risk factor for various perioperative and postoperative complications in several orthopaedic procedures, the most recent literature has focused mainly on the impact that the severity of CKD has on outcomes and complication rates after elective primary TJA.

There remains a paucity of literature as to whether this trend holds true for revision total knee arthroplasty (rTKA). Warth et al. previously established an independent association between the increasing severity of CKD and outcomes after primary TJA of the hips and knees.[12] Caution should be exercised in extrapolating the results of similar, yet distinct, procedures as differences in complication rates between primary TKA and rTKA in specific comorbid patient subpopulations have been previously demonstrated.[13,14] These demonstrated differences in complications between primary TKA and rTKA warrant further investigation as to how CKD affects postoperative complications in revision TKA. This current study seeks to (1) analyze differences in patient demographics and prevalence of specific comorbidities in differing levels of CKD severity and (2) establish whether increasing CKD severity is an independent risk factor for increased failure and complication rates in rTKA by utilizing The American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database, a multi-institutional clinical registry consisting of 5,608,708 total surgical patient files from 680 participating institutions.[15] By understanding the effects that different severity classes of CKD have on increasing the risk for adverse rTKA outcomes, surgeons can more readily identify patients who are good or poor candidates for rTKA with respect to CKD status.

2. Methods and materials

2.1. Patient cohort selection

Patients who had undergone rTKA procedures were analyzed by querying the ACS-NSQIP database and isolating rTKA patients by Current Terminology Procedure (CPT) codes. 16,428 patients who underwent elective revision knee arthroplasty procedures from 2005 to 2016, corresponding with CPT codes 27486 and 27487, initially met our inclusion criteria. 13,951 total rTKA patients from 2005 to 2016 were ultimately included in our study after selectively excluding those who had incomplete creatinine, age, and sex information in order mitigate influence by absent data. Patients who had undergone primary total knee arthroplasty procedures (CPT codes: 27446, 27447) were also excluded from this study in an effort to provide guidance specifically for those pondering revisional procedures for their TKA knees. All included patients were ≥18 years old, had complete gender data, and complete serum creatinine levels.

2.2. Variables

Each surgical patient file in the ACS-NSQIP database is characterized by over 270 variables that all serve to provide detailed medical histories for those undergoing surgery.[15,16] These variables are categorized into demographic characteristics, pre-operative comorbidities, laboratory values, and peri-operative/post-operative outcomes (including both medical and surgical complications).

Demographic factors, including age, sex, and race, were assessed for the purpose of analyzing these patients on a larger, more holistic scale for population-based findings. Preoperative comorbidities were also analyzed to gain better insight into the medical conditions that our patient sample of interest had previously been diagnosed with, independent of their main indication for the rTKA procedure. A comprehensive list of comorbidities, laboratory values, and operative variables that were included for analysis in this current retrospective study can be found in Table 1. Pre-operative comorbidities reported by the NSQIP were excluded from the current study if less than 85% of the included patients had complete data entries for those conditions (i.e. pre-operative pneumonia and angina). Postoperative complications considered for analysis in accordance with severity of CKD can be found in Table 4.

2.3. Chronic kidney disease severity and eGFR

The final patient sample that was utilized for the current study comprised of 13,951 patients who had undergone rTKA and also had complete serum creatinine levels, gender, and age information. The inclusion criteria was very specific to patients with these characteristics, since the severity of CKD was measured by calculating each individual patient's estimated glomerular filtration rate (eGFR) using the Modified Diet in Renal Disease Equation[17] (eGFR = 186.3 x serum creatinine^-1.154 x age^- 0.203 × 1.212 if patient is Black/African American x 0.743 if the patient is female [if the patient is not Black/African American or not female, then replace the 1.212 and 0.743, respectively, with 1]). Previous studies in the surgical literature, including primary joint arthroplasties, laparoscopic procedures, and urological surgeries, have assessed the severity of CKD on various surgical outcomes in a similar manner.[14,17–19] Following standard guidelines from the National Kidney Foundation, the rTKA patients were assigned to one of five CKD severity classes based on the calculated eGFR values: Normal/Stage 1 (eGFR ≥ 90 mL/min/1.73 m^2); Mild/Stage 2 (90 mL/min/1.73 m^2 > eGFR ≥ 60 mL/min/1.73 m^2); Moderate/Stage 3 (60 mL/min/1.73 m^2 > eGFR ≥ 30 mL/min/1.73 m^2); Severe/Stage 4 (30 mL/min/1.73 m^2 > eGFR ≥ 15 mL/min/1.73 m^2); and Kidney Failure/Stage 5 (eGFR < 15 mL/min/1.73 m^2).[20]

Patients were stratified into two cohorts for analysis: Normal/Mild CKD (Stages 1 and 2) and Moderate/Severe CKD (Stages 3, 4, and 5). The analyses conducted in the current study compared differences in demographics, comorbidities, and perioperative/postoperative complication rates between the two cohorts. Moderate/Severe CKD was also analyzed for its impact on increasing the risk for post-operative complications in comparison to the Normal/Mild CKD cohort.

2.4. Statistical analysis

In order to analyze the differences between two cohorts of rTKA patients stratified by their CKD severity, propensity score matching without replacement was first employed for the purpose of developing a cohort of Normal/Mild CKD patients matching with the Moderate/Severe CKD patient cohort in a 1:1 manner. This method generated a matched cohort of 2602 normal/mild CKD patients based on those patients' demographics and pre-operative comorbidities while minimizing selection bias; patients were non-randomly assigned to the Normal/Mild CKD and Moderate/Severe CKD cohorts due to CKD's association with a variety of other diseases. Demographics, comorbidities, and perioperative/post-operative complications were assessed for differences between the two cohorts utilizing Pearson's chi-squared tests or Fischer's exact test (for expected cell sizes <5) for categorical variables expressed

Table 1
Demographics and comorbidities stratified by CKD stage.

	Mild or Normal CKD (11349)	%	Matched Mild or Normal CKD (2602)	%	Moderate to Severe CKD (2602)	%	Unadjusted P-value	Propensity Matched P-value
DEMOGRAPHICS								
Age (Mean ± SD)[a]	64.23 ± 10.706		67.70 ± 10.055		70.90 ± 9.665		**<0.001**	**<0.001**
Sex							**<0.001**	**<0.001**
Female	6509	57.35%	1556	59.80%	1712	65.80%		
Male	4840	42.65%	1046	40.20%	890	34.20%		
Race							**<0.001**	0.052
American Indian or Alaska Native	75	0.66%	13	0.50%	16	0.61%		
Asian or Pacific Islander	170	1.50%	33	1.27%	51	1.96%		
Black or African American	1580	13.92%	245	9.42%	235	9.03%		
Hispanic	12	0.11%	5	0.19%	0	0.00%		
White	9512	83.81%	2306	88.62%	2300	88.39%		
PRE-OPERATIVE COMORBIDITIES								
Diabetes Mellitus							**<0.001**	**<0.001**
No Diabetes Mellitus	9131	80.46%	2016	77.48%	1790	68.79%		
Non-Insulin Dependent	1551	13.67%	383	14.72%	445	17.10%		
Insulin Dependent	667	5.88%	203	7.80%	367	14.10%		
Smoke	1466	12.92%	229	8.80%	218	8.38%	**<0.001**	0.586
Dyspnea							**<0.001**	**<0.001**
No Dyspnea	10605	93.44%	2387	91.74%	2306	88.62%		
Moderate Exertion	709	6.25%	200	7.69%	282	10.84%		
At Rest	35	0.31%	15	0.58%	14	0.54%		
Ventilator Dependence	4	0.04%	2	0.08%	2	0.08%	0.356	1.000
COPD	583	5.14%	157	6.03%	221	8.49%	**<0.001**	**0.001**
Congestive Heart Failure	63	0.56%	26	1.00%	45	1.73%	**<0.001**	**0.023**
Hypertension	7407	65.27%	1931	74.21%	2137	82.13%	**<0.001**	**<0.001**
Ascites	3	0.03%	2	0.08%	0	0.00%	0.407	0.157
Acute Renal Failure	2	0.02%	1	0.04%	19	0.73%	**<0.001**	**0.001**
Dialysis	3	0.03%	1	0.04%	61	2.34%	**<0.001**	**<0.001**
Disseminated Cancer	29	0.26%	7	0.27%	17	0.65%	**0.001**	**0.041**
Wound Infection	215	1.89%	52	2.00%	102	3.92%	**<0.001**	**<0.001**
Steroid Use	508	4.48%	114	4.38%	169	6.50%	**<0.001**	**0.001**
Weight Loss	40	0.35%	7	0.27%	19	0.73%	**0.007**	**0.018**
Bleeding Disorders	494	4.35%	132	5.07%	198	7.61%	**<0.001**	**<0.001**
Blood Transfusions	63	0.56%	18	0.69%	36	1.38%	**<0.001**	**0.014**
Systemic Sepsis	254	2.24%	67	2.57%	147	5.65%	**<0.001**	**0.001**
Functional Status							**<0.001**	**<0.001**
Independent	10866	95.74%	2480	95.31%	2383	91.58%		
Partially Dependent	382	3.37%	98	3.77%	184	7.07%		
Totally Dependent	26	0.23%	8	0.31%	10	0.38%		
Not Reported	75	0.66%	16	0.61%	25	0.96%		
OPERATIVE VARIABLES								
Anesthesia Administered							**<0.001**	**0.001**
Epidural	142	1.25%	2	0.08%	35	1.35%		
General	7145	62.96%	1623	62.38%	1772	68.10%		
Local/Regional	293	2.58%	66	2.54%	59	2.27%		
MAC/IV Sedation	794	7.00%	178	6.84%	135	5.19%		
Spinal	2949	25.98%	702	26.98%	593	22.79%		
Other	18	0.16%	4	0.15%	4	0.15%		
Not Reported	8	0.07%	4	0.15%	4	0.15%		
ASA Classification							**<0.001**	**<0.001**
1-No Disturb	125	1.10%	20	0.77%	11	0.42%		
2-Mild Disturb	4619	40.70%	909	34.93%	586	22.52%		
3-Severe Disturb	6284	55.37%	1564	60.11%	1770	68.02%		
4-Life Threat	308	2.71%	105	4.04%	233	8.95%		
5- Moribund	3	0.03%	1	0.04%	0	0.00%		
Not Reported	10	0.09%	3	0.12%	2	0.08%		
LABORATORY VALUES[a]								
Sodium (mEq/L)	139.220 ± 2.940		139.324 ± 2.932		138.978 ± 3.337		**<0.001**	**<0.001**
Blood Urea Nitrogen (mg/dL)	16.334 ± 6.059		19.026 ± 6.575		26.233 ± 11.475		**<0.001**	**<0.001**
Creatinine (mg/dL)	0.837 ± 0.179		1.018 ± 0.145		1.512 ± 0.984		**<0.001**	**<0.001**
Albumin (g/dL)	3.990 ± 0.504		3.956 ± 0.507		3.785 ± 0.586		**<0.001**	**<0.001**
White Blood Cells (10^3 c/mL)	7.157 ± 2.510		7.238 ± 2.360		7.740 ± 3.198		**<0.001**	**<0.001**
Hematocrit (%)	39.840 ± 4.732		39.486 ± 4.794		37.149 ± 5.283		**<0.001**	**<0.001**
Platelets (per mL)	250.253 ± 77.059		247.113 ± 76.887		242.155 ± 81.514		**<0.001**	**0.026**
INR	1.057 ± 0.254		1.070 ± 0.316		1.111 ± 0.311		**<0.001**	**<0.001**

CKD: Chronic kidney disease; SD: standard deviation; COPD: Chronic obstructive pulmonary disease; MAC/IV: monitored anesthesia care/intravenous; ASA: American Society of Anesthesiology; INR: International Normalized Ratio.
All other values expressed as (%) and N.
*Pneumonia & Angina were excluded due to <85% of patients containing data on Pre-operative Pneumonia/Angina status.
**Started with 16428 rTKA patients, then 15424 (Creatinine), then 13951 (age and race).
[a] Values expressed as Mean ± Standard Deviation.

as number and frequency of occurrences. For continuous variables such as age, laboratory values, and time, one-way analysis of variance (ANOVA) was used to assess significant differences between the two cohorts; these variables are expressed as mean values with standard deviations. All statistical findings with p-values less than or equal to 0.05 were considered significant in the univariate analyses.

The current retrospective study further analyzed the post-operative complications in order to assess moderate/severe CKD (and established kidney failure) as an independent risk factor for the complications included in the univariate analyses. Multivariate regression analyses were conducted on the propensity matched cohorts to control for patient demographics and pre-operative comorbidities and to assess the impact of higher stages of CKD on independently increasing the risk for postoperative complications. The multivariate logistic regression models were generated by controlling for statistically significant covariates—age, sex, diabetes mellitus, dyspnea, COPD, CHF, hypertension, acute renal failure, dialysis dependence, disseminated cancer, open wound/wound infection, steroid use, significant weight loss, hematologic disorders, pre-operative blood transfusions, systemic sepsis, and functional status—and calculating odds ratios (OR) with 95% confidence intervals (CI). All statistical analyses with p-values less than or equal to 0.05 were considered significant in the multivariate regression analyses. All statistical analyses were performed using the IBM® SPSS® Statistics Version 25 software. (IBM Corporation, Armonk, NY).

3. Results

After propensity score matching, a cohort of 2602 normal/mild CKD patients were generated for comparison against the moderate/severe CKD cohort of 2602 patients. When comparing the matched cohorts, significant differences in age ($p < 0.001$) and sex ($p < 0.001$) were observed, while race was not statistically significant in the propensity-matched analysis ($p = 0.052$; Table 1).

Significant differences that were observed in several preoperative comorbidities can be observed in Table 1. Univariate analyses results initially conducted to assess differences in the occurrence of postoperative complications between the two propensity-matched cohorts can also be observed in Table 2. Results of analyses of operation-related variables between rTKA patients with normal/mild CKD and moderate/severe CKD are listed in Table 3.

Controlling for patient demographic factors and pre-operative comorbidities, multivariate logistic regression models yielded moderate/severe CKD to be a significant independent risk factor for five post-operative complications. Suffering from moderate/severe CKD independently increased the risk for postoperative acute renal failure (OR 18.097, 95% CI 4.970–65.902, $p < 0.001$), blood transfusions (OR 1.697, 95% CI 1.50–1.919, $p < 0.001$), return to the operating room (OR 1.257, 95% CI 1.009–1.566, $p = 0.041$), extended length of stay of 10 or more days (OR 1.707, 95% CI 1.292–2.255, $p < 0.001$), and mortality (OR 2.165, 95% CI 1.116–4.20, $p = 0.022$). Moderate/Severe CKD, however, did not independently increase the risk for several complications—unplanned intubation, urinary tract infections, and septic shock—even though univariate analyses demonstrated higher prevalence rates in the postoperative period (Table 4).

4. Discussion

CKD and the vast spectrum of comorbidities affecting the afflicted patient population have significant surgical complications in rTKA that have been documented in the literature for the general population.[21,22] The physiology of the increased morbidity and mortality in this population is multifactorial but thought to be due to metabolic and electrolyte disturbances, volume dysregulation, and inadequate renal perfusion.[23] One challenge to studying the specific relationship between CKD and morbidity and mortality from rTKA lies in the significantly increased comorbidities in this population including diabetes mellitus, congestive heart failure, hypertension, and acute renal failure – all of which have their own established surgical and anesthesia complications. These conditions can often present together due to the common risk factors that link their pathophysiology. As the elderly population continues to grow, so too does the incidence of obesity and other features of metabolic syndrome that can lead to CKD.[24,25] Additionally, some of the same behavioral and epidemiologic trends account for the increasing rates of OA, TKA, and subsequently rTKA procedures. The significant comorbidities in the CKD population shroud the etiology of surgical complications from rTKA in these patients, and while the rates of both are increasing, it is important to understand why the

Table 2
Univariate analyses for postoperative medical complications by severity of chronic kidney disease.

Postoperative complications	Mild or Normal CKD		Matched Mild or Normal CKD		Moderate to Severe CKD		Unadjusted P-value	Propensity Matched P-value
	(N)	(%)	(N)	(%)	(N)	(%)		
	11349		2602		2602			
Superficial Incisional SSI	92	0.81%	13	0.50%	17	0.65%	0.411	0.464
Deep Incisional SSI	92	0.81%	21	0.81%	20	0.77%	0.829	0.875
Organ/Space SSI	159	1.40%	29	1.11%	43	1.65%	0.333	0.097
Wound Disruption	55	0.48%	10	0.38%	17	0.65%	0.279	0.177
Pneumonia	66	0.58%	17	0.65%	27	1.04%	**0.010**	0.130
Unplanned Intubation	23	0.20%	5	0.19%	15	0.58%	**0.001**	**0.025**
Pulmonary Embolism	47	0.41%	10	0.38%	6	0.23%	0.170	0.317
Ventilator Dependence (>48 h)	14	0.12%	4	0.15%	5	0.19%	0.391	0.739
Progressive Renal Insufficiency	23	0.20%	9	0.35%	18	0.69%	**<0.001**	0.082
Acute Renal Failure	3	0.03%	1	0.04%	17	0.65%	**<0.001**	**<0.001**
Urinary Tract Infection	95	0.84%	22	0.85%	37	1.42%	**0.005**	**0.050**
CVA/Stroke	9	0.08%	4	0.15%	4	0.15%	0.262	1.000
Cardiac Arrest	13	0.11%	3	0.12%	6	0.23%	0.148	0.317
Myocardial Infarction	33	0.29%	15	0.58%	13	0.50%	0.094	0.705
Blood Transfusions	1223	10.78%	319	12.26%	489	18.79%	**<0.001**	**<0.001**
Deep Venous Thromboembolism	104	0.92%	19	0.73%	24	0.92%	0.977	0.444
Systemic Sepsis	147	1.30%	39	1.50%	53	2.04%	**0.004**	0.141
Septic Shock	20	0.18%	5	0.19%	17	0.65%	**<0.001**	**0.010**

CKD: Chronic kidney disease; SSI: Surgical Site Infection; CVA: Cerebral Vascular Accident.

Table 3
Comparison of operative variables by severity of chronic kidney disease.

PERIOPERATIVE COMPLICATIONS	Normal or Mild CKD (11349)		Matched Normal or Mild CKD (2602)		Moderate to Severe CKD (2602)		Unadjusted P-value	Propensity Matched P-value
Operation Related Time Variables[a]								
Days to Operation from Admission	0.33 ± 7.013		0.32 ± 7.204		0.33 ± 1.301		0.959	0.938
Total Operating Time (Minutes)	134.65 ± 67.465		133.06 ± 68.656		132.61 ± 66.816		0.164	0.811
Total Hospital Stay Length (Days)	3.42 ± 3.194		3.55 ± 3.190		4.22 ± 4.326		**<0.001**	**<0.001**
Days from Operation to Death	11.00 ± 9.301		7.63 ± 7.927		13.60 ± 9.941		0.344	0.133
Days from Operation to Discharge	3.22 ± 2.608		3.36 ± 2.967		3.88 ± 3.771		**<0.001**	**<0.001**
	(n)	(%)	(n)	(%)	(n)	(%)		
Death	24	0.21%	7	0.27%	23	0.88%	**<0.001**	**0.012**
Return to Operating Room	412	3.63%	78	3.00%	126	4.84%	**0.004**	**0.001**
Extended Length of Stay (≥ 10 days)	190	1.67%	46	1.77%	100	3.84%	**<0.001**	**<0.001**
Discharge Destination							**<0.001**	**<0.001**
Home	6285	55.38%	1352	51.96%	1094	42.04%		
Other than Home	2196	19.35%	576	22.14%	775	29.78%		
Not Reported	2868	25.27%	674	25.90%	733	28.17%		

CKD: Chronic Kidney Disease.
Other values expressed as (n) and (%).
[a] Values expressed as Mean ± Standard Deviation for Time Variables.

Table 4
Multivariate analyses assessing moderate to severe CKD as an independent risk factor for complications.

Complications[a]	Odds Ratio	95% Confidence Interval		P-Value
Superficial Incisional SSI	1.247	0.722	2.154	0.429
Deep Incisional SSI	0.842	0.499	1.423	0.521
Organ/Space SSI	1.016	0.701	1.474	0.931
Wound Disruption	1.055	0.581	1.915	0.861
Pneumonia	1.258	0.770	2.056	0.359
Unplanned Intubation	1.731	0.835	3.592	0.140
Pulmonary Embolism	1.778	0.621	5.088	0.283
Ventilator Dependence (>48 h)	1.055	0.328	3.395	0.928
Progressive Renal Insufficiency	1.692	0.743	3.852	0.210
Acute Renal Failure	18.097	4.970	65.902	**<0.001**
Urinary Tract Infection	1.177	0.784	1.766	0.432
CVA/Stroke	1.326	0.378	4.655	0.659
Cardiac Arrest	1.479	0.500	4.376	0.479
Myocardial Infarction	1.056	0.512	2.182	0.882
Blood Transfusions	1.697	1.500	1.919	**<0.001**
Deep Venous Thromboembolism	1.007	0.635	1.598	0.976
Systemic Sepsis	1.099	0.757	1.595	0.620
Septic Shock	1.789	0.846	3.784	0.128
Death	2.165	1.116	4.200	**0.022**
Return to Operating Room	1.257	1.009	1.566	**0.041**
Extended Length of Stay (≥10 days)	1.707	1.292	2.255	**<0.001**

CKD: Chronic kidney disease; SSI: Surgical site infection; CVA: Cerebral vascular accident; COPD: Chronic obstructive pulmonary disease; CHF: Congestive heart failure.
[a] Controlled for age, sex, race, diabetes mellitus, dyspnea, COPD, CHF, hypertension, acute renal failure, dialysis dependence, disseminated cancer, wound infections, steroid use, bleeding disorders, pre-operative transfusions, sepsis, functional status.

adverse events are happening and how we can remedy them.

In this retrospective analysis, we were unable to delineate the specific comorbidity associations when accounting for the increased rate of unplanned intubation, UTI, or septic shock among those with moderate/severe CKD compared to normal/mild. However, we were able to identify statistically significant relationships between patients with moderate/severe CKD and increased risk for postoperative acute renal failure, blood transfusions, return to the operating room, extended length of hospital stay, and mortality after rTKA. These findings were all independent of the aforementioned comorbidities. This suggests there is more to the pathology of CKD that a surgeon must consider before agreeing to perform an elective rTKA. We require more coordination with our nephrology colleagues and collaboration into the pathophysiologic etiology of the various risks that are significantly increased in order to recommend the best treatment modality for patients needing new prostheses for their knee arthroplasties. In addition, CKD may also inform routine changes to the anesthesia care of these patients. The specific factors are yet to be elucidated in the current literature, aside from the knowledge that the dosage of renally excreted drugs must be modified. The current study stratified the adverse event risk by GFR staging independently, while controlling for comorbidities, and necessitates exploration into changes in management for these patients with a goal of either mitigating said risks or having a better understanding of the risk/benefit to management of OA with rTKA. Furthermore, blood transfusions are often responsible for broad recipient sensitization against donor human leukocyte antigen and can contribute to difficulties in finding appropriate donor organs.[26] The increased risk of postoperative blood transfusions following rTKA in the more severe CKD cohort is especially important as many of these patients are awaiting organ transplantation to improve their quality of life.

One of the ways we can try to combat these outcomes for CKD patients lies in understanding the physiology that predisposes them to increased incidences of acute renal failure, blood transfusions, and overall mortality. Acute renal failure can be subdivided by cause into prerenal, intrinsic, or postrenal. Mostly prerenal etiologies contribute to the increased rate of acute renal failure in CKD patients in surgery. Whether due to the operation itself or the anesthetics, decreased renal blood flow and poor perfusion can manifest as prerenal acute renal failure especially in CKD patients where kidney function is already partially compromised. Intraoperative hypotension and drastic fluid shifting can exacerbate a poorly perfused renal system, further contributing to acute renal failure in these patients.[27] Furthermore, increased need for blood transfusions in moderate/severe CKD patients can be explained by the role of the kidney in the production of erythropoietin (EPO). When this function is compromised in CKD patients, their homeostatic mechanism to control hemoglobin and RBC cell mass is insufficient. Synthetic EPO is often used as treatment of anemia in CKD patients outside of perioperative care.[28] However, in an acute setting of significant blood loss, transfusion is often required in these patients in order to maintain oxygenation and perfusion. These two complications in particular, necessitating transfusion and acute renal failure, likely contribute to the increased risk for mortality, increased hospital stay, and reoperation.

This study supports future research that should aim to delineate more specific renal insults and correlate them with specific complications following rTKA. Although CKD severity was established as an independent risk factor for such complications, more research into the direct etiologies of the adverse outcomes in association with CKD is warranted. Furthermore, it has yet to be determined if CKD itself increases the risk of failure of TKA, which may necessitate revision and contribute to increased morbidity and mortality thereafter. A review of rTKA and risk factors to revision did not specifically identify CKD, although it did find hypertension and diabetes mellitus as risk factors increasing the failure rate of the initial prosthesis.[29] It is not clear what proportion of the patients in those studies with hypertension, diabetes, or otherwise may have carried a diagnosis of CKD. Understanding this connection would further help orthopaedic surgeons better manage CKD patients considering initial TKA, who may present with increased risks for requiring rTKA.

4.1. Limitations

As laboratory values are markers of underlying pathologies, one limitation of this study was not explicitly controlling for electrolyte status when accounting for the increased complications represented by the comorbidities described in this study. It is routine standard of care to measure these electrolytes preoperatively in patients with overt risk factors including prior diagnosis of CKD or evidence of renal failure. Another limitation of this study lies in stratifying into two groups, and not each of the five stages of CKD; however, this current study modelled the analyses previously reported by Warth et al., in 2015 in primary total hip and knee arthroplasty procedures.[14] A smaller distinct division in risk stratification that allows for even stronger clinical applicability may be missed due to the wide range of GFR values in the two cohort groups. Although CKD is solely differentiated by GFR, it by nature does not reflect the pathophysiology of the renal insult but only the remaining renal function. Until we gain a better understanding of the causes of increased adverse events following rTKA in patients with CKD, the management of these patients cannot be appreciably different aside from increased monitoring for complications and more preoperative risk versus benefit discussion with these patients.

The present study only analyzed factors in which $\geq$85% of the patient files had recorded information for the variables in question. Several other demographic factors, comorbidities, and postoperative complications that may actually be significant may have not been reported due to the aforementioned inclusion criteria. A limitation inherent to all nationwide-database studies is the inability to verify the information being entered into the database. As a result, healthcare providers should consider the results of this study and other database studies within the appropriate clinical context. Finally, using CPT codes introduces the possibility of coding bias based on financial reimbursement as these codes were not originally intended for research purposes.[30]

5. Conclusion

We know that stages III, IV, and V CKD, independently of common comorbidities, increase the risk of postoperative acute renal failure, blood transfusions, return to the operating room, extended length of hospital stay, and mortality after rTKA. These significant complications should be accounted for in the clinical management of these patients suffering from OA of the knee requiring TKA and subsequent rTKA. However, before elucidating the cause of the increased risk for morbidity and mortality, surgeons and healthcare professionals should take the initiative to help reduce such complications from arising through routine postoperative surveillance and increased risk benefit discussions preceding the choice to operate.

Conflicts of interest

All conflict of interest forms have been submitted with the original manuscript. The authors declare no conflict of interest. No funding was obtained for the completion of this work.

Declaration of interests

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

This study was exempt from Institutional Review Board (IRB) approval, since it utilized de-identified patient data that was publicly available through the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database.

This research was conducted at The George Washington University School of Medicine and The George Washington University Hospital Department of Orthopaedic Surgery.

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