Impact of diabetes mellitus on surgical complications in patients undergoing revision total knee arthroplasty: Insulin dependence makes a difference

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ABSTRACT

Objectives: Assessing the effects of diabetes mellitus (DM), non-insulin-dependent diabetes mellitus (NIDDM), and insulin-dependent diabetes mellitus (IDDM) on revision TKA (rTKA) has become increasingly imperative due to the increased rates of revisions associated with DM. This study sought to identify complications in rTKA that were independently associated with NIDDM/IDDM compared to non-diabetic (Non-DM) patients and whether IDDM was associated with specific postoperative complications compared to NIDDM.

Methods and materials: 16,428 rTKA patients were identified from the ACS-NSQIP database from 2005 to 2016 and stratified into three separate cohorts. 12,922 (78.66%) were Non-DM, 2335 (14.21%) had NIDDM, and 1171 (7.13%) had IDDM. Univariate analyses were utilized to assess for differences in demographics, preoperative comorbidities, and postoperative complication rates. Multivariate logistic regression analyses were then employed to control for significant differences in patients characteristics to assess NIDDM and IDDM as independent risk factors for complications in comparison to Non-DM. IDDM was further analyzed as a risk factor in comparison to NIDDM for the purpose of elucidating the impact of insulin dependence on risk for postoperative complications.

Results: NIDDM was an independent risk factor for deep incisional surgical site infections (Odds Ratio (OR): 2.477) and urinary tract infections (UTI) (OR 1.862) ($p < 0.05$). Compared to NIDDM, IDDM was independently associated with greater risk for pneumonia (OR 2.603), septic shock (OR 6.597), blood transfusions (OR 1.326), and an extended length of stay (OR: 1.331) ($p < 0.05$). IDDM additionally increased the risk for acute renal failure (OR 3.269) and cardiac arrest (OR 3.268) ($p < 0.05$) when compared to Non-DM. DM patients overall had increased rates of worse outcomes and infectious complications.

Conclusion: Although differences between diabetes and non-diabetes rTKA patients were seen, differences in complication rates between diabetes patients further divided based on insulin dependence status were also noted. Future work examining whether targeting perioperative glucose levels < 200 mg/dL in DM rTKA patients decreases infectious complications is warranted. Future work analyzing the role of tranexamic acid administration and 24-h postoperative antibiotics in rTKA IDDM patients may be warranted given the elevated risk of pneumonia, septic shock, and blood transfusions.

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1. Introduction

Diabetes mellitus (DM) has been one of the most pressing public health issues facing the global health system in the last three decades.¹ The prevalence of DM in the United States has been showing patterns of rapid increase – vastly contributing to the burden of disease and its associated economic costs in the US.^{2–4} In recent

years, there has been growing interest on the effects of DM on surgical outcomes. Previous studies have established DM with increased rates of numerous complications in orthopedic procedures such as surgical site/periprosthetic joint infections,^{5–7} mortality,⁸ poorer functional outcomes,⁹ pneumonia,¹⁰ and aseptic loosening.¹¹ Interestingly, although DM increases the rates of various complications, it most notably increases the rate of revision amongst primary total knee arthroplasty (TKA).¹² However, the increasing demand and necessity of revision procedures for TKA should be met with careful consideration as these patients are likely at elevated risk for complications following their revision procedures due to their DM status.

DM encompasses a multitude of disease processes causing poor glycemic control and manifests as insulin-dependent DM (IDDM) and non-insulin-dependent DM (NIDDM). Previous literature has established the effect of IDDM and NIDDM on surgical complications and outcomes following primary TKA and various other orthopedic procedures.^{13,14} However, to the author's knowledge, there has been no previous study examining the effect of DM on surgical complications in revision total knee arthroplasty (rTKA). As DM has been associated with increased rates of revision following primary TKA, it is imperative to know how DM affects the subsequent revision procedure as well.

The main objectives of the current study are to: (1) establish the impact of DM and insulin dependence on the risk for various perioperative/postoperative complications following rTKA, (2) evaluate differences in comorbidities that diabetic patients present with and (3) describe and elucidate the differences in patient demographics between rTKA patients with diabetes. Surgeons can better risk-stratify candidates for rTKA by DM status for experiencing certain complications in order to implement optimal management in the preoperative and postoperative periods.

2. Materials and methods

The American College of Surgeons (ACS) maintains the National Surgical Quality Improvement Program (NSQIP) – a multi-institutional clinical registry of surgical patients aimed at recording data for improving outcomes. The database contains 274 variables for each patient that serve to provide complete medical histories and outcome measures for the surgical patient files provided by 680 participating institutions. This retrospective study was exempt from Institutional Review Board (IRB) review/approval, since the patient data is de-identified and publicly available for individuals at participating institutions to access.

2.1. Patient selection

The ACS-NSQIP database was queried to identify patients who had undergone rTKA in order to analyze the impact of diabetes mellitus and specifically insulin dependence, on increased risks for surgical complications in rTKA. Patients corresponding with Current Procedure Terminology (CPT) codes 27486 and 27487 only for rTKA from 2005 to 2016 were isolated and included for analysis. All included patients were ≥ 18 years old and had complete medical profiles and surgical outcome. 16,428 patients were identified and stratified into three separate cohorts by their diabetes mellitus status—Non-DM, NIDDM, and IDDM—in order to assess differences in prevalence of demographics/comorbidities and rates of complications between the three cohorts.

2.2. Variables

The ACS-NSQIP database maintains 274 relevant variables for each surgical patient case. Patient demographic factors were

analyzed between the three cohorts of rTKA patients in order to gain better insight into population-based differences in progressive stages of diabetes mellitus. Included demographic factors were age, sex, and race in order to better provide orthopaedic surgeons with the necessary risk-stratifications for patients who present as candidates for rTKA. Preoperative comorbidities were analyzed for differences in order to gain better insight into the patients' medical histories and assess possible associations between existing disease states and surgical complications in rTKA. Only preoperative comorbidities where more than 85% of the patient sample had complete data for were included in this study in order to minimize possible statistical errors when evaluating prevalence and associations with specific surgical complications. A complete list of comorbidities analyzed can be found in [Table 1](#) ([Table 1](#)).

Patients were also analyzed for differences in their operative variables to evaluate whether operation-specific parameters were significantly different between patients in three separate stages of diabetes mellitus progression – a complete set of operation-specific variables analyzed can be found in [Table 2](#) ([Table 2](#)). Post-operative outcomes were included in this retrospective study in order to assess the effect of diabetes mellitus severity on adverse events following revision total knee arthroplasty. Complications of interest that were included for analyses are displayed in [Table 3](#) ([Table 3](#)). These variables were assessed for differences in incidence rates, as well as increased levels of risk in diabetic patients.

2.3. Statistical analysis

Univariate analyses were utilized for statistical difference in prevalence of the aforementioned variables ([Table 1](#))([Table 2](#))([Table 3](#)). Pearson's chi-squared tests and Fischer's exact tests (expected cell sizes < 5) were used to evaluate differences in rates of categorical variables, while one-way analysis of variance (ANOVA) was utilized for differences in mean values of continuous variables (ie. age, laboratory values, time). Continuous variables are expressed as mean values with respective standard deviations. Categorical variables are expressed as proportions to represent prevalence rates among each cohort. Statistical findings with p -values ≤ 0.05 were considered significant.

Postoperative complications were further analyzed with multivariate analyses in order to establish both NIDDM and IDDM as independent risk factors for complications found to be significantly more prevalent in the NIDDM and IDDM cohorts. Multivariate logistic regression models were generated by controlling for significant patient demographic factors and pre-operative comorbidities to assess the impact of NIDDM and IDDM in independently increasing the risk for the complications included in the current study. The multivariate logistic regression model controlled for sex, race, dyspnea, COPD, CHF, hypertension, acute renal failure, dialysis dependence, open wound/wound infections, steroid use, hematologist disorders, preoperative blood transfusions, systemic sepsis, and functional dependence as categorical indicators, and for age as a covariate. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for each complication to assess the increased levels of risk.

In the multivariate analyses, NIDDM was first assessed as an independent risk factor for the complications of interest when compared to Non-DM patients. IDDM was analyzed in comparison to Non-DM separately to evaluate risk levels for these adverse events following surgery. For further analysis, another multivariate logistic regression model (controlling for the same patient factors and comorbidities) was generated to assess IDDM as a risk factor when compared to NIDDM for the purpose of establishing the role of insulin dependence specifically (a marker for advanced stages of diabetes mellitus) on increased levels of risk for complications

Table 1
Demographics and preoperative characteristics of patients undergoing revision total knee arthroplasty.

	IDMM ^a	NIDDM ^b	Non-DM ^c	P-Value
DEMOGRAPHICS				
Age (years; mean $\pm$ SD ^d)	66.19 $\pm$ 9.902	66.91 $\pm$ 9.726	65.10 $\pm$ 11.251	<0.001*
Sex				<0.001*
Female	626 (53%)	1325 (57%)	7727 (60%)	
Male	544 (46%)	1010 (43%)	5190 (40%)	
Race				<0.001*
American Indian or Alaska Native	10 (1%)	14 (1%)	69 (1%)	
Asian or Pacific Islander	18 (2%)	46 (2%)	174 (1%)	
Black or African American	159 (14%)	348 (15%)	1395 (11%)	
Hispanic	1 (0%)	4 (0%)	10 (0%)	
White	884 (75%)	1683 (72%)	10032 (78%)	
PRE-OPERATIVE COMORBIDITIES				
Smoke	138 (12%)	249 (11%)	1585 (12%)	0.088
Dyspnea				<0.001*
No Dyspnea	1019 (87%)	2137 (92%)	12067 (93%)	
Moderate Exertion	146 (12%)	184 (8%)	823 (6%)	
At Rest	6 (1%)	14 (1%)	32 (0%)	
Ventilator Dependence	0 (0%)	1 (0%)	5 (0%)	0.791
COPD ^e	114 (10%)	145 (6%)	660 (5%)	<0.001*
Congestive Heart Failure	30 (3%)	12 (1%)	80 (1%)	<0.001*
Hypertension	1039 (89%)	1996 (85%)	7970 (62%)	<0.001*
Ascites	0 (0%)	0 (0%)	3 (0%)	0.666
Acute Renal Failure	7 (1%)	3 (0%)	12 (0%)	<0.001*
Dialysis	21 (2%)	7 (0%)	44 (0%)	<0.001*
Disseminated Cancer	6 (1%)	4 (0%)	41 (0%)	0.221
Wound Infection	51 (4%)	57 (2%)	262 (2%)	<0.001*
Steroid Use	68 (6%)	78 (3%)	638 (5%)	0.001*
Weight Loss (>10% in past 6 months)	7 (1%)	15 (1%)	46 (0%)	0.083
Bleeding Disorders ^f	93 (8%)	118 (5%)	563 (4%)	<0.001*
Blood Transfusions	18 (2%)	19 (1%)	72 (1%)	<0.001*
Systemic Sepsis	61 (5%)	71 (3%)	339 (3%)	<0.001*
Functional Status				<0.001*
Independent	1075 (92%)	2223 (95%)	12330 (95%)	
Partially Dependent	84 (7%)	92 (4%)	466 (4%)	
Totally Dependent	9 (1%)	3 (0%)	31 (0%)	
LABORATORY VALUES (mean $\pm$ SD^d)				
Sodium (mEq/L)	138.42 $\pm$ 3.344	139.06 $\pm$ 3.042	139.22 $\pm$ 3.00	<0.001*
Blood Urea Nitrogen (mg/dL)	21.74 $\pm$ 10.741	19.22 $\pm$ 8.939	17.69 $\pm$ 7.869	<0.001*
Creatinine (mg/dL)	1.20 $\pm$ 0.988	0.98 $\pm$ 0.409	0.93 $\pm$ 0.478	<0.001*
Albumin (g/dL)	3.71 $\pm$ 0.643	3.96 $\pm$ 0.561	3.97 $\pm$ 0.510	<0.001*
White Blood Cells (10^3 c/mL)	7.98 $\pm$ 2.802	7.58 $\pm$ 2.523	7.17 $\pm$ 2.653	<0.001*
Hematocrit (%)	37.79 $\pm$ 5.280	38.78 $\pm$ 4.935	39.64 $\pm$ 4.860	<0.001*
Platelets (per mL)	244.05 $\pm$ 89.926	246.54 $\pm$ 77.018	249.67 $\pm$ 77.854	0.024*
INR ^g	1.09 $\pm$ 0.232	1.07 $\pm$ 0.292	1.06 $\pm$ 0.260	0.002*

*statistically significant.

^a Insulin-Dependent Diabetes Mellitus.

^b Non-Insulin Dependent Diabetes Mellitus.

^c No Diabetes Mellitus.

^d Chronic Obstructive Pulmonary Disease.

^e Standard Deviation.

^f Vitamin K deficiency, hemophilias, thrombocytopenia, etc.

^g International Normalized Ratio.

following rTKA. All statistical analyses, both univariate and multivariate, were completed using the IBM® SPSS® Statistics Version 25 software. (IBM Corporation, Armonk, NY).

3. Results

By querying the ACS-NSQIP database, 16,428 patients who had undergone rTKA procedures between 2005 and 2016 were isolated, of which 12,922 (78.66%) were not diabetic, 2335 (14.21%) were NIDDM, and 1171 (7.13%) were IDDM. When comparing these three separate cohorts of rTKA patients stratified by their diabetes mellitus status, IDDM and NIDDM patients (66.19 years, SD 9.902 and 66.91 years, SD 9.726) were significantly older than non-diabetic patients (65.10 years, SD 11.251; $p < 0.001$; Table 1). Compared to Non-DM patients, of which 40.16% were male, NIDDM and IDDM

patients were comprised of significantly more male patients (43.25% and 46.46%, respectively; $p < 0.001$). Between the three cohorts, there was also a significant difference in the race distribution among patients ($p < 0.001$).

Patients with NIDDM and IDDM were significantly more likely to have preoperative dyspnea ($p < 0.001$), COPD ($p < 0.001$), hypertension ($p < 0.001$), acute renal failure ($p < 0.001$), open wounds or wound infections ($p < 0.001$), hematologic disorders ($p < 0.001$), blood transfusions ($p < 0.001$), systemic sepsis ($p < 0.001$), and be functionally dependent ($p < 0.001$). Patients with IDDM, but not NIDDM, were significantly more likely to have preoperative CHF ($p < 0.001$), dialysis dependence ($p < 0.001$), and steroid use for chronic conditions ($p = 0.001$; Table 1).

Among the Non-DM, NIDDM, and IDDM patients respectively, there was an increasingly greater operative time (131.95 min vs.

Table 2
Operation-specific variables.

OPERATIVE VARIABLES	IDDM ^a	NIDDM ^b	Non-DM ^c	P-value
	1171	2335	12922	
Total Operating Time (Minutes)	137.35 ± 62.855	135.85 ± 69.281	131.95 ± 66.685	0.002*
Days to Operation from Admission	0.46 ± 2.231	0.59 ± 10.895	0.26 ± 4.789	0.036*
Total Hospital Stay Length (Days)	4.57 ± 4.805	3.87 ± 3.979	3.61 ± 3.819	<0.001*
Days from Operation to Death	10.33 ± 10.062	15.00 ± 10.564	12.70 ± 9.409	0.648
Days from Operation to Discharge	4.10 ± 3.659	3.59 ± 2.951	3.41 ± 3.248	<0.001*
Discharge Destination				<0.001*
Home	537 (46%)	1168 (50%)	7157 (55%)	
Other than Home	348 (30%)	569 (24%)	2411 (19%)	
Not Reported	286 (24%)	598 (26%)	3354 (26%)	
Care Type				0.011*
Inpatient	1166 (100%)	2316 (99%)	12760 (99%)	
Outpatient	5 (0%)	19 (1%)	162 (1%)	
Wound Class				<0.001*
Clean	962 (82%)	2035 (87%)	11371 (88%)	
Clean/Contaminated	32 (3%)	66 (3%)	366 (3%)	
Contaminated	42 (4%)	39 (2%)	255 (2%)	
Dirty/Infected	135 (12%)	195 (8%)	930 (7%)	
Anesthesia Administered				0.010*
Epidural	15 (1%)	27 (1%)	170 (1%)	
General	799 (68%)	1480 (63%)	7964 (62%)	
Local/Regional	14 (1%)	59 (3%)	321 (2%)	
MAC ^d /IV Sedation	68 (6%)	147 (6%)	846 (7%)	
Spinal	273 (23%)	618 (26%)	3591 (28%)	
Other	1 (0%)	3 (0%)	18 (0%)	
Not Reported	1 (0%)	1 (0%)	12 (0%)	
ASA ^e Classification				<0.001*
1-No Disturb	0 (0%)	5 (0%)	189 (1%)	
2-Mild Disturb	131 (11%)	505 (22%)	5649 (44%)	
3-Severe Disturb	915 (78%)	1702 (73%)	6679 (52%)	
4-Life Threat	122 (10%)	120 (5%)	390 (3%)	
5- Moribund	1 (0%)	2 (0%)	1 (0%)	
Not Reported	2 (0%)	1 (0%)	4 (0%)	

*statistically significant.

^a Insulin-Dependent Diabetes Mellitus.^b Non-Insulin Dependent Diabetes Mellitus.^c No Diabetes Mellitus.^d Monitored Anesthesia Care.^e American Society of Anesthesiologists.

135.85 min vs. 137.35 min; $p = 0.002$), total length of hospital stay (3.61 days vs. 3.87 days vs. 4.57 days; $p < 0.001$), and inpatient stay following the rTKA procedure (3.41 days vs. 3.59 days vs. 4.10 days; $p < 0.001$; Table 2). NIDDM and IDDM patients also experienced significantly longer wait periods from admission to operation time (0.59 days and 0.46 days) when compared to Non-DM patients (0.26 days; $p = 0.036$). NIDDM and IDDM patients undergoing rTKA were significantly more likely to be inpatient ($p = 0.011$) and be discharged to destinations other than their homes ($p < 0.001$; Table 2).

There were significantly different rates of several postoperative complications between the three cohorts: deep incisional surgical site infection (SSI) ($p = 0.044$), pneumonia ($p < 0.001$), unplanned intubation ($p < 0.001$), progressive renal insufficiency ($p = 0.043$), acute renal failure ($p < 0.001$), UTIs ($p = 0.002$), cardiac arrest ($p = 0.002$), bleeding requiring transfusions ($p < 0.001$), systemic sepsis ($p < 0.001$), septic shock ($p < 0.001$), and an extended length of stay greater than or equal to 5 days ($p < 0.001$; Table 3).

In multivariate analyses, NIDDM was found to be a significant independent risk factor for two complications when compared to Non-DM patients: deep incisional SSI (OR 2.477, 95% CI 1.192–5.145, $p = 0.015$) and UTIs (OR 1.862, 95% CI 1.22–2.842, $p = 0.004$; Table 4).

IDDM independently increased the risk for six postoperative complications compared to Non-DM patients. Patients with IDDM were at an increased risk for pneumonia (OR 1.793, 95% CI 1.019–3.156, $p = 0.043$), acute renal failure (OR 3.269, 95% CI

1.124–9.507, $p = 0.030$), cardiac arrest (OR 3.268, 95% CI 1.155–9.247, $p = 0.026$), blood transfusions (OR 1.41, 95% CI 1.178–1.687, $p < 0.001$), septic shock (OR 2.719, 95% CI 1.238–5.969, $p = 0.013$), and extended length of stay (≥ 5 days) (OR 1.422, 95% CI 1.199–1.687, $p < 0.001$; Table 5) when compared to the non-diabetic patients.

In assessing the impact of insulin dependence, multivariate regression models were generated to analyze the impact of IDDM in comparison to NIDDM on the risk levels for postoperative complications. IDDM was found to be a significant independent risk factor for pneumonia (OR 2.603, 95% CI 1.141–5.936, $p = 0.023$), blood transfusions (OR 1.326, 95% CI 1.068–1.647, $p = 0.011$), septic shock (OR 6.597, 95% CI 1.678–25.929, $p = 0.007$), and an extended length of stay (≥ 5 days) (OR 1.331, 95% CI 1.083–1.636, $p = 0.007$; Table 6).

4. Discussion

As DM has been shown to increase the risk for poorer functional outcomes and even mortality following surgery, the implications of DM on postoperative complications in a variety of procedures have been increasingly important as the number of patients living with DM continues to rise.^{2–4,8,9} The effects of DM on TKA have been previously reported – however, there is a lack of literature analyzing the effects of DM on rTKA. As DM has been associated with higher rates of revision surgeries of TKA, it is important to delineate the specific complications that DM subsequently

Table 3

Univariate analyses of postoperative complication rates by diabetes mellitus status.

	IDDM ^a	NIDDM ^b	Non-DM ^c	P- Value
POSTOPERATIVE COMPLICATIONS	1171	2335	12922	
Superficial Incisional SSI ^d	5 (0%)	23 (1%)	114 (1%)	0.217
Deep Incisional SSI ^d	12 (1%)	9 (0%)	110 (1%)	0.044*
Organ/Space SSI ^d	19 (2%)	43 (2%)	181 (1%)	0.245
Wound Disruption	6 (1%)	12 (1%)	71 (1%)	0.967
Pneumonia	19 (2%)	11 (0%)	75 (1%)	<0.001*
Unplanned Intubation	10 (1%)	7 (0%)	28 (0%)	<0.001*
Pulmonary Embolism	3 (0%)	8 (0%)	55 (0%)	0.604
Ventilator Dependence (>48 h)	4 (0%)	1 (0%)	22 (0%)	0.112
Progressive Renal Insufficiency	4 (0%)	12 (1%)	29 (0%)	0.043*
Acute Renal Failure	7 (1%)	2 (0%)	13 (0%)	<0.001*
Urinary Tract Infection	15 (1%)	34 (1%)	98 (1%)	0.002*
CVA ^e /Stroke	2 (0%)	4 (0%)	9 (0%)	0.211
Cardiac Arrest	6 (1%)	2 (0%)	15 (0%)	0.002*
Myocardial Infarction	7 (1%)	9 (0%)	40 (0%)	0.248
Blood Transfusions	207 (18%)	288 (12%)	1446 (11%)	<0.001*
Deep Venous Thromboembolism (DVT)	10 (1%)	22 (1%)	109 (1%)	0.893
Systemic Sepsis	31 (3%)	38 (2%)	164 (1%)	<0.001*
Septic Shock	12 (1%)	3 (0%)	26 (0%)	<0.001*
Death	7 (1%)	6 (0%)	39 (0%)	0.193
Return to Operating Room	53 (5%)	83 (4%)	483 (4%)	0.336
Extended Length of Stay (≥5 days)	272 (23%)	387 (17%)	1874 (15%)	<0.001*
Readmission	77 (7%)	142 (6%)	696 (5%)	0.120

*statistically significant.

^a Insulin-Dependent Diabetes Mellitus.^b Non-Insulin Dependent Diabetes Mellitus.^c No Diabetes Mellitus.^d Surgical Site Infection.^e Cerebral Vascular Accident.**Table 4**Multivariate analyses assessing NIDDM^a as an independent risk factor for post-operative complications compared to Non-DM.^b

POSTOPERATIVE COMPLICATIONS	Odds Ratio	95% Confidence Interval	P-Value
Superficial Incisional SSI ^c	1.132	0.682 1.879	0.631
Deep Incisional SSI ^c	2.477	1.192 5.145	0.015*
Organ/Space SSI ^c	1.272	0.87 1.859	0.214
Wound Disruption	0.903	0.468 1.74	0.76
Pneumonia	0.699	0.354 1.379	0.301
Unplanned Intubation	1.097	0.407 2.955	0.854
Pulmonary Embolism	0.82	0.384 1.753	0.609
Ventilator Dependence (>48 h)	0	0	0.985
Progressive Renal Insufficiency	1.956	0.954 4.013	0.067
Acute Renal Failure	0.665	0.136 3.245	0.614
Urinary Tract Infection	1.862	1.22 2.842	0.004*
CVA/Stroke ^d	2.496	0.737 8.456	0.142
Cardiac Arrest	0.286	0.037 2.223	0.232
Myocardial Infarction	1.071	0.493 2.325	0.863
Blood Transfusions	1.063	0.918 1.232	0.414
Deep Venous Thromboembolism (DVT)	1.106	0.689 1.775	0.678
Systemic Sepsis	1.205	0.811 1.79	0.356
Septic Shock	0.602	0.172 2.106	0.427
Death	0.621	0.236 1.634	0.334
Return to OR	0.828	0.64 1.07	0.148
Extended Length of Stay (≥5 days)	1.101	0.957 1.267	0.179
Readmission	1.008	0.825 1.231	0.937

*statistically significant.

^a Non-insulin Dependent Diabetes Mellitus.^b No Diabetes Mellitus.^c Surgical Site Infection.^d Cerebral Vascular Accident.**Table 5**Multivariate analyses assessing IDDM^a as an independent risk factor for post-operative complications compared to Non-DM.^b

POSTOPERATIVE COMPLICATIONS	Odds Ratio	95% Confidence Interval	P-Value
Superficial Incisional SSI ^c	2.493	0.899 6.919	0.079
Deep Incisional SSI ^c	1.127	0.585 2.17	0.722
Organ/Space SSI ^c	1.045	0.629 1.735	0.866
Wound Disruption	1.222	0.514 2.905	0.650
Pneumonia	1.793	1.019 3.156	0.043*
Unplanned Intubation	2.142	0.94 4.882	0.070
Pulmonary Embolism	5.50	0.751 40.271	0.093
Ventilator Dependence (>48 h)	1.053	0.296 3.742	0.937
Progressive Renal Insufficiency	1.359	0.375 4.93	0.641
Acute Renal Failure	3.269	1.124 9.507	0.030*
Urinary Tract Infection	1.247	0.686 2.266	0.469
CVA ^d /Stroke	1.124	0.14 9.053	0.912
Cardiac Arrest	3.268	1.155 9.247	0.026*
Myocardial Infarction	1.282	0.542 3.033	0.572
Blood Transfusions	1.41	1.178 1.687	<0.001*
Deep Venous Thromboembolism (DVT)	1.149	0.572 2.31	0.696
Systemic Sepsis	1.387	0.864 2.228	0.175
Septic Shock	2.719	1.238 5.969	0.013*
Death	1.01	0.405 2.517	0.983
Return to Operating Room	1.025	0.755 1.392	0.873
Extended Length of Stay (≥5 days)	1.422	1.199 1.687	<0.001*
Readmission	1.069	0.821 1.393	0.620

*statistically significant.

^a Insulin-Dependent Diabetes Mellitus.^b No Diabetes Mellitus.^c Surgical Site Infection.^d Cerebral Vascular Accident.

increases the risk for in these revision procedures. In doing so, anticipated complications can guide preoperative and post-operative management in order to decrease the risk of adverse events in these NIDDM/IDDM patients undergoing rTKA.

There were several limitations to this study analyzing diabetes

mellitus in rTKA patients. The ACS-NSQIP database lacks information regarding Type I or Type II diabetes for each patient, although NIDDM or IDDM information is given. While the NIDDM and IDDM patients together make up the diabetic patient cohort, these patients could not be differentiated based on whether they had Type I

Table 6Multivariate Analyses Assessing IDDM^a as an Independent Risk Factor for Postoperative Complications vs. NIDDM^b.

POSTOPERATIVE COMPLICATIONS	Odds Ratio	95% Confidence Interval	P-Value
Superficial Incisional SSI ^c	0.355	0.114 1.108	0.074
Deep Incisional SSI ^c	0.648	0.407 1.033	0.068
Organ/Space SSI ^c	0.921	0.514 1.648	0.781
Wound Disruption	1.025	0.373 2.819	0.961
Pneumonia	2.603	1.141 5.936	0.023*
Unplanned Intubation	2.653	0.785 8.965	0.116
Pulmonary Embolism	0.236	0.026 2.184	0.204
Ventilator Dependence (>48 h)	>999.99	0 .	0.982
Progressive Renal Insufficiency	0.299	0.067 1.34	0.115
Acute Renal Failure	4.623	0.864 24.726	0.074
Urinary Tract Infection	0.733	0.372 1.443	0.369
CVA ^d /Stroke	1.663	0.142 19.506	0.686
Cardiac Arrest	8.916	0.979 81.218	0.052
Myocardial Infarction	1.147	0.37 3.555	0.812
Blood Transfusions	1.326	1.068 1.647	0.011*
Deep Venous Thromboembolism (DVT)	0.813	0.366 1.808	0.612
Systemic Sepsis	1.107	0.618 1.985	0.732
Septic Shock	6.597	1.678 25.929	0.007*
Death	1.678	0.355 7.924	0.514
Return to Operating Room	1.213	0.83 1.772	0.319
Extended Length of Stay (≥5 days)	1.331	1.083 1.636	0.007*
Readmission	1.032	0.755 1.409	0.844

*statistically significant.

^a Insulin-Dependent Diabetes Mellitus.^b Non-Insulin Dependent Diabetes Mellitus.^c Surgical Site Infection.^d Cerebral Vascular Accident.

or Type II diabetes mellitus. However, given that 95% of diabetes mellitus cases are Type II diabetes, it's more likely that the overwhelming majority of IDDM represents later stages of Type II DM, where pancreatic beta cells are no longer functional due to cellular injury induced by chronic overactivity in the progressing earlier stages of the disease, though there may be a small number of these IDDM patients who were insulin-dependent due to Type I diabetes rather than Type II diabetes; NIDDM represents less severe forms of Type II DM where pancreatic beta cells are still functional.¹⁵ Though this poses a limitation with the small number of Type I diabetics, the authors believe its effects are minimal, as 95% of diabetics are Type II diabetics, with previous studies following a similar method.¹⁵ Therefore, although this study was able to study insulin dependence in DM, it was unable to assess the effects of Type I or Type II DM specifically on rTKA since our patients were presumed to have Type II DM. Another limitation lies in the inability to further stratify patients based on their HbA1c levels to assess their glycemic control – the increased risk in various complications seen in IDDM patients could be due to a subset of patients with severely elevated HbA1c levels. In addition, this study did not differentiate patients based on their indications for rTKA procedures (peri-prosthetic infections, fractures, life-span, etc.) and may present as potential confounding variables in assessing the impact of diabetes mellitus and insulin dependence on complications in the 30-day postoperative period. Furthermore, the inability to verify the provided data is a limitation inherent to all large clinical registry studies.

This retrospective study identified both NIDDM and IDDM to be associated with various infectious complications following rTKA. The two statistically significant complications found to be associated with NIDDM were deep incisional SSI and UTIs. These associations are in concordance with prior literature. Previously, Martin et al.¹⁴ had conducted a meta-analysis of the current literature and found that diabetes in general was a significant independent risk factor for SSIs across multiple different types of surgery, including

arthroplasty. Furthermore, patients with NIDDM, in comparison to non-diabetics, have been shown to experience worse outcomes and increased rates of complications, specifically with UTIs.¹⁶ Therefore, blood glycemic control should also be carefully monitored in the preoperative and perioperative period as the hyperglycemic state in DM is likely a contributory factor in the development of infectious complications in DM patients.¹⁷ Jansen et al. previously reported that preoperative hyperglycemia is a strong predictor of knee infection following primary TKA, and that preoperative testing for hyperglycemia can be an effective screening tool for patients at high risk for experiencing SSIs.¹⁸ Umpierrez et al. previously conducted a randomized control trial assessing the effectiveness of basal-bolus insulin regimen for inpatient management of patients with type 2 diabetes undergoing general surgery.¹⁹ The report concluded that treatment reduced postoperative complication rates of pneumonia, bacteremia, respiratory failure, and acute renal failure.¹⁹ Additionally, the CDC strongly recommends with high to moderate-quality evidence that perioperative glycemic control with blood glucose targets less than 200 mg/dL in patients decreases the risk of SSIs.²⁰ More consistent postoperative glycemic control and perioperative glucose levels of less than 200 mg/dL in NIDDM and IDDM patients undergoing rTKA may prove useful in decreasing infectious complications in rTKA. Given the higher risk of infection seen in diabetic patients, the results of this current study suggest that future randomized controlled trials assessing the efficacy of keeping perioperative blood glucose levels under 200 mg/dL in both NIDDM and IDDM patients undergoing rTKA to prevent infectious complications are warranted.

Interestingly, the present study identified an increased risk of pneumonia and septic shock in IDDM patients undergoing rTKA. It is crucial to elucidate this risk for sepsis as it indicates a complicated and arduous hospital course and must therefore be prevented with the highest precautionary measures.²¹ Furthermore, infection is the most common predisposing factor in precipitating diabetic ketoacidosis.²² Therefore, in the setting of rTKA, it is extremely important to identify IDDM as a potential risk factor for septic shock for potential candidates of rTKA. The current guidelines from the Center for Disease Control and Prevention on prevention of SSI maintains that a single preoperative dose of antibiotics is adequate for prophylaxis – however, the guidelines recommend against postoperative dosing.²⁰ In contrast, the American Association of Hip and Knee Surgeons (AAHKS) recommends that postoperative medication be continued for 24 h. To the best of the author's knowledge, there is no evidence suggesting that a 24-h postoperative course of microbial prophylaxis leads to increased complications, such as antibiotic resistance, in comparison to a single preoperative dose. Given the increased risk of pneumonia and septic shock in IDDM compared to NIDDM, a more aggressive infection prophylaxis regiment for IDDM patients may be warranted. Therefore, the authors support the AAHKS protocol for postoperative antimicrobial administration in IDDM patients for rTKA.²³ Future work analyzing the effectiveness of postoperative antibiotic prophylaxis in decreasing rates of infectious complications in NIDDM and IDDM patients undergoing rTKA is warranted.

IDDM was also shown to independently increase the risk for acute renal failure and severe cardiac arrest requiring cardiopulmonary resuscitation (CPR) in patients following rTKA. While diabetes mellitus has been well established in causing diabetic nephropathy, such kidney function deterioration is more associated with a chronic setting.^{24,25} Khan et al. found sepsis to be the single most common cause of acute renal failure in patients with diabetes mellitus.²⁵ This is in accordance with the aforementioned association of septic shock in IDDM patients following rTKA that the current retrospective study reports. Glycemic control in patients with IDDM being considered for rTKA is encouraged to reduce the risk of

postoperative renal failure. Additionally, IDDM was found to increase the risk for postoperative blood transfusions following rTKA when compared with Non-DM and NIDDM. Although diabetes mellitus has been demonstrated to increase rates of postoperative transfusions in orthopedic procedures,²⁶ to our knowledge, no prior literature has identified IDDM status as increasing the risk for bleeding requiring blood transfusion compared to NIDDM. As tranexamic acid (TXA) has been found to reduce blood loss in TJA without a corresponding increase in complication rates, TXA administration to IDDM patients may be warranted given the increased risk that IDDM poses.^{27–29} However, the administration of TXA in patients with diabetes in preventing blood loss has not been previously examined. As diabetes patients have been well reported in the literature to have increased rates of thromboembolic events compared to non-diabetic patients, the pro-coagulative effects of TXA in diabetic patients must be more thoroughly examined before TXA administration in diabetic patients undergoing rTKA to prevent blood loss resulting in transfusion becomes a standard of care. Finally, length of stay was also increased following rTKA specifically in IDDM patients. The abundance of specific complications associated with IDDM over NIDDM likely offer a plausible explanation behind the extended length of stay. Compared to primary TKA, rTKA is also independently known to be associated with increased length of stay and operative costs.³⁰ Therefore, revision and complications related to IDDM together can cause a synergistic burden.

In conclusion, careful preoperative optimization of diabetics patients undergoing rTKA may prove useful in decreasing infectious complications in rTKA. Furthermore, given the elevated risk of pneumonia and sepsis in IDDM patients undergoing rTKA, more aggressive antimicrobial prophylaxis via postoperative antibiotics administration may be warranted. Future work analyzing the efficacy of TXA in IDDM patients undergoing rTKA to decrease risk of blood transfusions is warranted.

Conflicts of interest

The authors report no conflict of interest or funding/payment of any kind for this study.

CRediT authorship contribution statement

Danny Lee: Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Project administration. **Ryan Lee:** Conceptualization, Methodology, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Project administration. **Nikhil B. Gowda:** Investigation, Writing - original draft, Writing - review & editing, Project administration. **William V. Probasco:** Investigation, Writing - original draft, Writing - review & editing, Project administration. **Seth Stake:** Investigation, Writing - original draft, Writing - review & editing, Project administration. **George Ibrahim:** Investigation, Writing - original draft, Writing - review & editing, Project administration. **Rajeev Pandarinath:** Investigation, Writing - original draft, Writing - review & editing, Project administration, Supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcot.2019.07.009>.

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