Complication Rates Associated with GLP-1 Receptor Agonist Use in Patients with Type-2 Diabetes Undergoing Total Knee Arthroplasty: A Retrospective Cohort Study

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INTRODUCTION: Diabetes is a well-established risk factor for a number of complications after total knee arthroplasty (TKA), including poor wound healing and periprosthetic joint infection (PJI). In recent years, Glucagon-like Peptide-1 (GLP-1) receptor agonists have emerged as a powerful diabetic treatment adjunct; however, its effect on outcomes following TKA is unknown. The purpose of this study was to characterize this relationship, as well as compare risk of complications in patients on GLP-1 agonists to those on other classes of diabetic medications, including metformin.

METHODS: Patients undergoing primary TKA between 2016-2021 were retrospectively reviewed utilizing the IBM MarketScan database. Only those with a preoperative diagnosis of type-2 diabetes were included. Propensity score matching was employed to match patients 1-to-1 within 4 comparison cohorts based on their diabetes medication: 1) GLP-1 agonist vs. no GLP-1 agonist, 2) GLP-1 agonist vs. metformin, 3) GLP-1 agonist and metformin (combination therapy) vs. all other diabetes treatments, and 4) GLP-1 agonist and metformin (combination therapy) vs. metformin (without GLP-1 agonist). Subjects were matched on factors including age, sex, insulin status, utilization of additional diabetic medications, comorbidities, complexity of diabetes, and smoking status. Multivariate logistic regressions were performed on matched cohorts to examine 90-day and 1-year primary TKA outcomes.

RESULTS SECTION: 34,696 patients were initially queried from the database. After matching, 7,620 patients were included in the first comparison group, 1,716 patients in the second, and 5,904 patients in both the third and fourth comparison groups. Baseline characteristics were similar amongst matched cohorts. Within the first comparison cohort (Table 1), patients not on GLP-1 receptor agonists were had no increased risks for 90-day surgical complications. However, those not on GLP-1 agonists had increased likelihood of stroke (OR 1.93, P=0.049) and readmission (OR 1.21, P=0.03) at 90-days, longer length of hospital stay (OR 1.16, P=0.006), and 1-year revision TKA at 1-year (OR 1.54, P=0.02). No differences in complications were observed between patients on GLP-1 agonists compared to those taking metformin. In the third comparison cohort (Table 2), patients not on a combination therapy of GLP-1 agonist and metformin had higher odds of 90-day readmission (OR 1.23, P=0.03), longer length of hospital stay (OR 1.23, P<0.001), and revision TKA at 1-year (OR 1.70, P=0.01) compared to patients on the combination therapy. Analysis of the fourth comparison cohort demonstrated that patients on metformin without a GLP-1 agonist were more likely to have longer length of hospital stay (OR 1.25, P<0.001) compared to those on combination GLP-1 agonist and metformin therapy.

DISCUSSION: After controlling for disease severity and medical comorbidity burden in diabetic patients undergoing primary TKA, the current study demonstrates that GLP-1 receptor agonist use appears safe and is associated with lower odds for developing post-surgical complications. This includes stroke, revision TKA procedures, extended length of hospital stays, and readmissions. Conversely, there were no differences in post-surgical complications between diabetic patients treated with GLP-1 agonists and those treated with metformin. Patients treated with both agents were observed to have lower odds of developing post-surgical complications following TKA compared to patients not on the combination therapy. Given the high prevalence of diabetic patients undergoing TKA in combination with the recent surge in GLP-1 agonist usage in this population, the results of this study show promise in improving preoperative optimization protocols for the diabetic population in an effort to minimize post-surgical complications.

SIGNIFICANCE/CLINICAL RELEVANCE: With recent emergence of GLP-1 receptor agonist usage for effective glycemic control and weight loss in patients with type-2 diabetes, there is a lack of understanding surrounding postoperative outcomes in patients utilizing these diabetes medications who undergo primary TKA. Therefore, this study characterized differences in surgical and medical complications, as well as differences in resource utilization, in patients on varying diabetic medications who underwent primary TKA. The results of the study have the potential to improve preoperative medical management protocols in order to optimize postoperative outcomes following TKA.

IMAGES AND TABLES:

Table 1

Cohort 1. Univariate and Multivariate Analysis of Complications - *GLP-1 Agonist vs. No GLP-1 Agonist

Characteristic	GLP1-Agonist n=3,810	No GLP-1 Agonist n=3,810	Univariate *P*-value	Odds Ratio** (95% CI)	Multivariate *P*-value
90-Day Surgical Complications					
Surgical Site infection (SSI)	191 (5.01%)	221 (5.80%)	0.13	1.17 (0.96 - 1.44)	0.12
Prosthetic Joint Infection (PJI)	80 (2.09%)	83 (2.18%)	0.81	1.01 (0.74 - 1.38)	0.96
Wound Dehiscence	55 (1.44%)	61 (1.60%)	0.57	1.12 (0.78 - 1.63)	0.53
Periprosthetic Fracture	4 (0.10%)	6 (0.16%)	0.53	1.29 (0.34 - 4.89)	0.7
90-Day Medical Complications					
Cardiac Arrest	5 (0.13%)	6 (0.16%)	0.76	1.21 (0.36 - 4.14)	0.76
Stroke	14 (0.37%)	30 (0.79%)	**0.02**	1.93 (0.99 - 3.73)	**0.049**
Pneumonia	65 (1.71%)	48 (1.26%)	0.11	0.75 (0.51 - 1.10)	0.14
Deep Vein Thrombosis (DVT)	54 (1.41%)	64 (1.68%)	0.35	1.15 (0.79 - 1.69)	0.46
Urinary Tract Infection (UTI)	253 (6.64%)	251 (6.59%)	0.93	0.98 (0.82 - 1.19)	0.89
Acute Kidney Injury (AKI)	146 (3.83%)	169 (4.44%)	0.19	1.15 (0.91 - 1.47)	0.24
C. difficile infection	4 (0.10%)	9 (0.24%)	0.17	2.34 (0.66 - 8.27)	0.19
Hypoglycemic events	71 (1.86%)	65 (1.71%)	0.60	0.90 (0.64 - 1.28)	0.56
Resource Utilization					
90-Day Readmission	272 (7.14%)	322 (8.45%)	**0.03**	1.21 (1.02 - 1.44)	**0.03**
Extended Length of Stay (>= 3 days)	974 (25.56%)	1,110 (29.13%)	**<0.001**	1.16 (1.04 - 1.28)	**0.006**
1 Year Outcomes					
1-Year Revision Surgery	49 (1.29%)	75 (1.97%)	**0.02**	1.54 (1.06 - 2.23)	**0.02**
1-Year Prosthetic Joint Infection	113 (2.97%)	111 (2.91%)	0.89	0.96 (0.73 - 1.25)	0.74
1-Year Periprosthetic Fracture	5 (0.13%)	8 (0.21%)	0.41	1.44 (0.45 - 4.59)	0.53

**Values are given as the odds ratio for the no GLP-1 agonist group, with the 95% CI in parentheses
*GLP-1 = Glucagon-like peptide 1 agonist;

Table 2

Cohort 3. Univariate and Multivariate Analysis of Complications - *GLP-1 Agonist & Metformin (Combination Therapy) vs. All Other Diabetes Treatments

Characteristic	Combination GLP-1 & Metformin n=2,952	All Other Diabetes Treatments n=2,952	Univariate *P*-value	Odds Ratio** (95% CI)	Multivariate *P*-value
90-Day Surgical Complications					
Surgical Site infection (SSI)	150 (5.08%)	167 (5.66%)	0.33	1.13 (0.89 - 1.42)	0.31
Prosthetic Joint Infection (PJI)	58 (1.96%)	76 (2.57%)	0.12	1.26 (0.89 - 1.80)	0.20
Wound Dehiscence	41 (1.39%)	38 (1.29%)	0.73	0.87 (0.55 - 1.36)	0.53
Periprosthetic Fracture	4 (0.14%)	3 (0.10%)	0.71	0.54 (0.10 - 2.82)	0.46
90-Day Medical Complications					
Cardiac Arrest	3 (0.10%)	4 (0.14%)	0.71	1.56 (0.38 - 7.25)	0.57
Stroke	12 (0.41%)	21 (0.71%)	0.12	1.77 (0.84 - 3.71)	0.13
Pneumonia	42 (1.42%)	49 (1.66%)	0.46	1.19 (0.77 - 1.82)	0.44
Deep Vein Thrombosis (DVT)	36 (1.22%)	50 (1.69%)	0.13	1.44 (0.92 - 2.26)	0.11
Urinary Tract Infection (UTI)	177 (5.99%)	176 (5.96%)	0.96	0.99 (0.79 - 1.23)	0.91
Acute Kidney Injury (AKI)	100 (3.39%)	129 (4.37%)	0.05	1.12 (0.85 - 1.49)	0.41
C. difficile infection	3 (0.10%)	8 (0.27%)	0.13	3.43 (0.76 - 15.43)	0.11
Hypoglycemic events	58 (1.96%)	55 (1.86%)	0.76	0.86 (0.59 - 1.26)	0.45
Resource Utilization					
90-Day Readmission	200 (6.78%)	250 (8.47%)	**0.01**	1.23 (1.01 - 1.50)	**0.03**
Extended Length of Stay (>= 3 days)	690 (23.37%)	835 (28.29%)	**<0.001**	1.23 (1.09 - 1.38	**<0.001**
1 Year Outcomes					
1-Year Revision Surgery	39 (1.32%)	66 (2.24%)	**0.01**	1.70 (1.14 - 2.56)	**0.01**
1-Year Prosthetic Joint Infection	87 (2.95%)	110 (3.73%)	0.09	1.23 (0.92 - 1.64)	0.16
1-Year Periprosthetic Fracture	4 (0.14%)	3 (0.10%)	0.71	1.85 (0.35 - 9.70)	0.46

**Values are given as the odds ratio for the "All Other Diabetes Treatments" group, with the 95% CI in parentheses
*GLP-1 = Glucagon-like peptide 1 agonist;