Arthroplasty Today 30 (2024) 101506

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Original Research

Glucagon-Like Peptide-1 Receptor Agonist Use is Not Associated With Increased Complications After Total Knee Arthroplasty in Patients With Type-2 Diabetes

Kevin Y. Heo, BS[a, *], Rahul K. Goel, MD[b], Andrew Fuqua, BS[a], Jeffrey S. Holmes, MD[a], Brian T. Muffly, MD[c], Greg A. Erens, MD[a], Jacob M. Wilson, MD[a], Ajay Premkumar, MD, MPH[a]

[a] Department of Orthopaedic Surgery, Emory University School of Medicine, Atlanta, GA, USA
[b] Department of Orthopaedic Surgery, Duke University School of Medicine, Durham, NC, USA
[c] Department of Orthopaedic Surgery, Hospital for Special Surgery, New York, NY, USA

ARTICLE INFO

Article history:
Received 23 April 2024
Received in revised form
3 July 2024
Accepted 13 August 2024
Available online 11 October 2024

Keywords:
GLP-1 receptor agonist
Glucagon-like Peptide-1 receptor agonist
Complications
Total knee arthroplasty
Diabetes

ABSTRACT

Background: Glucagon-like peptide-1 (GLP-1) agonists have emerged as a powerful diabetic treatment adjunct; however, its effects on outcomes following total knee arthroplasty (TKA) are not well known. The purpose of this study was to compare the risk of complications after TKA in patients with type-2 diabetes who were on GLP-1 agonists with those who were not.

Methods: In total, 34,696 type 2 diabetes patients undergoing primary TKA between 2016 and 2021 were retrospectively reviewed utilizing a large national database. Propensity score matching was employed to match patients on GLP-1 agonists to controls at a 1:1 ratio (n = 2388 each). Multivariable logistic regression was utilized to examine 90-day and 1-year TKA outcomes between cohorts.

Results: Controls had higher odds of extended hospital stays (≥3 days) (odds ratio 1.29, $P < .001$). However, surgical complication rates at 90-days including surgical site infection and prosthetic joint infection were not significantly different. Similarly, no differences were seen in medical complications. There were also no significant differences in rates of all-cause revision TKA and aseptic revision TKA at 1 year postoperatively.

Conclusions: This study found that GLP-1 agonist use was not associated with increased medical or surgical complication rates in patients with diabetes undergoing TKA and was associated with lower rates of extended hospital stays after surgery. Given the potential for increased glycemic control and weight loss in patients using GLP-1 agonists, more data are needed to delineate the potential role of GLP-1 agonists in preoperative optimization of patients with diabetes prior to joint arthroplasty to minimize postoperative complications.

Introduction

Knee osteoarthritis is a leading cause of disability in the elderly, resulting in significant pain and impaired function [1,2]. Total knee arthroplasty (TKA) has been a consistently effective therapeutic option for severe osteoarthritis [3-6]. Despite low revision rates, adverse postoperative events are not uncommon, with the incidence of major complications reported to be 5.5% at 30 days and 14.4% at 6 months [7,8]. A number of studies have examined risk factors for complications following TKA [9].

Metabolic disease is a common comorbidity with critical implications for TKA outcomes. Elevated body mass index (>30) has been linked to increased number of in-hospital events, deep infections, and early revisions [10,11]. Similarly, diabetes mellitus has been shown to be an independent risk factor for multiple complications, most notably prosthetic joint infection (PJI) and deep surgical site infection (SSI) [12,13]. Studies examining

* Corresponding author. Department of Orthopaedic Surgery, Emory University School of Medicine, 21 Ortho Ln, Atlanta, GA 30329, USA. Tel.: +1 978 729 3690.
E-mail address: kevin.heo@emory.edu

https://doi.org/10.1016/j.artd.2024.101506

controlled vs uncontrolled diabetes in this population have demonstrated increased risks only in uncontrolled diabetes, suggesting glycemic control is an important factor for optimizing outcomes [14,15].

From 1999 to 2018, age-controlled prevalence of diabetes rose from 9.8% to 14.3% with only 21.0% of these patients achieving optimal control of hemoglobin A1c and blood pressure [16]. In 2015, metformin, insulin, and sulfonylureas were the most commonly prescribed antiglycemic medications [17]. The advent of newer agents such as glucagon-like peptide-1 (GLP-1) agonists and sodium-glucose cotransporter-2 inhibitors, however, have revolutionized diabetic management, especially in patients undergoing orthopaedic surgery [18]. In particular, GLP-1 agonists have demonstrated high efficacy in treating diabetes and obesity, as well as providing potential benefits to hospitalized patients who have hyperglycemia [19,20]. A 2021 study found that irrespective of disease severity and glycemic control, metformin use was associated with significantly fewer adverse outcomes after TKA [21]. Currently, there is a paucity of evidence comparing the association of GLP-1 agonists with complication rates after TKA.

The aim of this study was to compare the relative rates of complications in patients on GLP-1 agonists compared to patients not on GLP-1 agonists following TKA, while accounting for disease severity and other comorbidities. We hypothesized that patients who were on GLP-1 agonists would experience fewer postoperative complications compared to those not taking these agents.

Material and methods

Data source

Patients were identified from the IBM MarketScan Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefit databases (Ann Arbor, Michigan). Institutional review board approval was not required as this study was a retrospective review of deidentified data. This database is a collection of medical insurance claims databases from over 300 employer-sponsored and Medicare supplemental plans, containing more than 240 million deidentified patient records. It provides information on inpatient admissions, outpatient visits, and pharmaceutical encounters. The authors chose to use this database because it contains data on a large quantity of continuously enrolled patients that allows for longitudinal follow-up. It has been successfully utilized in previous orthopaedic studies [21,22].

Patient identification: inclusion and exclusion criteria

Current procedural terminology code “27447” (primary TKA) was used to identify patients over 18 years of age who underwent unilateral TKA from January 1, 2016, to December 31, 2021. Only patients who had a preoperative diagnosis of type 2 diabetes were included. Nondiabetics and those with type 1 diabetes mellitus were excluded. Those with an operative diagnosis of periarticular knee or lower extremity fracture were also excluded from the study in order to remove any potential emergent TKA. Patients with a history of pancreatitis or medullary thyroid cancer were excluded as these are potential contraindications to GLP-1 agonist use [23]. The International Classification of Disease codes and the Elixhauser method were used to identify comorbidities, including diabetes [24]. To be included in the final analyses, patients were required to be continuously enrolled within the database for at least 6 months preoperatively and 3 months postoperatively.

After the initial study population was established (n = 34,696), patients were divided into 2 cohorts: GLP-1 agonist (n = 2388) vs no GLP-1 agonist (n = 26,117). Cohorts were determined utilizing prescription claims based on National Drug Codes. Patients were included in the GLP-1 agonist cohort if the database recorded at least 3 fills of their GLP-1 agonist prescription within 6 months preoperatively, or if they received at least 1 fill corresponding to a 90-day or greater supply within 6 months preoperatively. Patients in the control group were identified as those who did not receive any GLP-1 agonists within the 6-month period prior to their TKA. Patients who did not meet strict criteria for the GLP-1 agonist or control cohorts were excluded from the study.

Baseline patient information

Baseline patient demographic characteristics, diabetic prescription status, comorbidity data, and smoking status were collected. This included comorbidity status using the Elixhauser comorbidity index as previously described (grouped categorically on the basis of the number of comorbidities present), insulin status (grouped categorically as insulin-dependent or not), and usage of other diabetic medications such as sulfonylureas, thiazolidinediones, dipeptidyl peptidase 4 inhibitors, meglitinides, sodium-glucose cotransporter-2 inhibitors, and alpha-glucosidase inhibitors. In accordance with the convention established by Wilson et al [21], usage of other diabetic medications was grouped binomially based on the presence of additional diabetic medication usage or not. Likewise, diabetes was classified as complicated or uncomplicated based on the Elixhauser comorbidity index, as this was believed to approximate disease severity that may influence the results.

Postoperative complications and healthcare utilization data

Postoperative resource utilization, SSIs, and medical complications were collected for the 90-day postoperative period. These included the following utilization and complication parameters: SSI, PJI, wound dehiscence, periprosthetic fracture, cardiac arrest, stroke, pneumonia, deep vein thrombosis, urinary tract infection, acute kidney injury (AKI), *Clostridium difficile* infection, hypoglycemic events, 90-day all-cause hospital readmission, and extended hospital length of stay (LOS) (defined as 3 days). Additionally, 1-year postoperative outcomes were collected, including revision TKA (defined by current procedural terminology codes shown in Appendix A), aseptic revision TKA, PJI, and periprosthetic fracture.

Data analyses and baseline patient characteristics

The propensity score matching at a 1-to-1 ratio was utilized to control for baseline variables between cohorts with 0.2 standard deviation caliper size to ensure the closest possible match [25]. Propensity score models included potential confounders of age, sex, insulin-dependent diabetes status, Elixhauser comorbidity index (1, 2, and 3+ comorbidities), presence of congestive heart failure, smoking status, utilization of additional diabetic medications, and diabetic complexity.

Chi-squared tests were used to determine differences in categorical comorbidity variables, and Student *t*-tests were used to analyze differences in continuous comorbidity variables, as indicated. Before matching, patients on GLP-1 agonists were younger (61.2 vs 64.6 years of age, $P < .001$) and had a higher percentage of having at least 3 comorbidities compared to patients who were not on GLP-1 agonists (76.5 vs 70.2%, $P < .001$) (Table 1). Furthermore, those who were taking GLP-1 agonists were more likely to be insulin-dependent (22.0 vs 6.5%, $P < .001$), more likely to be on additional diabetic medications (76.8 vs 72.0%, $P < .001$), and more likely to have a diagnosis of complicated diabetes (50.2 vs

Table 1
Glucagon-like peptide-1 (GLP-1) receptor agonist use by patient demographic characteristics and comorbidities: unmatched and matched cohorts.

Characteristic	Unmatched cohort			Matched cohort		
	GLP-1 agonist	No GLP-1 agonist	*P*-value	GLP-1 agonist	No GLP-1 agonist	*P*-value
Total (%)	2388 (8.4%)	26,117 (91.6%)		2388 (50.0%)	2388 (50.0%)	
Age (range)	61.2 (40-88)	64.6 (24-95)	**<.001**	61.2 (40-88)	61.0 (32-88)	.49
Sex						
Men	1013 (42.4%)	11,508 (44.1%)	.12	1013 (42.4%)	1040 (43.6%)	.43
Women	1375 (57.6%)	14,609 (55.9%)		1375 (57.6%)	1348 (56.4%)	
Elixhauser			**<.001**			.94
1	136 (5.7%)	2804 (10.7%)		136 (5.7%)	129 (5.4%)	
2	424 (17.8%)	4980 (19.1%)		424 (17.8%)	425 (17.8%)	
>3	1828 (76.5%)	18,333 (70.2%)		1828 (76.5%)	1834 (76.8%)	
Insulin-dependent diabetes mellitus			**<.001**			.23
No	1863 (78.0%)	24,407 (93.4%)		1863 (78.0%)	1897 (79.4%)	
Yes	525 (22.0%)	1710 (6.5%)		525 (22.0%)	491 (20.6%)	
Other diabetes mellitus medication			**<.001**			.13
No	554 (23.2%)	7311 (28.0%)		554 (23.2%)	510 (21.4%)	
Yes	1834 (76.8%)	18,806 (72.0%)		1834 (76.8%)	1878 (78.6%)	
Congestive heart failure			.89			.69
No	2156 (90.3%)	23,603 (90.4%)		2156 (90.3%)	2164 (90.6%)	
Yes	232 (9.7%)	2514 (9.6%)		232 (9.7%)	224 (9.4%)	
Complicated diabetes			**<.001**			.49
No	1189 (49.8%)	17,305 (66.3%)		1189 (49.8%)	1165 (49.8%)	
Yes	1199 (50.2%)	8812 (33.7%)		1199 (50.2%)	1223 (50.2%)	
Smoking status			.18			.69
No	2084 (87.3%)	22,538 (86.3%)		2084 (87.3%)	2093 (87.6%)	
Yes	304 (12.7%)	3579 (13.7%)		304 (12.7%)	295 (12.4%)	

Values are given as number of patients, with the percentage in parentheses, except for age, which is given as the mean and the range.
Bold values indicate statistical significance ($P < .05$).
GLP-1, glucagon-like peptide 1 agonist.

33.7%, $P < .001$) compared to patients who were not on GLP-1 agonists.

Following propensity-score matching, 2388 patients were matched to each cohort. All standardized mean differences for the covariates were below 0.1, indicating negligible cohort differences. Covariate balance was visualized by plotting the propensity score distributions in both the unmatched and matched data sets [21] (Fig. 1). Propensity score distributions between GLP-1 agonist users and controls more closely resembled each other in the matched data set. Furthermore, prior preoperative baseline differences between cohorts in the unmatched data set were successfully balanced within the matched data set of patients who were on GLP-1 agonists and controls (Table 1).

After propensity-score matching, multivariable logistic regressions were utilized to control for any remaining cohort differences to examine the association of GLP-1 agonist use on 90-day and 1-year postoperative outcomes. All statistical analyses were conducted using R Studio (PBC, Boston, MA).

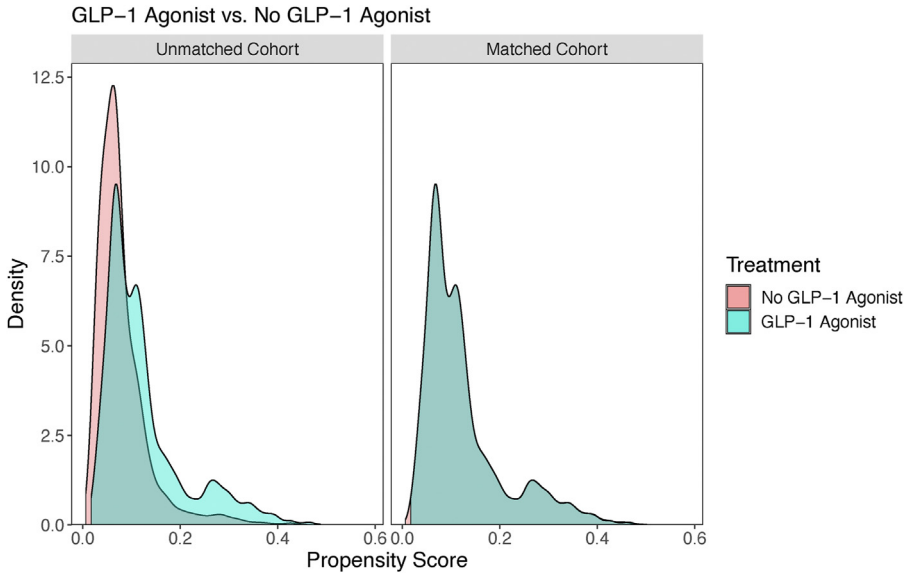

Figure 1. Propensity-score distribution in unmatched and matched datasets: cohort 1 – glucagon-like peptide (GLP)-1 agonist vs no GLP-1 agonist.

Table 2
Multivariable analyses of complications − glucagon-like peptide-1 (GLP-1) agonist vs no GLP-1 agonist.

Characteristic	GLP1-agonist, n = 2388	No GLP-1 agonist, n = 2388	Odds ratio[a] (95% CI)	Multivariate *P* value
90-d surgical complications				
Surgical site infection	112 (4.7%)	108 (4.5%)	0.95 (0.73 - 1.26)	.74
Prosthetic joint infection	53 (2.2%)	55 (2.3%)	0.99 (0.69 - 1.46)	.96
Wound dehiscence	34 (1.4%)	38 (1.6%)	1.14 (0.71 - 1.82)	.53
Periprosthetic fracture	3 (0.1%)	1 (0.1%)	0.38 (0.03 - 4.29)	.43
90-d medical complications				
Cardiac arrest	3 (0.1%)	4 (0.2%)	1.19 (0.25 − 5.71)	.83
Stroke	10 (0.4%)	18 (0.8%)	1.53 (0.67 - 3.48)	.32
Pneumonia	37 (1.5%)	38 (1.6%)	0.99 (0.62 - 1.59)	.98
Deep vein thrombosis	39 (1.6%)	45 (1.9%)	1.16 (0.74 - 1.82)	.53
Urinary tract infection	150 (6.3%)	151 (6.3%)	1.01 (0.80 - 1.28)	.91
Acute kidney injury	84 (3.5%)	90 (3.8%)	1.06 (0.77 - 1.46)	.71
C. difficile infection	2 (0.1%)	9 (0.4%)	4.02 (0.73 - 22.05)	.11
Hypoglycemic events	45 (1.9%)	35 (1.5%)	0.73 (0.46 - 1.15)	.18
Resource utilization				
90-d readmission	168 (7.0%)	187 (7.8%)	1.14 (0.91 - 1.42)	.25
Extended length of stay (≥ 3 d)	607 (25.4%)	746 (31.2%)	1.29 (1.14 - 1.47)	**<.001**
1-y outcomes				
All-cause revision TKA	37 (1.5%)	42 (1.8%)	1.15 (0.73 - 1.81)	.54
Aseptic revision TKA	24 (1.0%)	27 (1.1%)	1.16 (0.66 - 2.02)	.61
Prosthetic joint infection	81 (3.4%)	76 (3.2%)	0.91 (0.66 - 1.25)	.55
Periprosthetic fracture	4 (0.2%)	2 (0.1%)	0.70 (0.12 - 4.03)	.69

Bold values indicate statistical signifcance ($P < .05$).
GLP-1, glucagon-like peptide 1 agonist; TKA, total knee arthroplasty.
[a] Values are given as the odds ratio for the no GLP-1 agonist group, with the 95% CI in parentheses.

Results

Multivariable logistic regression analyses revealed that patients who were not on GLP-1 agonists had significantly higher rates of extended hospital LOS after TKA compared to those on GLP-1 agonists (31.2 vs 25.4%; odds ratio [OR] 1.29, $P < .001$; Table 2). There were no significant differences between cohorts for surgical complications at 90 days, including SSI (4.5 vs 4.7%; OR 0.95, $P = .74$) and PJI (2.3 vs 2.2%; OR 0.99, $P = .96$). There were also no significant differences in medical complications at 90 days, including deep vein thrombosis (1.9 vs 1.6%; OR 1.16, $P = .53$), acute kidney injury (3.8 vs 3.5%; OR 1.06, $P = .71$), or hypoglycemic events (1.5 vs 1.9%; OR 0.73, $P = .18$). Furthermore, there were no significant differences in 90-day readmission rates between the control and GLP-1 cohorts (7.8 vs 7.0%; OR 1.14, $P = .25$). At the 1-year postoperative period, there were no significant differences in rates of all-cause revision TKA (1.8 vs 1.5; OR 1.15, $P = .54$) or aseptic revision TKA (1.1 vs 1.0%; OR 1.16, $P = .61$). There were also no significant differences in rates of 1-year PJI (3.2 vs 3.4%; OR 0.91, $P = .55$) or 1-year periprosthetic fracture (0.1 vs 0.2%; OR 0.70, $P = .69$).

Discussion

These results of this investigation revealed that after controlling for patient comorbidities, disease severity, and use of other antiglycemic medications, GLP-1 agonist use was not associated with increased risk of 90-day surgical or medical complications in patients undergoing TKA. Additionally, we observed a potential signal for reduced hospital length of stay in patients on these agents. Additionally, no differences were seen in rates of all-cause revision TKA, aseptic revision TKA, or PJI after 1 year postoperatively.

On a physiological level, GLP-1 is a hormone released by the intestines in response to food ingestion, which stimulates pancreatic insulin secretion while inhibiting glucagon release [26]. The purpose of GLP-1 receptor agonists is to mimic this hormone, helping restore insulin homeostasis in patients who have type-2 diabetes [27]. These medications have been shown to induce considerable weight loss in both diabetics and nondiabetics [27]. In addition to their effects on blood glucose and weight, GLP-1 agonists have been shown to reduce cardiovascular events, all-cause mortality, and worsening renal function [28]. An increasing body of evidence supports its potential utility for preoperative medical optimization, with purported benefits of decreased incidence of hyperglycemia and reduced insulin use without increased risk of hypoglycemic events [29].

On a cellular level, emerging data suggest GLP-1 agonists exert anti-inflammatory effects by dampening production of proinflammatory cytokines and impairing immune cell tissue infiltration [30,31]. Such anti-inflammatory effects, as well as concomitant improved glycemic control, may help explain our study's results indicating decreased hospital LOS. These anti-inflammatory effects may also play a role in postoperative pain, as spinal GLP-1 agonists have been shown to suppress pain hypersensitivity by 60%-90% [32]. More data are needed to fully capture the relationship between anti-inflammatory effects of GLP-1 agonists and outcomes after TKA.

Several studies have focused on diabetes and poor glycemic control as risk factors for PJI and poorer joint function following arthroplasty [33,34]. Patients taking GLP-1 agonist monotherapy or combination therapy may have relatively tighter glycemic control and improved cardiovascular health. This may subsequently allow for earlier mobilization after surgery, translating into shorter length of stays, and reduced risk of hospital-acquired infections [35]. While diabetic complexity was controlled for within our analyses, future evaluation that accounts for preoperative A1C and perioperative glucose may help to fully understand whether addition of GLP-1 agonists results in superior outcomes and decreased infection rates. Nevertheless, the reduction in extended hospital stays observed in our study may signal and add benefit with regard to patient morbidity and quality of life. Reducing length of stay may also have significant economic implications to the healthcare system as well, as hospital costs for TKA increased by 52.4% from 2002 to 2013 [36].

Although GLP-1 agonists have several potential benefits, they are not without potential adverse effects − most commonly gastrointestinal symptoms such as nausea and vomiting [37]. In the perioperative state, delayed gastric emptying can occur, resulting in increased gastric residual contents [38,39]. Due to this concern and

subsequent potential risk for aspiration, the American Society of Anesthesiologists does recommend holding these agents a week preoperatively [40]. Despite ample evidence regarding the benefits of GLP-1 agonists in general, little is known regarding their influence on outcomes of surgical interventions in diabetic patients undergoing joint arthroplasty, especially compared to other standard diabetic medications.

A recent study by Magruder et al [41] comparing the usage of semaglutide in patients with type-2 diabetes undergoing TKA found that use of this agent was associated with decreased risk of 90-day sepsis and readmission rates, as well as 2-year PJI, but an increased risk of myocardial infarction, acute kidney injury, pneumonia, and hypoglycemic events. In contrast, our study did not show increased risks of medical complications for patients on GLP-1 agonists in the perioperative period and only demonstrated decreased rates of extended hospital LOS between cohorts. Inherent differences in the databases may have contributed to these discordant findings. Our study also included all GLP-1 agonists, rather than only semaglutide, as done by Magruder et al [41]. Furthermore, while the aforementioned study by Magruder et al [41] utilized propensity-score matching to control for covariates, they noted the possibility of incomplete control of confounders, including diabetic severity. It is also unclear if other comorbidities that were not included in the propensity-score match were controlled for within their logistic regression analyses. Increased MI would be unexpected with GLP-1 agonist use as several randomized controlled trials have shown semaglutide to have protective cardiovascular effects in patients with type-2 diabetes [42,43]. After ensuring thorough control of confounders through propensity-score matching and logistic regression, we found no associated increased risks with GLP-1, suggesting confounding may have influenced the prior results.

This study is also not without potential limitations. As with any database study, data are reliant on the accuracy and sensitivity of diagnostic coding. Moreover, specific measures of both short-term and long-term glycemic control such as hemoglobin A1c and perioperative hyperglycemia were not accessible, which might introduce bias into the results. No significant differences in the outcome measures of PJI, SSI, or wound complications between cohorts were observed, suggesting the majority of patients were matched to similar levels of glycemic control. The database also does not have access to anesthesia, nursing, or operative documentation; therefore, episodes of pulmonary aspiration or regurgitation, as well as information regarding type of anesthesia utilized for surgery were not obtainable for the study. Another potential limitation of the study is the dependence on prescription claim accuracy within the database. Our study incorporated several measures to identify the patients who were on chronic GLP-1 agonist use prior to their TKA, including requirement of least 3 refills of their GLP-1 prescription within 6 months preoperatively or at least 1 fill of at least 90-day supplies within 6 months before surgery. However, patients on GLP-1 agonists not recorded in the database could have been included in the control cohort. Similarly, due to the usage of an insurance claims database, the exact timing of when patients discontinued their GLP-1 agonist prior to their TKA is uncertain. The American Society of Anesthesiologists recommends holding these agents 1 week preoperatively, and since patients who underwent a TKA in a potential emergent setting were excluded from the study, it is likely that most of the patients in this study had their medications stopped 1 week prior to surgery. Nevertheless, further prospective study is needed to investigate the timing of preoperative GLP-1 cessation and outcomes after TKA. Additionally, the database does not include patients' body mass index. While diagnostic codes for obesity were captured utilizing the Elixhauser comorbidity index and were controlled for, this is still an inherent limitation. Further research is needed to examine the potential use of GLP-1 agents in improving outcomes as compared to other diabetic medications with equivalent glycemic control and understand the short-term risks associated with perioperative use. Additionally, the effects of GLP-1 agonists on complications rates following TKA in obese, nondiabetic patients have not been well-studied. With the rising use of GLP-1 agonists for weight loss, it is important to understand the risks and benefit profiles within this high-risk population. [42]

Conclusions

In conclusion, unlike previous evidence, we did not find GLP-1 agonists linked to increased rates of postoperative complications in patients with type 2 diabetes undergoing primary TKA, including revision procedures at 1 year. In contrast, GLP-1 agonists were associated with lower rates of extended hospital LOS. Our findings reinforce the potential low risk profile from a medical and surgical standpoint of GLP-1 agonist use in diabetic patients undergoing TKA. Additional prospective studies are needed to confirm the findings of this study, as well as delineate proper perioperative protocols given the side-effect profile of GLP-1 agonists.

Conflicts of interest

The authors declare there are no conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2024.101506.

CRediT authorship contribution statement

Kevin Y. Heo: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Rahul K. Goel:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Andrew Fuqua:** Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **Jeffrey S. Holmes:** Writing – review & editing, Writing – original draft, Methodology. **Brian T. Muffly:** Writing – review & editing, Writing – original draft, Methodology. **Greg A. Erens:** Writing – review & editing, Validation, Supervision, Resources, Investigation. **Jacob M. Wilson:** Conceptualization, Supervision, Validation, Writing – review & editing. **Ajay Premkumar:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Conceptualization.

References

[1] Neogi T. The epidemiology and impact of pain in osteoarthritis. Osteoarthritis Cartilage 2013;21:1145–53.
[2] Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89:780–5.
[3] Viganò R, Marega L, Breemans E, Miró RL. A systematic literature review of the Profix in primary total knee arthroplasty. Acta Orthop Belg 2012;78:55–60.
[4] Sayah SM, Karunaratne S, Beckenkamp PR, Horsley M, Hancock MJ, Hunter DJ, et al. Clinical course of pain and function following total knee arthroplasty: a systematic review and meta-regression. J Arthroplasty 2021;36:3993–4002.e37.
[5] Yong TM, Young EC, Molloy IB, Fisher BM, Keeney BJ, Moschetti WE. Long-term implant survivorship and modes of failure in simultaneous concurrent bilateral total knee arthroplasty. J Arthroplasty 2020;35:139–44.
[6] Mont MA, Pivec R, Issa K, Kapadia BH, Maheshwari A, Harwin SF. Long-term implant survivorship of cementless total knee arthroplasty: a systematic review of the literature and meta-analysis. J Knee Surg 2014;27:369–76.
[7] Belmont Jr PJ, Goodman GP, Waterman BR, Bader JO, Schoenfeld AJ. Thirty-day postoperative complications and mortality following total knee arthroplasty: incidence and risk factors among a national sample of 15,321 patients. J Bone Joint Surg Am 2014;96:20–6.

[8] Heo SM, Harris I, Naylor J, Lewin AM. Complications to 6 months following total hip or knee arthroplasty: observations from an Australian clinical outcomes registry. BMC Musculoskelet Disord 2020;21:602.
[9] Castano-Betancourt MC, Fruschein Annichino R, de Azevedo E Souza Munhoz M, Gomes Machado E, Lipay MV, Marchi E. Identification of high-risk groups for complication after arthroplasty: predictive value of patient's related risk factors. J Orthop Surg Res 2018;13:328.
[10] Abdulla I, Mahdavi S, Khong H, Gill R, Powell J, Johnston KD, Sharma R. Does body mass index affect the rate of adverse outcomes in total hip and knee arthroplasty? A retrospective review of a total joint replacement database. Can J Surg 2020;63:E142–9.
[11] Feng B, Lin J, Jin J, Qian WW, Wang W, Weng XS. Thirty-day postoperative complications following primary total knee arthroplasty: a retrospective study of incidence and risk factors at a single center in China. Chin Med J 2017;130:2551–6.
[12] Ahmad MA, Ab Rahman S, Islam MA. Prevalence and risk of infection in patients with diabetes following primary total knee arthroplasty: a global systematic review and meta-analysis of 120,754 knees. J Clin Med 2022;11:3752.
[13] Everhart JS, Altneu E, Calhoun JH. Medical comorbidities are independent preoperative risk factors for surgical infection after total joint arthroplasty. Clin Orthop Relat Res 2013;471:3112–9.
[14] Ojemolon PE, Shaka H, Edigin E, Gomez TMA, Eseaton P, Bello J, et al. Impact of diabetes mellitus on outcomes of patients with knee osteoarthritis who underwent knee arthroplasty: an analysis of the nationwide inpatient sample. Cureus 2020;12:e8902.
[15] Na A, Middleton A, Haas A, Graham JE, Ottenbacher KJ. Impact of diabetes on 90-day episodes of care after elective total joint arthroplasty among Medicare beneficiaries. J Bone Joint Surg Am 2020;102:2157–65.
[16] Wang L, Li X, Wang Z, Bancks MP, Carnethon MR, Greenland P, et al. Trends in prevalence of diabetes and control of risk factors in diabetes among US adults, 1999-2018. JAMA 2021;326:1–13.
[17] Raval AD, Vyas A. National trends in diabetes medication use in the United States: 2008 to 2015. J Pharm Pract 2020;33:433–42.
[18] Diaz R, DeJesus J. Managing patients undergoing orthopedic surgery to improve glycemic outcomes. Curr Diab Rep 2022;21:68.
[19] Mendez CE, Umpierrez GE. Pharmacotherapy for hyperglycemia in noncritically ill hospitalized patients. Diabetes Spectr 2014;27:180–8.
[20] Yeh TL, Tsai MC, Tsai WH, Tu YK, Chien KL. Effect of glucagon-like peptide-1 receptor agonists on glycemic control, and weight reduction in adults: a multivariate meta-analysis. PLoS One 2023;18:e0278685.
[21] Wilson JM, Farley KX, Broida SE, Bradbury TL, Guild GN. Metformin use is associated with fewer complications in patients with type-2 diabetes undergoing total knee arthroplasty: a propensity score-matched analysis. J Bone Joint Surg Am 2021;103:601–8.
[22] Karlson NW, Nezwek TA, Menendez ME, Tybor D, Salzler MJ. Increased utilization of American administrative databases and large-scale clinical registries in orthopaedic research, 1996 to 2016. J Am Acad Orthop Surg Glob Res Rev 2018;2:e076.
[23] Brown E, Heerspink HJL, Cuthbertson DJ, Wilding JPH. SGLT2 inhibitors and GLP-1 receptor agonists: established and emerging indications. Lancet 2021;398:262–76.
[24] Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8–27.
[25] Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011;10:150–61.
[26] Müller TD, Finan B, Bloom SR, D'Alessio D, Drucker DJ, Flatt PR, et al. Glucagon-like peptide 1 (GLP-1). Mol Metab 2019;30:72–130.
[27] Vilsbøll T, Christensen M, Junker AE, Knop FK, Gluud LL. Effects of glucagon-like peptide-1 receptor agonists on weight loss: systematic review and meta-analyses of randomised controlled trials. BMJ 2012;344:d7771.
[28] Sattar N, Lee MMY, Kristensen SL, Branch KRH, Del Prato S, Khurmi NS, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. Lancet Diabetes Endocrinol 2021;9:653–62.
[29] Hulst AH, Plummer MP, Hollmann MW, DeVries JH, Preckel B, Deane AM, et al. Systematic review of incretin therapy during peri-operative and intensive care. Crit Care 2018;22:299.
[30] Lee YS, Jun HS. Anti-inflammatory effects of GLP-1-based therapies beyond glucose control. Mediators Inflamm 2016;2016:3094642.
[31] Helmstädter J, Keppeler K, Aust F, Küster L, Frenis K, Filippou K, et al. GLP-1 analog liraglutide improves vascular function in polymicrobial sepsis by reduction of oxidative stress and inflammation. Antioxidants 2021;10.
[32] Gong N, Xiao Q, Zhu B, Zhang CY, Wang YC, Fan H, et al. Activation of spinal glucagon-like peptide-1 receptors specifically suppresses pain hypersensitivity. J Neurosci 2014;34:5322–34.
[33] Yang Z, Liu H, Xie X, Tan Z, Qin T, Kang P. The influence of diabetes mellitus on the post-operative outcome of elective primary total knee replacement. Bone Joint J 2014;96-B:1637–43.
[34] Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, INFORM Team. Patient-Related risk factors for periprosthetic joint infection after total joint arthroplasty: a systematic review and meta-analysis. PLoS One 2016;11:e0150866.
[35] Jeon CY, Neidell M, Jia H, Sinisi M, Larson E. On the role of length of stay in healthcare-associated bloodstream infection. Infect Control Hosp Epidemiol 2012;33:1213–8.
[36] Molloy IB, Martin BI, Moschetti WE, Jevsevar DS. Effects of the length of stay on the cost of total knee and total hip arthroplasty from 2002 to 2013. J Bone Joint Surg Am 2017;99:402–7.
[37] Filippatos TD, Panagiotopoulou TV, Elisaf MS. Adverse effects of GLP-1 receptor agonists. Rev Diabet Stud 2014;11:202–30.
[38] Silveira SQ, da Silva LM, de Campos Vieira Abib A, de Moura DTH, de Moura EGH, Santos LB, et al. Relationship between perioperative semaglutide use and residual gastric content: a retrospective analysis of patients undergoing elective upper endoscopy. J Clin Anesth 2023;87:111091.
[39] Kobori T, Onishi Y, Yoshida Y, Tahara T, Kikuchi T, Kubota T, et al. Association of glucagon-like peptide-1 receptor agonist treatment with gastric residue in an esophagogastroduodenoscopy. J Diabetes Investig 2023;14:767–73.
[40] Joshi GP, Abdelmalak BB, Weigel WA, Soriano SG, Harbell MW, Kuo CI, et al. American society of anesthesiologists consensus-based guidance on preoperative management of patients (adults and children) on glucagon-like peptide- 1 (GLP-1) receptor agonists. Press Release. Schaumburg, IL: American Society of Anesthesiologists; 2023.
[41] Magruder ML, Yao VJH, Rodriguez AN, Ng MK, Sasson V, Erez O. Does semaglutide use decrease complications and costs following total knee arthroplasty? J Arthroplasty 2023;38:2311–2315.e1.
[42] Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, et al. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med 2019;381:841–51.
[43] Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med 2016;375:1834–44.

Appendix A

Current procedural terminology (CPT) codes for revision total knee arthroplasty.

Procedure	CPT
Revision of total knee arthroplasty, with or without allograft; 1 component	27486
Revision of total knee arthroplasty, with or without allograft; femoral and entire tibial component	27487
Removal of prosthesis, including total knee prosthesis, methylmethacrylate with or without insertion of spacer, knee	27488