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Research Article

Preoperative GLP-1 Receptor Agonist Use Improves Thromboembolic, Infectious, and Wound-Related Outcomes Following Unicompartmental Knee Arthroplasty

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Background

Glucagon-like peptide-1 (GLP-1) receptor agonists have demonstrated benefits in diabetes and obesity management, but their impact on outcomes following unicompartmental knee arthroplasty (UKA) remains unexplored. This study evaluates the influence of preoperative GLP-1 agonist use on postoperative complications following UKA.

Methods

A national claims database was queried to identify patients undergoing primary UKA between 2010 and 2021. Patients with preoperative GLP-1 prescriptions were 1:1

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Conflicts of Interest Statement for Dr. Zachary Fuller

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propensity-matched to non-users based on age, sex, Charlson Comorbidity Index, diabetes, obesity, and tobacco use, yielding two balanced cohorts of 1,138 patients each (mean age 61.1 years, 53% female). Successful matching was confirmed with standardized mean differences <0.001 for all variables. Primary outcomes included 90-day and 2-year complications. Categorical variables were compared using chi-square tests with relative risk reduction (RRR) and 95% confidence intervals.

Results

At 90 days, GLP-1 users demonstrated significantly lower rates of deep vein thrombosis (0.4% vs. 1.4%; RRR = 75%; 95% CI: 15-93%; P = 0.013), wound complications (0.0% vs. 1.2%; RRR = 100%; P < 0.001), and surgical site infections (0.1% vs. 1.2%; RRR = 93%; 95% CI: 34-99%; P = 0.002) compared to non-users. No significant differences were observed in pulmonary embolism, acute kidney injury, urinary tract infection, hematoma, transfusion requirements, or readmissions. At 2 years, GLP-1 users had significantly lower rates of prosthetic joint infection (0.4% vs. 1.4%; RRR = 75%; 95% CI: 15-93%; P = 0.013). All-cause revision rates showed a favorable trend in GLP-1 users but did not reach statistical significance (2.3% vs. 3.6%; RRR = 37%; P = 0.083).

Conclusion

Preoperative GLP-1 receptor agonist use was associated with lower rates of thromboembolic, infectious, and wound-related complications following UKA without an observed increase in other adverse events. These findings may reflect both medication-related effects and broader improvements in metabolic optimization. Prospective studies with detailed metabolic data are needed to further evaluate these associations.

INTRODUCTION

Unicompartmental knee arthroplasty (UKA) represents a joint-preserving alternative to total knee arthroplasty (TKA) for patients with isolated unicompartmental osteoarthritis (Walgrave and Parker 2024; Wang et al. 2025; R et al. 2023). Compared to TKA in patients with unicompartmental disease, UKA has demonstrated advantages including faster recovery, reduced blood loss, and greater preservation of native knee kinematics (Pongcharoen et al. 2023; Brilliant et al. 2023; Hao et al. 2024). However, UKA outcomes remain susceptible to complications, including thromboembolic events, impaired wound healing, and implant failure, particularly in patients with significant comorbidity burden (Albishi et al. 2024; Schneider et al. 2020). As the arthroplasty population becomes increasingly complex with rising rates of obesity and type 2 diabetes mellitus (T2DM), optimizing preoperative metabolic health has emerged as a critical priority for reducing postoperative adverse events (Cao et al. 2025).

Glucagon-like peptide-1 (GLP-1) receptor agonists have gained widespread adoption in managing obesity and T2DM due to their ability to promote sustained weight loss, improve glycemic control, and reduce systemic inflammation (Kaye et al. 2024; Baggio and Drucker 2021; Pang et al. 2022). These agents have demonstrated significant reductions in cardiovascular morbidity and improvements in metabolic indices, making them increasingly popular in surgical populations (Monami et al. 2009; Zheng et al. 2018; ElSayed et al. 2023; Westermeier and Fisman 2025). Emerging evidence suggests that GLP-1 receptor agonists may exert beneficial effects on periarticular tissue physiology through mechanisms including enhanced angiogenesis, improved tissue regeneration, and modulation of inflammatory signaling pathways (Alharbi 2024; Halabitska et al. 2024). Considering their recent widespread adoption as a weight loss agent, the implications of their use in the perioperative period require even further attention (Buddhiraju et al. 2024b; Katzman et al. 2025).

In the arthroplasty literature, recent studies have suggested that GLP-1 use may be associated with lower rates of infection, thromboembolic events, and hospital readmission following TKA, particularly in high-risk patients with morbid obesity (Katzman et al. 2025; Kim et al. 2025; Xie et al. 2025). However, the impact of GLP-1 agonists on outcomes following UKA remains unexplored. To our knowledge, no study has comprehensively evaluated whether preoperative GLP-1 use confers protective effects in this population or introduces new risks. Furthermore, prior studies have often lacked adequate adjustment for confounding variables that influence both medication use and surgical outcomes.

The present study addresses this knowledge gap by utilizing a large national claims database to compare postoperative outcomes between UKA patients prescribed GLP-1 agonists and propensity-matched controls. We hypothesized that GLP-1 agonist therapy would be associated with lower rates of medical and surgical complications, particularly prosthetic joint infection (PJI) and all-cause revisions at 2 years, supporting its safety and potential benefit in patients undergoing UKA.

METHODS

STUDY DESIGN AND DATA SOURCE

This retrospective cohort study utilized the PearlDiver Mariner170 dataset (PearlDiver Technologies, Colorado Springs, CO, USA), which contains over 170 million U.S. patients who received health coverage under commercial insurance, Medicare, Medicaid, government insurance, and self-pay between 2010 and 2023. Patient records were retrieved using procedural and diagnostic codes from the International Classification of Diseases Ninth (ICD-9) and Tenth (ICD-10) Revision, and Current Procedural Terminology (CPT). The dataset has been deidentified for public access, and institutional review board approval was waived.

STUDY POPULATION

Adult patients aged 18 years and older who underwent primary UKA (CPT-27446) between January 2010 and December 2021 with minimum 2-year follow-up eligibility were included. Patients with a history of infection, trauma, tumor, or metastases were excluded using appropriate ICD-9 and ICD-10 diagnostic codes. Eligible patients were subsequently stratified by preoperative GLP-1 agonist use (exenatide, liraglutide, dulaglutide, semaglutide, tirzepatide) within 1 year prior to surgery and propensity-matched 1:1 by age, sex, Charlson Comorbidity Index (CCI), diabetes, obesity, and tobacco use history. Propensity matching was performed to achieve statistical balance in confounding variables across the two cohorts. Covariates were selected based on their documented impact on outcomes of interest, with CCI included to ensure equivalent comorbidity burden between groups. Following 1:1 propensity matching, two cohorts of 1,138 patients each were identified. The mean age was 61.1 years (SD 8.54), with 53% female patients and 94% with diabetes, which reflects the predominant indication for GLP-1 therapy during the study period. No significant differences existed between GLP-1 users and non-users in demographics or baseline comorbidities (all $p = 1.000$), with standardized mean differences <0.001 for all matched variables, confirming matching balance.

OUTCOME MEASURES

Primary outcomes included 90-day complications and 2-year implant-related complications. 90-day complications encompassed acute kidney injury (AKI), deep venous thrombosis (DVT), pulmonary embolism (PE), wound complications, surgical site infection (SSI), hematoma, transfusion requirements, urinary tract infection (UTI), and 90-day readmissions. Implant-related complications included aseptic loosening, instability/dislocation, mechanical failure, periprosthetic fracture, osteolysis, PJI, and all-cause revisions. Additionally, 90-day episode-of-care costs were analyzed.

STATISTICAL ANALYSIS

Postoperative complications were compared using chi-square tests or Fisher's exact tests when appropriate. Relative risk reduction (RRR) with 95% confidence intervals were calculated for statistically significant findings. All analyses were conducted using the built-in R statistical software within PearlDiver and SPSS Statistics for Windows, Version 29.0 (IBM Corp, Armonk, NY). A p-value <0.05 was considered statistically significant.

RESULTS

90-DAY OUTCOMES

At 90 days, GLP-1 users demonstrated significantly lower rates of DVT (GLP-1 User = 0.4% vs. GLP-1 Non-User = 1.4%, RRR = 0.75, $p = 0.013$), wound complications (0.0% vs. 1.2%, RRR = 1.00, $p < 0.001$), and SSI (0.1% vs. 1.2%, RRR = 0.93, $p = 0.002$). However, rates of PE (0.2% vs. 0.4%, RRR = 0.49, $p = 0.683$), AKI (1.0% vs. 1.1%, RRR = 0.15, $p = 0.837$), UTI (2.4% vs. 3.3%, RRR = 0.29, $p = 0.208$), hematoma (0.1% vs. 0.5%, RRR = 0.83, $p = 0.130$), and transfusion (0.0% vs. 0.4%, RRR = 1.00, $p = 0.133$) were comparable between groups. The 90-day readmission rates were also comparable (0.4% vs. 0.4%, RRR = 0.00, $p = 1.000$).

Mean 90-day episode-of-care costs were marginally higher in the GLP-1 group ($11,418 vs. $10,472), though this difference was not statistically significant ($p = 0.116$). The 90-day complications are summarized in Table 2.

2-YEAR OUTCOMES

At 2 years, GLP-1 users had significantly lower rates of PJI (0.4% vs. 1.4%, RRR = 0.75, $p = 0.013$), while other implant-related complications, including aseptic loosening (0.5% vs. 1.1%, RRR = 0.54, $p = 0.167$), mechanical failure (0.1% vs. 0.6%, RRR = 0.85, $p = 0.077$), and all-cause revision surgery (2.3% vs. 3.6%, RRR = 0.37, $p = 0.083$), were lower but did not reach statistical significance. Rates of instability/dislocation (0.3% vs. 0.3%, RRR = 0.00, $p = 1.000$) and periprosthetic fracture (0.2% vs. 0.1%, RRR = -1.00, $p = 1.000$) were equivalent between groups. No cases of osteolysis were observed in either cohort. The 2-year complications and all-cause revisions are summarized in Table 3.

DISCUSSION

This national matched cohort analysis represents the first comprehensive evaluation of GLP-1 receptor agonist use in patients undergoing UKA. Our findings suggest that preoperative GLP-1 agonist therapy is associated with lower rates of thromboembolic, infectious, and wound-related complications. Most notably, GLP-1 users exhibited lower rates of DVT, SSI, wound complications at 90 days, and PJI at 2 years postoperatively. These findings are most applicable to patients with diabetes undergoing UKA, who represent the primary population receiving GLP-1 therapy within this study.

Our findings align with and extend previous research by Kim et al., who demonstrated significantly lower 90-day PJI rates among GLP-1 users undergoing TKA (1.0% vs. 1.8%; P = 0.037) and THA (1.6% vs. 3.2%; P = 0.03) compared to matched controls (Kim et al. 2025; 2024). These results are further corroborated by a large database study reporting a 42% RRR in PJI among GLP-1 users across total joint arthroplasty populations (Buddhiraju et al. 2024a). Poor perioperative glycemic control is a well-established risk factor for postoperative infection, with current guidelines recommending optimization to HbA1c ⩽7.5% and blood glucose ⩽137 mg/dL prior to arthroplasty (Kheir et al. 2018). The consistency of these findings across different arthroplasty procedures suggests a robust protective effect of GLP-1 against infectious complications.

The 75% reduction in DVT among GLP-1 users represents another clinically significant benefit. While UKA patients typically have lower baseline thrombotic risk compared to TKA patients, venous thromboembolism remains a serious complication with potential for significant morbidity and mortality. GLP-1 agonists may reduce thrombotic risk through multiple pathways, including weight reduction, improved endothelial function, reduced systemic inflammation, and favorable effects on coagulation parameters (Kalyani 2021; Lee et al. 2025; Marsico et al. 2020). These cardiometabolic improvements, combined with reduced mechanical stress on lower extremity joints from weight loss, may contribute to the observed reduction in thromboembolic events (Porto et al. 2025).

The protective effects of GLP-1 agonists likely result from multiple synergistic mechanisms rather than reductions in adiposity alone. GLP-1 agonists enhance glucose regulation while promoting wound healing through multiple mechanisms, including improved angiogenesis, enhanced collagen synthesis, and modulation of inflammatory responses (Chan et al. 2024; Ihnat et al. 2025; de Vries et al. 2017). In addition, these agents demonstrate potent anti-inflammatory properties through modulation of adipokines and cytokines in joint tissues, potentially reducing the inflammatory milieu that predisposes to complications (Meurot et al. 2022; Heckmann et al. 2025). Additionally, GLP-1-mediated weight loss in obese patients reduces mechanical stress on implants and surrounding tissues while improving overall metabolic health (Porto et al. 2025). The cardiovascular benefits, including reduced blood pressure and improved endothelial function, may further contribute to the observed reduction in complications (Kalyani 2021; Lee et al. 2025; Marsico et al. 2020).

Our findings have important implications for perioperative management of UKA patients. The demonstrated safety profile, combined with significant reductions in major complications, supports the continuation of GLP-1 therapy in the perioperative period for appropriate patients. However, recent concerns regarding aspiration risk during anesthesia require careful perioperative medication management, particularly regarding the timing of GLP-1 discontinuation (Elkin et al. 2025).

The modest 9% increase in episode-of-care costs among GLP-1 users, while not statistically significant, warrants consideration in the context of potential cost savings from reduced complications. The prevention of even a single PJI or deep vein thrombosis could offset multiple episodes of routine care, suggesting potential cost-effectiveness despite higher initial treatment costs.

This study's strengths include its large, nationally representative dataset providing excellent generalizability, 1:1 propensity matching that successfully balanced baseline characteristics, and comprehensive evaluation of both 90-day and mid-term implant-related outcomes. Importantly, this represents the first study specifically examining GLP-1 use in the UKA population, addressing a significant knowledge gap in the literature. However, several limitations warrant consideration. First, the retrospective nature of administrative database studies inherently limits causal inference, and unmeasured confounding cannot be completely excluded despite rigorous matching. Second, the dataset does not permit analysis of individual GLP-1 agents, dosing regimens, or duration of therapy, which may have varying efficacy and safety profiles. In particular, we were unable to determine medication adherence or whether patients continued GLP-1 therapy postoperatively or throughout the duration of follow-up, potentially introducing heterogeneity in exposure. Third, important clinical variables such as HbA1c levels, body mass index changes, or other metabolic parameters were unavailable. Likewise, while GLP-1 receptor agonists are associated with gastrointestinal side effects and reduced caloric intake, concerns regarding malnutrition or malabsorption were not directly assessable within this administrative database. Furthermore, although propensity matching achieved balance across selected demographic and comorbidity variables, unmeasured confounders such as glycemic control, diabetes severity, insulin use, duration of disease, and perioperative metabolic optimization were not captured either. Fifth, selection bias may exist regarding which patients receive GLP-1 prescriptions, and the lack of information on perioperative medication management protocols represents another limitation. Finally, the high prevalence of diabetes in our cohort reflects contemporary prescribing patterns of GLP-1 receptor agonists and may limit generalizability to non-diabetic populations. Not to mention, the lack of granular metabolic data, including glycemic control (e.g., HbA1c), and inability to account for temporal changes in treatment practices may introduce residual confounding. Finally, the study period spans over a decade during which GLP-1 utilization increased substantially alongside evolving perioperative care pathways. As a result, patients receiving GLP-1 therapy may represent a more contemporary cohort benefiting from broader improvements in metabolic and surgical management.

CONCLUSION

In this predominantly diabetic UKA cohort, preoperative GLP-1 receptor agonist use in UKA patients is associated was associated with lower rates of DVT, SSI, and wound complications at 90 days, as well as PJI at 2 years postoperatively, without increasing other adverse events or com-

plications. These findings, consistent with trends observed in TKA and THA cohorts, may reflect both GLP-1-specific effects in orthopaedic surgery and broader improvements in metabolic optimization. While prospective studies are needed to confirm causality and optimize perioperative management protocols, these results suggest that GLP-1 therapy may play a role in preoperative optimization for select UKA patients. Future prospective studies should evaluate specific GLP-1 agents and dosing protocols, assess optimal perioperative management strategies, and incorporate detailed metabolic parameters to better understand mechanisms of benefit. Cost-effectiveness analyses would help inform healthcare policy decisions, while randomized controlled trials could establish definitive causal relationships. Investigation of dose-response relationships and identification of patient subgroups most likely to benefit would further refine clinical applications.

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SUPPLEMENTARY MATERIALS

Table 1

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Table 2

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Table 3

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