

GLP-1 Receptor Agonists and Total Knee Arthroplasty Outcomes: A Systematic Review

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Received: September 15, 2026; Accepted: September 22, 2026; Published: September 30, 2026

ABSTRACT

Introduction: Optimizing outcomes in total knee arthroplasty (TKA) is a priority in orthopaedics. GLP-1 receptor agonists (GLP-1 RA) help control blood sugar in diabetics and promote weight loss in obese patients. Studies show they contribute to decreased complications and improved outcomes after orthopedic surgery, but there are inconsistencies regarding its safety and efficacy. Some studies demonstrate reduced infection, readmission, and wound complications in diabetic patients, while others raise concerns about delayed healing, malnutrition, and increased complication rates among non-diabetics. This review evaluates the association between perioperative GLP-1 RA use and postoperative outcomes in TKA.

Methods: A systematic review was conducted using PRISMA 2020 guidelines. PubMed/MEDLINE, Embase, Web of Science, and Cochrane CENTRAL were searched (2015–2025). Eligible studies included adults undergoing primary TKA with reported perioperative GLP-1 RA use and postoperative outcomes.

Results: Eighteen studies met inclusion criteria. Perioperative GLP-1 RA use was associated with lower 90-day complications, fewer readmissions, and reduced prosthetic joint infection, particularly in morbidly obese and diabetic TKA patients. Studies demonstrated at 90 days and 2 years, obese GLP-1 RA users were found to have lower rates of aseptic loosening. Another study showed 45% lower odds of 1-year implant complications among GLP-1 RA users. There were varying outcomes reported in other studies demonstrating no statistically significant differences in short- or long-term PJI or revision rates between GLP-1 RA users and nonusers.

Conclusions: This systematic review shows GLP-1 RA represents a promising adjunct in optimizing obese patients prior to TKA. While encouraging, the current evidence is limited. Future research should focus on large prospective studies which stratify outcomes by surgical procedure, baseline metabolic status, and duration of GLP-1 therapy. Investigation into potential risks, including delayed wound healing or nutritional deficiencies, is necessary to ensure it is safe and effective. The use of GLP-1 RA appears to offer a meaningful opportunity to improve surgical outcomes in high-risk TKA patients.

Keywords: Metabolic Health, GLP-1 Analogues, Knee Replacement, Total Knee Arthroplasty, Obesity

Introduction

Diabetes Mellitus and obesity are prevalent conditions that impact the outcomes in orthopedic surgery, particularly total joint arthroplasty. Both are strongly associated with the development

of osteoarthritis (OA) and increased rates of post-operative complications such as infection, readmission, and early revision [1]. Patients with elevated body mass index (BMI), especially those with a BMI ≥ 40 kg/m², are more likely to require surgical intervention. Due to these associations, preoperative management of modifiable risk factors such as weight and glycemic control has become an essential part of surgical planning. Glucagon-like

Citation: Damon Ross, Lucy Fisher, Tegshjargal Baasansukh, Rolanda Willacy, Regan Burgess, et al. GLP-1 Receptor Agonists and Total Knee Arthroplasty Outcomes: A Systematic Review. J Ortho Physio. 2026. 4(3): 1-4. DOI: doi.org/10.61440/JOP.2026.v4.64

peptide-1 receptor agonists (GLP-1 RAs), including semaglutide and liraglutide, have recently emerged as effective treatments for type 2 diabetes and obesity. In addition to improving glycemic control and promoting weight loss, GLP-1 RAs may improve perioperative outcomes. Recent orthopedic literature illustrates that GLP-1 RA use is associated with reduced rates of prosthetic joint infection, readmission, and overall complications in patients undergoing total hip and total knee arthroplasty. Similar benefits were observed in spinal surgery, including lower infection rates and improved fusion outcomes [2-4].

Optimizing outcomes in total knee arthroplasty (TKA) is a priority amongst orthopaedic surgeons, and has been a focus of research on how to best predict outcomes. Decreasing modifiable risk factors, such as obesity, are often one-way surgeons can help improve outcomes due to its well-known correlation with increased complications. GLP-1 RAs have emerged as an effective way to help control blood sugar in diabetics, but also contribute to significant weight loss in obese patients effectively optimizing their weight prior to surgery. Currently, there is a growing body of evidence studying the association of GLP-1 RAs with decreased complications and improved outcomes after orthopedic surgery, including in TKA [1-4].

Despite promising results, current literature remains inconsistent regarding the safety and efficacy of GLP-1 RAs in orthopaedic surgery, particularly among non-diabetic patients. While several studies have demonstrated reduced rates of infection, readmission, and wound complications in diabetic patients, other findings raise concerns about delayed healing, malnutrition, and increased complication rates among non-diabetics [2-4]. These conflicting results highlight the need to clarify the role of GLP-1 RAs in orthopaedic surgery optimization [5]. The aim of this study is to systematically evaluate existing literature from the past twenty years on the perioperative use of GLP-1 RAs and their association with postoperative outcomes in TKA patients to help determine if GLP-1 RAs should be incorporated into preoperative optimization protocols or approached with caution.

Methods

The systematic search was conducted following the PRISMA 2020 guidelines to evaluate the impact of GLP-1 RAs (e.g. semaglutide [Ozempic/Wegovy], dulaglutide, liraglutide, victoza, exenatide) on postoperative outcomes in the context of primary total knee arthroplasty (TKA) outcomes. The following sources from 2023-2026 were reviewed: PubMed/MEDLINE, Embase, Web of Science Core Collection, and Cochrane CENTRAL. Key terms used were "total knee arthroplasty" and "GLP-1 receptor agonists". Two independent reviewers assessed the abstracts and full studies based on the following criteria: peer-reviewed study, all included subjects were over the age of 18, subjects underwent a primary total knee arthroplasty, subjects were on a GLP-1 RA, and the study included perioperative and postoperative outcomes. Studies that were published in a non-English language were excluded along with studies with pediatric patients and papers that were not related to orthopedics.

Two reviewers independently extracted data from the included studies and placed it into an online spreadsheet. For each paper, the title, authors' names, publication year, paper title, publication journal, and page numbers were documented. The sample size

of each study was documented along with the type of study that was conducted (prospective, case study, retrospective, systematic review, etc.). The reviewers then extracted data from these studies including early (within 90 days) and long-term postoperative complications, including surgical site infection, prosthetic joint infection, wound dehiscence, readmission, revision surgery, nonunion or pseudoarthrosis, and mortality. Any disagreements between the two reviewers were resolved through a third-party consensus.

Results

Study Characteristics

We identified a total of 18 studies that met inclusion criteria. Fifteen were observational studies, with most being retrospective cohort or database analyses. Several used propensity score matching to account for differences in baseline patient characteristics. There was one systematic review and meta-analysis, one clinical commentary, and one trial protocol. Because the commentary and protocol did not report independent outcomes, they were considered separately from the clinical outcome studies.

Progression to TKA

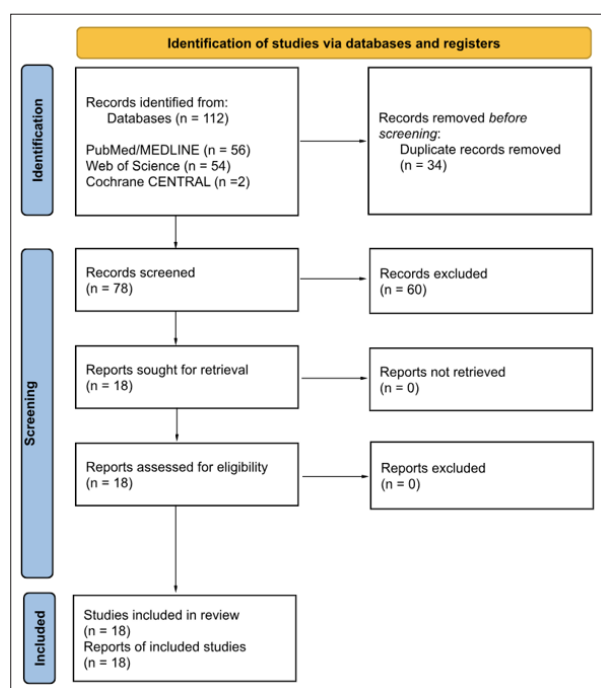
In a single-center analysis of 300 patients on a TKA waiting list, 40% were obese (BMI ≥ 35 kg/m²), with only 13 (10.3%) of them using GLP-1 Ras [6]. In patients with type 2 diabetes (T2DM), and knee osteoarthritis (OA), GLP-1 RA treatment was associated with lower rate of subsequent TKA, with an adjusted hazard ratio of 0.913 (95% CI, 0.885-0.977; $P = 0.15$) [7]. A retrospective database analysis similarly found lower TKA incidence among patients with knee OA receiving GLP-1 RAs across treatment durations and follow-up intervals [8]. One year of GLP-1 RA exposure was associated with an 8-year absolute risk difference of -2.80 percentage points (HR, 0.90; 95% CI, 0.83 to 0.98).

Medical Outcomes and Healthcare Utilization

Lower odds of minor adverse events among patients initiating semaglutide less than a month before TKA were found (OR, 0.16; $P < 0.001$), with reduction in minor adverse events across longer exposure durations; lower odds of severe adverse events became significant with at least 2-3 months of preoperative semaglutide exposure (OR, 0.25; $P < 0.001$) [9]. In patients with BMI ≥ 40 kg/m², perioperative GLP-1 RA use was significantly associated with any medical complication, pulmonary embolism (PE), and readmission compared to matched nonusers [2]. Similarly, Ranson et. al, reported an association of GLP-1 RA use within 6 months of surgery with lower odds of 90-day readmission, arrhythmia, mortality, and deep vein thrombosis (DVT) in a national database, although GLP-1 RA use was associated with increased odds of acute renal failure [10]. Among patients with T2DM treated with metformin, GLP-1 RA use was associated with lower 90-day readmission and emergency department visits in both obese and nonobese patients; obese patients also showed lower odds of postoperative anemia and acute kidney injury (Lee, 2026) [11]. Katzman, found GLP-1 RA users having shorter length of stay and higher rate of home discharge, but more 90-day emergency department visits compared to nonusers [12]. Similarly, Heo, and Box, found that nonusers had higher odds of an extended hospital stay [13,14]. Pooled analysis of the systematic review demonstrated lower odds of 90-day readmission among GLP-1 RA users (OR, 0.76; 95% CI, 0.61 to 0.94; $P = .01$) [15].

Surgical Outcomes

In regard to periprosthetic joint infection after TKA, (PJI), obese patients with a BMI of 30.0-39.9 kg/m² on semaglutide were associated with lower odds of 90-day PJI (OR, 0.543; 95% CI 0.38 to 0.76), and 2-year PJI (OR, 0.65; 95% CI, 0.52 to 0.81), while patients with BMI $\geq$ 40 kg/m² on GLP-1 RAs were significantly associated with lower 90-day rates of PJI [3,16]. Conversely, Heo, found similar rates of 90-day surgical site infection and PJI, with no difference in all-cause or aseptic revision at 1 year [13]. In obese semaglutide users, 90-day revision rates were lower (OR, 0.54; 95% CI, 0.35 to 0.85), while Katzman, found all-cause revision rates at final follow-up among GLP-1 RA users to be lower, although Kaplan-Meier implant survival did not differ between users and non-users [12,16]. At 90 days and 2 years, obese GLP-1 RA users were found to have lower rates of aseptic loosening [16,17]. Another study showed 45% lower odds of 1-year implant complications among GLP-1 RA users (OR, 0.55; 95% CI, 0.33 to 0.90; $P = .02$) (Box, 2026). Both Kim, and Ranson reported no differences in 2-year surgical outcomes between cohorts [3,11]. Consistent with the mixed findings across individual studies, pooled analyses found no statistically significant differences in short- or long-term PJI or revision rates between GLP-1 RA users and nonusers [15].



Comparison with Bariatric Surgery

Among matched patients with a BMI of $\geq$ 35 kg/m², those with prior bariatric surgery had higher odds of PJI (OR, 1.70) and all-cause revision (OR, 1.69) compared with patients receiving GLP-1 RAs after TKA; GLP-1 RA users also demonstrated lower risks of surgical complications than patients receiving no weight-loss optimization across most time points and BMI subgroups [18]. In another cohort study, bariatric surgery patients had more 90-day emergency department visits than semaglutide users and obese controls (7.9% vs 5.7% vs 4.0%; $P < .001$), all while bariatric surgery independently predicted emergency department utilization (OR, 1.79; $P = .005$) and revision (OR, 1.71; $P = .028$) [12]. Sharma, found bariatric surgery patients had higher 90-day rates of periprosthetic fracture (RR, 2.4; $P = .016$), PJI (RR, 1.7; $P = .002$), revision surgery (RR, 1.926;

$P = .005$), cardiac events (RR, 1.255; $P < .001$), readmission (RR, 1.316; $P = .015$), and emergency department utilization (RR, 1.2; $P < .001$) [19]. Higher rates of DVT or pulmonary embolism (2.18% vs 4.42%; $P < .001$), transfusion (0.30% vs 1.03%; $P = .016$), any surgical complication (1.64% vs 3.45%; $P = .001$), any medical complication (9.09% vs 12.30%; $P = .003$), and combined readmission or emergency department utilization (21.33% vs 25.33%; $P = .007$) among bariatric surgery patients compared with GLP-1 RA users [20].

Conclusions

This systematic review shows that GLP-1 receptor agonists represent a promising adjunct in optimizing obese patients prior to total knee arthroplasty. Even though many studies have shown a benefit of GLP-1 receptor agonists being associated with lower complication rates and reduced admissions in diabetic patients undergoing orthopaedic procedures, few studies have focused on their effect in obese patients specifically undergoing TKA. The studies which have focused on GLP-1 receptor agonists on TKA have shown decreases in 90 day prosthetic joint infection, any medical complications, pulmonary embolism, and later readmission.

While encouraging, the current evidence base is limited by heterogeneity in study design, small sample sizes in some cohorts, and a lack of randomized controlled trials. Future research should focus on large-scale, prospective studies that stratify outcomes by surgical procedure, baseline metabolic status, and duration of GLP-1 therapy. Additionally, investigation into potential risks, including delayed wound healing or nutritional deficiencies, is necessary to ensure safe and effective clinical application. Additionally, GLP-1 receptor agonists have been shown to contribute to delayed gastric emptying, increasing the aspiration risk during anesthesia requiring specific protocols to be followed on holding the medication at least 1 week prior to surgery to minimize risk [21]. Ultimately, GLP-1 receptor agonists appear to offer a meaningful opportunity to improve surgical outcomes in high-risk patients, but their use should be guided by further evidence that clarifies both their benefits and limitations within total knee arthroplasty so subsequent protocols can be created [22].

Integrating GLP-1 receptor agonists into the perioperative course for obese patients undergoing TKA could lead to a shift in how orthopedic surgeons optimize their patients prior to surgery. The evidence shows these patients will have improved outcomes post-surgery, but they will also need to understand that this is a lifelong intervention. Orthopedic surgeons who place their TKA patients on a GLP-1 RA should coordinate their patient's care with their primary care provider along with an endocrinologist as needed to ensure the patient is able to maintain their improved surgical outcome past the 90-day mark [21]. As this medication and its effects on patients continues to be investigated, GLP-1 RAs could become a key player for obese and diabetic patients in their perioperative optimization, ultimately reducing complications, lowering healthcare costs, and improving total knee arthroplasty outcomes.

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