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Research Article

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

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ABSTRACT

Introduction: The rising prevalence of obesity has contributed to an increased burden of orthopedic complications, including higher risks of infection, thromboembolism, and revision surgery following total hip arthroplasty (THA). Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), initially developed for type 2 diabetes, have recently been evaluated for their impact on THA outcomes. Emerging evidence suggests that GLP-1 RAs may reduce postoperative complications such as prosthetic joint infection, readmissions, and revisions, particularly among patients with obesity and diabetes. However, findings remain inconsistent, as some studies report significant benefits and others show no difference. This systematic review synthesizes the current evidence, highlights areas of consensus and variability, and identifies directions for future research relevant to orthopedic practice.

Methods: A systematic review of PubMed and Google Scholar was conducted August 2025, for primary articles published between August 2015 to 2025 using the terms: GLP-1 receptor, Glucagon-Like Peptide 1, agonist, semaglutide, liraglutide, dulaglutide, total hip arthroplasty, hip replacement, complications, infection, revision, outcomes, complications, infection, revision. Boolean terms AND and OR were used to refine results. Inclusion criteria: full-text English-language human studies from the United States involving adults (≥ 18 years old) and primary studies. Exclusion criteria included non-English studies, studies outside the time window or outside the United States, secondary literature, insufficient information, and studies lacking specification of THA, GLP-1 RA use, or postoperative outcomes.

Results: Thirty-nine records were identified (see Figure 1). After removing duplicates and automated exclusions, 23 studies were screened and 12 were excluded for reasons including lack of GLP-1 RA focus , not specific to THA, or omitting surgical outcomes. Eleven studies met the inclusion criteria. Across these studies, perioperative GLP-1 RA use in THA was consistently safe. Several analyses demonstrated no increase in infection, revision, or periprosthetic fracture rates, while others showed reduced rates of readmission, prosthetic joint infection, or acute blood loss anemia.

Conclusion: Current literature suggests GLP-1 RAs are safe in the perioperative period of THA and may improve outcomes postoperatively. Further investigation is warranted to clarify benefits in high-risk populations such as patients with morbid obesity and both diabetic and nondiabetic cohorts.

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Introduction

Nearly 1 in 11 adults has severe obesity in the United States. This is defined by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and NHANES as individuals with a BMI greater than 40 [1]. More importantly, it is known that obesity is negatively correlated with orthopedic surgical outcomes. Likewise, type 2 diabetes mellitus (T2DM) affects roughly 1 in 6 Americans. Both populations are more likely to experience adverse postoperative outcomes. Thus, to decrease risk, patients undergoing total hip arthroplasty (THA) are generally recommended to have a BMI less than 40 [2]. Consequently, the multifaceted use of glucagon-like peptide receptor agonists has been of recent interest.

Glucagon-Like peptide-1 receptor agonists (GLP-1 RAs), are an increasingly popular class of medications that act as incretin mimetics [3]. Incretins, which include GLP-1 and glucose-dependent insulinotropic peptide (GIP), are derived from the gut after eating and function to lower blood sugar by stimulating glucose-dependent insulin secretion. GLP-1 RAs, such as Exenatide, Liraglutide, Dulaglutide, and Semaglutide, play a major role in cardiovascular health, several endocrine disorders, and bone metabolism [4]. Although GLP-1 RAs have been associated with several adverse effects, such as nausea, vomiting, diarrhea, and, less commonly, acute pancreatitis, they are relatively safe in orthopedic practice. Therefore, GLP-1 RAs remain of great interest to orthopedic clinicians aimed at decreasing modifiable risk factor complications related to orthopedic surgery and its outcomes.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) saw a rise in use in 2018-2019. Originally used for the treatment of type 2 diabetes mellitus (T2DM), GLP-1 RAs have expanded their use to chronic weight management in patients who are overweight or obese, with FDA approval in 2021. This led to a major increase in the prescription and use of GLP-1 RAs, especially semaglutides. The use of GLP-1 RAs has shown promise to be advantageous to a variety of specialties, in particular, orthopedics. Individuals with obesity or morbid obesity and/or T2DM are associated with higher postoperative orthopedic complications.

Given what is known about GLP-1 RAs' ability to lower blood sugar and promote weight reduction, there is growing clinical interest in their application within orthopedic practice. The metabolic effects of GLP-1 RAs may contribute to improved perioperative physiologic stability in patients with obesity or type 2 diabetes mellitus. Some studies have also reported that GLP-1 RA therapy is associated with improved glycemic control and reduced inflammatory markers, which may be relevant in reducing surgical site complications in arthroplasty populations [2,4]. Emerging literature suggests that GLP-1 RAs are associated with reduced prosthetic joint infections, fewer 90-day readmission rates, and reduced 2-year revision procedures in total knee and hip arthroplasty populations [5-8]. Specifically, in total hip arthroplasty (THA), obesity and T2DM are known to negatively impact postoperative orthopedic outcomes. One study showed that individuals with a BMI > 50 kg/m², or super obesity, were associated with higher postoperative complications such as venous thromboembolism, infection, 90-day readmission, and medical complications following THA [9]. Thus, the use of GLP-1 RAs' effects on total hip arthroplasty postoperative outcomes remains a developing topic in the discussion of chronic weight management and glycemic control in patients undergoing THA. This systematic review, therefore, synthesizes the current evidence, highlights areas of consensus and variability, and identifies directions for future research relevant to orthopedic practice.

Methods

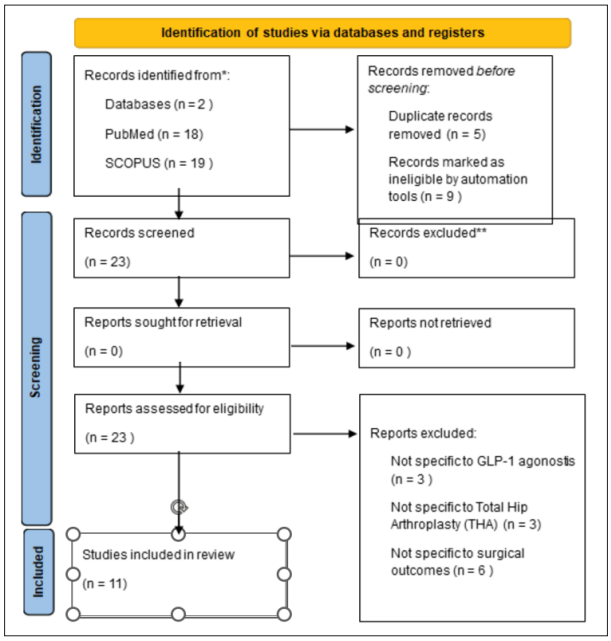
A systematic review of PubMed, SCOPUS, and Google Scholar was conducted August 2025, for primary articles published between August 2015 to 2025 using the terms: GLP-1 receptor, Glucagon-Like Peptide 1, agonist, semaglutide, liraglutide, dulaglutide, total hip arthroplasty, hip replacement, complications, infection, revision, outcomes, complications, infection, revision. Boolean terms AND and OR were used to acquire relevant studies. Inclusion criteria: full-text studies written in English, human studies performed in the United States, adult patients (≥ 18 years old), primary studies (retrospective, prospective, cohort studies). Studies not written in English, performed outside of the United States, published outside of the 10-year window, with secondary information (i.e., systematic reviews, editorials), or with insufficient information (i.e., brief reports, abstracts, no full-text available) were excluded. Studies that did not specify total hip arthroplasty, use of GLP-1 receptor agonist, or patient outcomes were also excluded.

All studies were assessed for eligibility by five independent reviewers. This review adhered to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [10,11]. In case of disagreement, consensus on which articles to screen full-text was reached by discussion. If necessary, the first researcher was consulted to make the final decision on inclusion.

All studies were assessed for: author, publication year, study type, number of participants (n), demographic information (age range, mean age, genders, ethnicities), patient outcomes, and follow-up time. Given the limited amount of research on this topic there were no validation systems or bias assessment tools used in selection of our studies.

Results

A total of 39 records were identified through database searching (PubMed = 18; SCOPUS = 19; other databases = 2). After removal of duplicates (n = 5) and automated ineligible records (n = 9), 23 studies underwent full-text screening. Twelve studies were excluded for lack of GLP-1 receptor agonist specificity (n = 3), absence of total hip arthroplasty (THA)-specific data (n = 3), or failure to report postoperative surgical outcomes (n = 6). Eleven primary U.S.-based studies met inclusion criteria and were incorporated into the final synthesis (Figure 1), in accordance with PRISMA 2020 reporting guidance [5,6].



All included studies were retrospective cohort or administrative database analyses, encompassing heterogeneous populations including patients with type 2 diabetes, individuals prescribed GLP-1 receptor agonists for weight management, and morbidly obese patients undergoing primary THA. Follow-up intervals ranged from 90 days to two years postoperatively. Across studies, perioperative GLP-1 receptor agonist use was consistently not associated with increased postoperative complication risk in THA. No study demonstrated an increased risk of prosthetic joint infection (PJI), aseptic or all-cause revision, or periprosthetic fracture among GLP-1 users compared to matched controls, including large diabetic THA cohorts reported by Levidy et al. and Heo et al [7,10]. Several investigations instead reported favorable short-term outcomes, including lower 90-day readmission and reduced PJI in diabetic patients using semaglutide or other GLP-1 agonists undergoing THA, as well as lower rates of PJI, readmission, medical complications, and hematoma formation in morbidly obese THA patients receiving GLP-1 therapy [8,11,12]. A recent systematic review and meta-analysis further supported this pattern, demonstrating a reduced risk of PJI without increased revision, loosening, fracture, wound dehiscence, or length of stay in arthroplasty patients exposed to GLP-1 agonists [13].

Studies specifically evaluating non-diabetic patients using GLP-1 RAs for weight loss similarly demonstrated no increase in surgical or medical complication rates, suggesting safety beyond diabetic populations. In particular, Verhey et al. found that non-diabetic GLP-1 RA users undergoing primary THA had lower odds of acute blood loss anemia, postoperative transfusion, and 90-day emergency department visits, while showing no increased risk of DVT, PE, myocardial infarction, sepsis, periprosthetic joint infection, instability, fracture, loosening, or all-cause revision [14]. These findings are especially relevant given the increasing use of GLP-1 agonists for obesity treatment alone in modern arthroplasty candidates.

With respect to gastrointestinal complications, the available THA-specific literature suggests that GLP-1 agonist use may be associated with higher rates of transient postoperative nausea and vomiting, but not with worsened major THA outcomes. Magaldi et al. reported increased inpatient postoperative nausea/vomiting among GLP-1 users undergoing THA, although there were no significant differences in length of stay, readmissions, urinary retention, venous thromboembolism, or other major complications [15]. Similarly, Baum et al. reported an association between GLP-1 receptor agonist use and certain short-term gastrointestinal complications in arthroplasty patients. In the THA cohort, GLP-1 use was associated with gastrointestinal ulcer, ileus, and cholecystitis within 30–90 days postoperatively, although these findings did not correspond to increased rates of revision, infection, or mortality following THA [16]. Importantly, these gastrointestinal findings did not translate into increased rates of revision, infection, or other major perioperative complications in THA cohorts [15,16].

Although complication rates were generally similar between groups, reported reductions in prosthetic joint infection and 90-day readmission varied across patient populations and study designs. Methodological limitations were common, including retrospective design, reliance on administrative coding for medication exposure and outcomes, limited data on medication adherence and timing of perioperative discontinuation, and lack of granular metabolic or BMI change data [7,8,10-16].

Discussion

Current evidence suggests that perioperative GLP-1 RAs do not increase the incidence or severity of postoperative medical or surgical complications and appear to be safe in the perioperative period of total hip arthroplasty (THA). Perioperative GLP-1 RA use may even confer protective effects against postoperative complications, particularly in high-risk patients. Several investigations report reduced periprosthetic joint infection and 90-day readmission in obese and diabetic cohorts [11,12,1-4]. While the evidence is promising, further investigation is warranted to clarify the magnitude of their role in improving postoperative outcomes, particularly in populations such as patients with morbid obesity (BMI > 40) and both diabetic and nondiabetic cohorts.

Apart from perioperative safety and complication risk, recent studies have also examined how GLP-1RA use influences osteoarthritis (OA) progression and the incidence of THA. Available evidence does not demonstrate an increase in the incidence of THA among GLP-1 RA users, regardless of OA or diabetes status [5,7]. Among patients with preexisting OA, GLP-1 RA use was associated with a lower odd of conversion to THA within 1 year.16 However, one study reported finding that in diabetic patients and those without prior OA, there was an increase in the rate of OA progression and utilization of major joint injections among GLP-1 RA users [6]. Overall, current evidence does not demonstrate a strong relationship between GLP-1 RAs and the incidence of THA; however, their effects on OA progression justify further investigation, as they may be influenced by baseline disease status, residual confounding, and underlying metabolic factors.

Importantly, the long term complications of GLP-1 RA use have just recently begun to reach the threshold for longitudinal studies to review the 5-year to 10-year risk of GLP-1 RA usage. One

study, focused on the 5-year complications of GLP-1 RAs use among patients with diabetes and obesity, found that glucagon-like peptide receptor agonists were independently associated with a significant increase in osteoporosis, osteomalacia, and gout compared to their matched cohort of nonusers [5].

Taken together, the current literature suggests that GLP-1 RA use does not increase the incidence of total hip arthroplasty and may be associated with favorable outcomes in select populations with osteoarthritis. However, emerging data on long-term metabolic and musculoskeletal complications highlight the need for continued surveillance as longer follow-up studies become available [17,18].

There are several limitations in this study. Most of the included studies in this systematic review are retrospective database analyses, and were therefore potentially subject to selection bias, coding inaccuracies, and residual confounding that cannot be fully accounted for. Differences in study design, follow-up duration, GLP-1 RA agent type, and perioperative management protocols may limit direct comparison across studies. At the review level, restricting the review to primarily U.S.-based and English-language studies may limit global generalizability and the breadth of the evidence.

Conclusion

In conclusion, the literature suggests that GLP-1RAs are safe in the perioperative period of total hip arthroplasty and may even demonstrate protective effects against certain postoperative complications. Furthermore, current evidence does not demonstrate an increased incidence of THA among GLP-1RA users, helping to address concerns that these medications may accelerate or increase the need for joint replacement.

Despite these encouraging findings, additional research is needed to better define the patient populations most likely to benefit from perioperative GLP-1RA therapy. Future studies should stratify outcomes by factors such as diabetic status, obesity classification, glycemic control, and comorbidity burden. Additionally, comparative investigations of GLP-1-based preoperative protocols may help guide orthopedic surgeons on best practices for the perioperative management of patients using these medications. Long-term follow-up studies evaluating outcomes beyond the early postoperative period are also necessary to further assess the safety profile of prolonged GLP-1RA use, particularly given emerging reports suggesting potential associations with osteoporosis, osteomalacia, and gout.

Future studies should further stratify outcomes by factors such as diabetic status, obesity classification, glycemic control, and comorbidity burden to better identify subpopulations most likely to benefit from perioperative GLP-1 RA therapy. Long-term follow-up studies, including 1-5-year outcomes, are needed to evaluate complications beyond just the early postoperative period. Additionally, studies comparing GLP-1 RA based preoperative protocols should be conducted to help guide orthopedic surgeons on best practices for the perioperative management of GLP-1 RA users.

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