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Glucagon-Like Peptide-1 Receptor Agonists

Impact of Glucagon-Like Peptide-1 Receptor Agonists on Postoperative Outcomes in Arthroplasty: A Systematic Review

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ABSTRACT

Background: The use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has expanded due to their effectiveness in weight management, with increasing applications beyond diabetes care. Given the strong association between obesity and suboptimal total joint arthroplasty outcomes, evaluating how GLP-1 RAs affect postoperative outcomes is essential. However, few studies have synthesized available evidence.

Methods: A systematic review was conducted following the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. PubMed, Embase, and Scopus were searched for studies published until January 29, 2025, using terms related to GLP-1 RAs and arthroplasty. Studies analyzing postoperative outcomes in patients undergoing total knee arthroplasty or total hip arthroplasty while taking GLP-1 RAs were included. Articles were screened, and data on study characteristics and key findings were extracted. There were seven studies, totaling 16,467 patients undergoing arthroplasty who were taking GLP-1 RAs, which met inclusion criteria, with six utilizing national databases and one based on institutional data. There were three that focused on diabetic GLP-1 users; four included both diabetic and nondiabetic GLP-1 RA users.

Results: Among the included studies, GLP-1 RA use was most commonly associated with reduced postoperative complications, including lower rates of periprosthetic joint infection, readmissions, and wound complications following total knee arthroplasty or total hip arthroplasty. Some studies reported no differences in outcomes or increased rates of adverse events such as myocardial infarction, hypoglycemia, or postoperative nausea. Overall, five studies reported primarily beneficial effects, while one showed mixed results and one reported predominantly negative findings.

Conclusions: Current evidence suggests GLP-1 RAs may improve total joint arthroplasty outcomes, particularly by reducing infection risk and readmission. However, conflicting findings highlight the need for further research, particularly well-designed multicenter studies and randomized controlled trials, to clarify the effects of GLP-1 RAs on surgical outcomes.

The use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has rapidly expanded in recent years, largely due to their effectiveness in weight management. Currently, approximately 6% of Americans use GLP-1 RAs [1]. By 2030, an estimated 50% of U.S. adults will have obesity, defined as a body mass index (BMI) of 30 or higher, with even higher rates in certain states [2]. Reflecting

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this trend, GLP-1 RAs are being developed for weight loss beyond diabetes mellitus (DM) management, underscoring their expanding role in obesity-related care [3,4].

With obesity rates rising, the burden of related conditions, including osteoarthritis (OA), is expected to increase. Osteoarthritis is a leading cause of joint degeneration and the primary indication for total joint arthroplasty (TJA) [5]. Excess weight accelerates OA, necessitating surgical intervention. By 2040, the volume of total hip arthroplasty (THA) and total knee arthroplasty (TKA) is projected to increase by 176 and 139%, respectively, mirroring obesity trends [6]. Given the link between obesity and suboptimal arthroplasty outcomes, evaluating the potential of GLP-1 RAs to mitigate these risks is essential [7,8].

Many surgeons set a BMI threshold of 40 for arthroplasty eligibility due to the correlation between higher BMI and poorer postoperative outcomes [9]. However, studies indicate that 21.9% of patients excluded due to this cutoff have symptomatic lower extremity OA, highlighting a major gap in care [10]. The GLP-1 RAs help obese patients lose weight, improving eligibility or reducing the need for TJA [11,12]. Notably, semaglutide (Ozempic) has been shown to induce weight loss of 6 to 16% of baseline body weight, offering a promising option for preoperative weight management [13].

Research on the impact of GLP-1 RAs on postoperative TJA outcomes remains limited. While studies have examined their effects on total knee, hip, and shoulder arthroplasty, the literature is still sparse, with most publications emerging only recently. Although individual studies and expert opinions suggest benefits, no comprehensive review has synthesized the evidence [11,13]. This study aimed to fill this gap by evaluating current research on the association between GLP-1 RA therapy and postoperative outcomes in total knee and hip arthroplasty. By summarizing existing research, this review seeks to clarify potential implications for orthopaedic surgeons and researchers in this emerging area.

Materials and Methods

A systematic review was conducted using the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [14]. A literature search was performed using PubMed, Embase, and Scopus for articles published from inception until January 29, 2025, using the search terms ([GLP-1 OR Semaglutide] AND [TKA OR THA OR joint replacement OR arthroplasty]). The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD4202510000206). We identified 102 articles that were screened through four phases: identification, screening, eligibility, and inclusion.

All search results were uploaded to Rayyan (Rayyan Systems Inc., Cambridge, Massachusetts, USA). After removing duplicates, 43 articles remained. There were two reviewers (VL and SD) who independently screened abstracts, selecting eight articles for full-text review. There was one study excluded for focusing only on preoperative outcomes, leaving seven for inclusion (Figure 1). Disagreements were resolved by a third author (PG).

Studies analyzing postoperative outcomes in TKA or THA patients on GLP-1 RAs were included. Exclusion criteria included non-English publications, case reports, reviews, meta-analyses, editorials, letters, commentaries, expert opinions, and laboratory studies. Studies on other orthopaedic procedures or lacking postoperative outcomes were excluded. Extracted data from the included studies included the author and year of publication, journal, patient data source, GLP-1 cohort size, study population, follow-up duration points, and main findings.

Study Characteristics

This review included seven studies analyzing 16,467 TKA and THA patients on GLP-1 RAs. There were six published in 2024 and one in 2023. The most frequently represented journal was *The Journal of Arthroplasty* (five out of seven). There were six studies that utilized national databases: four from PearlDiver, one from TriNetX, and one from IBM MarketScan databases. There was one study that analyzed single-institution patient data.

All seven used a case-control design, comparing GLP-1 RA users to nonusers. There were three studies that included only patients who had DM in the case group, while the other four included both diabetic and nondiabetic GLP-1 RA users. There were none that differentiated between type 1 and 2 DM: three included only patients who had type 2 DM, three did not specify the type of diabetes among GLP-1 RA users, and one did not report the indication for GLP-1 RA use. By arthroplasty type, two studies examined TKA and four focused on THA. There was one study that evaluated outcomes in a combined THA and TKA cohort.

All studies assessed 90-day complications as a standardized short-term outcome. Additionally, four studies extended their analysis to complications occurring up to two years postsurgery. Tables 1 and 2 summarize study characteristics and key findings: Table 1 (TKA) and Table 2 (THA). The combined THA/TKA study is presented in both Tables 1 and 2.

Results

Findings from TKA Studies

A 2023 study by Magruder et al. evaluated GLP-1 RA semaglutide in diabetic TKA patients [17]. Among 7,051 users at the time of surgery, there were decreased odds of sepsis (0 versus 0.4%; odds ratio [ORs] 0.23) and periprosthetic joint infection (PJI) (2.1 versus 3.0%; OR 0.7) compared to the control group [17]. These reductions corresponded with lower readmission rates (7.0 versus 9.4%; OR 0.71), revision surgeries (4.0 versus 4.5%; OR 0.86), and lower 90-day costs ($15,292 versus $16,798) [17]. However, semaglutide use was associated with increased rates of myocardial infarction (MI) (1.0 versus 0.7%; OR 1.49), acute kidney injury (AKI) (4.9 versus 3.9%; OR 1.28), pneumonia (PNA) (2.8 versus 1.7%, OR 1.67), and hypoglycemic events (1.9 versus 1.2%; OR 1.55) [17].

In contrast, Buddhiraju et al. assessed 90-day outcomes in patients taking GLP-1 RAs for weight loss compared to a control group not using these medications, regardless of diabetic status [15]. The GLP-1 RA use was associated with a 47% reduction in hospital readmission following surgery [15].

Kim et al. evaluated the use of GLP-1 RA in morbidly obese (BMI $\geq$ 40) patients undergoing TKA [16]. Users had decreased rates of PJI and wound dehiscence [16]. Additionally, GLP-1 RA use was associated with lower readmission and pulmonary embolism (PE) rates than another cohort of morbidly obese patients [16]. Notably, there was no observed increase in the risk of MI, AKI, or deep venous thrombosis (DVT) in patients taking GLP-1 RAs [16].

Findings from THA Studies

Buddhiraju et al. evaluated the preoperative use of GLP-1 RAs in patients undergoing THA [15]. Compared to the control group, GLP-1 RA use was associated with a 42% lower risk of PJI (2.1 versus 3.6%) [15]. The study also found no increased risk of adverse events, including aspiration, DVT, PE, or hospital readmission [15]. Magruder et al. similarly found that patients using semaglutide at the time of surgery had lower rates of readmission (6.2 versus 8.8%; OR 0.68) and PJI (1.6 versus 2.9%; OR 0.56) [21]. However, no

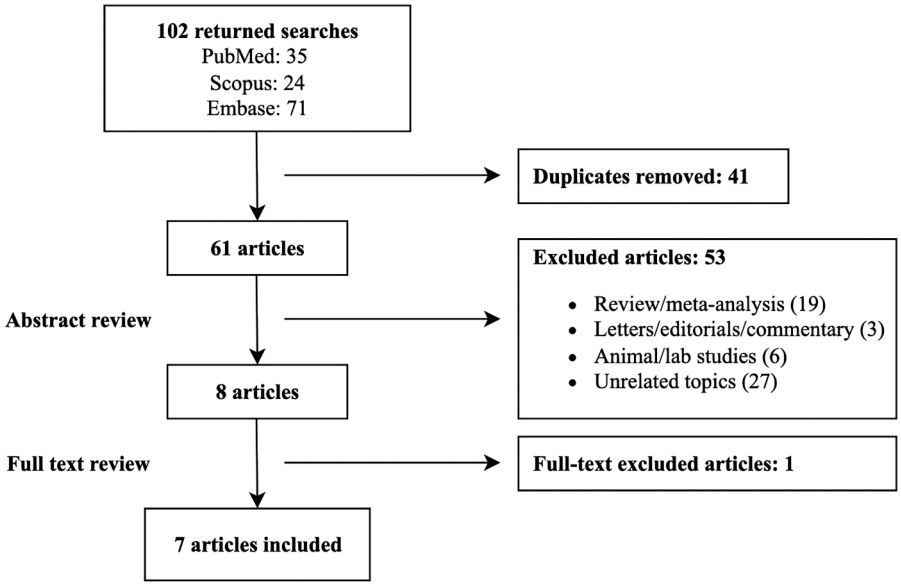

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram.

significant differences were observed in other medical complications, including MI, DVT, PE, hospitalization costs, or length of stay [21]. A separate study by Heo et al. examined GLP-1 RA use in diabetic patients undergoing THA [18]. Patients not using GLP-1 RAs had a higher likelihood of extended hospital stays (31.2 versus 25.4%; OR 1.29) [18]. However, no significant differences were observed in surgical complications, including DVT, PNA, or PJI [18]. Another 2024 study by Magaldi et al. assessed the safety of GLP-1 RAs in patients undergoing THA [20]. Their findings indicated no significant differences in length of stay, readmission rates, or other complications between the GLP-1 RA group and the control group [20]. However, patients taking GLP-1 RAs experienced significantly higher rates of postoperative nausea and vomiting [20]. Unlike other studies, this study did not rely on a large national database, and the GLP-1 RA cohort consisted of only 66 patients. Kim et al. investigated GLP-1 RA use in morbidly obese patients undergoing THA [19]. The study found no significant differences in the rates of PNA, PE, AKI, DVT, cardiac arrest, or urinary tract infection between the GLP-1 RA and control groups [19]. However, patients taking GLP-1 RAs experienced lower rates of PJI, hematoma formation, and hospital readmission at 90 days than controls [19].

Discussion

Among the seven studies reviewed, five reported primarily improved postoperative outcomes with GLP-1 RA use in TKA or THA, while one found predominantly negative effects, and one had mixed findings.

With obesity on the rise, its negative impact on arthroplasty outcomes is a growing concern. As GLP-1 RAs gain widespread use for both diabetes management and weight loss, their influence on TJA outcomes is becoming increasingly relevant. By 2029, nearly 69% of TKA patients are projected to be classified as obese or morbidly obese [8]. Given this trend, optimizing surgical outcomes in patients undergoing TJA is essential. While primarily recognized for weight loss, GLP-1 RAs also affect glycemic control and systemic inflammation, both of which may influence postoperative recovery and complications. Notably, prescriptions among nondiabetic patients in the United States surged from approximately 21,000 in 2019 to over 174,000 in 2023—an increase of over 700% [22]. This rapid expansion raises questions about how outcomes differ between diabetic and nondiabetic GLP-1 RA users.

To better understand the broader effects of GLP-1 RAs, the largest study to date on GLP-1 RA patients—a January 2025 analysis of Veterans Affairs data, including over 215,000 users—examined their impact beyond weight and musculoskeletal health [23]. The study found that GLP-1 RA use was associated with a lower risk of neurocognitive disorders, cardiometabolic conditions, and certain infections, while also identifying an increased risk of gastrointestinal issues, hypotension, syncope, and nephrolithiasis [23]. Overall, patients taking GLP-1 RAs were less likely to develop 42 health conditions but had a higher risk of 19 others [23]. Given these widespread effects, it is unclear why similar benefits and risks were not consistently observed in arthroplasty patients within the studies reviewed here. Differences in study populations, sample sizes, or data granularity may contribute to these discrepancies.

Beyond perioperative considerations, GLP-1 RAs may also play a role in reducing the need for arthroplasty before surgery is even considered. A 2025 study reported lower conversion rates to TKA (1.4 versus 2.1%) and THA (1.1 versus 2.2%) among OA patients using GLP-1 RAs within one year [12]. Another study found no difference in arthroplasty rates between GLP-1 RA users and nonusers, underscoring the need for further research [24]. While not the primary focus of this review, these findings suggest that GLP-1 RAs could be integrated into a broader nonoperative treatment strategy. When combined with nonsteroidal anti-inflammatory drugs, corticosteroid injections, and physical therapy, they may aid in symptom management and slow OA progression, potentially delaying or even preventing the need for surgery.

As GLP-1 RAs become more prevalent among surgical patients, debate continues over when they should be discontinued before surgery. These medications slow gastric emptying, which may increase the risk of aspiration and pneumonia under anesthesia. The 2024 American Society of Anesthesiologists guidelines recommend holding GLP-1 RAs the day of surgery for daily formulations and one week prior for weekly formulations [25]. However, a 2024 meta-analysis challenged these recommendations, arguing that stopping GLP-1 RAs at these timepoints could

Table 1
Study Characteristics and Main Findings for Studies on GLP-1 Receptor Agonist Use in Total Knee Arthroplasty.

Author and Year	Journal	Patient Data Source	GLP-1 Cohort Size	Case Group	Control Group	Comparison Group	Matching Strategy	Surgery Type	Follow-Up Duration	Main Findings
Buddhiraju et al., 2024 [15]	*The Journal of Arthroplasty*	TriNetX Database	3,139	Patients prescribed GLP-1 RAs between 1 year and 15 days before surgery	Patients not using GLP-1 RAs	None	Propensity score matching (1:1) by clinical characteristics	Mix of TKA (n = 2,095) and THA (n = 1,044)	90-day	The use of GLP-1 RAs was linked to a reduced 90-day risk of readmission (1.1 versus 2.0%, RR = 0.53, $P = 0.017$) after TKA. No significant differences were found between the comparison groups for other outcomes.
Kim et al., 2024 [16]	*Journal of Bone and Joint Surgery*	PearlDiver Database	2,975	Patients who had morbid obesity (BMI ≥40.0) who were on GLP-1s for at least 3 months before and after surgery	Patients who had morbid obesity (BMI ≥40.0) without GLP-1 RA use	Patients who had severe obesity (BMI 35.0 to 39.9) without GLP-1 RA use	Propensity score matching by clinical characteristics between the treatment group and morbid obesity controls (1:1) and between the treatment group and severe obesity comparison group (2:1)	TKA	90 day, 2 year	Patients who had a BMI ≥40 on GLP-1 RAs had lower rates of 90-day PJI (1.0 versus 1.8%; $P = 0.037$), medical complications (10.6 versus 12.7%; $P = 0.033$), pulmonary embolism (<0.4 versus 0.6%; $P = 0.05$), and readmissions (5.3 versus 8.9%; $P < 0.001$) compared to controls. No differences were observed in 2-year surgical complications ($P > 0.05$). Additionally, patients who had a BMI ≥40 on GLP-1 RAs had similar infection and complication rates at 90 days and 2 years ($P > 0.05$) compared to those who had a BMI of 35.0 to 39.9.
Magruder et al., 2023 [17]	*The Journal of Arthroplasty*	PearlDiver Database	7,051	Patients who had DM and an active prescription for semaglutide at the time of surgery	Patients not using GLP-1 RAs	None	Propensity score matching (1:5) by clinical characteristics	TKA	90 day, 2 year	Semaglutide cohorts had higher incidence and odds of myocardial infarction (1.0 versus 0.7%; OR 1.49; $P = 0.003$), acute kidney injury (4.9 versus 3.9%; OR 1.28; $P < 0.001$), pneumonia (2.8 versus 1.7%; OR 1.67; $P < 0.001$), and hypoglycemic events (1.9 versus 1.2%; OR 1.55; $P < 0.001$), but lower odds of sepsis (0 versus 0.4%; OR 0.23; $P < 0.001$). Semaglutide cohorts also had lower odds of PJI (2.1 versus 3.0%; OR 0.70; $P < 0.001$) and readmission (7.0 versus 9.4%; OR 0.71; $P < 0.001$), and trended toward lower odds of revisions (4.0 versus 4.5%; OR 0.86; $P = 0.02$) and 90-day costs ($15,291.66 versus $16,798.46; $P = 0.012$)

GLP-1 RA, glucagon-like peptide-1 receptor agonist; DM, diabetes mellitus; BMI, body mass index; TKA, total knee arthroplasty; THA, total hip arthroplasty; PJI, periprosthetic joint infection; OR, odds ratio; RR; relative risk.

Table 2
Study Characteristics and Main Findings for Studies on GLP-1 Receptor Agonist Use in Total Hip Arthroplasty.

Author and Year	Journal	Patient Data Source	GLP-1 Cohort Size	Case Group	Control Group	Comparison Group	Matching Strategy	Surgery Type	Follow-Up Duration	Main Findings
Buddhiraju et al., 2024 [15]	*The Journal of Arthroplasty*	TriNetX Database	3,139	Patients prescribed GLP-1 RAs between 1 year and 15 days before surgery	Patients not using GLP-1 RAs	None	Propensity score matching (1:1) by clinical characteristics	Mix of TKA (n = 2,095) and THA (n = 1,044)	90 day	The use of GLP-1 RAs was linked to a reduced 90-day risk of PJI (2.1 versus 3.6%, RR = 0.58, $P = 0.042$) after THA. No significant differences were found between the comparison groups for other outcomes.
Heo et al., 2024 [18]	*The Journal of Arthroplasty*	IBM MarketScan Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefit databases	812	Patients who had type 2 DM taking a GLP-1 RA preoperatively	Patients not using GLP-1 RAs	None	Propensity score matching (1:5) by clinical characteristics	THA	90 days, 1 year	Patients not using GLP-1 RAs had higher rates of prolonged hospital stays (more than 3 days, $P = 0.001$), while those on GLP-1 RAs showed no significant differences in surgical or medical complications, revision surgeries, or infections within the first year postoperatively.
Kim et al., 2024 [19]	*The Journal of Arthroplasty*	PearlDiver Database	771	Patients who had morbid obesity (BMI $\geq$ 40.0) and GLP-1 RA use for at least 3 months before and after surgery	Patients who had morbid obesity (BMI $\geq$40.0) without GLP-1 RA use	Patients who had severe obesity (BMI 35.0 to 39.9) without GLP-1 RA use	Propensity score matching (1:4:4) by clinical characteristics	THA	90 day, 2 year	Patients who had morbid obesity on GLP-1 RAs had lower rates of 90-day PJI (1.6 versus 3.2%; $P = 0.03$), readmission (6.9 versus 9.7%; $P = 0.04$), medical complications (10.5 versus 14.1%; $P = 0.03$), and postoperative hematoma formation (0 versus 1.3%; $P < 0.01$) compared to controls. Additionally, hematoma formation was lower in morbidly obese patients on GLP-1 RAs (0 versus 1.0%; $P < 0.01$) than in those who had severe obesity (BMI 35.0 to 39.9). No significant differences were observed in surgical complications at 2 years.
Magaldi et al., 2024 [20]	*JAAOS: Global Research and Reviews*	Single institution	66	Patients who had a GLP-1 RA listed on their preoperative medication list	Patients without a GLP-1 RA listed on their preoperative medication list	None	Covariate matching by sex, age, and BMI (1:2)	THA	90 day, 6 months, 1 year	The GLP-1 cohort experienced a markedly higher rate of inpatient postoperative nausea and vomiting (18.2 versus 6.0%, $P = 0.011$). Although more patients taking GLP-1 RA returned to the ED for nausea and vomiting among the GLP-1 cohort, no notable differences in ED volume were found between the two groups. Furthermore, no differences were reported in race, ethnicity, laterality, LOS, or readmissions between the two cohorts
Magruder et al., 2024 [13]	*The Journal of Arthroplasty*	PearlDiver Database	1,653	Patients who had DM and a semaglutide prescription at the time of surgery	Patients without a semaglutide prescription at the time of surgery	None	Propensity score matching by clinical characteristics	THA	90 day, 2 year	Semaglutide users exhibited lower 90-day readmission rates (6.2 versus 8.8%; OR 0.68; $P < 0.01$) and reduced PJI (1.6 versus 2.9%; OR 0.56; $P < 0.01$). However, medical complication rates, hospital stays, same-day surgical costs, and 90-day episode costs showed no significant differences.

GLP-1 RA, glucagon-like peptide-1 receptor agonist; DM, diabetes mellitus; BMI, body mass index; THA, total hip arthroplasty; TKA, total knee arthroplasty; ED, emergency department; LOS, length of stay; PJI, periprosthetic joint infection; OR, odds ratio; RR; relative risk.

worsen blood glucose control in diabetic patients and noting that the American Society of Anesthesiologist guidelines were not based on empirical data [25,26]. Further research is needed to determine the optimal timing for discontinuation, balancing potential perioperative risks with metabolic stability.

To our knowledge, beyond TKA, THA, and total shoulder arthroplasty, no studies have examined the effects of GLP-1 RAs in total ankle or total elbow arthroplasty, despite their potential relevance. This gap in research is particularly notable for total ankle arthroplasty, as the ankle is weight-bearing but biomechanically distinct from the hip and knee. Additionally, emerging orthopaedic studies have explored GLP-1 RA effects in other surgical contexts. A 2024 study on single-level posterior lumbar fusion found that semaglutide use was associated with fewer postoperative complications [27]. Another study on tibiotalar and subtalar fusion reported increased postoperative infection rates among GLP-1 RA users [28]. These conflicting findings suggest that GLP-1 RAs may have variable effects depending on the type of surgery, underscoring the need for further research into their role in orthopaedic outcomes. Moreover, evidence indicates that GLP-1 RAs influence fracture healing and bone metabolism, potentially affecting implant integration and surgical recovery. Current research remains inconclusive, highlighting the need for further study into broader musculoskeletal effects [29,30].

Potential Limitations

This study has potential limitations, the most notable being the quality of the included studies. All seven studies were published within the past two years, with six relying on national databases that often lack detailed clinical information [31]. There were five studies that utilized TriNetX, a clinical database derived from electronic health records, though inconsistencies in data entry and coding across individual physicians and participating institutions are recognized limitations [32]. PearlDiver, used in three studies, is an administrative database compiled from billing data and was not originally designed for clinical research, further limiting its applicability [33]. Similarly, the last study relied on two IBM MarketScan databases, which included commercial claims and Medicare supplemental data. These databases offer insights, but definitive conclusions remain difficult. The one study not based on a national database was constrained by a small sample of 66 GLP-1 users from a single institution and an inability to determine the indication for GLP-1 RA use, both acknowledged as major limitations [20]. A formal risk of bias or quality assessment was not conducted. Given the heterogeneity in data sources, study designs, and reporting quality—and the fact that six of the seven studies relied on databases with major, acknowledged limitations—such an evaluation was not pursued for the included studies.

Additionally, no study compared postoperative arthroplasty outcomes between diabetic and nondiabetic GLP-1 RA users, despite potential differences in baseline risk profiles. Likewise, none differentiated between type 1 and 2 DM among GLP-1 RA users. Given the distinct pathophysiological mechanisms, degrees of insulin dependence, and metabolic responses in these subgroups, the lack of stratification may limit the interpretation of GLP-1 RA effects on arthroplasty outcomes.

Another potential limitation involves follow-up duration. Although two years is typically recommended for assessing surgical outcomes, only four studies included this duration [34]. Furthermore, none of the studies provided definitive explanations for the biologic mechanisms underlying the observed effects of GLP-1 RAs, further limiting causal interpretations.

Conclusions

Overall, as GLP-1 RA use expands in both diabetic and nondiabetic patients—with usage rising over 700% among nondiabetics in the past four years—further research is urgently needed to clarify their impact on arthroplasty outcomes [22]. The GLP-1 RAs may improve TKA and THA outcomes through weight loss, glycemic control, and reduced inflammation, but findings remain inconsistent. High-level evidence, such as randomized controlled trials and multicenter prospective studies, is needed to better define their role. The GLP-1 RAs should be carefully considered in surgical planning, with close monitoring.

CRediT authorship contribution statement

Vincent Lee: Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Stephen M. Durkee:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Brent A. Ponce:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Nino Coutelle:** Writing – review & editing, Investigation. **Paul Gerges:** Writing – original draft, Visualization, Data curation, Conceptualization. **Diego Lima:** Writing – review & editing, Supervision.

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