

Preoperative GLP-1 Receptor Agonist Use and Total Knee Arthroplasty Outcomes: A Matched Cohort Study

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INTRODUCTION: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used for weight management, a key concern in total knee arthroplasty (TKA). While GLP-1 RAs show promise, their consistent usage has unclear impact on perioperative and long-term outcomes. This study investigates the association between consistent preoperative GLP-1 RA use and postoperative primary TKA outcomes assessed at 90 days, 1, 2, and 5 years.

METHODS: This retrospective study utilized TriNetX (multicenter database) to identify adult patients undergoing primary TKA from 2005-2023 with consistent preoperative GLP-1 RA exposure (≥ 3 prescriptions within 1 year of surgery) versus controls with no exposure, with minimum 2-year follow-up. 1:1 propensity score matching balanced for demographics, comorbidities, and baseline labs. Outcomes included 90-days medical complications (perioperative pulmonary aspiration, sepsis, venous thromboembolism, myocardial infarction, mortality, renal failure) and surgical complications (periprosthetic joint infection (PJI), periprosthetic fracture, aseptic loosening, all-cause revisions) evaluated 1, 2, and 5 years. Statistical analyses were performed to calculate risk ratios (RR) and Kaplan-Meier survivorship curves.

RESULTS: 2,895 matched patients were included in each cohort. At 90 days, the GLP-1 RA cohort had significantly decreased risks of readmission (RR 0.765, $p=0.002$) and PJI (RR 0.618, $p=0.008$). Reduced PJI risk was also observed at 1-year (RR 0.67, $p=0.008$). No statistically significant differences were observed in other evaluated 90-day medical complications including aspiration pneumonia; no significant differences were found for risk of aseptic loosening, periprosthetic fracture, and all-cause revision at 1, 2, and 5 years.

DISCUSSION AND CONCLUSION: Consistent preoperative GLP-1 RA use in patients undergoing TKA is associated with a significantly reduced risk of 90-day hospital readmission and PJI, with the PJI benefit extending to 1-year. This use did not show an increased risk of other short-term complications or adverse mechanical outcomes up to 5 years postoperatively. These findings suggest that GLP-1 RAs may not confer additional risks, and may offer protective benefits, particularly against PJI within 1 year of surgery.

Table I: 90-Day Postoperative Outcomes in GLP-1 RA-TKA vs Control-TKA

| Outcome | % of Outcomes in GLP-1 RA | % of Outcomes in Control | Risk Ratio (RR) | 95% Confidence Interval (CI) | P-value |
|--------------------------------|---------------------------|--------------------------|-----------------|------------------------------|--------------|
| Hospital Readmission | 7.3% | 9.6% | 0.765 | (0.645, 0.908) | 0.002 |
| Periprosthetic Joint Infection | 1.6% | 2.6% | 0.618 | (0.431, 0.886) | 0.008 |
| Renal Failure | 4.4% | 4.9% | 0.895 | (0.709, 1.130) | 0.351 |
| Sepsis | 1.0% | 1.0% | 1.000 | (0.594, 1.684) | 1.000 |
| Deep Vein Thrombosis | 2.3% | 2.6% | 0.882 | (0.637, 1.219) | 0.446 |
| Myocardial Infarction | 0.6% | 0.9% | 0.630 | (0.344, 1.153) | 0.130 |
| Pulmonary Aspiration | 0.3% | 0.3% | 1.000 | (0.417, 2.399) | 1.000 |
| Mortality | 0.3% | 0.3% | 1.000 | (0.417, 2.399) | 1.000 |

Table II: 1-Year and 2-Year Implant-Related Outcomes in GLP-1 RA-TKA vs Control-TKA

| Outcome | 1-Year | | | | 2-Year | | | |
|--------------------------------|----------|----------|-------|--------------|----------|----------|-------|---------|
| | %GLP-1RA | %Control | RR | P-value | %GLP-1RA | %Control | RR | P-value |
| Periprosthetic Joint Infection | 2.4% | 3.6% | 0.670 | 0.008 | 3.2% | 4.1% | 0.783 | 0.070 |
| Revision | 1.4% | 1.5% | 0.953 | 0.826 | 2.6% | 2.3% | 1.136 | 0.443 |
| Aseptic Loosening | 0.8% | 0.8% | 0.957 | 0.881 | 1.2% | 1.0% | 1.200 | 0.458 |
| Periprosthetic Fx | 0.4% | 0.4% | 1.091 | 0.835 | 0.6% | 0.6% | 1.000 | 1.000 |

Table III: 5-Year Kaplan-Meier Survival Analysis Summary

| Outcome | Group | Patients with Outcome | Survival Probability at 5 Years | Log-Rank Test (p-value) |
|--------------------------------|----------|-----------------------|---------------------------------|-------------------------|
| All-Cause Revision TKA | GLP-1 RA | 127 | 94.6% | 0.103 |
| | Control | 109 | 95.8% | |
| Periprosthetic Joint Infection | GLP-1 RA | 128 | 94.9% | 0.629 |
| | Control | 140 | 94.8% | |
| Aseptic Loosening | GLP-1 RA | 72 | 96.8% | 0.118 |
| | Control | 59 | 97.7% | |
| Periprosthetic Fracture | GLP-1 RA | 30 | 98.7% | 0.259 |
| | Control | 42 | 98.3% | |