Comparison of Postoperative Outcomes Between Semaglutide and Tirzepatide in Patients Undergoing Total Hip Arthroplasty: A Propensity Score-Matched Cohort Study

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INTRODUCTION: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are widely used for glycemic control and weight reduction in patients with type 2 diabetes mellitus (T2DM). Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA, has demonstrated greater weight loss and improved glycemic control compared to Semaglutide in recent clinical trials. These pharmacologic differences may influence perioperative outcomes in orthopedic procedures such as total hip arthroplasty (THA), where obesity, metabolic status, and frailty are known risk factors for complications. Prior studies suggest GLP-1 RA use may reduce postoperative risk in joint arthroplasty, but no study has directly compared outcomes between Semaglutide and Tirzepatide in patients undergoing THA. We hypothesized that Tirzepatide users would have similar or potentially improved short-term complication profiles compared to Semaglutide users.

METHODS: We conducted a retrospective cohort study using the TriNetX research network, a federated electronic health record database. Adults with T2DM who underwent primary THA between June 1, 2022, and December 31, 2024, and had an active prescription for either Semaglutide or Tirzepatide within 90 days before surgery were included. Patients with dual GLP-1 RA use or type 1 diabetes were excluded. Propensity score matching (1:1) was performed based on age, sex, race, BMI, HbA1c, comorbidity burden, and concurrent diabetes medication use, yielding 206 matched pairs. Outcomes assessed included 90-day medical complications, 180-day surgical complications, and healthcare utilization. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression.

RESULTS: No significant differences were observed in 90-day medical complications (OR 0.929, 95% CI 0.545-1.583, *P* = 0.786) or 180-day surgical complications (OR 1.000, 95% CI 0.407-2.456, *P* = 1.000) between groups. Individual outcomes, including myocardial infarction, stroke, pneumonia, sepsis, pulmonary embolism, deep vein thrombosis, acute kidney injury (OR 0.825, 95% CI 0.348-1.954, *P* = 0.661), urinary tract infection (OR 0.918, 95% CI 0.409-2.063, *P* = 0.837), surgical site infection, periprosthetic joint infection, revision surgery, and dislocation, were statistically similar (all *P* > 0.05). Emergency department visits and hospital readmissions at 90 (OR 0.781, 95% CI 0.493-1.238, *P* = 0.292) and 180 days (OR 0.790, 95% CI 0.516-1.210, *P* = 0.278) also did not differ. Several outcomes had low event counts, resulting in wide confidence intervals and ORs of 1.000.

DISCUSSION AND CONCLUSION:

In this propensity-matched analysis of T2DM patients undergoing THA, Semaglutide and Tirzepatide demonstrated comparable short-term postoperative safety profiles. Despite pharmacologic differences, both agents appear equally safe for perioperative use. Further study is warranted to assess longer-term outcomes and patient-reported measures of recovery and function.

Table 1. Demographic and clinical characteristics of patients undergoing total hip arthroplasty who were prescribed semaglutide or tirzepatide.

	Before PSM, Mean ± SD or No. (%)			After PSM, Mean ± SD or No. (%)		
	Semaglutide (N=696)	Tirzepatide (N=214)	*P* Value	Semaglutide (N=206)	Tirzepatide (N=206)	*P* Value
Age	64.3 ± 9.0	63.8 ± 8.7	0.501	64.2 ± 8.5	63.8 ± 8.6	0.631
Race						
White	510 (73.3)	160 (74.8)	0.665	164 (79.6)	156 (75.7)	0.344
Black or African American	121 (17.4)	29 (13.6)	0.186	26 (12.6)	29 (14.1)	0.664
Asian	10 (1.4)	10 (4.7)	0.005	10 (4.9)	10 (4.9)	>0.999
Native Hawaiian or Other Pacific Islander	10 (1.4)	0 (0.0)	0.078	0 (0.0)	0 (0.0)	>0.999
American Indian or Alaska Native	10 (1.4)	0 (0.0)	0.078	0 (0.0)	0 (0.0)	>0.999
Other Race	12 (1.9)	10 (4.7)	0.022	10 (4.9)	10 (4.9)	>0.999
Unknown Race	33 (4.7)	19 (8.9)	0.023	10 (4.9)	15 (7.3)	0.302
Sex						
Male	283 (40.7)	88 (41.1)	0.905	87 (42.2)	85 (41.3)	0.842
Female	394 (56.6)	111 (51.9)	0.222	113 (54.9)	110 (53.4)	0.767
Unknown	19 (2.7)	15 (7.0)	0.004	10 (4.9)	11 (5.3)	0.823
Medical Comorbidities						
Hypertension	531 (76.3)	167 (78.0)	0.598	164 (79.6)	162 (78.6)	0.808
Chronic Ischemic Heart Disease	131 (18.8)	32 (15.0)	0.197	37 (18.0)	32 (15.5)	0.509
Heart Failure	81 (11.6)	18 (8.4)	0.185	15 (7.3)	18 (8.7)	0.586
CKD	107 (15.4)	36 (16.8)	0.611	37 (18.0)	34 (16.5)	0.696
Acute Kidney Failure	33 (4.7)	11 (5.1)	0.812	13 (6.3)	11 (5.3)	0.674
Cerebral Infarction	10 (1.4)	10 (4.7)	0.005	0 (0.0)	10 (4.9)	0.001
Atherosclerosis	21 (3.0)	10 (4.7)	0.243	10 (4.9)	10 (4.9)	>0.999
COPD	44 (6.3)	13 (6.1)	0.896	17 (8.3)	12 (5.8)	0.336
Asthma	99 (14.2)	26 (12.1)	0.441	24 (11.7)	26 (12.6)	0.763
Nicotine Dependence	121 (17.4)	27 (12.6)	0.098	31 (15.0)	27 (13.1)	0.571
Mood (Affective) Disorders	178 (25.6)	57 (26.6)	0.756	58 (28.2)	56 (27.2)	0.826
Metformin Use	299 (43.0)	88 (41.1)	0.634	89 (43.2)	86 (41.7)	0.765
Insulin Use	213 (30.6)	58 (27.1)	0.327	62 (30.1)	57 (27.7)	0.587
Laboratory Investigations						
Average BMI (kg/m²)	35.3 ± 6.3	34.9 ± 5.9	0.401	35.0 ± 6.4	34.9 ± 6.0	0.925
Average HbA1c (%)	6.4 ± 0.9	6.2 ± 0.9	0.031	6.4 ± 0.9	6.2 ± 0.9	0.014

BMI = Body Mass Index; *CKD* = Chronic Kidney Disease; *COPD* = Chronic Obstructive Pulmonary Disease; *GLP-1* = Glucagon-Like Peptide 1; HbA_{1c} = Glycated Hemoglobin; *PSM* = Propensity Score Matching; *SD* = Standard Deviation