Association Between Semaglutide Use in Patients with Type 2 Diabetes or Significant Adiposity and the Incidence of Osteoarthritis and Total Joint Arthroplasty

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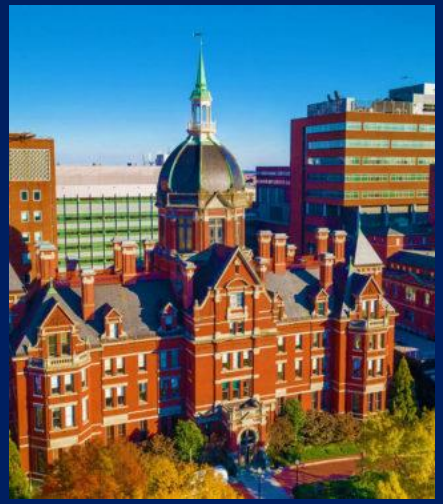

Disclosures

- Dr. Weber:
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  - Editorial or Governing board of Archives of Orthopaedic And Trauma Surgery, Arthroscopy, Journal of Shoulder and Elbow Surgery, SLACK Incorporated
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Introduction

- The rising prevalence of diabetes and obesity highlights the importance of understanding the musculoskeletal effects of anti-obesity medications.[1]

- Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), is widely used for glucose regulation and weight loss.[2]

Introduction

- Type 2 diabetes mellitus (T2DM) and obesity are associated with higher risks of osteoarthritis (OA) and adverse orthopaedic outcomes, including joint replacement and complications.[3]

- Existing literature suggests semaglutide may improve metabolic health, but its impact on musculoskeletal outcomes remains unclear.[4,5]

Objective

- Compare first-year musculoskeletal outcomes in patients with T2DM or obesity treated with semaglutide versus non-GLP-1 diabetes medications.

Materials and Methods

- **Study Design**: Retrospective cohort study using the TriNetX US Research Network.

- **Patient Selection:**
  - Included patients with T2DM or obesity newly prescribed semaglutide or non-GLP-1 RA between 2017-2023.
  - Excluded patients with prior osteoarthritis, bariatric surgery, or use of other antidiabetic medications.

Materials and Methods

- **Subgroup Formation:**
  - T2DM patients: Semaglutide users vs. non-GLP-1 RA users.
  - Obese patients: Semaglutide users vs. non-GLP-1 RA users.

Materials and Methods

- **Statistical Analysis:**
  - Propensity score matching (1:1) to control for baseline differences.
  - Outcomes analyzed using Student t-tests and chi-square tests with significance set at $p < 0.05$.

Results

- **Diabetes Cohort:**
  - 541,803 total patients (Semaglutide: 8,566; Non-GLP-1 RA: 533,237); after propensity score matching, 8,565 per cohort.
- **Obesity Cohort:**
  - 71,466 total patients (Semaglutide: 21,055; Non-GLP-1 RA: 50,411); after matching, 20,549 per cohort.

- **Demographics (After Matching, Both Cohorts):** No significant imbalance in age, gender, race, BMI, or comorbidities between cohorts.

Table 1: Matched Outcomes For Patients With Type 2 Diabetes Mellitus After Initial Prescriptions For Semaglutide Or Non-glp-1 RA

	Diabetes-Semaglutide Cohort: N(%)	Diabetes-Non-GLP-1 Cohort: N(%)	P-Value	Risk Ratio (95% CI)
BMI ≥ 30	4903 (57.2)	3812 (44.5)	**<.0001**	1.3 (1.2–1.3)
Duration of follow-up, d	322 ± 106[†]	259 ± 155[†]	**<.0001**	
Death	93 (1.1)	264 (3.1)	**<.0001**	0.4 (0.3–0.4)
New-onset joint pain	1349 (15.8)	591 (6.9)	**<.0001**	2.3 (2.1–2.5)
New-onset osteoarthritis				
Shoulder	52 (0.6)	49 (0.6)	.76	1.1 (0.7–1.6)
Hip	77 (0.9)	49 (0.6)	**.01**	1.6 (1.1–2.2)
Knee	210 (2.5)	146 (1.7)	**<.001**	1.4 (1.2–1.8)
Arthroplasty				
Total shoulder	10 (0.1)	10 (0.1)	>.99	1.0 (0.4–2.4)
Reverse total shoulder	10 (0.1)	10 (0.1)	>.99	1.0 (0.4–2.4)
Total knee	15 (0.2)	10 (0.1)	.32	1.5 (0.7–3.3)
Total hip	10 (0.1)	10 (0.1)	>.99	1.0 (0.4–2.4)

Table 2: Matched Outcomes For Patients With Obesity After Initial Prescriptions For Semaglutide Or Non-glp-1 RA

	Obese-Semaglutide Cohort: N(%)	Obese-Non-GLP-1 Cohort: N(%)	P-Value	Risk Ratio (95% CI)
BMI ≥ 30	14,228 (69.2)	15,004 (73.0)	**<.0001**	1.0 (0.9–1.0)
Duration of follow-up, d	294 ± 113[†]	250 ± 145[†]	**<.0001**	
Death	54 (0.3)	243 (1.2)	**<.0001**	0.2 (0.2–0.3)
New-onset joint pain	1599 (7.8)	1420 (6.9)	**<.0001**	1.3 (1.2–1.4)
New-onset osteoarthritis				
Shoulder	87 (0.4)	89 (0.4)	.88	1.0 (0.7–1.3)
Hip	112 (0.5)	135 (0.7)	.14	0.8 (0.7–1.1)
Knee	503 (2.4)	444 (2.2)	**.05**	1.1 (1.0–1.3)
Arthroplasty				
Total shoulder	0 (0)	11 (0.1)	**<.001**	
Reverse total shoulder	0 (0)	10 (0.1)	**.002**	
Total knee	17 (0.1)	43 (0.2)	**<.001**	0.4 (0.2–0.7)
Total hip	12 (0.1)	22 (0.3)	.09	0.6 (0.3–1.1)

Discussion/Conclusion

- Findings challenge the assumption that semaglutide may protect against OA and reduce joint replacement needs.
- Further research is needed to clarify the musculoskeletal effects of semaglutide, particularly its impact on joint pain and OA progression.
- Longer follow-up studies to assess the long-term impact of semaglutide on musculoskeletal health.

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