Preoperative GLP-1 Receptor Agonist Exposure Is Associated With Increased Risk of Repeat Flexor Tendon Sheath Tenolysis and Diagnosis in Diabetic Patients: A Propensity-Matched Cohort Study

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INTRODUCTION: Stenosing flexor tenosynovitis, commonly known as trigger finger, disproportionately affects individuals with type 2 diabetes mellitus (T2DM), often necessitating surgical intervention via flexor tendon sheath tenolysis. While glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used for glycemic control and possess anti-inflammatory properties in cardiovascular and metabolic tissues, their role in tendon remodeling and fibroproliferative pathology remains unclear. This study evaluates whether GLP-1 RA exposure prior to tenolysis is associated with increased risk of subsequent trigger finger recurrence, both surgically and diagnostically, in diabetic patients.

METHODS: A retrospective cohort study was performed evaluating adult patients with T2DM who underwent flexor tendon sheath tenolysis (CPT 26055) between 2003 and 2023. Patients were stratified by GLP-1 RA use within the 12 months preceding surgery. Eligible agents included liraglutide, semaglutide, dulaglutide, exenatide, albiglutide, and lixisenatide. Individuals were excluded if they underwent additional hand procedures or had a diagnosis of trigger finger within 30 days postoperatively to eliminate early treatment failure. Propensity score matching (1:1) was performed based on age, sex, race, body mass index, hemoglobin A1c, hypertension, obesity, chronic kidney disease, heart failure, and concurrent metformin use. Primary outcomes were defined as (1) repeat flexor tendon sheath tenolysis and (2) repeat diagnosis of trigger finger (ICD-10-CM M65.3) within three years. Kaplan-Meier analysis and Cox proportional hazards modeling were used to estimate hazard ratios (HR) with 95% confidence intervals (CI).

RESULTS: Among 1,213 GLP-1 RA users and 18,630 non-users identified, 1,180 patients per group were successfully matched with standardized mean differences <0.1 across all covariates. At three-year follow-up, GLP-1 RA users demonstrated significantly higher rates of repeat surgery (25.0% vs 13.6%; HR 2.06, 95% CI 1.71–2.49; p<0.001) and repeat diagnosis (41.6% vs 29.8%; HR 1.61, 95% CI 1.41–1.85; p<0.001). Risk differences for surgery and diagnosis were 11.4% and 11.8%, respectively. Dulaglutide (22.9%) and semaglutide (17.4%) were the most commonly prescribed agents among the exposed group. No significant differences in baseline HbA1c, BMI, or insulin use were observed after matching.

DISCUSSION AND CONCLUSION: Preoperative exposure to GLP-1 receptor agonists was independently associated with increased three-year risk of both repeat flexor tendon sheath tenolysis and recurrent trigger finger diagnosis in diabetic patients. These findings contradict assumptions that GLP-1 RAs confer general anti-inflammatory benefit across tissues and suggest the need for further investigation into their effects on tendon homeostasis and fibroproliferative signaling pathways. Hand surgeons should consider GLP-1 RA exposure as a potential risk factor when counseling diabetic patients undergoing tenolysis.

Table 1. Baseline Demographic and Clinical Characteristics Before and After Propensity Matching

Characteristic	Tendon Sheath Incision + GLP-1-RA Use Unmatched (N = 1,213)	Tendon Sheath Incision with No GLP-1-RA Use Unmatched (N = 18,630)	P-Value (Unmatched)	Tendon Sheath Incision + GLP-1-RA Use Matched (N = 1,206)	Tendon Sheath Incision with No GLP-1-RA Use Matched (N = 1,206)	P-Value (Matched)
Age at Index (mean ± SD)	60.3 ± 10.0	63.8 ± 11.6	<0.001	60.2 ± 10.0	60.0 ± 12.0	0.602
Female (%)	66.40%	63.60%	0.049	66.30%	66.50%	0.896
Male (%)	30.20%	32.70%	0.072	30.30%	30.30%	0.964
White (%)	66.40%	68.70%	0.102	66.80%	68.70%	0.311
Black or African American (%)	17.50%	15.50%	0.059	16.90%	16.50%	0.783
Asian (%)	2.00%	3.90%	0.001	1.90%	1.50%	0.431
Other Race (%)	2.60%	2.60%	0.941	2.60%	2.50%	0.794
Hispanic or Latino (%)	11.40%	10.20%	0.186	11.40%	8.70%	0.034
Not Hispanic or Latino (%)	70.00%	69.90%	0.944	69.60%	74.40%	0.009
Overweight and Obesity (%)	38.50%	22.50%	<0.001	38.50%	37.80%	0.735
Diabetes Mellitus (%)	81.00%	65.10%	<0.001	81.00%	79.20%	0.279
Hypertensive Diseases (%)	67.40%	57.90%	<0.001	67.30%	68.10%	0.692
Heart Failure (%)	6.50%	7.00%	0.517	6.40%	5.80%	0.548
Chronic Kidney Disease (%)	2.30%	1.40%	0.013	2.40%	3.20%	0.212
BMI (mean ± SD)	35.5 ± 7.4	32.4 ± 7.0	<0.001	35.5 ± 7.4	35.1 ± 7.5	0.311
HbA1c (mean ± SD)	7.6 ± 1.7	7.0 ± 1.5	<0.001	7.6 ± 1.7	7.5 ± 1.6	0.111
Metformin Use (%)	0.412	0.231	<0.001	0.409	0.383	0.192

Table 2. Distribution of GLP-1 RA Agents Among Treated Patients (N = 1,213)

GLP-1 RA Agent	Tendon Sheath Incision + GLP-1-RA Use (N = 1,213)
Any GLP-1 RA	53.2% (645 patients)
Lixisenatide	0.8% (10 patients)
Albiglutide	0.8% (10 patients)
Dulaglutide	22.9% (278 patients)
Semaglutide	17.4% (211 patients)
Liraglutide	13.0% (158 patients)
Exenatide	4.7% (57 patients)

Table 3. Three-Year Risk of Surgical and Diagnostic Recurrence After Flexor Tendon Sheath Tenolysis

Outcome	TFS + GLP (N = 1,180)	TFS Never GLP (N = 1,180)	Risk Difference	Risk Ratio	Odds Ratio	P-Value
Repeat Trigger Finger Surgery (Tendon Sheath Incision)	295 patients (25.0%)	161 patients (13.6%)	11.4% (95% CI: 8.2%, 14.5%)	1.83 (95% CI: 1.54–2.18)	2.11 (95% CI: 1.71–2.61)	< 0.001
Repeat Trigger Finger Diagnosis	491 patients (41.6%)	352 patients (29.8%)	11.8% (95% CI: 7.9%, 15.6%)	1.40 (95% CI: 1.25–1.56)	1.68 (95% CI: 1.42–1.99)	< 0.001