Increased Tendon Rupture Risk in GLP-1 Receptor Agonist Users: A Five-Year Cohort Study With Obese and Diabetic Subgroup Analysis

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INTRODUCTION: The use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has increased significantly in the treatment of type 2 diabetes and obesity, owing to their effectiveness in improving glycemic control and promoting weight loss. However, emerging research suggests a potential association between GLP-1 RA use and an increased risk of tendon injuries.

METHODS:

A retrospective cohort study was conducted using a large, multi-institutional electronic health record database. Adults prescribed GLP-1 receptor agonists were matched 1:1 to non-users (n = 72,691 per group) using propensity scores based on age, sex, body mass index (BMI), race, and diabetes status. To ensure consistency and minimize bias, only patients with at least five years of continuous follow-up were included, and those with a documented history of tendon rupture prior to the index date were excluded. After matching, baseline demographic and clinical characteristics were well-balanced between groups. The five-year incidence of ten specific tendon rupture types was assessed, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to compare risk between cohorts. Pre-specified subgroup analyses were conducted to evaluate rupture risk in patients with obesity (defined as BMI >30) and those with type 2 diabetes

RESULTS: In patients with obesity, GLP-1 receptor agonist use was associated with a significantly increased risk of several major tendon ruptures. The incidence of rotator cuff rupture was higher in the GLP-1 group compared to controls (2.69% vs. 1.72%; HR 1.48, 95% CI: 1.38–1.59; $p < 0.0001$). The risk of Achilles tendon rupture was also elevated (0.24% vs. 0.16%; HR 1.403, 95% CI: 1.11–1.77; $p = 0.004$), as was the risk of pectoralis major tendon rupture (0.80% vs. 0.57%; HR 1.34, 95% CI: 1.18–1.52; $p = 0.0002$). No statistically significant differences were observed between groups for other tendon rupture types, including the quadriceps, biceps, flexor, patellar, triceps, anterior tibial, and peroneal tendons

DISCUSSION AND CONCLUSION:

This study identifies a significant association between GLP-1 receptor agonist therapy and an increased risk of specific tendon ruptures, most notably involving the rotator cuff, Achilles tendon, and pectoralis major tendon. These findings raise concern for a potential adverse musculoskeletal effect associated with GLP-1 RA use, particularly in patients with obesity. Possible contributing mechanisms may include rapid weight loss, associated muscle atrophy, and nutritional deficiencies—especially protein or micronutrient insufficiency that could compromise tendon integrity. Further research is needed to clarify causality and underlying pathophysiology. Clinicians should maintain a high index of suspicion for tendon-related complications in patients receiving GLP-1 receptor agonists, particularly those undergoing significant changes in body composition.

Table 1: Baseline Demographic and Clinical Characteristics Before and After Propensity Score Matching Between GLP-1 Receptor Agonist Users and Non-Users

Variable	Pre-Match Cohort 1 (N = 72,691)	Pre-Match Cohort 2 (N = 72,691)	Pre-Match P-Value	Post-Match Cohort 1 (N = 72,691)	Post-Match Cohort 2 (N = 72,691)	Post-Match P-Value
Age at Index	54.3 ± 13.2	54.6 ± 13.0	0.002	54.6 ± 12.9	54.6 ± 13.0	0.847
Male	27,100 (37.3%)	26,678 (36.7%)	0.04	26,620 (36.6%)	26,678 (36.7%)	0.752
Female	39,100 (53.8%)	39,761 (54.7%)	0.036	39,774 (54.7%)	39,761 (54.7%)	0.945
White	42,002 (57.8%)	43,193 (59.4%)	0.015	43,112 (59.3%)	43,193 (59.4%)	0.665
Black	14,600 (20.1%)	13,775 (19.0%)	0.007	13,768 (18.9%)	13,775 (19.0%)	0.963
Unknown Race	12,400 (17.1%)	11,666 (16.0%)	0.088	11,630 (16.0%)	11,666 (16.0%)	0.797
Hispanic	5,600 (7.7%)	6,195 (8.5%)	0.022	6,203 (8.5%)	6,195 (8.5%)	0.94
Other Race	3,000 (4.1%)	2,682 (3.7%)	0.05	2,714 (3.7%)	2,682 (3.7%)	0.657
Asian	850 (1.2%)	897 (1.2%)	0.082	938 (1.3%)	897 (1.2%)	0.335
American Indian	310 (0.4%)	360 (0.5%)	0.044	376 (0.5%)	360 (0.5%)	0.554
Native Hawaiian	100 (0.1%)	118 (0.2%)	0.026	153 (0.2%)	118 (0.2%)	0.033
Diabetes Mellitus	37,200 (51.2%)	36,577 (50.3%)	<0.001	36,573 (50.3%)	36,577 (50.3%)	0.983
BMI	38.0 ± 7.7	37.1 ± 7.3	<0.001	37.6 ± 7.5	37.1 ± 7.3	<0.001

Table 2: Five-Year Hazard Ratio and Incidence of Tendon Tears in Obese Patients that Received GLP-1-RA (Cohort 1) Agonists and Patients with no GLP-1-RA Use (Cohort 2)

Tendon Rupture	GLP Incidence	Non-GLP Incidence	Hazard Ratio	95% CI	p-value
Achilles Tendon Rupture	0.24%	0.16%	1.403	1.113–1.767	0.004
Triceps Tendon Rupture	0%	0%	1.359	0.517–3.571	0.519
Biceps Tendon Rupture	0%	0%	1.836	0.336–10.026	0.213
Patellar Tendon Rupture	0%	0%	0.616	0.219–1.730	0.347
Quadriceps Tendon Rupture	0.18%	0.13%	1.264	0.969–1.649	0.086
Anterior Tibial Tendon Rupture	0%	0%	1.327	0.59–2.99	0.479
Flexor Tendon Rupture	0%	0%	3.173	0.87–11.53	0.107
Rotator Cuff Rupture	2.69%	1.72%	1.481	1.379–1.590	0.0001
Peroneal Tendon Rupture	0.12%	0.11%	1.071	0.787–1.458	0.629
Pectoralis Major Tendon Rupture	0.80%	0.57%	1.336	1.178–1.516	0.0002

Table 3: Five-Year Analysis of Tendon Tears in **Diabetic, Obese Patients** that Received GLP-1-RA (Cohort 1) Agonists and Patients with no GLP-1-RA Use (Cohort 2)

Tendon Rupture Outcome	GLP-1 Users (Diabetes + BMI > 30) Incidence	Non-GLP-1 Users (Diabetes + BMI > 30) Incidence	Hazard Ratio (HR)	95% Confidence Interval	Log-Rank p-value
Achilles Tendon Rupture	0.24%	0.19%	1.246	0.920–1.687	0.154
Quadriceps Tendon Rupture	0.20%	0.14%	1.322	0.931–1.878	0.118
Rotator Cuff Rupture	2.87%	1.84%	1.46	1.328–1.605	0.001
Peroneal Tendon Rupture	0.11%	0.06%	1.82	1.088–3.042	0.021
Pectoralis Major Tendon Rupture	0.83%	0.61%	1.269	1.071–1.503	0.006