The Effect of GLP-1 Receptor Agonists on Bone Mineral Density in the Lumbar Spine

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INTRODUCTION: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly prescribed for type 2 diabetes and obesity, with recent data suggesting neutral or modestly beneficial skeletal effects. Large, randomized trials and meta-analyses have reported small but statistically significant improvements in lumbar spine bone mineral density (BMD), as measured by dual-energy X-ray absorptiometry (DXA), without an increased fracture risk. However, the magnitude of BMD change is modest, and the clinical significance in populations experiencing weight loss remains unclear. Computed tomography (CT) Hounsfield units (HU) represent an opportunistic and validated measure of bone quality that strongly correlates with DXA-derived BMD. However, no study has investigated lumbar spine density in patients on GLP-1 therapy using both CT HU and DXA. The objective of this study was to evaluate longitudinal changes in lumbar spine density before and after initiation of GLP-1 using complementary imaging modalities in a large retrospective cohort.

METHODS: After Institutional Review Board approval, a retrospective cohort study was conducted of adult patients prescribed GLP-1 receptor agonists at a tertiary academic medical center between 2018 and 2024. Patients with lumbar spine imaging (CT and/or DXA) available both prior to GLP-1 initiation (pre-GLP) and approximately 1–2 years following initiation (post-GLP) were included. Exclusion criteria included spinal hardware or imaging artifacts that precluded measurement. Lumbar density was quantified using mean CT Hounsfield units (HU) at L1–L5 using a standardized 1 cm² mid-vertebral region of interest protocol under musculoskeletal radiologist supervision, and DXA-derived T-scores at L1–L4. CT analyses were performed as unpaired (independent pre- vs. post-GLP scans) and paired (patients with imaging in both windows). Outlier values reflecting poor image quality were excluded. Analyses were stratified by sex, and comparisons used parametric or nonparametric tests according to distributional assumptions. A p-value < 0.05 was considered statistically significant.

RESULTS: A total of 304 patients contributed CT scans for the unpaired analysis (168 females, 136 males). Pre-GLP scans were obtained a median of 104 days prior to GLP-1 initiation, and post-GLP scans were performed at 477 days. In females, the L1-L5 composite HU declined from 157.5 ± 40.7 to 147.7 ± 42.8 (Δ = -9.8 HU, p = 0.224), with nonsignificant decreases at each level. In males, the composite decreased from 157.3 ± 40.6 to 150.6 ± 37.5 (Δ = -6.7 HU, p = 0.425), with the largest nonsignificant reductions at L4 (Δ = -11.5 HU) and L5 (Δ = -10.5 HU). In the paired CT cohort (n = 28; 16 females, 12 males), the median time intervals between pre- and post-GLP scans were -143 and +497 days, respectively. Females demonstrated nonsignificant reductions in the L1-L5 composite (Δ = -3.1 HU, p = 0.638). Males demonstrated larger decreases (166.2 ± 34.1 to 151.4 ± 36.5, Δ = -14.8 HU, p = 0.078), with significant reductions at L4 (Δ = -23.1 HU, p = 0.008) and L5 (Δ = -27.7 HU, p = 0.044). In the DXA cohort (n = 22 females), pre- and post-GLP scans were performed at a median of -122 and +451 days, respectively. Post-GLP mean T-scores increased modestly at L1 (+0.26), L2 (+0.66), L3 (+0.53), and the L1-L4 composite (+0.36), though none reached statistical significance (all p > 0.5). Overall, GLP-1 initiation was associated with nonsignificant HU declines in unpaired analyses, significant HU reductions at L4-L5 in paired male patients, and modest nonsignificant T-score improvements in females by DXA.

DISCUSSION: To our knowledge, this is the most extensive study to date evaluating the effect of GLP-1 receptor agonist therapy on lumbar spine bone density using both CT Hounsfield units and DXA. Unpaired analyses demonstrated consistent but nonsignificant declines in vertebral HU in both sexes, while paired analyses identified significant reductions at L4-L5 in males. In contrast, DXA analysis in females demonstrated modest, nonsignificant improvements in lumbar T-scores. The magnitude of HU decline in males at the lower lumbar spine exceeded the expected age-related loss of 0.4-1.2% per year reported in longitudinal studies, suggesting a possible site- and sex-specific effect of GLP-1 therapy. Conversely, the small gains in DXA-derived T-scores in females compared favorably with the typical annual decline observed in postmenopausal women, aligning with prior meta-analyses that report neutral or modestly favorable skeletal effects of GLP-1 therapy. Taken together, these findings support the complementary use of CT and DXA in characterizing nuanced skeletal changes in this population.

SIGNIFICANCE/CLINICAL RELEVANCE: GLP-1 receptor agonists are rapidly expanding in use for the treatment of diabetes and obesity. Our findings highlight potential sex- and site-specific skeletal effects, including significant HU reductions in the lower lumbar spine of male patients and modest improvements in DXA in females. These results underscore the importance of longitudinal bone health monitoring in patients receiving GLP-1 therapy and support the complementary use of CT and DXA in assessing bone quality in this growing population.

TABLES:

Table 1. Unpaired CT HU analysis of lumbar vertebrae before and after GLP-1 initiation.

Sex	Level	n	Pre-GLP	Post-GLP	Δ	p-value
Female	L1	63, 50	163.4	153.2	-10.2	0.199
	L2	64, 49	161.7	152.1	-9.6	0.268
	L3	63, 49	155.6	147.2	-8.4	0.323
	L4	62, 48	150.4	146.8	-3.6	0.688
	L5	47, 40	153.3	148.6	-4.7	0.649
	L1-L5	64, 48	157.5	147.7	-9.8	0.224
Male	L1	66, 33	158.9	156.7	-2.1	0.882
	L2	67, 31	155.3	157.3	2.0	0.830
	L3	65, 31	154.4	151.1	-3.2	0.736
	L4	65, 28	153.5	141.9	-11.5	0.191
	L5	47, 24	156.1	145.6	-10.5	0.351
	L1-L5	65, 32	157.3	150.6	-6.7	0.425

Table 2. Paired CT HU analysis of lumbar vertebrae before and after GLP-1 initiation.

Sex	Level	n	Pre-GLP	Post-GLP	Δ	p-value
Female	L1	16	159.0	154.8	-4.2	0.851
	L2	15	152.8	148.1	-4.7	0.523
	L3	15	140.2	139.5	-0.7	0.918
	L4	15	144.7	140.3	-4.4	0.647
	L5	12	153.6	148.4	-5.3	0.433
	L1-L5	16	147.1	144.0	-3.1	0.638
Male	L1	12	166.6	154.4	-12.1	0.136
	L2	12	172.0	154.6	-17.4	0.126
	L3	11	160.8	153.4	-7.4	0.618
	L4	**11**	**164.4**	**141.3**	**-23.1**	**0.008**
	L5	**8**	**159.8**	**132.1**	**-27.7**	**0.044**
	L1-L5	12	166.2	151.4	-14.8	0.078