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GLP-1 Receptor Agonists and Low Back Pain: A Divergent-Effects Model for Pain Medicine

Zackary T. Park, MD[1], Felix A. Zayas Rodriguez, MD[1], Yuichi Igarashi, MD[1], Justin Nguyen, MD[1], Kaivalya Deshpande, MD[1]

[1] Department of Physical Medicine and Rehabilitation, Christine E. Lynn Rehabilitation Center, University of Miami Miller School of Medicine, Miami, FL, USA

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INTRODUCTION

- Low back pain (LBP) is a leading cause of disability worldwide, and high BMI is a rising, modifiable contributor.[1]
- GLP-1 receptor agonists (GLP-1 RAs) result in about 15% (semaglutide) to 21% (tirzepatide) weight loss. Use in adults without diabetes rose approximately 700% from 2019 to 2023.[2,3]
- Pain clinicians may encounter patients with LBP, radicular pain, or functional decline during therapy. These signals are **hypothesis-generating, not causal**.
- **Working model:** divergent effects, with benefit for many and vulnerability in a susceptible subgroup.
- **Aim:** synthesize the evidence and provide pain clinicians with a practical monitoring and rehabilitation framework.

METHODS

- **Design:** focused narrative review; targeted PubMed searches (June 2026) plus selected preprint and conference-level evidence.
- **Searched:** GLP-1 RA therapy, obesity, LBP, degenerative disease and spine surgery, paraspinal muscle, lean mass, physical activity, pharmacovigilance, neurologic and nutritional mimics.
- **Synthesis:** narrative, yielding a six-pathway model and monitoring framework. No formal screening, risk-of-bias assessment, or pooling.

Evidence base by study design (strongest to weakest)

RCT	Semaglutide 2.4 mg in knee osteoarthritis (analogue)
Prospective	Pilot cohort: obesity + chronic LBP
Retrospective	Serial lumbar MRI; propensity-matched spine cohorts
FAERS	Pharmacovigilance: noncausal signals
Case reports	Neuropathy and nutritional-deficiency mimics

No GLP-1 RA RCT with a prespecified LBP outcome exists yet.

FIGURE AND TABLE

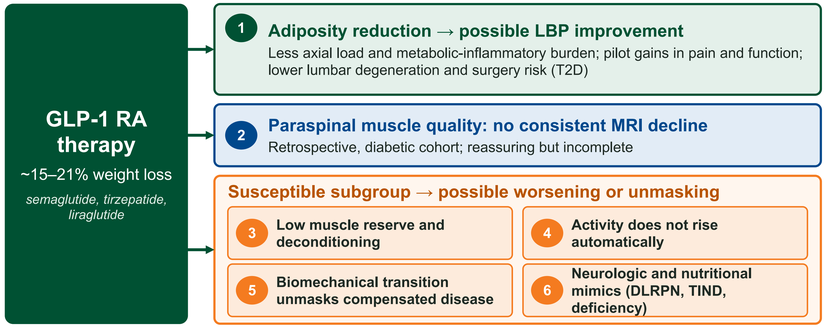


Figure 1. Six proposed pathways linking GLP-1 RA therapy and spine pain (hypothesis-generating).

Table 1. Practical monitoring framework for GLP-1 RA–treated patients with or at risk for LBP

Domain	Screen / high-risk finding	Action
Baseline spine history	Prior LBP, stenosis, surgery; baseline ODI and NRS	Record baseline metrics; early PT; inform GLP-1 prescriber
Muscle reserve and function	Grip strength, 30-s chair stand, gait speed, trunk endurance, falls	Progressive resistance training; PT if frail; retest at 3–6 months
Nutrition	Protein intake, nausea, bariatric history, dietary restriction	Dietitian-set protein target; micronutrient labs when indicated
Weight-loss velocity	% body weight lost over 1–3 months, with weakness, fatigue, or falling intake	Reassess tolerance, intake, and exercise; discuss dose with prescriber
Physical activity	Daily steps, walking tolerance, resistance training, sedentary time	Walking progression plus resistance training; PT if pain-limited
Neurologic red flags	Asymmetric leg pain, progressive weakness, allodynia, gait change, rapid HbA1c drop	**Bowel/bladder symptoms or rapid weakness: urgent evaluation; else neurology, EMG/NCS, nutritional labs**

Pragmatic framework, not a validated guideline. ODI, Oswestry Disability Index; NRS, numeric rating scale; PT, physical therapy.

RESULTS

POSSIBLE BENEFIT Pilot cohort (obesity + chronic LBP): pain, disability, and function improved.[4] Type 2 diabetes (T2D) cohort: lower long-term risk of lumbar degeneration and spine surgery.[5] Knee osteoarthritis RCT: pain improved (analogue).[6]

LEAN MASS ≠ MUSCLE DXA lean mass falls, yet in SEMALEAN handgrip strength rose and sarcopenic obesity decreased.[7]

PARASPINAL: NO SIGNAL Serial MRI: no significant loss of psoas, erector spinae, or multifidus quality (retrospective, diabetic).[8]

ACTIVITY Conference-level wearable data suggest daily steps and moderate-to-vigorous activity fall after initiation.[9]

SAFETY SIGNALS FDA adverse-event reports (FAERS) flag back pain, myalgia, and muscle atrophy; noncausal.[10,11]

MIMICS Diabetic lumbosacral radiculoplexus neuropathy (DLRPN),[12] treatment-induced neuropathy of diabetes (TIND; onset within 8 weeks of a ≥2-point HbA1c drop), and deficiency polyradiculopathy can mimic radiculopathy.

DISCUSSION

- **Divergent effects:** outcomes diverge with muscle reserve, weight-loss velocity, protein, activity, glycemia, and spine disease.
- Avoid reflexively attributing symptoms to GLP-1 RA therapy alone; **track function, not weight or DXA lean mass**.
- Exclude neurologic and nutritional mimics before spine procedures.
- **Importance of Rehabilitation:** resistance training, protein across meals, supervised PT when needed.
- Weight returns to baseline within ~1.7 years of stopping.[13] Patients need to sustain lifestyle changes for long-lasting results.
- **Future directions:** prospective cohorts with prespecified LBP outcomes and paraspinal MRI/CT.

TAKE-HOME: GLP-1 RA therapy may improve LBP in some patients, but pain clinicians should monitor function, nutrition, activity, and neurologic red flags rather than weight alone.

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