Glp-1 Receptor Agonists Increase Fracture Risk In Non-diabetic Patients With Obesity

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BACKGROUND

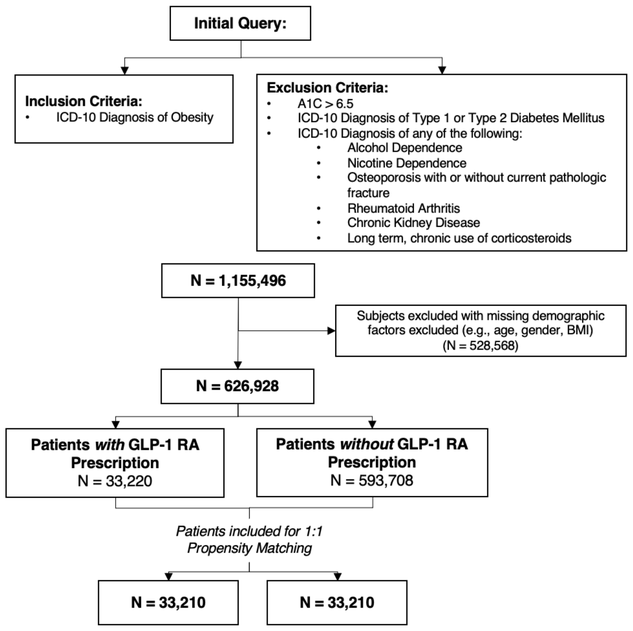
- GLP-1 receptor agonists (GLP-1 RA) promote insulin secretion and satiety and are prescribed to improve glycemic control in patients with type 2 diabetes mellitus (T2DM).
- GLP-1 RAs, such as dulaglutide (Trulicity), exenatide (Byetta), liraglutide (Victoza), and semaglutide (Ozempic), also have potential to promote weight loss.
- GLP-1 RAs in patients with diabetes have shown variable results related to fracture risk, including evidence of both an increase and decrease risk of fracture while taking GLP-1 RAs[1,2].
- The effect of GLP-1 RAs on bone health in patients without T2DM has not been studied.

PURPOSE

The purpose of this study was to assess fracture risk in obese patients without diabetes following their use of GLP-1 RAs.

METHODS

- A retrospective case-control study was conducted using deidentified data from the TriNetX database. Patients were included based on the ICD-10 diagnosis of obesity between 2018-2022. Patients were excluded based on ICD-10 diagnosis of type 1 or type 2 diabetes mellitus, A1c > 6.5 and ICD-10 diagnosis of conditions that would increase the risk of fragility fracture[3]
- Multiple GLP-1 RAs were included (semaglutide, liraglutide, exenatide, dulaglutide, tirzepatide, and lixisenatide).
- Propensity score matching was performed for two groups of 33,210 patients per group.
- The primary outcome was fracture instance indicated by ICD-10 diagnosis code (S02 – S92) within 1 year of GLP-1 RA prescription.
- Risk and odds ratio with 95% CI's were estimated using multiple logistic regression to account for covariate variability.



3: Obesity (ICD-10-CM-E66, ICD-10-CM-E66.3, ICD-10-CM-E66.8, ICD-10-CM-E66.9), Diabetes Mellitus (ICD-10-CM-E08, ICD-10-CM-E09, ICD-10-CM-E10, ICD-10-CM-E11, ICD-10-CM-E12, ICD-10-CM-E13), Osteoporosis with or without current pathological fracture (ICD-10-CM-M80, ICD-10-CM-M81), Chronic Kidney Disease (ICD-10-CM-N18), Rheumatoid Arthritis (ICD-10-CM-M05.9, ICD-10-CM-M06.0, ICD-10-CM-M06.9), Nicotine Dependence (ICD-10-CM-F17), Alcohol Abuse (ICD-10-CM- F10.1, ICD-10-CM-F10.2), Long term (current) use of systemic steroids (ICD-10-CM-Z79.52)

REFERENCES

1. Cai, T.A.-O., et al., Effects of GLP-1 Receptor Agonists on Bone Mineral Density in Patients with Type 2 Diabetes Mellitus: A 52-Week Clinical Study. (2314-6141).
2. Cheng, L., et al., Glucagon-like peptide-1 receptor agonists and risk of bone fracture in patients with type 2 diabetes: A meta-analysis of randomized controlled trials. (1520-7560)

RESULTS

- Fracture risk was significantly increased in patients with obesity without diabetes who were prescribed a GLP-1 RA (3.05%) compared to patients who were not (2.61%) (OR 1.19 CI [1.09, 1.31]; RR 1.09 CI [1.04, 1.14]) **(Fig. 1)**
- There was a significant increase in fracture risk in the GLP-1 RA group with a BMI >40 compared to those of the same BMI not prescribed GLP-1 RA (OR 1.26 CI[1.04, 1.52]) **(Fig. 2)**
- There was a significant increase in fracture odds in those older than 67 years, which included those ages, 68-77 (OR 2.25 CI[1.62, 3.13]) and 78-88 (OR 4.99 CI[2.68, 9.26]) compared to those who were not prescribed a GLP-1 RA. **(Fig 3)**
- Subjects with BMI >40 with a GLP-1 RA prescription had the most significant change in fracture location when compared to control, including foot or toe (OR 2.18 CI[1.67, 2.85]), lumbar spine or pelvis (OR 1.60 CI[1.16, 2.18]), ribs, sternum, or thoracic spine (OR 2.04 CI[1.40, 2.97]), and skull or facial bones (OR 1.83 CI[1.11, 3.00]) **(Fig. 4)**
- There was no significant difference in type of GLP-1 RA

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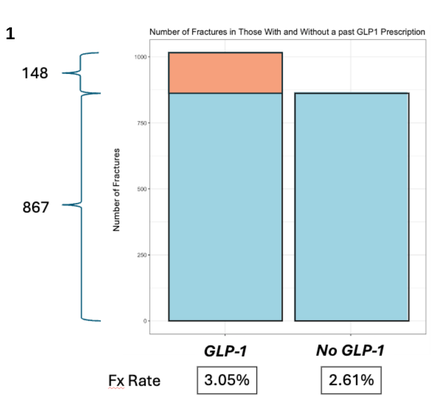

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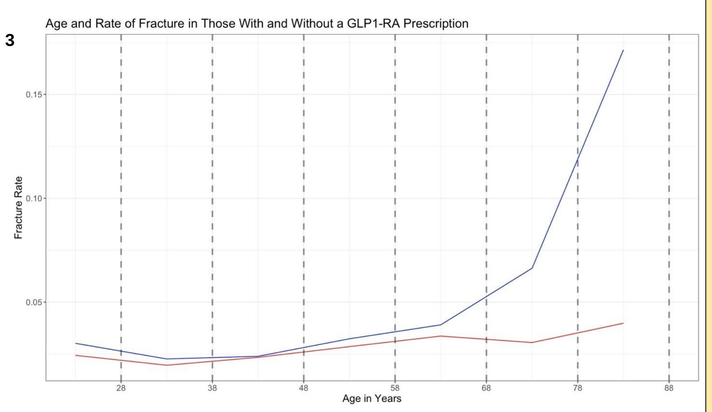

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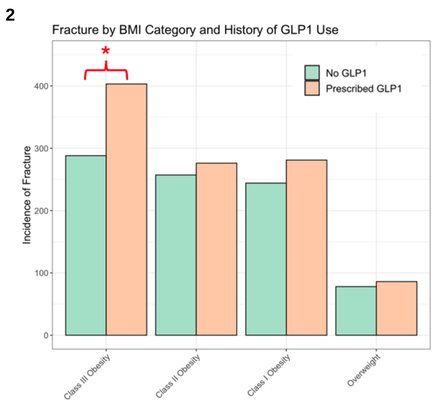

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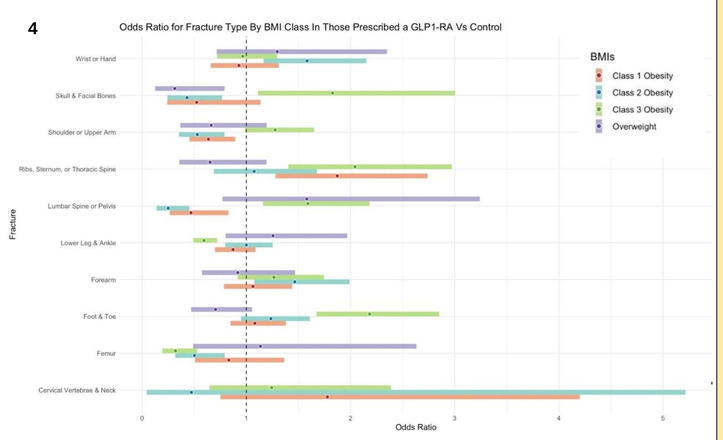

CONCLUSION

- GLP-1 RAs are associated with an increased fracture risk in obese patients without diabetes, specifically those with BMI >40 and age >68.
- GLP-1 RA associated weight loss may increase the risk of fracture due to associated muscle loss and trabecular bone loss from the decreased mechanical load on bone.
- Limitations include inability to determine amount of weight lost, the dosage of the GLP-1 RA, the duration of treatment, or the adherence by the patient.
- A large, prospective study exploring the risk of fractures following utilization of GLP-1 RAs that accounts for amount of weight loss, specific time on therapy as well as specific dosage would be useful.