The Influence of GLP-1RA Medications on Fracture Risk in the Diabetic Foot and Ankle Patient Population

Samantha Nikole Olson, BS*; Alexandra Vaughan-Masamitsu, BS; Michael Levidy, MD; Lincoln Dutcher, MD; Jana Davis, MD*

Purpose: Diabetes mellitus (DM) is associated with an elevated risk for sustaining a fracture, driven by both direct and indirect mechanisms. Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs) are a newer class of medication being used in the management of DM. Prior studies have demonstrated that certain GLP-1RAs promote bone formation by reducing osteoclast activity and stimulating osteoblast differentiation. However, the evidence of their impact on fracture risk remains inconclusive. This study seeks to investigate the association between GLP-1RAs and ankle fracture risk in diabetic patients, aiming to clarify their potential clinical effects.

Methods: The global collaborative network on the TriNetX online health record database retrospectively compared ankle fracture risk across diabetic patients. Patents were excluded if they were taking any alternative diabetes medication aside from metformin, had a diagnosis of diabetic neuropathy or osteoporosis with or without a current pathologic fracture, or used corticosteroids. The two cohorts either included or excluded GLP- 1RA. Propensity score matching for age, sex, tobacco use, and alcohol abuse yielded 129,332 patients. ICD-10 codes for ankle fracture types included bimalleolar, trimalleolar, lateral malleolar, medial malleolar, and fracture of the lower leg including the ankle.

Results: The mean age of patients was 56±15 years. The patient demographics included 52.9% female, 60.6% not Hispanic or Latino, and 54.5% White. In all ankle fracture cohorts, GLP-1RA usage was associated with a significant reduction in risk ($P<0.05$). The risk of bimalleolar fracture of the lower leg had the highest risk ratio of 2.195 (95% CI:1.517–3.175), odds ratio of 2.196 (95% CI: 1.518–3.177), and nearly double the risk for those not taking GLP-1RA medications ($P<0.0001$). The risk ratios of all the remaining cohorts were statistically significant and ranged from 1.865 to 1.482.

Conclusion: The results of this study demonstrate a statistically significant lower risk of ankle fracture in diabetic patients who are taking a GLP-1RA medication as compared to those who are not. This study's findings contribute to the growing body of evidence that GLP-1RA medications may exert a protective effect on bone and could potentially reduce fracture risk in patients with DM.