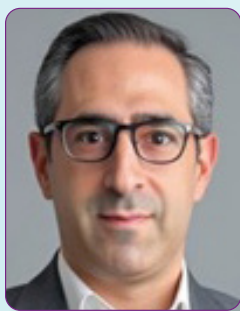




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Glucagon-Like Peptide-1 Receptor Agonists and Risk for Gastroesophageal Reflux Disease in Patients With Type 2 Diabetes: A Population-Based Cohort Study

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Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which include Ozempic®, Rybelsus® and other widely-prescribed drugs for type 2 diabetes and obesity management, are associated with delayed gastric emptying, which is a risk factor for gastroesophageal reflux disease (GERD). However, evidence linking these drugs to GERD is limited.

GLP-1 RAs work by stimulating insulin secretion, slowing gastric emptying, and reducing appetite, which contribute to their therapeutic effects. However, the delayed gastric emptying caused by these drugs may also lead to gastrointestinal side effects such as nausea, vomiting, gastroparesis, and as this study highlights, an increased risk of GERD. GERD is a condition characterized by acid reflux that can severely impact quality of life and lead to serious complications including Barrett esophagus and esophageal adenocarcinoma.

Our study analyzed data from a large cohort of patients with type 2 diabetes, comparing those using GLP-1 RAs to those on SGLT-2 inhibitors. It was found that the incidence of GERD and related complications was significantly higher among GLP-1 RA users. This increased risk was especially notable in patients who were ever-smokers, obese, or had other comorbidities affecting gastric motility. The results were consistent across multiple sensitivity analyses, strengthening the validity of the findings.

In addition, we utilized the UK Clinical Practice Research Datalink (CPRD) to conduct an active-comparator new-user cohort analysis, minimizing bias and increasing the clinical relevance of the results. The research focused on newly developed GERD cases among adults with type 2 diabetes and accounted for a broad range of lifestyle and clinical factors.

Our research adds to a limited but growing body of evidence highlighting gastrointestinal adverse effects linked to GLP-1 RAs. Prior studies and clinical trials have suggested similar trends, but this is among the first to use a rigorous, population-based design to compare GLP-1 RAs with an active comparator, SGLT-2 inhibitors, which do not affect gastric emptying.

Despite these findings, we emphasize that the well-established benefits of GLP-1 RAs in managing type 2 diabetes and obesity remain significant. We recommend that healthcare providers balance these benefits against the potential for increased GERD risk and monitor patients accordingly. Further studies are needed to confirm these results and to explore the risks in populations without diabetes but using GLP-1 RAs for obesity management.