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**Shorter-acting glucagon-like peptide-1 receptor agonists are associated with increased development of gastro-oesophageal reflux disease and its complications in patients with type 2 diabetes mellitus**

Liu B, Udemba S, Liang K, et al. [Shorter-acting glucagon-like peptide-1 receptor agonists are associated with increased development of gastro-oesophageal reflux disease and its complications in patients with type 2 diabetes mellitus: a population-level retrospective matched cohort study.](https://gut.bmj.com/content/73/2/246) Gut 2024; 73: 246-254. doi: 10.1136/gutjnl-2023-329651

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which cause delayed gastric emptying, are increasingly preferred in the treatment of type 2 diabetes mellitus (T2DM) and obesity. Liu et al. investigated whether GLP-1 RAs increased the risk of developing gastro-oesophageal reflux disease (GORD), and whether the use of short-acting (liraglutide, exenatide, lixisenatide) versus long-acting GLP-1 RAs (dulaglutide, semaglutide) had any effect.

1,543,351 patients diagnosed with T2DM over a 20-year period, on a large platform spanning 14 countries, were analysed after propensity score matching. Cohorts were separated by index prescription of a GLP-1 RA versus other second-line diabetes medications. Cohorts were propensity-matched according to baseline characteristics, including possible confounders such as BMI (body mass index), HbA1c (glycated haemoglobin A1c), nicotine dependence, NSAID (non-steroidal anti-inflammatory drug) use and alcohol. Patients with connective tissue disease, dysmotility, prior radiation exposure and major prior surgery were excluded.

12.87% of patients on GLP-1 RAs developed GORD vs. 6.38% of controls (HR (hazard ratio) 1.15). Patients on short-acting GLP-1 RAs were more likely to develop erosive oesophagitis (HR 1.22) compared to patients on long-acting GLP1-RAs (HR 0.99). Risks of secondary complications such as oesophageal strictures (HR 1.28), Barrett’s without dysplasia (HR 1.37) and Barrett’s with dysplasia (1.52) were also increased in patients on short-acting GLP-1 RAs. These risks were increased in patients on longer-acting GLP-1 RAs only if they had a pre-existing diagnosis of GORD.

In conclusion, Liu et al., demonstrate that GLP-1 RAs, particularly short-acting GLP-1 RAs, are not without risks of important gastrointestinal side effects, particularly as GORD is a disease which carries high morbidity and economic cost.