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**Glucagon-like peptide-1 receptor agonist use is associated with a lower risk of major adverse liver-related outcomes**

Celsa C, Pennisi G, Tulone A, et al. Glucagon-like peptide-1 receptor agonist use is associated with a lower risk of major adverse liver-related outcomes: a meta-analysis of observational cohort studies. Gut 2025; 74: 815-824. doi: 10.1136/gutjnl-2024-334591.

The hepatoprotective effects of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been promising according to the findings of phase 2 trials on patients with metabolic dysfunction-associated steatotic liver disease (MASLD). However, the impact of GLP-1RAs on the long-term risk of major adverse liver- related outcomes (MALOs) remains unclear.

In this study, Celsa et al. conducted a meta-analysis of observational cohort studies to elucidate the association between GLP-1RAs and MALOs in patients with type 2 diabetes (T2D). Cohort studies comparing GLP-1RA new users versus users of other glucose-lowering medications were included. The primary outcome was the cumulative incidence rates of MALOs. Secondary outcomes included hepatic decompensation events, hepatocellular carcinoma (HCC) and liver-related mortality.

Eleven retrospective cohort studies, including data from over 1.4 million patients with type 2 diabetes (T2D), were analysed. Use of GLP-1 RAs was associated with a 29% reduction in the incidence of MALOs and a 30% reduction in liver decompensation. Although the incidence of HCC was reduced by 18%, this finding was not statistically significant. Compared to sodium-glucose cotransporter-2 (SGLT2) inhibitors, GLP-1 RAs demonstrated a 7% greater reduction in MALOs. A 26% reduction in liver decompensation was also observed when compared with Dipeptidyl peptidase-4 (DPP-4) inhibitors. Furthermore, GLP-1 RA use was associated with a 68% lower incidence of HCC compared to insulin therapy. Ten of the eleven studies were rated as having a moderate risk of bias.

This meta-analysis demonstrated that the benefits of GLP-1 RAs extended beyond their well-established cardiometabolic effects, showing a reduction in long-term liver-related complications in patients with T2D. Future well-designed observational studies, particularly those with emulated trial designs and long-term follow-up, are needed to better characterize the long-term impact of GLP-1 RAs on liver-related complications and HCC development.