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SGLT-2 inhibitors versus GLP-1 receptor agonists and risk of mortality, chronic kidney disease and hospitalisation for heart failure in patients with type 2 diabetes

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Background: Two promising classes of second-line glucose-lowering drugs, the sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA), have both been shown to lower the risk of cardiovascular (CV) outcomes in patients with type 2 diabetes, however no head-to-head comparisons exist.

Purpose: The aim of this study was to examine the risk of CV and all-cause mortality, incident chronic kidney disease (CKD) and hospitalisation for heart failure (HF) in association with SGLT-2i versus GLP-1RA use.

Methods: New users of SGLT-2i and GLP-1RA, with no prior use of drugs from the comparison class, were identified between 2012-2016, using individual-level linkage of Danish nationwide registries. The absolute risk of CV was calculated using the Aalen-Johansen Estimator with non-CV mortality as competing risk. The hazard ratios (HR) of CV and all-cause mortality, incident CKD and hospitalisation for HF were estimated using Cox regression and adjusted for age, sex, diabetes duration and other outcome specific risk factors.

Results: The study included a total of 8,304 SGLT-2i users (median age: 63 years [interquartile range (IQR): 54-70], males: 63%, dapagliflozin: 60.5%, empagliflozin: 36.5%) and 13,318 GLP-1RA users (median age: 60 years [IQR: 50-68], males: 54%, liraglutide: 97.4%) with a median follow-up time of 2.0 [(IQR): 1.5-2.9] years and 3.6 [IQR: 2.1-5.0] years, respectively. At baseline 29% of SGLT-2i and 30% of GLP-1RA users had CV disease. The absolute risks are shown in Figure 1. Compared with GLP-1RA, initiation of SGLT-2i was in adjusted analyses associated with a lower risk of CV mortality (HR: 0.49 [confidence interval (CI): 0.37-0.65]), all-cause mortality [HR: 0.79 [CI: 0.68-0.93], incident CKD (HR: 0.42 [CI: 0.34-0.53] and hospitalisation for HF (HR: 0.68 [CI: 0.59-0.78]).

Conclusion: SGLT-2i use was associated with a significantly lower risk of CV and all-cause mortality, incident CKD and hospitalisation for HF in comparison with GLP-1RA use.
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