01. Comparative Cardiovascular Outcomes of GLP-1 Receptor Agonists Versus SGLT2 Inhibitors in Type 2 Diabetes Mellitus: A Multicenter Propensity-Matched Cohort Study

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Background: Type 2 diabetes mellitus (T2DM) is associated with a substantially increased risk of cardiovascular morbidity and mortality, including myocardial infarction, stroke, heart failure, and premature death. Among contemporary glucose-lowering therapies, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter-2 inhibitors (SGLT2i) have demonstrated cardiovascular benefits in randomized clinical trials; however, comparative real-world evidence evaluating their relative cardiovascular effectiveness remains limited. This study aimed to compare major cardiovascular outcomes and all-cause mortality among patients with T2DM treated with GLP-1 analogues versus SGLT2 inhibitors using a large multicenter federated electronic health records network.

Methods: A retrospective comparative outcomes analysis was conducted using the TriNetX Research Network comprising 111 healthcare organizations. Adult patients aged ≥18 years with T2DM (ICD-10-CM: E11) treated with either GLP-1 analogues (liraglutide, semaglutide, exenatide, or dulaglutide) or SGLT2 inhibitors (empagliflozin, dapagliflozin, canagliflozin, or ertugliflozin) were identified. Patients receiving medications from the alternate drug class were excluded from each cohort. The index event was defined as first exposure to the respective drug class after T2DM diagnosis. Outcomes included myocardial infarction, atherosclerosis, cerebral infarction, heart failure, and all-cause mortality. Propensity score matching (1:1) was performed to balance demographic and clinical characteristics between cohorts, resulting in 419,760 patients in each group. Risk analysis, Kaplan–Meier survival analysis, and number of instances analysis were performed.

Results: Following propensity score matching, patients treated with GLP-1 analogues demonstrated significantly lower risks of adverse cardiovascular outcomes compared with those treated with SGLT2 inhibitors. The risk of myocardial infarction was lower in the GLP-1 cohort (4.1% vs 7.8%; risk ratio [RR] 0.522, 95% CI 0.513–0.532; hazard ratio [HR] 0.487, 95% CI 0.478–0.496; $p<0.001$). Similarly, GLP-1 analogue use was associated with reduced risk of atherosclerosis (6.7% vs 7.9%; RR 0.843, 95% CI 0.830–0.856; HR 0.795, 95% CI 0.783–0.808; $p<0.001$), cerebral infarction (4.8% vs 6.3%; RR 0.773, 95% CI 0.759–0.787; HR 0.731, 95% CI 0.718–0.745; $p<0.001$), and heart failure (12.2% vs 25.0%; RR 0.488, 95% CI 0.484–0.493; HR 0.430, 95% CI 0.426–0.435; $p<0.001$). All-cause mortality was also significantly lower among GLP-1 analogue users (6.0% vs 7.3%; RR 0.815, 95% CI 0.802–0.828; HR 0.767, 95% CI 0.755–0.780; $p<0.001$).

Conclusions: In this large real-world propensity score–matched analysis of patients with T2DM, treatment with GLP-1 analogues was associated with significantly lower risks of myocardial infarction, cerebral infarction, heart failure, atherosclerosis, and all-cause mortality compared with SGLT2 inhibitors. These findings suggest that GLP-1 receptor agonists may provide superior overall cardiovascular protection in selected patients with T2DM. Prospective randomized head-to-head trials are warranted to validate these observational findings and further guide individualized therapeutic decision-making.

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