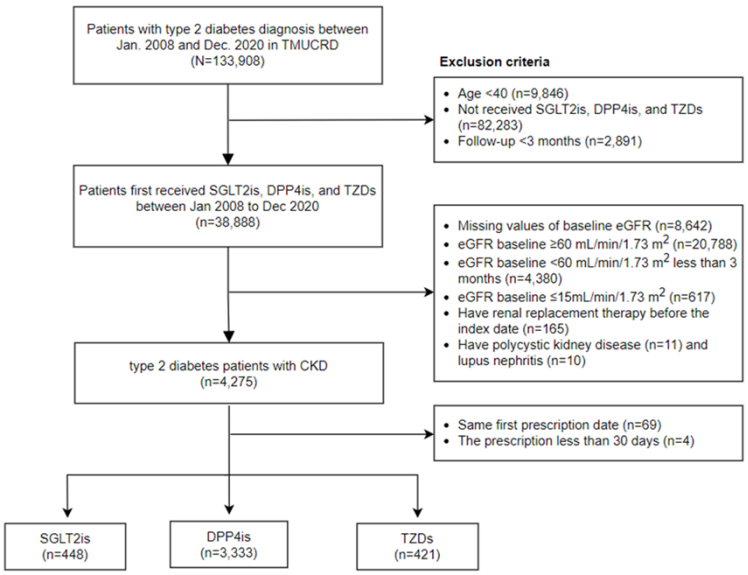
SGLT2 Inhibitors Mitigate Renal Decline and Cardiovascular Events in T2D Patients with CKD, Slowing CKM Syndrome Progression

Protective Effects of SGLT2 Inhibitors on Cardiovascular-Kidney-Metabolic (CKM) Syndrome Progression in Type 2 Diabetes with Chronic Kidney Disease: A Multi-Center Data Analysis Using OMOP-CDM

Background: This study aims to evaluate the protective effects of sodium-glucose co-transporter 2 inhibitors (SGLT2is) on renal and cardiovascular events in type 2 diabetes (T2D) patients with chronic kidney disease (CKD) within the context of Cardiovascular-Kidney-Metabolic (CKM) Syndrome. Specifically, we assess whether SGLT2is can reduce the progression of renal dysfunction and cardiovascular risks, providing real-world insights using multi-center clinical data.

Methods: We conducted a retrospective cohort study using the OMOP-common data model (CDM) with data sourced from the Taipei Medical University Clinical Research Database (TMUCRD) across three hospitals: Taipei Medical University Hospital, Wanfang Hospital, and Shuang Ho Hospital. The study included patients with T2D and CKD who received antidiabetic medications between 2008 and 2020. Propensity score matching was used to balance patient characteristics across SGLT2is, dipeptidyl peptidase-4 inhibitors (DPP4is), and thiazolidinediones (TZD) groups. A total of 5,005 patients were included, with 524 in the SGLT2is group. Primary outcomes were renal function markers (e.g., sustained ≥50% eGFR reduction, eGFR ≤15 mL/min/1.73 m², and initiation of kidney replacement therapy [KRT]), and the incidence of 4-point major adverse cardiovascular events (4P-MACE).

Figure 1: Cohort Selection Process



Results： The SGLT2is group exhibited significantly lower rates of renal function decline, with an adjusted hazard ratio (HR) of 0.49 (95% CI: 0.29-0.82) for a ≥50% reduction in eGFR, and an HR of 0.41 (95% CI: 0.22-0.77) for eGFR ≤15 mL/min/1.73 m², compared to the DPP4is and TZD groups. Additionally, the incidence of 4P-MACE was significantly reduced in the SGLT2is group (HR: 0.65, 95% CI: 0.47-0.90), including a notable reduction in cardiovascular deaths (HR: 0.37, 95% CI: 0.21-0.65) compared to both DPP4is and TZDs. Subgroup analyses indicated that male patients with pre-existing heart disease particularly benefited from SGLT2is (HR: 0.38, 95% CI: 0.15-0.97).

Conclusion： The use of SGLT2is in T2D patients with CKD significantly mitigates both renal function decline and cardiovascular events, supporting their efficacy in slowing the progression of CKM Syndrome. These findings, based on real-world clinical data from multiple centers, highlight SGLT2is as a valuable therapeutic option for reducing the burden of renal and cardiovascular complications in this high-risk population. This study is expected to be developed into a multinational cooperative research using OHDSI tools and OMOP CDM in the future.

Figure 2: 4P-MACE Outcomes in Patients with SGLT2i or Other Hypoglycemic Agents in Propensity-matched Cohort (1:4)

	Events, No.	Participant-years of follow up	Incidence rate (Events/100 participants)	Crude model		Adjusted model¶	
				Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
4P-MACE							
SGLT2i	42	2842	8.0				
vs. non-SGLT2i	254	11433	12.1	0.65 (0.47, 0.90)	0.010	0.68 (0.49, 0.95)	0.024
SGLT2i	42	2842	8.0				
vs. DPP4i	253	11430	12.1	0.65 (0.47, 0.91)	0.012	0.72 (0.52, 1.00)	0.053
SGLT2i	26	1615	12.3				
vs. TZD	40	1556	19.0	0.54 (0.34, 0.85)	0.008	0.56 (0.35, 0.88)	0.012

*Abbreviations: DPP4i, dipeptidyl peptidase 4 inhibitor; MACE, major adverse cardiovascular events; SGLT2i, sodium–glucose cotransporter 2 inhibitors; TZD, thiazolidinediones.

¶Adjusted for age, duration of type 2 DM, Charlson Comorbidity Index (CCI), and eGFR.

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