Superior Benefits of SGLT2 Inhibitors Over DPP4 Inhibitors for Diabetic Kidney Disease: A Cohort Study

Chen HL[1], Wang IT[1], Lee YH[2], Huang WM[1], Cheng HM[2], Tsai YW[1]

[1]National Yang Ming Chiao Tung University, Taipei, Taiwan, [2]Taipei Veterans General Hospital, Taipei, Taiwan

Background

Novel antidiabetic drugs show cardiorenal benefits but direct comparisons among patients with diabetic kidney disease (DKD) in real-world settings are lacking.

Objectives

To compare cardiorenal outcomes of dipeptidyl peptidase-4 (DPP-4i) and sodium-glucose cotransporter-2 (SGLT-2i) inhibitors in a national DKD population.

Method

We conducted a cohort study utilizing data from Taiwan's National Health Insurance Research Database and Laboratory Databases. Adults with diabetic kidney disease (DKD) and an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 were identified between 2017 and 2018. Propensity score matching was performed to select 1,524 new users of sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and 6,005 new users of dipeptidyl peptidase-4 inhibitors (DPP-4i). The primary renal composite outcomes included sustained eGFR decline, renal failure, and renal mortality. The primary cardiovascular composite outcomes comprised acute myocardial infarction, stroke, hospitalization for heart failure, and cardiovascular death. Cox proportional hazard models were employed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Result

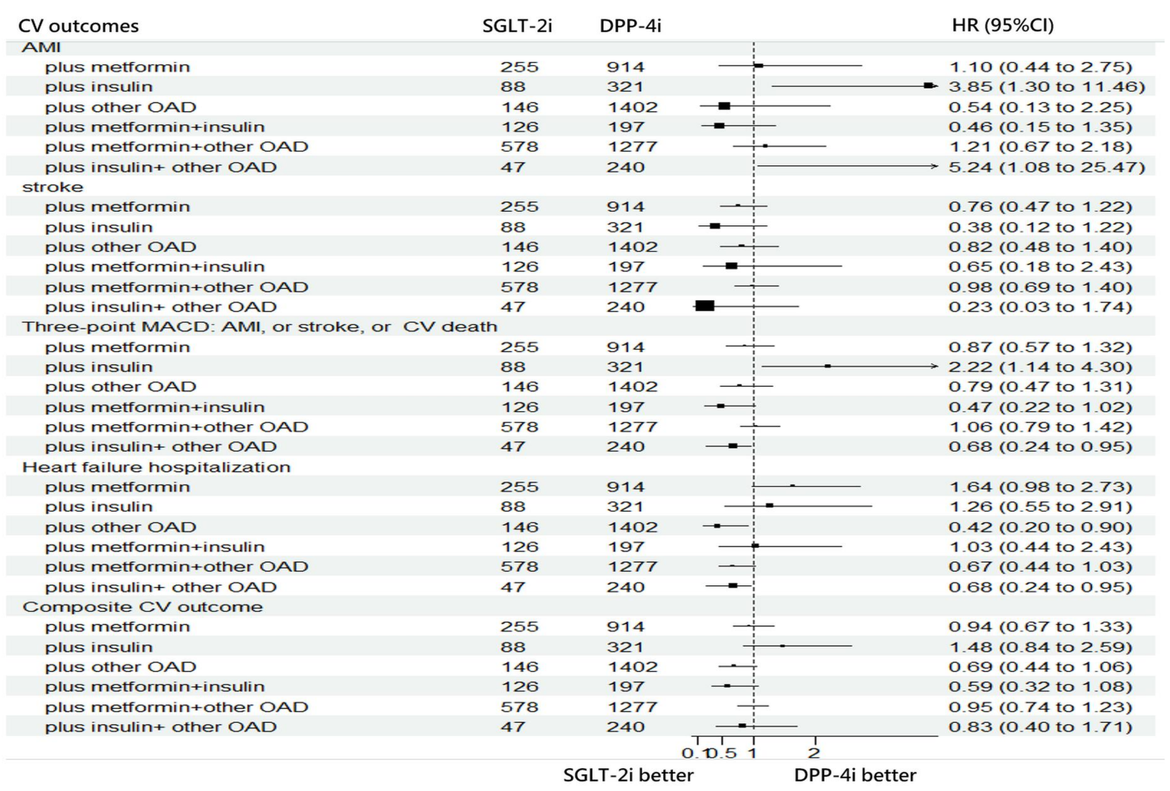
Compared with DPP-4i users, SGLT-2i users had a reduced risk of composite renal endpoint (HR: 0.165; 95% CI: 0.115-0.237), consistently for a prolonged time to ≥50% eGFR decrease (HR 0.175; 95% CI: 0.113-0.271), renal failure (HR: 0.136; 95% CI: 0.081-0.227), and decreased renal death (HR: 0.096; 95% CI: 0.013-0.695). SGLT-2i users had a better composite CV outcome than DPP-4i users (HR: 0.739; 95% CI: 0.643-0.848) and lower risks of stroke (HR: 0.761; 95% CI: 0.624-0.925) and hospitalization for heart failure (HR: 0.681; 95% CI:0.551-0.842). Findings were consistent in analyses stratified by concomitant antidiabetic agents or intervals between DKD diagnosis and study drug initiation.

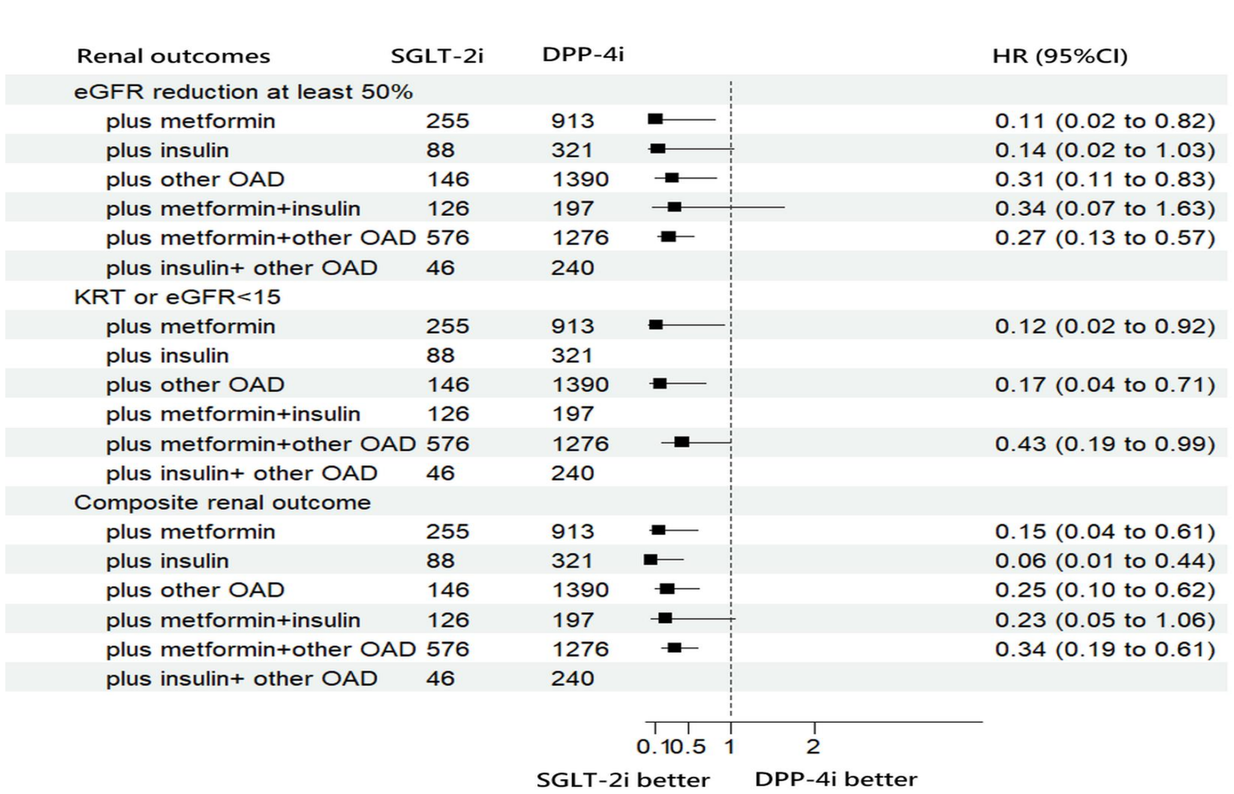
		Stratify by time interval, HR (95% CI)			
	HR (95% CI)	< 30 days	30-365 days	> 365 days	*P* for interaction[a]
Renal outcomes					
eGFR reduction at least 50%	0.175 (0.113, 0.271)	0.209 (0.124, 0.351)	0.054 (0.008, 0.392)	0.171 (0.07, 0.421)	.3963
KRT or eGFR < 15	0.136 (0.081, 0.227)	0.248 (0.135, 0.455)	NA[b]	0.077 (0.029, 0.208)	.1869
Renal death	0.096 (0.013, 0.695)	0.138 (0.019, 1.021)	NA[b]	NA[b]	.9998
Composite outcome	0.165 (0.115, 0.237)	0.219 (0.141, 0.34)	0.034 (0.005, 0.244)	0.133 (0.068, 0.26)	.1295
Cardiovascular outcomes					
AMI	1.092 (0.797, 1.497)	1.159 (0.781, 1.718)	0.831 (0.343, 2.014)	1.054 (0.542, 2.051)	.7573
Stroke	0.761 (0.624, 0.925)	0.828 (0.643, 1.065)	0.776 (0.456, 1.321)	0.602 (0.401, 0.902)	.24
Cardiovascular death	0.857 (0.294, 2.501)	1.466 (0.394, 5.454)	NA[b]	0.629 (0.076, 5.168)	.769
3-point MACE	0.82 (0.696, 0.967)	0.954 (0.776, 1.173)	0.727 (0.444, 1.19)	0.585 (0.421, 0.814)	.0427
hFH	0.681 (0.551, 0.842)	0.816 (0.632, 1.053)	0.32 (0.148, 0.695)	0.563 (0.361, 0.878)	.0536
Composite outcome	0.739 (0.643, 0.848)	0.874 (0.735, 1.04)	0.553 (0.363, 0.842)	0.556 (0.42, 0.736)	.0083

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; DKD, diabetic kidney disease; DPP-4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; hFH, hospitalization for heart failure; HR, hazard ratio; KRT, kidney replacement therapy; MACE, major adverse cardiovascular events (including AMI, stroke or cardiovascular death); NA, not available; SGLT-2i, sodium-glucose co-transporter-2 inhibitor.

[a]The multiplicative interaction term (exposure to SGLT-2i or DPP-4i × time interval) was tested to determine if the time interval acts as an effect modifier.

[b]The number of patients in each cell was less than six. Because of privacy protection, the data for this cell should be combined with other groups for





Conclusion

This study demonstrated the superior cardiorenal benefits of SGLT-2i over DPP-4i in DKD population, regardless of concomitant antidiabetic agents or time from DKD onset to study drug initiation. SGLT2i should be prioritized in adult patients with DKD.

Chen HL : hlchen369@gmail.com