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Heterogeneous Kidney Patterns In Diabetic Patients Following SGLT2 Inhibitor Use

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Objectives : Although sodium-glucose cotransporter 2 inhibitors (SGLT2is) slow the progression of kidney disease in diabetic patients, whether certain subsets of diabetic patients present heterogeneous phenotypes, such as a rapid deterioration of kidney function, following SGLT2i use remains unclear. This study aimed to clarify these heterogeneous responses and identify the factors contributing to them through a kidney function trajectory analysis.

Methods : This retrospective cohort study included 66,375 patients who visited the diabetes clinic for type 2 diabetes management, 5,209 of whom were prescribed SGLT2is. Patterns of estimated glomerular filtration rate (eGFR) trajectories were analyzed using a latent class linear mixed model, and factors associated with these patterns were evaluated via multinomial logistic regression analysis.

Results : Four distinct eGFR trajectory patterns were identified: class 1 (high baseline, stable eGFR; n = 3,357), class 2 (low baseline, stable eGFR; n = 611), class 3 (high baseline, rapidly declining eGFR; n = 96), and class 4 (low baseline, rapidly declining eGFR; n = 121). A rapid eGFR decline was more common in younger male patients with substantial albuminuria, anemia, and hypoalbuminemia. Patients in the rapidly declining eGFR classes had higher risks of adverse kidney outcomes and mortality than those in stable eGFR classes did.

Conclusions : The heterogeneity in eGFR trajectories following SGLT2i use suggests that not all patients benefit equally from this therapy. Identifying patients at risk of a rapid eGFR decline is critical for providing timely warnings and optimizing treatment strategies.

Figure.jpg

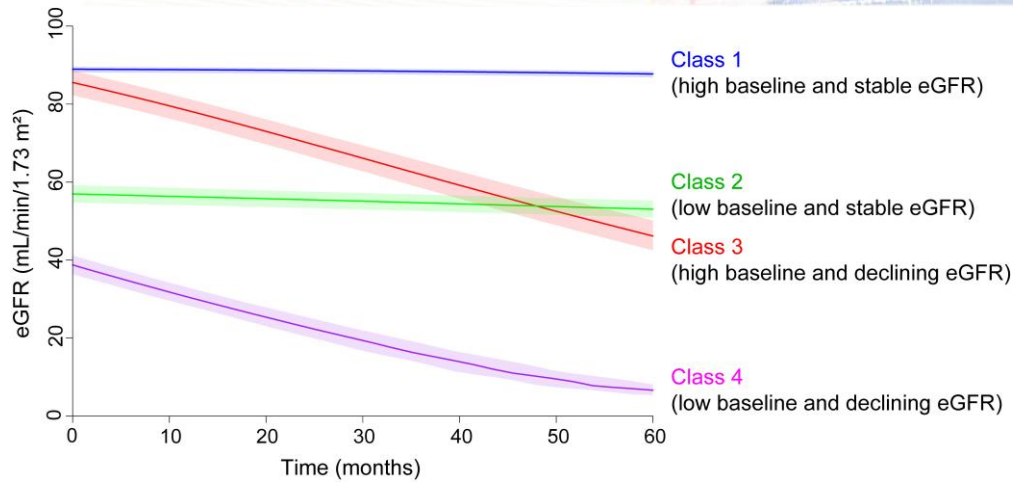


Figure.jpg

Table 2. Factors associated with the pattern of estimated glomerular filtration rates

Variables	Class 3 (vs. class 1)		Class 4 (vs. class 2)	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age (per 1 year)	0.95 (0.94–0.97)	0.008	0.92 (0.90–0.94)	<0.001
Male (vs. female)	1.99 (1.20–3.29)	<0.001		
eGFR (per 1 mL/min/1.73 m ²)	0.98 (0.97–1.00)	0.031	0.95 (0.94–0.97)	<0.001
ACR (per 100 mg/g)	1.22 (1.10–1.34)	<0.001	1.20 (1.10–1.31)	<0.001
Hemoglobin (per 1 mg/dl)	0.75 (0.65–0.86)	<0.001	0.82 (0.72–0.93)	0.002
Serum albumin (per 1 mg/dl)	0.51 (0.31–0.84)	0.009	0.35 (0.21–0.56)	<0.001
Hemoglobin A1c (per 1%)	1.19 (1.03–1.39)	0.020		
Total cholesterol (per 1 mg/dl)				
LDL cholesterol (per 1 mg/dl)				
Ischemic heart disease (vs. none)				
Stroke (vs. none)				

Backward stepwise variable selection was performed based on the Akaike Information Criteria.

Classes 1 and 2 were used as the reference groups.

eGFR, estimated glomerular filtration rate; OR, odds ratio; CI, confidence interval; ACR, random urine albumin-to-creatinine ratio; LDL, low-density lipoprotein.