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Association between Plasma Fibroblast Growth Factor 21 levels and Incident Chronic Kidney Disease

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Objectives : Fibroblast growth factor 21 (FGF21) plays a critical role in glucose, lipid, and energy metabolism. However, the relationship between FGF21 and the risk of chronic kidney disease (CKD) has not yet been explored.
Methods : We analyzed 17,107 participants without CKD from UK biobank cohort who measured baseline plasma FGF21 levels using proximity extension assay. The primary outcome was a composite CKD outcome, defined as the development of an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m^2 or urine albumin-creatinine ratio (uACR) >30 mg/g on at least two occasions 90 days apart. The secondary outcomes were individual occurrences of eGFR-based CKD and the development of albuminuria.
Results : Participants with higher FGF21 levels were older and more likely to be male, smokers, and obese. They exhibited more comorbidities and concomitant medication use, and less favorable metabolic and lipid profiles. During 127,832 person-years of follow-up, the composite outcome occurred in 853 (5.0%) participants. The incidence of CKD increased progressively in participants with higher FGF21 levels (2.7%, 4.4%, 5.0%, and 7.8% from Q1 to Q4, respectively; P-for-trend <0.001). In Cox regression analysis, compared with Q1, the adjusted hazard ratios (aHRs) (95% CIs) for composite CKD outcome were 1.41 (1.11-1.79), 1.65 (1.30-2.09), and 2.07 (1.65-2.60) for Q2, Q3, and Q4, respectively (P-for-trend <0.001). Similar results were observed in secondary analysis for the occurrence of eGFR < 60 mL/min/1.73 m^2 (aHR [95% CI]; Q2, 1.46 [1.13-1.88]; Q3, 1.69 [1.32-2.17]; Q4, 2.03 [1.59-2.58] versus Q1; P-for-trend <0.001) and the development of albuminuria (aHR [95% CI]; Q2, 1.10 [0.57-2.14]; Q3, 1.62 [0.88-2.99]; Q4, 2.49 [1.40-4.42] versus Q1; P-for-trend <0.001).
Conclusions : Higher FGF21 levels were associated with an increased risk of incident CKD in UK adults, suggesting that FGF21 may serve as a potential biomarker for predicting the development of CKD.

Table1.jpg

Table. Incidence rates of CKD outcomes according to FGF21 quartiles

	Total	Q1	Q2	Q3	Q4	P for trend
Primary outcome						
Composite CKD						
Person-years	127,833	32,187	31,930	32,195	31,521	
Events	853 (5.0%)	117 (2.7%)	186 (4.4%)	216 (5.0%)	334 (7.8%)	<0.001
Incidence rate [a]	66.8 (62.4-71.4)	36.4 (30.3-40.6)	58.3 (50.5-67.3)	67.1 (58.7-76.7)	105.9 (95.2-117.9)	
Secondary outcome						
eGFR <60mL/min/1.73m^2						
Person-years	128,105	32,221	31,957	32,245	31,683	
Events	760 (4.4%)	105 (2.5%)	172 (4.0%)	198 (4.6%)	285 (6.7%)	<0.001
Incidence rate [a]	59.3 (55.3-63.7)	32.6 (26.9-39.5)	53.8 (46.4-62.5)	61.4 (53.4-70.6)	90.0 (80.1-101)	
uACR > 30mg/g						
Person-years	130,624	32,573	32,535	32,926	32,590	
Events	144 (0.8%)	16 (0.4%)	20 (0.5%)	31 (0.7%)	77 (1.8%)	<0.001
Incidence rate [a]	11.0 (9.4-13.0)	4.9 (3.0-8.0)	6.1 (4.0-9.5)	9.4 (6.6-13.4)	23.6 (18.9-29.5)	

[a] Incidence rate is presented as per 10,000 person-year

Abbreviation: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FGF21, fibroblast growth factor 21; uACR, urine albumin-to-creatinine ratio.

Table1.jpg

Table. Hazard ratios for primary and secondary outcomes according to FGF21 levels

	Univariable			Multivariable [a]		
Composite CKD outcome	HR	95% CI	P value	HR	95% CI	P value
Continuouse	1.29	1.23 - 1.35	<0.001	1.17	1.11 - 1.22	<0.001
Quartiles						
Q1		(Reference)			(Reference)	
Q2	1.60	1.27 - 2.02	<0.001	1.41	1.11 - 1.79	0.005
Q3	1.85	1.47 - 2.31	<0.001	1.65	1.30 - 2.09	<0.001
Q4	2.92	2.36 - 3.60	<0.001	2.07	1.65 - 2.60	<0.001
		P for trend	<0.001		P for trend	<0.001
eGFR <60mL/min/1.73m^2 outcome	HR	95% CI	P value	HR	95% CI	P value
Continuouse	1.26	1.20 - 1.32	<0.001	1.15	1.09 - 1.21	<0.001
Quartiles						
Q1		(Reference)			(Reference)	
Q2	1.65	1.30 - 2.10	<0.001	1.46	1.13 - 1.88	0.004
Q3	1.88	1.49 - 2.39	<0.001	1.69	1.32 - 2.17	<0.001
Q4	2.76	2.21 - 3.45	<0.001	2.03	1.59 - 2.58	<0.001
		P for trend	<0.001		P for trend	<0.001
uACR > 30mg/g outcome	HR	95% CI	P value	HR	95% CI	P value
Continuouse	1.55	1.40 - 1.71	<0.001	1.32	1.18 - 1.48	<0.001
Quartiles						
Q1		(Reference)			(Reference)	
Q2	1.25	0.65 - 2.40	0.512	1.10	0.57 - 2.14	0.771
Q3	1.91	1.05 - 3.49	0.035	1.62	0.88 - 2.99	0.120
Q4	4.80	2.80 - 8.23	<0.001	2.49	1.40 - 4.42	0.002
		P for trend	<0.001		P for trend	<0.001

[a] Adjusted for age, sex, race, BMI, hypertension, diabetes, CVD, eGFR, uACR, hsCRP, fasting glucose, total cholesterol, and RASBs use.

Abbreviation: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; FGF21, fibroblast growth factor 21; HR, hazard ratio; hsCRP, high-sensitivity C-reactive protein; uACR, urine albumin-to-creatinine ratio; RASBs, renin-angiotensin system blockades.