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Identification of Mineral Metabolism Phenotypes Using Multiple Trajectory Modeling and Their Association with Kidney Outcomes: Findings from the KNOW-CKD Cohort

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Objectives : Disorders of mineral and bone metabolism (CKD-MBD) are clinical hallmarks of chronic kidney disease (CKD) progression, characterized by a complex interplay between serum calcium, phosphate, and parathyroid hormone (PTH). In this study, we aimed to identify distinct mineral metabolism phenotypes using multiple group-based trajectory modeling (GBTM) and evaluate their association with long-term kidney outcomes.
Methods : Using data from the KNOW-CKD cohort, we performed multiple GBTM to identify distinct phenotypes based on the longitudinal patterns of serum calcium, phosphate, and PTH. The primary outcome was a composite kidney outcome (≥50% decline in eGFR, doubling of serum creatinine, initiation of dialysis, or kidney transplantation). To evaluate the independent prognostic value of the identified trajectory phenotypes, model performance was validated by comparing the C-index and assessing risk reclassification through Net Reclassification Improvement (NRI) with scatter plots.
Results : Among the 1,541 patients analyzed, multiple GBTM identified five distinct mineral metabolism phenotypes. In a multivariable Cox model, Group 1 was associated with a significantly elevated risk of kidney failure compared to the other groups (Hazard Ratio [HR], 1.703; 95% CI, 1.291–2.246; $P < 0.001$) compared to the rest of the cohort. Conversely, Group 2 demonstrated the most favorable prognosis, showing a marked reduction in risk (HR, 0.477; 95% CI, 0.346–0.658; $P < 0.001$). Using the MICE-imputed dataset, the C-index improved from 0.7746 in the baseline model to 0.7824 in the full model ($P = 0.022$). The scatter plot of predicted risks visually confirms this redistribution, illustrating that longitudinal mineral trajectories offer refined risk stratification beyond traditional static measurements.
Conclusions : This study demonstrates that the integrated longitudinal patterns of mineral metabolism markers provide superior prognostic information for CKD progression compared to single-point measurements. Our findings suggest that accounting for these dynamic patterns allows for earlier intervention and more personalized management within the CKD-MBD framework.

Figure 1.PNG

Figure 1A. Distinct trajectories of mineral metabolism markers

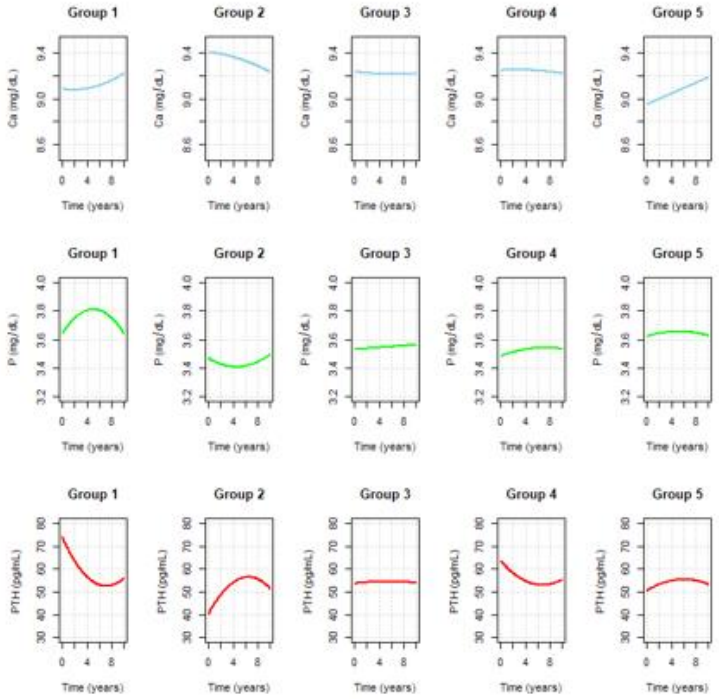

Figure 1B. Cumulative incidence of kidney outcomes according to the mineral metabolism trajectory groups

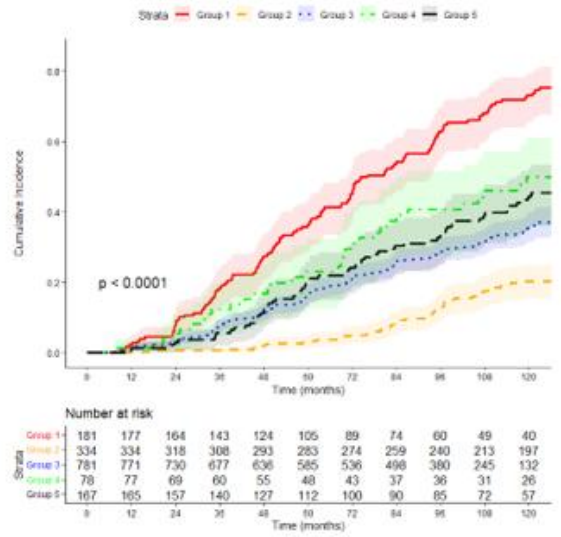

Figure 1.PNG

Table 2A. Univariable and multivariable Cox regression analyses for kidney outcome

	Univariable		Multivariable	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Trajectory phenotype	3.179 (2.604, 3.880)	<0.001	1.703 (1.291, 2.245)	<0.001
Age	1.003 (0.996, 1.010)	0.356	0.912 (0.960, 0.983)	<0.001
Male sex	1.043 (0.874, 1.244)	0.644	1.622 (0.960, 0.983)	0.012
Smoking	1.126 (0.949, 1.337)	0.175	0.921 (1.110, 2.370)	0.603
BMI	1.012 (0.987, 1.038)	0.337	1.032 (0.994, 1.071)	0.099
DM	1.843 (1.539, 2.207)	<0.001	1.493 (1.115, 1.999)	0.007
HTN	4.136 (2.057, 8.315)	<0.001	1.125 (0.377, 3.355)	0.833
CVD	1.149 (0.891, 1.480)	0.284	1.020 (0.700, 1.487)	0.916
eGFR	0.965 (0.960, 0.969)	<0.001	0.966 (0.959, 0.973)	<0.001
UPCR	1.271 (1.212, 1.332)	<0.001	1.151 (1.058, 1.252)	0.001
Hemoglobin	0.770 (0.734, 0.808)	<0.001	0.900 (0.818, 0.990)	0.031
Albumin	0.375 (0.311, 0.452)	<0.001	0.799 (0.528, 1.209)	0.288
Total cholesterol	1.001 (0.999, 1.003)	0.456	1.003 (0.999, 1.007)	0.099
RAAS blocker	1.490 (1.116, 1.989)	0.007	1.370 (0.880, 2.132)	0.164
Beta blocker	1.616 (1.339, 1.950)	<0.001	1.350 (1.024, 1.781)	0.033
Diuretics	1.710 (1.427, 2.049)	<0.001	0.992 (0.755, 1.303)	0.951
CCB	1.659 (1.397, 1.969)	<0.001	1.334 (1.020, 1.744)	0.035
Statin	1.382 (1.162, 1.643)	<0.001	0.796 (0.603, 1.051)	0.108

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; UPCR, urine protein-creatinine ratio; RAAS blocker, renin-angiotensin-aldosterone system blocker; CCB, calcium channel blocker

Figure 2B. Scatter plot of predicted probabilities for kidney outcome between the standard and trajectory-integrated models