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Low klotho/fibroblast growth factor 23 ratio is an independent risk factor for renal progression in chronic kidney disease: the KNOW-CKD study

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Objectives: We aimed to evaluate soluble klotho and circulating fibroblast growth factor 23 (FGF23) ratio as a risk factor for renal progression, cardiovascular (CV) events, and mortality in chronic kidney disease (CKD).

Methods: We analyzed 2,099 subjects from a CKD cohort whose soluble klotho and C-terminal FGF23 levels were measured at enrollment. The klotho to FGF23 ratio was calculated as klotho values divided by FGF23 values + 1 (hereinafter called the klotho/FGF23 ratio). Participants were categorized into quartiles according to klotho/FGF23 ratio. The primary outcome was renal events, defined as the doubling of serum creatinine, 50% reduction of estimated glomerular filtration rate from the baseline values, or development of end-stage kidney disease. The secondary outcomes consisted of CV events and death.

Results: During the follow-up period of 64.0 ± 28.2 months, 735 (35.1%) and 273 (13.0%) subjects developed renal events and composite outcomes of CV events and death, respectively. After adjustment, the first (hazard ratio [HR]: 1.39; 95% confidence interval [CI]: 1.10–1.76, $P = 0.006$), second (HR: 1.44; 95% CI: 1.14–1.82, $P = 0.002$), and third (HR: 1.27; 95% CI: 0.99–1.63, $P = 0.059$) quartiles with regard to the klotho/FGF23 ratio showed elevated risk of renal events as compared to the fourth quartile group. There was no significant association between klotho/FGF23 ratio and the composite outcome of CV events and death. The prevalence of left ventricular hypertrophy and vascular calcification was higher in the low klotho/FGF23 ratio quartiles at baseline and at the fourth-year follow-up.

Conclusions: Low klotho/FGF23 ratio was significantly associated with increased renal events in the cohort of Korean predialysis CKD patients.