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Proteinuria Modifies the Relationship Between Urinary Sodium Excretion and Adverse Kidney Outcomes: Findings from KNOW-CKD

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Objectives: High sodium intake is strongly associated with increased risk of proteinuria, hypertension and adverse cardiovascular events in patients with chronic kidney disease (CKD). Despite the importance of salt restriction, there are discrepancies regarding the relationship between salt intake and kidney outcomes. The aim of this study is to investigate whether proteinuria can modify the association between urinary sodium excretion and adverse kidney outcomes in patients with CKD.

Methods: In this prospective observational cohort study, we included 967 participants with CKD G1-G5 between 2011-2016, who measured 24-hour urinary sodium and protein excretion at baseline. The main predictors were urinary sodium and protein excretion levels. The primary outcome was CKD progression, which was defined as a ³50% decline in the estimated glomerular filtration rate or the onset of kidney replacement therapy.

Results: During a median follow-up of 4.1 years, the primary outcome events occurred in 287 participants (29.7%). There was a significant interaction between proteinuria and sodium excretion for the primary outcome (P=0.006). In patients with proteinuria of <0.5 g/day, sodium excretion was not associated with the primary outcome. However, in patients with proteinuria of ≥0.5g/day, a 1.0g/day increase in sodium excretion was associated with a 29% higher risk of adverse kidney outcomes. Moreover, in patients with proteinuria of ≥0.5g/day, the hazard ratios (95% confidence intervals) for sodium excretion of <3.4 and ≥3.4g/day were 2.32 (1.50–3.58), and 5.71 (3.58–9.11), respectively, compared with proteinuria of <0.5g/day and sodium excretion of <3.4g/day.

Conclusions: Higher urinary sodium excretion was more strongly associated with an increased risk of adverse kidney outcomes in patients with higher proteinuria levels.

Table 1. Hazard ratios for primary outcomes based on the baseline 24-hour urinary sodium and hazard ratio per 1.0g/day of urinary sodium excretion