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The association of metabolic acidosis with renal progression in chronic kidney disease: Results from the KNOW-CKD Study

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Objectives : Metabolic acidosis, usually manifested by low serum bicarbonate level, is prevalent in chronic kidney disease (CKD). However, its relationship to long-term outcomes is unclear in Korean CKD patients. The purpose of the present study is to evaluate serum bicarbonate as a risk factor for renal outcomes, cardiovascular events and mortality in large-scale Korean CKD cohort patients.

Methods : Between 2011 and 2016, 2,238 CKD patients were enrolled in the KoreaNCohort Study for Outcome in Patients With Chronic Kidney Disease (KNOW-CKD). We analyzed 1,809 participants from this cohort who had been measured for serum bicarbonate levels. Serum bicarbonate level was categorized into quartiles. We used Cox proportional hazards models to analyze the association between serum bicarbonate and outcomes. The primary outcome was renal events. Renal events were defined as doubling of serum creatinine, 50% reduction in eGFR from the baseline values, or end-stage renal disease (either initiation of dialysis or kidney transplantation). The secondary composite outcome consisted of cardiovascular events and death.

Results : Patients were 53.6 ± 12.3 years old and 1,111 patients (61.4%) were male. The mean eGFR was 50.1 ± 30.1 mL/min/1.73m2 and serum bicarbonate level was 25.7 ± 3.7 mEq/L. During follow-up for 36.3 ±17.5months, primary outcomes were 31.2%, 16.9%, 9.1%, and 6.6%; secondary outcomes were 9.0%, 4.5%, 3.3%, and 4.0% in bicarbonate quartiles 1,2,3, and 4, respectively. In unadjusted analyses, the risk of developing renal outcomes was 17% lower per mEq/L increase in serum bicarbonate (HR, 0.83; 95% CI, 0.80-0.85; $P < 0.001$) and the 1st quartile was associated with a HR of 5.88 (95% CI, 3.92-8.81; $P < 0.001$) compared with the 4th quartile. There was significant interaction of serum bicarbonate with eGFR (interaction $P = 0.029$). In an analysis adjusted for demographic factors and proteinuria, in a subgroup with eGFR ≤ 45ml/min/1.73m2, the risk of developing renal outcomes was 9% lower

per mEq/L increase in serum bicarbonate (HR, 0.91; 95% CI, 0.87–0.94; P < 0.001) and the 1st quartile was associated with a HR of 2.38 (95% CI, 1.39–4.08; P=0.002) compared with the 4th quartile. Serum bicarbonate was not independently associated with renal outcomes in those with eGFR > 45ml/min/1.73m2 (HR 0.91; 95% CI, 0.78–1.07; P = 0.253). Serum bicarbonate was not independently associated with secondary outcomes neither in eGFR ≤ 45 (HR 0.96; 95% CI, 0.89–1.04; P = 0.339) nor in eGFR > 45ml/min/1.73m2 (HR 0.90; 95% CI, 0.79–1.02; P = 0.086).

Conclusions : In a cohort of participants with CKD, low serum bicarbonate was an independent risk factor for renal progression, particularly for those with decreased kidney function.

Keywords : metabolic acidosis, serum bicarbonate, chronic kidney disease, renal progression; mortality; cardiovascular event