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Intrarenal renin-angiotensin system activation alters relationship between systolic blood pressure and progression of chronic kidney disease: Findings From KNOW-CKD Study

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Objectives: Elevated blood pressure (BP) and intrarenal renin-angiotensin system (RAS) activity are closely related to chronic kidney disease (CKD) progression. However, interrelationship between BP and intrarenal RAS activity on the risk of CKD progression is unknown. We determined whether intrarenal RAS activity alters relationship between SBP and CKD progression.

Methods: We analyzed 2,076 participants from the Korean Cohort Study for Outcomes in Patients With CKD. The main exposure was systolic BP (SBP). The urinary angiotensinogen-to-creatinine (u-AGT/Cr) ratio was stratified according to the median value (3.65 μg/gCr). The primary outcome was a composite kidney outcome of a ≥50% decline in estimated glomerular filtration rate (eGFR) from baseline measurement or initiation of kidney replacement therapy.

Results: During 10,550 person-years of follow-up (median, 5.2 years), the composite outcome occurred in 800 (38.5%) participants. In the multivariable cause-specific hazard model, higher SBP was associated with an increased risk of CKD progression. There was a significant interaction between SBP and u-AGT/Cr ratio on the risk of the primary outcome (*P*-for-interaction=0.019). In patients with u-AGT/Cr <3.65 μg/gCr, the hazard ratios (HRs) (95% confidence intervals [CIs]) for SBP 120–129, 130–139, and ≥140 mmHg were 1.46 (1.07-1.99), 1.71 (1.25-2.35), and 2.40 (1.73-3.32), respectively, compared with SBP <120 mmHg. In addition, each 10 mmHg increase in SBP was associated with an 18% higher risk of CKD progression. Moreover, there was a greater decline in the eGFR among the higher SBP categories. However, these associations were not observed in patients with u-AGT/Cr ³3.65 μg/gCr.

Conclusions: Urinary angiotensinogen levels may modify the association between SBP and adverse kidney outcomes.

Graphical abstract

Cohort

KNOW-CKD study

Nine tertiary-care hospitals

N=2,076

Median eGFR 43.4ml/min/1.73m^2

Median follow-up 5.2 years

Exposure

Systolic blood pressure

Urinary angiotensinogen-to-creatinine ratio

Endpoint

Composite kidney outcome*

Result