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The greater difference between cystatin C- and creatinine-based estimated glomerular filtration rate is associated with adverse cardiovascular outcome in patients with chronic kidney disease: Results for KNOW-CKD

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Objectives: Although cystatin C and creatinine are established markers of kidney function, non-renal factors can differently affect circulating levels of each marker. Cystatin C levels are more likely to be increased when high blood pressure and inflammation are present, which are well-known cardiovascular risk factors. Here, we aimed to evaluate whether the difference in eGFR between creatinine- and cystatin C- based equations could be used to predict adverse cardiovascular outcome in patients with chronic kidney disease (CKD).

Methods: Using a database from the KoreaN cohort study for Outcome in patients with CKD (KNOW-CKD), we studied 2018 patients with CKD stage 1 to 5 prior to dialysis. The eGFR difference ($eGFR_{diff}$) was calculated by subtracting cystatin C-based eGFR ($eGFR_{cys}$) from creatinine-based eGFR ($eGFR_{cr}$). Coronary arterial calcification score (CACS) was measured by computed tomography. The primary outcome was the occurrence of fatal and non-fatal cardiovascular events.

Results: The mean $eGFR_{diff}$ was 0.5±11.1 mL/min/1.73m^2, and the difference was higher in advanced CKD stages (P for trend < 0.001). When patients were categorized into $eGFR_{diff}$ tertiles, patients in the middle and highest tertiles had significantly higher blood pressure, C-reactive protein levels, and CACS than those in the lowest tertile (P for trend <0.001). The highest $eGFR_{diff}$ tertile was associated with significantly higher risk of cardiovascular outcome (hazard ratio, 2.18; 95% confidence interval [CI], 1.30-3.68; P = 0.003) as compared to the lowest tertile. This relationship was persistent after further adjustment of $eGFR_{cr}$, $eGFR_{cys}$, or $eGFR_{cr\text{-}cystatin\ C}$. In subgroup of 978 patients who measured follow-up CACS at year 4, $eGFR_{diff}$ was significantly associated with accelerated CAC progression (≥ 50/year) (odds ratio, 1.04; 95% CI, 1.01-1.06; P = 0.006).

Conclusions: A greater difference between $eGFR_{cr}$ and $eGFR_{cys}$ was associated with higher risk of adverse cardiovascular outcome and faster CAC progression in patients with CKD.