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High sensitivity C-reactive protein associates with an increased risk for cardiovascular disease and all-cause death, but not with progression of chronic kidney disease: The results from the KNOW-CKD cohort

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Objectives : Low grade inflammation is a distinct feature of chronic kidney disease (CKD) and associates with the development of cardiovascular disease (CVD), increased mortality, and CKD progression. However, this association is not consistent among studies. Thus, we aimed to clarify the clinical significance of inflammation in CKD.

Methods : Using the database from the KoreaN Cohort Study for Outcome in Patients with CKD (KNOW-CKD), we explored the relationship between high sensitivity C-reactive protein (hsCRP) level and adverse outcomes in 2048 patients with CKD. Patients were considered inflamed if they had hsCRP levels of ≥ 2 mg/L. The study endpoints were 1) a composite renal outcome defined as halving of the estimated glomerular filtration rate (eGFR) or the onset of end stage renal disease and 2) a composite outcome of CVD or all-cause mortality.

Results : The mean age of the participants was 53.6 years and 61.8 % were men. The median hsCRP level was 0.60 mg/L (IQR 0.22-1.70). During a median follow-up of 3.0 years, the composite renal outcome occurred in 243 (15.0%) non-inflamed patients and in 69 inflamed (16.3%) patients (P = 0.274). However, 32 (7.5%) inflamed patients developed the composite of CVD or death as compared to 69 (4.2%) non-inflamed patients (P = 0.005). A Kaplan-Meier curve also showed that time to the composite of CVD or death was significantly shorter in inflamed patients than in non-inflamed patients. In a multivariable analysis adjusted for confounders, there was no relationship between hsCRP levels and risk of CKD progression (per 1 log increase; hazard ratio [HR], 0.972; 95% confidential interval [CI], 0.886 - 1.068; P = 0.559). By

contrast, elevated hsCRP levels were significantly associated with an increased risk of the composite of CVD or death (per 1 log increase; HR, 1.189; 95% CI, 1.024 - 1.381; P = 0.023). The inflamed patients had a 1.6-fold increased risk of the composite of CVD or death as compared to non-inflamed patients (HR, 1.571; 95% CI, 1.006 -2.454; P = 0.047). However, adding hsCRP to a conventional Cox model did not improve c-statistics (P = 0.128).

Conclusions : In the KNOW-CKD participants, hsCRP is a significant predictor of CVD or mortality, but has limited value in improving predictability. In addition, it is not associated with CKD progression.

Keywords : C-reactive protein, Cardiovascular disease, Chronic kidney disease, Chronic kidney disease progression, Mortality