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CKD & associated complications

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Circulating TNF Receptors Predict Cardiovascular Disease in Patients with Chronic Kidney Disease

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Background: Cardiovascular disease (CVD) is the main public health problem in patients with chronic kidney disease (CKD); however, there is no established biomarker for predicting CVD morbidity and mortality in CKD. The aim of this study was to evaluate the role of circulating tumor necrosis factor receptors (cTNFRs) in predicting CVD risk in CKD patients.

Methods: We prospectively recruited 1,078 patients with CKD from 11 centers between 2006 and 2012. The levels of cTNFR1 and cTNFR2 were determined by performing an enzyme-linked immunosorbent assay. The primary outcome was CVD event and secondary outcomes were all-cause mortality and ESRD.

Results: During the mean follow-up period of 4 years, 59 patients experienced a CVD event. The median serum concentrations of TNFR1 and cTNFR2 were 2,318.6 pg/ml (Interquartile range [IQR] 225.6 - 13057.7 pg/ml) and 4,924.3 pg/ml (IQR 634.9 - 30599.6 pg/ml), respectively, and the log-transformed TNFR1 (ln cTNFR1) level was closely correlated with the ln cTNFR2 level ($r=0.86$, $P<0.0001$). The urinary protein-to-creatinine ratio (UPCR) and estimated glomerular filtration rate (eGFR) were significantly correlated with the ln cTNFR2 level ($r=0.21$ for UPCR, $r=-0.67$ for eGFR; $P<0.001$ for all). Similar correlations were observed for serum ln cTNFR1 ($r=0.20$ for UPCR, $r=-0.75$ for eGFR; $P<0.001$ for all). In the Cox proportional hazard analyses, ln cTNFR2 (HR 2.271, 95% CI 1.269-4.065, $P=0.006$) predicted CVD risk even after adjustment for clinical covariates, such as UPCR, eGFR, and high-sensitivity C-reactive protein. In addition, ln cTNFR2 was independently associated with all-cause mortality and ESRD.

Conclusion: cTNFR2 could predict CVD, all-cause mortality and ESRD outcome in CKD population, independently of eGFR and UPCR.

Keywords: cardiovascular disease ■ circulating TNF receptor ■ chronic kidney disease