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Clinical significance of creatinine variability and its impact on cardiovascular outcomes in general population

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Objectives: Linear decline of glomerular filtration rate (GFR) is known to aggravate patient outcomes. Serum creatinine, which is commonly used for estimating GFR, often fluctuates throughout the serial measurement. The clinical significance of creatinine fluctuation among the general population whose renal function is prior to chronic kidney disease (CKD) development had not been demonstrated yet. Thus, we investigated the study to evaluate the impact of creatinine variability on patient outcomes.

Methods: We investigated a nationwide retrospective cohort study using the database of Korean National Health Insurance System. Adult patients who received national health screening program and measured creatinine for ≥ 3 times between 2012 and 2016 were considered. Those who previously developed CKD were excluded. The variability of creatinine values were presented with variability independent of mean (VIM). The patients were classified into quartiles of the VIM and Q4 presented highest variability of creatinine. Then, the risks of myocardial infarction (MI), stroke and death were assessed according to the extent of variability.

Results: During the median follow up of 3.27 years, 3,509,899 participants were examined for association of creatinine variability and cardiovascular outcomes. Participants with higher creatinine variability were significantly associated with higher risk of MI (hazard ratio (HR); 1.08, 95% confidence interval (95% CI); 1.01-1.14), stroke (HR (95%CI) 1.08 (1.01-1.14)) and death (HR (95%CI) 1.22 (1.16-1.29)), compared to those with the lowest quartile of creatinine variability.

Conclusions: Increased creatinine variability exhibited association with elevated risk of MI, stroke and death. In general population, whose renal function is prior to CKD development, monitoring of creatinine variability needs to be considered as the parameter of predicting the adverse outcomes, in addition to the decline of GFR.