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**The difference of Cystatin C- and Creatinine-based estimated GFR may differently affect the risk of all-cause mortality according to renal function.**

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**Objectives:** Estimated glomerular filtration rate (eGFR) is a routine method for measuring renal function, and the formula by creatinine or cystatin is known as standard. However, the clinical significance of the difference in eGFR according to these formulas based on two molecules has not been evaluated well. In this study, the effect of eGFR difference by two different formulas on all-cause mortality according to the renal function was investigated.

**Methods:** The patients who measured serum creatinine and cystatin C simultaneously between 2003 and 2020 at Korea University Guro Hospital were enrolled. Based on the KDIGO guideline, patients with impaired renal function were defined as  $eGFR_{Cr} < 60 \text{ ml/min/1.73m}^2$  or dipstick proteinuria  $\geq 1+$ . eGFR difference between two different formulas was measured as eGFR ratio which defined as  $eGFR_{Cys}/eGFR_{Cr}$ . Main outcome was all-cause mortality according to eGFR ratio in patients who has normal renal function and renal function impairment.

**Results:** Among the 8680 patients who measured creatinine and cystatin C simultaneously, 6488 was included as renal dysfunction group and 2192 was included in normal renal function group. The median eGFR ratio of renal dysfunction group was  $1.6 \pm 0.8$  and the median eGFR ratio of normal renal function group was  $1.3 \pm 0.3$  ( $p < 0.001$ ). In renal dysfunction group, the risk of all-cause mortality was significantly elevated with eGFR ratio  $\geq 1.4$ , while low eGFR ratio  $< 1.0$  did not significantly affect mortality risk. In normal renal function group, the risk of all-cause mortality was elevated as U-shape, which increased risk in both eGFR ratio  $\geq 1.4$  and eGFR ratio  $< 0.6$ .

**Conclusions:** The patients with renal dysfunction showed widely distributed difference between  $eGFR_{Cys}$  and  $eGFR_{Cr}$ , and had significantly higher mortality risk with higher  $eGFR_{Cys}$  compared to  $eGFR_{Cr}$ . In normal renal function, the eGFR ratio of  $eGFR_{Cys}$  to  $eGFR_{Cr}$  were significantly elevated mortality risk with U-shape.