Change in GFR and Subsequent Mortality: Meta-Analysis of 32 Cohorts in the CKD Prognosis Consortium

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BACKGROUND: Change in estimated GFR (eGFR) is frequently used to track CKD progression in clinical practice, trials and cohort studies but its association with mortality has not been studied extensively.

METHODS: Change in eGFR was estimated as % change from the first to last eGFR (CKD-EPI creatinine) in a 2-year baseline period. We modeled the hazard ratios (HRs) of subsequent mortality as a spline function of %change in eGFR after adjusting for age, sex, race, first eGFR, and co-morbid conditions. We used random effects meta-analyses to combine results stratified by first baseline eGFR (<60 & ≥60) across studies.

RESULTS: Mortality follow-up of 910,660 participants from 32 cohorts for a mean of 4.2 years after the 2-year baseline period showed 91,398 deaths for baseline eGFR <60 (n=333,722) and 45,063 deaths for baseline eGFR ≥60 (n=576,938). Change in eGFR had a non-linear association with mortality (Figure for eGFR<60). A decline in eGFR was consistently associated with higher subsequent mortality risk (adjusted HR for -30% vs. 0% change in eGFR were: 1.8 at eGFR <60; and 1.5 at eGFR ≥60; p<0.001). Similar results were obtained for a 1- or 3-year change in eGFR. Hazards ratios were largely similar for those with eGFR ≥60 or when stratified by ACR levels.

CONCLUSIONS: Declines in eGFR are strongly and consistently associated with subsequent risk of mortality adjusted for the first eGFR and covariates. These findings support using smaller changes than -57% (equivalent to doubling of serum creatinine) in clinical research.

Figure. Adjusted mortality hazard ratio vs. % 2-year Change in eGFR: Baseline eGFR<60