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Urine Kidney Injury Biomarkers and
Risks of Cardiovascular Disease Events
and All-Cause Death: The CRIC Study

Meyoon Park^{*}, Chi-yuan Hsu^{*}, Alan S. Go[†], Harold I. Feldman[‡],
Dawei Xie[‡], Xiaoming Zhang[‡], Theodore Mifflin[‡], Sushrut S. Waikar^S,
Venkata S. Sabbiseti^S, Joseph V. Bonventre^S, Josef Coresh^{||},
Robert G. Nelson[¶], Paul L. Kimmel[¶], John W. Kusek[¶],
Mahboob Rahman^{**}, Jeffrey R. Schelling^{**}, Ramachandran S. Vasan^{††},
Kathleen D. Liu^{*} on behalf of the Chronic Renal Insufficiency Cohort
(CRIC) Study Investigators the CKD Biomarkers Consortium

+ Author Affiliations

Correspondence:

Dr. Meyoon Park, Department of Medicine, Division of Nephrology, University of
California, San Francisco, 533 Parnassus Avenue, U404, Box 0532, San Francisco,
CA 94143. Email: Meyoon.Park@ucsf.edu

Abstract

Background and objectives CKD is an important risk factor for cardiovascular disease (CVD) and death. We investigated whether select urine kidney injury biomarkers were associated with higher risk of heart failure (HF), CVD, and death in persons with CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) Study.

Design, setting, participants, & measurements Urine kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin, liver fatty acid-binding protein, and *N*-acetyl- β -D-glucosaminidase were measured in urine of a subset of CRIC participants ($n=2466$). We used Cox proportional hazards regression to examine associations between these biomarkers indexed to urinary creatinine (Cr) and (1) HF, (2) a composite of atherosclerotic CVD events (myocardial infarction, ischemic stroke, or peripheral artery disease), and (3) all-cause death.

Results At baseline, mean age of study participants was 59.5 ± 10.8 years, 46% were women, and 34% had a self-reported history of any CVD. Median follow-up was 6.5 (interquartile range, 5.6–6.8) years. A total of 333 HF events, 282 atherosclerotic CVD events, and 440 deaths were observed during a median follow-up of 6.5 (interquartile range, 5.6–6.8) years. Those in the highest two quintiles of KIM-1/Cr levels had a higher risk of HF relative to the lowest quintile (quintile 5 versus quintile 1 adjusted hazard ratio [aHR] of 1.73 [95% confidence interval, 1.05 to 2.85]). *N*-acetyl- β -D-glucosaminidase/Cr was associated with HF in continuous analyses (aHR per log SD higher 1.18 [95% confidence interval, 1.01 to 1.38]). Only KIM-1/Cr was independently associated with atherosclerotic CVD events (aHR per log SD higher 1.21 [95% confidence interval, 1.02 to 1.41]), whereas both KIM-1/Cr (quintile 5 versus quintile 1 aHR of 1.56 [95% confidence interval, 1.06 to 2.31]) and neutrophil gelatinase-associated lipocalin/Cr (quintile 5 versus quintile 1 aHR of 1.82 [95% confidence interval, 1.19 to 2.8]) were associated with all-cause death.

Conclusions Selected urine kidney injury biomarkers were independently associated with higher risk of HF, CVD events, and death in CRIC. Among the biomarkers examined, only KIM-1/Cr was associated with each outcome. Further work is needed to determine the utility of these biomarkers to improve risk prediction for these adverse outcomes.

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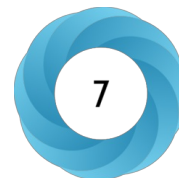
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