RISK FACTORS

Meta-analysis confirms relationship between eGFR, albuminuria and risk of mortality

Estimated glomerular filtration rate (eGFR) and albuminuria are associated with all-cause and cardiovascular mortality independently of each other and of traditional risk factors, according to a meta-analysis published by the Chronic Kidney Disease Prognosis Consortium. In a commentary published in the same issue of *The Lancet*, Giovanna Leoncini and colleagues express their hope that this study will promote greater clinical use of renal function tests for global risk assessment.

Chronic kidney disease (CKD) is a major health problem worldwide and is associated with an increased risk of cardiovascular and all-cause mortality. Although previous studies have reported an association between eGFR or albuminuria and outcomes in the general population; controversy exists over the ability of these parameters to define and stage CKD.

To address this controversy, the consortium performed a collaborative meta-analysis to evaluate the independent and combined associations of eGFR and albuminuria with mortality. The researchers performed a PubMed search to identify studies that met eligibility criteria, such as the inclusion of at least 1,000 participants from a general population, and baseline information about eGFR and urine albumin concentrations.

The researchers extended their search by reviewing references from eligible articles, and to minimize publication bias, they sought further data by discussion between collaborators, nephrologists, and cardiovascular epidemiologists. The consortium issued standard statistical programs to collaborating study groups and asked them to prepare a dataset with 12 variables, including follow-up time, event variable, and 10 predictors including eGFR and albuminuria. Guidelines for the definition of variables, such as hypertension, diabetes, and smoking, were circulated to minimize heterogeneity.

In total, 21 general population cohorts were included in the analysis. These studies included data on over 100,000 individuals with urine albumin-to-creatinine ratio (ACR) measurements and over 1 million individuals with urine protein dipstick measurements. The median study follow-up was 7.9 years.

The researchers found that eGFR and albuminuria were associated with all-cause mortality in the general population. Compared with an eGFR of 95 ml/min/1.73 m², hazard ratios (HRs) for all-cause mortality were 1.18 (95% CI 1.05–1.32) for an eGFR of 60 ml/min/1.73 m², 1.57 (95% CI 1.39–1.78) for an eGFR of 45 ml/min/1.73 m², and 3.14 (95% CI 2.39–4.13) for an eGFR of 15 ml/min/1.73 m². Similarly, compared with an ACR of 0.6 mg/mmol, HRs for all-cause mortality were 1.20 (95% CI 1.15–1.26) for an ACR of 1.1 mg/mmol, 1.63 (95% CI 1.50–1.77) for an ACR of 3.4 mg/mmol, and 2.22 (95% CI 1.97–2.51) for an ACR of 33.9 mg/mmol. These associations were independent of each other and of traditional cardiovascular risk factors. “The consistency in both continuous and categorical models for eGFR and ACR demonstrates that our findings are robust”, says corresponding author, Josef Coresh.

Similar findings for both eGFR and ACR were seen for cardiovascular mortality.

“Our study demonstrates that mortality risk is doubled at eGFR 30–45 ml/min/1.73 m² or ACR 11.3 mg/mmol compared with their normal ranges”, notes lead author Kunihiro Matsushita. “With 21 studies from 14 countries of Asia, Europe, North America, and Oceania, our study shows the range of association as well as summary estimates across the globe”.

The consortium also investigated the interaction of eGFR and ACR with age. A stratified analysis of eGFR and ACR by age showed largely similar associations of eGFR and ACR with mortality risk in younger (<65 years of age) and older (≥65 years of age) populations. Matsushita and colleagues say that their findings provide a quantitative basis for the use of eGFR and albuminuria for risk assessment in CKD. “Our study provides the most comprehensive assessment of the relationship between eGFR, albuminuria, and mortality performed to date”.

The consortium plan to expand their analyses with respect to outcomes and additional estimates of kidney function, for example, by use of the CKD-EPI equation to estimate GFR and by assessing the association of outcomes with kidney biomarkers, such as cystatin C. “We appreciate that the range of outcomes related to CKD is broad, and we plan to encourage more cohort studies to examine a wide range of outcomes, including heart failure and other subtypes of cardiovascular disease, infections, and acute kidney injury”, states Coresh.

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Original article Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 375, 2073–2081 (2010)

Further reading Leoncini, G. *et al.* Overall health assessment: a renal perspective. *Lancet* 375, 2053–2054 (2010)