Risk of death in general population independently predicted by both low kidney filtration rate and high albumin: creatin

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A meta-analysis of more than a million people in populations across Europe, the USA, Australia, and Asia has shown that both glomerular filtration rate (GFR) (the rate at which blood is filtered by the kidneys) and levels of protein in urine (albuminuria) independently predict the risk of death in the general population. The findings appear in an Online First Article, written by Dr Josef Coresh, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; Dr. Paul E de Jong, University Medical Center Groningen, Groningen, Netherlands; and Dr. Andrew Levey, Tufts Medical Center, Boston, and other colleagues from the Chronic Kidney Disease Prognosis Consortium.

Chronic kidney disease is recognised as a major global public health problem. The disease affects 10?% of the adult population in Asia, Australia, Europe, and the USA, and increases the risk of all-cause mortality, cardiovascular disease, and progression to kidney failure, even after accounting for traditional risk factors such as hypertension and diabetes. However, controversy surrounds the use of estimated GFR (eGFR) and albuminuria to define chronic kidney disease and assign its stages. In this new research, the authors collaborated with contributing cohorts to analyse data from around the globe using standardised methods and combined the results using meta-analysis techniques to assess the independent and combined associations of eGFR and albuminuria with mortality.

The analysis included around 105,000 people from 14 studies with urine albumin-to-creatinine ratio (ACR) measurements; and around 1.1 million participants from seven studies with urine protein dipstick measurements. eGFR was estimated from serum creatinine measured from a blood draw using a standard equation and ACR was calculated from measurements in a urine sample. In studies with ACR measurements, risk of mortality was unrelated to eGFR between 75 and 105 standard units (measured in mL/min/1•73 m²)-the optimal range in healthy people. However, risk increased at lower eGFRs. Compared with eGFR of 95 (around the middle of the healthy range), there was an 18% increased risk of death for eGFR of 60, rising to a 57% increased risk for a GFR of 45. When GFR fell to the dangerously low level of 15, risk of death was more than tripled.

Mortality was higher at progressively higher ACR. Compared with ACR 0•6 mg/mmol (a healthy baseline value), risk of death rose 20% for patients with ACR of 1.1 (a high-normal level), 63% for those with ACR of 3.4 (the threshold for defining chronic kidney disease often termed micro-albuminuria), and more than doubled for those with ACR values of 33.9 (the threshold for defining overt albuminuria, often termed macro-albuminuria).

The authors found that eGFR and ACR were multiplicatively associated with risk of mortality without evidence of interaction. Similar findings were recorded for cardiovascular mortality and in studies with dipstick measurements.

The authors say: "By contrast with previous claims, these findings suggest that mild to moderate reduction in eGFR is associated with adverse clinical outcomes."

They conclude: "eGFR less than 60 mL/min/1•73 m² and ACR 1•1 mg/mmol (10 mg/g) or more are independent predictors of mortality risk in the general population. This study provides quantitative data for use of both kidney measures for risk assessment and definition and staging of chronic kidney disease."

In an accompanying Comment, Drs Roberto Pontremoli, Giovanna Leoncini, and Francesca Viazzi University of Genoa, Italy, say that the organisation Kidney Disease: Improving Global Outcomes (KDIGO) has already appointed a workgroup to develop a revised global chronic kidney disease guideline.

They say: "Thanks to this well-conducted study, the kidney message for overall health might get some well deserved attention from the medical community... Today's results indicate that the kidney might provide useful information about our future health. Therefore, the study by the Chronic Kidney Disease Prognosis Consortium will hopefully promote greater use of renal function tests in clinical practice aimed at global risk assessment. Researchers should be further encouraged to evaluate the effect of including renal variables in algorithms and risk charts."

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