Nature Reviews Nephrology **8**, 611 (2012); published online 9 October 2012; doi:10.1038/nrneph.2012.199

CHRONIC KIDNEY DISEASE

Association of chronic kidney disease with adverse outcomes in the absence of hypertension and diabetes

Chronic kidney disease (CKD) is a strong predictor of mortality and end-stage renal disease (ESRD), even in the absence of diabetes and/or hypertension, say the authors of two large-scale meta-analyses. "Our findings suggest that several major health outcomes, including ESRD and death, are increased in individuals with chronic kidney disease, irrespective of the cause of their impaired kidney function", Caroline Fox and colleagues state in their paper.

CKD often coexists with comorbidities. Hypertension is both a cause and a consequence of CKD and is the most common cardiovascular risk factor associated with CKD. On the other hand, diabetes is the leading cause of CKD in developed countries. Outcomes for individuals with CKD and hypertension and/or diabetes are known to be poor; however, the extent to which these comorbidities modify the association of CKD with adverse outcomes is not well understood. The two meta-analyses, performed by members of the Chronic Kidney Disease Prognosis Consortium, aimed to explore the associations of estimated glomerular filtration rate (eGFR) and albuminuria with mortality and ESRD risk according to hypertensive and diabetes status.

One meta-analysis by Bakhtawar Mahmoodi *et al.* assessed whether hypertension modifies the association of decreased eGFR and increased albuminuria with adverse outcomes. The researchers analysed data from 1,127,656 participants from 25 general and high-risk populations and 13 CKD cohorts; 364,344 participants had hypertension. eGFR was determined using the Chronic Kidney Disease Epidemiology Collaboration equation.

Mahmoodi *et al.* found dose-dependent associations of low eGFR and high albuminuria with mortality in both hypertensive and nonhypertensive individuals from the general, high-risk and CKD cohorts. Risks of all-cause and

Don Farrall | Photodisc/Getty

cardiovascular mortality in individuals with eGFR >55 ml/min/1.73 m^2 and >45 ml/min/1.73 m^2, respectively, were higher in hypertensive individuals than in nonhypertensive individuals in the general and high-risk cohorts; however, a steeper relative risk gradient in nonhypertensive participants resulted in equivalent or greater mortality outcomes for nonhypertensive individuals with eGFR <45 ml/min/1.73 m^2. When separate reference eGFRs of 95 ml/min/1.73 m^2 were set in both hypertensive and nonhypertensive groups to assess the interaction between eGFR and hypertension, the researchers found significant pointwise interactions at eGFR <59 ml/min/1.73 m^2 for all-cause mortality and at eGFR <73 ml/min/1.73 m^2 for cardiovascular mortality. The adjusted hazard ratio for all-cause mortality at eGFR 45 ml/min/1.73 m^2 was 1.77 (95% CI 1.57–1.99) in nonhypertensive individuals and 1.24 (95% CI 1.11–1.39) in hypertensive individuals. Similarly, high albuminuria was more strongly associated with mortality in individuals without hypertension than in those with hypertension; the adjusted hazard ratio for all-cause mortality for an albumin-to-creatinine ratio of 300 mg/g (versus 5 mg/g) was 2.30 (95% CI 1.98–2.68) in nonhypertensive individuals compared with 2.08 (95% CI 1.84–2.35) in hypertensive individuals. In the CKD cohorts, the researchers found similar associations of mortality outcomes with eGFR and albuminuria. The associations of low eGFR and high albuminuria with ESRD were not affected by hypertensive status in this patient group. The interactions between eGFR and albuminuria with mortality outcomes in the general and high-risk populations were not attributable to the presence of diabetes.

The second meta-analysis by Fox *et al.* further investigated the interaction of kidney function with diabetes. This meta-analysis included data from 1,024,977 individuals from 30 general population and high-risk cohorts and 13 CKD cohorts; 128,505 participants had diabetes. Using one set reference point in the nondiabetes group, the mortality risks in the general and high-risk cohorts were 1.2–1.9-fold higher in individuals with diabetes than in those without. However, when separate reference points were set in the nondiabetes and diabetes groups to assess interaction between renal function and diabetes, Fox *et al.* found no difference in relative risks of mortality between the groups. No significant interactions with diabetes were identified at any eGFR or albuminuria category studied. Similarly, when the researchers set separate references in the diabetes and nondiabetes groups in the CKD cohorts, no significant interaction between diabetes and risk of ESRD was identified. "Taken together, these findings show the value of eGFR and albuminuria as predictors of these health outcomes and emphasise their importance as predictors in the presence or absence of diabetes", say the researchers.

Susan J. Allison

Original articles Mahmoodi, B. K. *et al.* Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without hypertension: a meta-analysis. *Lancet* doi:10.1016/S0140-6736(12)61272-0 | Fox, C. S. *et al.* Associations of kidney disease measures with mortality and end-stage renal disease in individuals with and without diabetes: a meta-analysis. *Lancet* doi:10.1016/S0140-6736(12)61350-6

© 2012 Macmillan Publishers Limited. All rights reserved