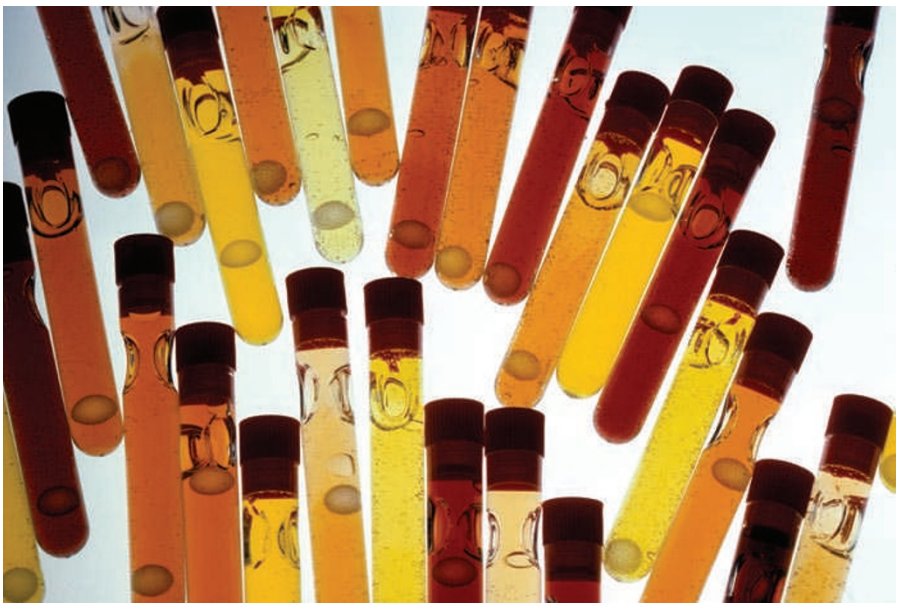
CHRONIC KIDNEY DISEASE

Proteinuria is an important indicator of adverse outcomes in CKD

Assessment of proteinuria in addition to estimated glomerular filtration rate (eGFR) in patients with chronic kidney disease (CKD) may help identify individuals at high risk of adverse outcomes, according to a new study. "Patients with higher levels of proteinuria within a given level of eGFR had an increased risk of adverse outcomes", explains Brenda Hemmelgarn of the study group. "These results suggest that proteinuria is an important marker that should be considered in future revisions of the CKD staging system".



Current methods for staging CKD are primarily based on calculations of eGFR. However, findings from prior studies suggesting that proteinuria is associated with adverse outcomes in CKD led Hemmelgarn and colleagues to investigate whether individuals with a low eGFR and proteinuria have a higher risk of adverse outcomes than individuals with one or neither of these characteristics.

The researchers assessed the association between eGFR, proteinuria, and adverse clinical outcomes in adults with CKD who were undergoing laboratory testing in Alberta, Canada. All participants in this cohort study had at least one outpatient serum creatinine measurement, did not require renal replacement therapy at baseline, and had proteinuria assessed either by dipstick ($n = 920{,}985$) or by measurement of their albumin:creatinine ratio (ACR; $n = 102{,}701$). Outcomes assessed were all-cause mortality, hospitalization for acute myocardial infarction, development of end-stage renal disease, and the occurrence of a doubling in serum creatinine from the baseline measurement.

Over a median follow-up of 35 months 27,959 participants (3%) died, 5,772 (0.6%) were hospitalized for myocardial infarction, 771 (0.08%) were started on renal replacement therapy, and 2,514 (0.4%) had a doubling of their serum creatinine level. The researchers stratified participants' eGFRs into four categories: ≥60 ml/min/1.73 m^2, 45–59.9 ml/min/1.73 m^2, 30–44.9 ml/min/1.73 m^2, and 15–29.9 ml/min/1.73 m^2.

Hemmelgarn *et al.* found that the risk of mortality within each eGFR category varied depending on the presence and severity of proteinuria. For example, the age-adjusted risk of mortality was over twofold higher in individuals with an eGFR ≥60 ml/min/1.73 m^2 and heavy proteinuria (as assessed by dipstick analysis) than in those with an eGFR within the range 45–59.9 ml/min/1.73 m^2 but without proteinuria. The risk of other adverse outcomes—myocardial infarction, need for renal replacement therapy, and progression of renal disease—were also increased for each eGFR category in individuals with moderate or heavy proteinuria compared with those without proteinuria. Similar results were achieved when the researchers used ACR as an alternative measure of proteinuria. Individuals with an ACR >2,000 mg/g had increased rates of adverse outcomes than those without proteinuria.

The researchers say that their results support the hypothesis that proteinuria is an important marker of CKD. "Patients with heavy proteinuria but without overtly abnormal eGFR seemed to have worse clinical outcomes than those with moderately reduced eGFR but without proteinuria". As current guidelines for the staging and classification of CKD do not explicitly consider the severity of concomitant proteinuria, Hemmelgarn and colleagues believe their findings have direct clinical implications. They say that risk categorization based on eGFR alone does not adequately define clinically relevant gradients of risk and that proteinuria should be considered in addition to eGFR in future revisions of CKD staging. They add that their results may also enable the identification of individuals who would benefit most from close monitoring, although Hemmelgarn acknowledges that further work is required to confirm this hypothesis. "The results from this study do not directly address which patients would benefit from referral to a nephrologist", she explains. The researchers plan to explore this question in the same large cohort in future studies.

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