

Reduced kidney function, high levels of protein in urine associated with adverse outcomes

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Patients with high levels of proteinuria (protein in urine) in addition to another marker of reduced kidney function had an associated increased risk of all-cause death, heart attack or progression to kidney failure, according to a study in the February 3 issue of *JAMA*.

As many as 26 million Americans have chronic [kidney](#) disease (CKD). The current system for determining the stage of CKD is based primarily on the estimated rate of glomerular filtration (eGFR; measure of the kidneys' ability to filter and remove waste products) with lower eGFR associated with higher risk of adverse outcomes. "... the guidelines have been criticized because they do not incorporate information about the presence and severity of proteinuria an important marker of CKD that is associated with adverse outcomes," the authors write.

Brenda R. Hemmelgarn, M.D., Ph.D., of the University of Calgary, Alberta, Canada, and colleagues examined the association between reduced eGFR, proteinuria, and adverse clinical outcomes, including all-cause death, heart attack, and progression to kidney failure. The researchers analyzed data from a province-wide (Alberta) laboratory registry that included eGFR and proteinuria measurements for 2002 to 2007. There were 920, 985 adults who had at least 1 outpatient serum creatinine measurement and who did not require renal replacement treatment (i.e., dialysis) at the beginning of the study.

The researchers found that within each level of eGFR, there was substantial variability in risk with participants who had greater amounts of proteinuria having increased adjusted rates of all 4 adverse outcomes (all-cause death, [heart attack](#), end-stage renal disease, and the doubling of serum creatinine measurement [corresponding to a

50 percent decline in [kidney function](#)]). Patients with heavy proteinuria but without overtly abnormal eGFR appeared to have worse clinical outcomes than those with moderately reduced eGFR but without proteinuria. Significant interactions between eGFR and proteinuria were observed for death, initiation of renal replacement, and doubling of serum creatinine.

"These findings are important because current guidelines for the classification and staging of CKD are based on eGFR without explicit consideration of the severity of concomitant proteinuria. In addition, computerized reporting of eGFR (generally without consideration of proteinuria) is increasingly used to assist physicians in identifying patients at high risk of adverse outcomes—or those who might benefit from specialist care. Although our findings do not directly address which patients would benefit from referral to a nephrologist, they do suggest that risk stratification performed in terms of eGFR alone is relatively insensitive to clinically relevant gradients in risk," the authors write. "These findings suggest that future revisions of the classification system for CKD should incorporate information from proteinuria."

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