Combined use of three markers for kidney disease may help predict risk of kidney failure, death

April 11 2011

Combining the chronic kidney disease markers of creatinine-based estimated glomerular filtration rate and urine albumin-to-creatinine ratio with the biomarker cystatin C was associated with improved prediction of end-stage kidney disease and all-cause death, according to a study that will appear in the April 20 issue of *JAMA*. The study is being published early online to coincide with its presentation at the World Congress of Nephrology.

Chronic kidney disease (CKD) is currently defined as certain levels of creatinine-based estimated glomerular filtration rate (GFR) or urine albumin-to-creatinine ratio (ACR). Clinical laboratories are routinely reporting estimated GFR, and electronic medical records often alert clinicians to the presence of CKD on estimated GFR alone, even though because of several factors, serum creatinine may misclassify individuals. Because routine assessment of the ACR is only recommended for persons with diabetes, initial CKD detection in routine practice is primarily limited to serum creatinine testing. Serum cystatin C, an alternative biomarker of kidney function, it is not routinely used in clinical practice, according to background information in the article. Combining these markers for CKD evaluation has not been well studied.

Carmen A. Peralta, M.D., M.A.S., of the San Francisco VA Medical Center, and colleagues conducted a study to evaluate whether combining creatinine, cystatin C, and urine ACR would improve identification of

risks associated with CKD compared with creatinine alone. The study, conducted from January 2003 to June 2010, included 26,643 U.S. adults. Participants were categorized into 8 groups, defined by estimated GFR determined by creatinine and by certain levels of cystatin C and ACR. The primary outcomes measured were the incidence of end-stage renal disease and all-cause death.

The study participants had an average age of 65 years. Overall, 40 percent were black, 54 percent were women, 21 percent had diabetes, and 59 percent had hypertension. Over a median (midpoint) follow-up period of 4.6 years, 1,940 participants died and 177 developed incident end-stage renal disease. Overall, 2,904 participants (11 percent) were classified as having CKD based on creatinine. Among them, 701 participants (24 percent) had CKD defined by creatinine alone and 148 participants (5 percent) had CKD defined by creatinine and ACR, whereas CKD was defined by creatinine and cystatin C for 1,172 participants (40 percent) and by all biomarkers for 883 participants (30 percent). Among 23,739 participants with no CKD defined by creatinine, 3,863 (16 percent) had CKD detected by ACR, cystatin C, or both.

The researchers found that by adding cystatin C to creatinine and albuminuria for risk prediction could more accurately reclassify persons and distinguish important prognostic differences, namely a 3-fold risk of death and 4-fold risk of end-stage renal disease. Cystatin C and albuminuria were both strongly and independently associated with all-cause death among persons with or without CKD defined by creatinine-based estimated GFR. "The risk of future end-stage renal disease was concentrated within the subset of participants who had CKD defined by all 3 markers. The second highest risk group for end-stage renal disease was missed by creatinine but was detected by cystatin C and ACR."

The authors note that several groups are currently advocating new

international guidelines that more accurately reflect prognosis of CKD and have proposed adding ACR to staging of CKD. "Our results suggest that a triple-marker approach using both ACR and cystatin C to confirm CKD more accurately discriminates prognosis for death and progression to end-stage renal disease than creatinine and ACR alone."

They add that the use of a triple-marker renal panel that improves prognostic ability could both reduce unwarranted referrals and unnecessary workups for low-risk individuals and would prioritize specialty care and interventions to individuals at highest risk.

"Our findings illustrate the potential implications of universal screening for CKD using a triple-marker approach," the researchers write. "Future studies are needed using the triple-marker approach to evaluate clinical strategies that may reduce these risks."

More information: *JAMA*. 2011;305[15]:doi.10.1001/jama.2011.468