



May 17, 2010, 6:30 pm ET

Study Documents a Consistent Risk of Mortality Associated with Kidney Disease in 14 Countries Across Four Continents

NEW YORK, NY – Simple tests of kidney function and damage predict total and cardiovascular mortality risk in a wide range of populations across the globe, according to a systematic analysis including more than 1.2 million participants.

In this week's issue of *The Lancet*, researchers from the Chronic Kidney Disease Prognosis Consortium, established last year by Kidney Disease: Improving Global Outcomes (KDIGO), show two simple measures of kidney disease are strongly related to total and cardiovascular mortality. One measure estimates the kidneys' filtration function using a blood test and the other estimates kidney damage using a urine test for protein or albumin.

The new findings are part of a comprehensive effort to refine the definition and staging of chronic kidney disease. Current guidelines from the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) define chronic kidney disease based on the presence for greater than three months of either: (1) estimated kidney filtration function below 60 ml/min/1.73 m² (approximately half the level in a young healthy adult) or (2) kidney damage most commonly detected by protein in the urine (the most sensitive test is an albumin-creatinine ratio (ACR) of 30 mg/g or greater).

"Data presented in this meta-analysis confirm beyond any doubt that the current thresholds are indicative of increased all-cause and cardiovascular mortality risk," Roberto Pontremoli of the University of Genoa in Italy and his colleagues write in a Comment accompanying the article.

-more-

“The overwhelming support by the community of researchers studying kidney disease with the call to assemble the best possible data to define kidney disease prognosis and improve its definition and staging was impressive” said Josef Coresh of Johns Hopkins University, one of the senior members of the consortium.

Staging aims to categorize the severity of an illness to help in guiding treatment. Based on the large amount of data analyzed, the study confirmed earlier suggestions that adding information about the level of protein in the urine can improve the current staging system for chronic kidney disease, which centers on the kidney’s filtration function. The level of protein in the urine added information about the risk of mortality at all levels of kidney function. Kidney filtration function was unrelated to mortality risk in the 75-105 ml/min/1.73 m² range; a reduction to 60 was already an independent risk factor for total and cardiovascular mortality and risk increased threefold at an estimated filtration rate of 15 ml/min/1.73 m², when people often need dialysis.

Mortality risk also increased progressively with increasing albumin in the urine starting at the lowest levels. The risk of mortality was elevated by approximately 50% at 30 mg/g albumin to creatinine ratio, the threshold for defining chronic kidney disease, and rose to more than four-fold at high levels of albuminuria (1 gram/g) compared to an optimal level of 5 mg/g. Even people with high normal levels of albumin in the urine were at statistically significantly greater risk of mortality than people with low (optimal) levels of albumin in the urine.

An inexpensive dipstick test was nearly as predictive as ACR for stratifying risk based on albuminuria. The study did not directly compare dipstick testing with the more precise albumin to creatinine ratio in the urine. However, in countries where only dipstick testing is affordable, the study’s authors say the less-precise test could be useful for risk stratification.

This sort of testing, while it bears “powerful prognostic value,” remains “largely underused in risk calculators as well as in daily clinical practice,” Dr. Pontremoli and his colleagues write in their editorial. “These results indicate that the kidney may provide useful information about our future health. Therefore, they will hopefully promote greater use of renal function parameters in clinical practice aimed at global risk assessment.”

About the Chronic Kidney Disease Prognosis Consortium

The Consortium is led by Josef Coresh at Johns Hopkins University in the US, Paul de Jong and Ron Gansevoort at the University of Groningen in The Netherlands, and Andrew Levey at Tufts University. It was initiated for a KDIGO's October 2009 Controversies Conference where leading investigators from 45 studies contributed data to examine kidney disease outcomes across the globe. This report focuses on mortality outcomes from 14 countries including 21 leading population based studies. Other meta-analyses will focus on high risk and kidney disease cohort and end-points beyond mortality. The lead author was Kunihiro Matsushita from Johns Hopkins Bloomberg School of Public Health.

Chronic Kidney Disease Prognosis Consortium Participating Investigators/Collaborators:

AKDN Marcello Tonelli, Brenda Hemmelgarn; **ARIC** Josef Coresh, Brad C Astor, Kunihiro Matsushita, Yaping Wang; **AusDiab** Robert C Atkins, Kevan R Polkinghorne, Steven J Chadban; **Beaver Dam** Anoop Shankar, Ronald Klein, Barbara E K Klein; Beijing HaiYan Wang, Fang Wang, Luxia Zhang, Lisheng Liu; **CHS** Michael Shlipak, Mark J Sarnak, Ronit Katz, Linda P Fried; **COBRA** Tazeen Jafar, Muhammad Islam, Juanita Hatcher, Neil Poulter, Nish Chaturvedi; **ESTHER** Dietrich Rothenbacher, Hermann Brenner, Elke Raum, Wolfgang Koenig; Framingham Caroline S Fox, Shih-Jen Hwang, James B Meigs; Gubbio Massimo Cirillo; **HUNT** Stein Hallan, Stian Lydersen, Jostein Holmen; **MESA** Michael Shlipak, Mark J Sarnak, Ronit Katz, Linda P Fried; **MRC Older People** Paul Roderick, Dorothea Nitsch, Astrid Fletcher, Christopher Bulpitt; **NHANES III** Brad Astor, Josef Coresh; Ohasama Takayoshi Ohkubo, Hirohito Metoki, Masaaki Nakayama, Masahiro Kikuya, Yutaka Imai; **PREVEND** Ron T Gansevoort, Paul E de Jong, Marije van der Velde; **Rancho Bernardo** Simerjot Kaur Jassal, Elizabeth Barrett-Connor, Jaclyn Bergstrom; **REGARDS** David G Warnock, Paul Muntner, Suzanne Judd, William M McClellan, Mary Cushman, George Howard, Leslie A McClure; Severance Sun Ha Jee, Heejin Kimm, Ji Eun Yun; Taiwan Chi-Pang Wen, Sung-Feng Wen, Chwen-Keng Tsao, Min-Kuang Tsai; **ULSAM** Johan Ärnlöv.

KDIGO Guideline Development Process

KDIGO is a global organization, managed by the National Kidney Foundation (NKF), with the mission to improve patient care and outcomes through the development and implementation of evidence-based clinical practice guidelines.

KDIGO employs an evidence-based approach that is modeled on the guideline development process used in the NKF-Kidney Disease Outcome Quality Initiative (KDOQI™) guidelines. It empowers an independent work group supported by evidence review experts to rigorously examine the published evidence and formulate practice guidelines. Before they are finalized, the draft guidelines undergo a two-stage review process: internal review by the KDIGO Board, followed by open peer review by interested organizations, agencies and individuals worldwide.

Reviewer comments are carefully reviewed by the work group, and incorporated as appropriate, before the guidelines are finalized and published in *Kidney International*.

#