Thursday, March 13, 2008 is World Kidney Day! World Kidney Day was proposed by the International Society of Nephrology and International Federation of Kidney Foundations in 2006 to broadcast a message about kidney diseases to the public, government health officials, general physicians, allied health professionals, individuals, and families. In 2007, the message on World Kidney Day was that kidney disease is common, harmful, and treatable.1 This issue of AJKD contains articles from around the world about the importance of chronic kidney disease (CKD), attesting to the growing recognition of CKD as a global public health problem. In this editorial, we highlight CKD in the elderly as a new challenge for research, clinical practice, and public health.

BACKGROUND

As the world’s population ages, a major challenge is to unravel the pathways to disease and disability in older persons. The elderly are the fastest growing subset of the US population, with the number of adults over 65 years of age expected to approach approximately 20% of the population by 2030.2 Age-associated increases in chronic disease and disability have led to a significant financial burden on the health care system, due to increases in testing, medication usage, hospitalizations, and institutionalization.3 CKD has recently been recognized as one of a number of chronic diseases primarily affecting the elderly; early stages are silent yet associated with substantially increased risk for cardiovascular disease, while later stages are also associated with a wide range of additional complications including kidney failure. The full extent of the burden of CKD is not known and many questions remain unanswered. Understanding the prevalence, causes, and associations of CKD with other chronic diseases in the elderly is essential for effective treatment and prevention.

TWO RECENT STUDIES

Recent studies from the United States and China provide new information about the prevalence of CKD in the elderly. In JAMA, Coresh and colleagues used data from the US National Health and Nutrition Examination Survey (NHANES) to estimate the prevalence of CKD among noninstitutionalized adults (aged ≥ 20 years).4 They found an increase in prevalence from approximately 10% in the period from 1988 to 1994 to 13% in the period from 1999 to 2004, corresponding to 26 million people in the year 2000. Among individuals aged 70 years or older, the prevalence of CKD increased from 38% to 47% (Fig 1, right bars). For this analysis, kidney damage was defined as persistent albuminuria (spot urine albumin-creatinine ratio > 30 mg/g), and glomerular filtration rate (GFR) was estimated from serum creatinine using an assay traceable to isotope dilution mass spectroscopy (IDMS) and the Modification of Diet in Renal Disease (MDRD) Study equation re-expressed for use with standardized creatinine.5

In this issue of AJKD, Zhang and colleagues report results from a representative sample of noninstitutionalized adults aged 18 years and older in Beijing.6 They used a similar definition of persistent albuminuria as in NHANES, but also included hematuria as a marker of kidney damage because of the higher prevalence of glomerular diseases in China than in the United States. They estimated GFR based on a serum creatinine assay traceable to IDMS and an equation which provides GFR estimates approximately 23% higher than the MDRD Study equation in white of the same age and sex.7 They demonstrated an overall prevalence of CKD of 13%, corresponding to 1.43 million Beijing residents in 2000. Among those aged 70 years and over, the prevalence was 31% (Fig 1, left bars).

While there are many differences between the 2 studies, both highlight the substantial prevalence of CKD in the elderly, which has generated...
many questions and much controversy. Currently available GFR estimating equations underestimate measured GFR in the normal population and surveys do not have data on persistence of decreased GFR, so it is likely that some people with reduced estimated GFR (eGFR) do not have CKD.8 Some have suggested modification of the definition of CKD to incorporate a lower threshold for the definition of reduced GFR in the elderly.9-11 We contend that the high prevalence of reduced eGFR in the elderly is related to the high prevalence of cardiovascular disease risk factors, leading to both kidney disease and cardiovascular disease, and that reduced eGFR in the elderly should not be considered as normal, simply because it is common.

AGE-RELATED CHANGES IN KIDNEY FUNCTION AND STRUCTURE

Normal GFR averages approximately 130 and 120 mL/min/1.73 m² (2.7 and 2.0 mL/s/1.73 m²) in healthy young men and women, respectively, with most individuals having a GFR greater than 90 mL/min/1.73 m² (1.50 mL/s/1.73 m²).12 In one cross-sectional study of healthy adults, a decline of approximately 10% per 10 years of age in GFR and renal blood flow was noted.13 These data gave rise to the hypothesis that a decline in GFR was a normal part of the aging process. However, a longitudinal study showed that the rate of decline in GFR was greater in people with hypertension than without.14 Among NHANES III participants, there was an increase in prevalence of albuminuria from 7% at age 20 to 39 years to 30% at age 70 years or older.15 Autopsy findings of older adults show increases in global glomerulosclerosis, arteriolar sclerosis, and tubular atrophy, with reduced cortical thickness and decreased kidney size.16,17 These findings are considered abnormal when observed in young adults. Overall, these findings challenge the traditional concept that age-related decline in kidney function is normal.

CONSEQUENCES OF CKD IN THE ELDERLY

There is substantial evidence for health risks associated with decreased GFR and albuminuria in the elderly. The median age of new dialysis patients is now 65 years and the fastest growing group of new dialysis patients are those older than 75 years of age (Fig 2).18 Traditionally recognized complications of decreased GFR include hypertension, anemia, malnutrition, bone and mineral disorders, neuropathy, and decreased quality of life, which are common in elderly patients with eGFR less than 30 mL/min/
1.73 m² (CKD stages 4-5). Recent studies also demonstrate increased prevalence of traditional age-related conditions such as cognitive impairment and frailty in elderly individuals with decreased eGFR. There is a strong association between decreased eGFR or albuminuria and higher rates of cardiovascular disease and mortality in the elderly. Indeed, this is particularly true among elderly individuals with CKD, even in those with CKD stage 4. In addition, susceptibility to acute kidney injury and other side effects of medications or diagnostic and therapeutic procedures, such as imaging studies, are more common in patients with decreased GFR and are a major source of morbidity and cost in the elderly. In the general population, therapeutic interventions can prevent or ameliorate many of the complications of decreased GFR. Comorbid conditions are frequent in the elderly, however, which may modify the effectiveness of these interventions.

**HYPOTHESIS: CKD IN THE ELDERLY AS A MICROVASCULAR DISEASE**

Several lines of evidence suggest that vascular disease, specifically microvascular disease, may be an important cause of CKD in the elderly. Hypertension and diabetes are associated with specific renal vascular lesions. There are clear epidemiological associations among vascular disease risk factors, cardiovascular disease, and kidney disease. Even in the absence of clinical cardiovascular disease, there is an association among subclinical cardiovascular disease, earlier stages of CKD, inflammation, and endothelial dysfunction in the elderly. Hypertension is a well recognized risk factor for CKD and CVD in the general population. Increased pulse pressure is common in the elderly and is now recognized as a surrogate marker for aortic stiffness and a predictor for cardiovascular disease events. In principle, aortic stiffness is most likely to be associated with microvascular disease in high-flow, low-impedance organs, such as the kidney, where excessive pressure pulsatility is transmitted through to the microcirculation.

**DIRECTIONS FOR THE FUTURE**

Clinicians need to identify albuminuria and reduced eGFR in the elderly. In patients found to have CKD, all relevant characteristics must be considered in estimating prognosis and formulating treatment plans, including, cause of kidney disease, presence or absence of comorbid conditions, level of eGFR and complications related to reduced GFR, and risk factors for kidney disease progression and cardiovascular disease. In the elderly, the risk for mortality and complications is higher than for progression to kidney failure, and in many older patients, the most important interventions may be to reduce cardiovascular disease risk and avoid kidney toxicity and other side effects of medications and procedures. As outlined in the editorial by Shlipak in this issue of *AJKD*, more studies are required to better understand GFR measurement and estimation in the elderly. In addition, clinically useful predictive instruments that incorporate all of the known risk factors are needed, as are clinical trials to test the impact of therapeutic interventions on survival and quality of life in older adults with CKD.

It seems likely that nephrologists will need to care for most patients with CKD stages 4 and 5. More effective integration of principles of geriatrics into nephrology care will be necessary for this older, impaired, and frail population. In particular, this may affect the way nephrologists approach decisions regarding treatment of kidney failure and end of life care. However, neph-
rologists cannot and do not need to care for all patients with earlier stages of CKD. Recent clinical practice guidelines suggest detailed treatment recommendations for many of the conditions affecting patients with earlier stages of CKD as well as indications for referral, which should enable primary care physicians and other specialists to deal more effectively with many of the routine problems.15,26-29,36-40

Public health programs are beginning to include initiatives for CKD.41 As discussed in last year’s World Kidney Day editorial in AJKD, outcomes for CKD can be improved, and it is not too early to think of preventing development of CKD.1 Surveillance programs for all stages of CKD and antecedent conditions, such as NHANES in the United States and the program in Beijing reported in this issue of AJKD, are the first steps in determining the burden of CKD in the elderly.

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