

The message for World Kidney Day 2009: hypertension and kidney disease: a marriage that should be prevented

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The kidney is both a cause and a victim of hypertension. High blood pressure is a key pathogenetic factor that contributes to deterioration of kidney function. The presence of kidney disease is a common and underappreciated preexisting medical cause of resistant hypertension.¹ Therefore, treatment of hypertension has become the most important intervention in the management of all forms of chronic kidney disease (CKD). For this reason, the forthcoming World Kidney Day (WKD) on 12 March 2009 will emphasize the role of hypertension in renal disease.

How does one recognize the presence of chronic kidney disease?

In contrast to a decade ago, today most laboratories around the world report estimated glomerular filtration rate (eGFR) instead of or in addition to serum creatinine. This now provides the physician with data about kidney function that are, in general, more informative. As a result, a greater percentage of patients with diabetes or hypertension and their physicians have a better knowledge of their kidney function. Assessment of eGFR as an index of kidney function should be complemented by assessment of urine for protein or, preferably, albumin.

In spite of these laboratory updates, recent data demonstrate that a given patient's knowledge that he or she has CKD is very low. In a recent analysis of almost half a million people in Taiwan who took part in a standard medical screening program, 12% had CKD.² It is noteworthy that less than 4% of those with CKD were aware of their condition. People with CKD are several times more likely to die from cardiovascular causes than those without CKD; hypertension is a major risk factor in this context.³ The combination of CKD and hypertension, therefore, is a major public-health issue; because of the costly treatments necessary for end-stage renal disease (ESRD), end-stage CKD has also become a substantial burden to health budgets.

What is the worldwide frequency of chronic kidney disease?

The frequency of CKD continues to increase worldwide, as does the prevalence of ESRD.^{4,5} The most common, but not the only, causes of CKD are hypertension and diabetes. The presence of CKD is associated with a large increase in cardiovascular risk. Moreover, cardiovascular risk increases proportionally as eGFR falls below 60 ml/min. As a result, the identification and reduction of CKD has become a public-health priority.⁶

The reported prevalence of CKD stages 1–4 in the most recent National Health and Nutrition Examination Survey (NHANES) between 1999 and 2006 was 26 million out of a population base of approximately 200 million. This represented United States residents aged 20 and older; of these, 65.3% had CKD stage 3 or 4. Those with diabetes and hypertension had a far greater prevalence of CKD (37% and 26%, respectively) compared with those without these conditions (11% and 8%, respectively).⁷ In a more recent, yet-unpublished report from the CKD surveillance group, the prevalence of CKD stages 1–4 in the general population increased 30% from 1994 to 2006.

The most recent report of the United States Renal Data System estimates that nearly one-half million patients in the United States were treated for ESRD in the year 2004,⁸ and by 2010 this figure is expected to increase by approximately 40%. Patients destined to progress to ESRD—that is, the elderly—are a growing segment of the population. Additionally, males and African Americans with preexisting hypertension and CKD are also at much higher risk for ESRD.⁹ This observation has also been confirmed throughout the developed world: Europe, Asia, Australia, and regions of India and Africa.^{4,5}

The role of hypertension

Hypertension is a global problem, and the situation is projected to get worse. It is the major risk factor for development and progression in nondiabetic and diabetic CKD.

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The world population is getting older, and aging is the most common risk factor for the development of hypertension and diabetes as well as CKD. Nearly one billion people worldwide have high blood pressure (defined as >140/90 mm Hg), and that number is expected to increase to 1.56 billion people by 2025.¹⁰ The prevalence of hypertension is predicted to increase by 24% in developed countries and by 80% in developing regions such as Africa and Latin America. One report noted that 333 million adults in economically developed regions such as North America and Europe had high blood pressure in 2000, and an additional 639 million people in developing countries have this condition.

In 1999–2006, the prevalence of hypertension, defined as >140/90 mm Hg, in US adults was 43.4%, and similar figures have been reported from many Western countries.⁹ The rates of hypertension were highest in participants who were 60 years or older—that is 68%, versus 25% in those between 20 and 39 years—and in non-Hispanic blacks—53%, versus 43% in whites and 34% in Mexican Americans. Furthermore, hypertension was more common in individuals with a higher body mass index (BMI) (60% for BMI \geq 35 versus 32% for BMI of 23). Slightly more than half of adults with hypertension were aware of their disease in 1999–2004; fewer than half were treated for their hypertension with medications; and less than two-thirds were controlled to <140/90 mm Hg with medication.⁹ This trend in poor blood pressure control is observed worldwide.

The hypertension control rate is substantially lower in patients with CKD, particularly among those with diabetes and CKD.^{1,9} This is illustrated by the US National Kidney Foundation's Kidney Early Evaluation Program (KEEP), a US-based health-screening program for individuals at high risk for kidney disease.⁹ The prevalence (86.2%), awareness (80.2%), and treatment (70.0%) of hypertension in the screened cohort were high; however, blood pressure control rates were low (13.2%). The proportion of hypertensive patients increased with advancing stages of CKD.

Which blood pressure component is most relevant for renal and cardiovascular risk, systolic or diastolic?

There is now consensus, based on the totality of the data, that systolic rather than diastolic blood pressure poses the greater risk for cardiovascular events and kidney disease progression. Against this background, it is relevant that in the KEEP study, elevated systolic blood pressure accounted for the majority of patients with inadequate

control. Male gender, non-Hispanic black race, and BMI of 30 kg/m² or more were inversely related to blood pressure control.

What is the blood pressure target for CKD patients? According to the different guidelines published by the major kidney societies, systolic blood pressure should be lowered to values less than 130 mm Hg. One has to be aware, however, that as a predictor of adverse CKD or cardiovascular events, office blood pressure may be inferior compared with ambulatory blood pressure.¹¹ This issue is particularly relevant in CKD because of the tendency for nighttime blood pressure to be elevated (little or no nocturnal dip in blood pressure) and the fact that central (aortic) blood pressure tends to be higher than peripheral (brachial) blood pressure.^{11,12} In patients with diabetes, guidelines all recommend that lower blood pressure targets may provide further benefit, but prospective trials have thus far failed to confirm this epidemiological observation.

The role of diabetic nephropathy

As is indicated above, diabetes and hypertension are the most common causes of CKD. There are currently over 240 million people with diabetes worldwide. This figure is projected to rise to 380 million by 2025, largely because of population growth, aging, urbanization, unhealthy eating habits, increased body fat, and a sedentary lifestyle. By 2025, the number of people with diabetes is expected to more than double in Southeast Asia, the Eastern Mediterranean and Middle East, and Africa. It is projected to rise by nearly 20% in Europe, 50% in North America, 85% in South and Central America, and 75% in the Western Pacific region. The five countries with the highest prevalence of diabetes, in order, are India, China, the United States, Russia, and Japan. Worldwide, more than 50% of people with diabetes are unaware of their condition and are not treated.

The same factors that increase obesity are those predisposing to diabetes: family history, presence of hypertension, aging, excess body weight, lack of exercise, and unhealthy dietary habits. It is important to identify these risks early to reduce the development of diabetes and CKD, since CKD greatly amplifies the risk of cardiovascular events in the diabetic patient.

The remaining challenge

Underdiagnosis and undertreatment of CKD are a worldwide problem: not only is CKD awareness low worldwide, but the relative lack of awareness of CKD risk factors—that is, hypertension and

diabetes—among physicians is even more disturbing. Moreover, even awareness of these risk factors does not ensure adequate treatment; this could relate to the behavior of the patient, the provider, or both. Thus, the problem of CKD remains a challenge, as exemplified by recent data showing that between 1999 and 2006, less than 5% of people with an eGFR less than 60 ml/min/1.73 m² and proteinuria were aware of having CKD; of those with CKD stage 3, awareness was only 7.5%; for stage 4, awareness was less than 50%. Awareness rates among those with CKD stage 3 or 4 were higher if comorbid diagnoses of diabetes and hypertension were present, but even then, they were quite low (20% and 12%, respectively).

One barrier to overcome in order to ensure greater awareness is a more focused education of physicians, as they are in charge of the patients' medical condition. In one survey, more than one-third of primary care physicians in the United States were not aware that family history was a risk factor for CKD, and almost one-quarter did not perceive African-American ethnicity as a CKD risk factor; in contrast, nearly all perceived diabetes (95%) and hypertension (97%) as risk factors for CKD. Even more problematic was the finding that although diabetes and hypertension were acknowledged as CKD risk factors, the achieved control rates (defined as reaching guideline goals), sadly, remained well below 50% among those treated.

What can be done about this problem?

There have been many consensus panels over the past decade to approach ways to achieve better blood pressure control and educate physicians to the stages of CKD.^{13,14} The road to improvement of outcomes is to focus on public awareness and screening programs as well as programs to educate both patients and physicians. Data from the KEEP screening program in the United States have also shown that blood pressure values are most likely to be at goal once a patient is aware he or she has kidney disease.¹⁵ Data from Bolivia highlight the observation that once kidney disease is diagnosed, more appropriate interventions to reduce CKD risk factors such as hypertension are instituted.¹³

Programs to address these issues have started around the world, including KEEP-type programs. As a major focus of World Kidney Day this year, the issue is hypertension in CKD (<http://www.worldkidneyday.org>).

Because of the aging world population and consequently increasing prevalence of hypertension and diabetes, CKD rates will continue to increase. This has placed and will continue to place an undue

economic burden on societies, given the costs of an ESRD program. In 2005, the United States spent \$32 billion on such programs. These facts mandate that measures be put forth to ensure timely detection and prevention of CKD progression. The keys to ensuring successful prevention of CKD are screening for hypertension, improved testing and diagnosis of predisposing comorbidities such as diabetes, and aggressive treatment to guideline goals.

The International Society of Nephrology and the International Federation of Kidney Foundations have an ambitious long-term goal that, worldwide, every individual, particularly the patient with diabetes, know his or her blood pressure values. Additionally, he or she should be aware that prompt treatment is necessary once blood pressure values are no longer in the normal range. Finally, our societies must strongly encourage public-health authorities to support efforts to raise public awareness of CKD and promote moves to reduce the risk of developing hypertension. Such governmental public-health initiatives to reduce salt in the diet or to mandate that labels give sodium content are illustrated by the activities in the United Kingdom, Finland, and Japan. These initiatives have proven highly successful on the basis of reduction in cardiovascular mortality and morbidity.

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