Control of Hypertension in Adults With Chronic Kidney Disease in the United States

Carmen A. Peralta, Leroi S. Hicks, Glenn M. Chertow, John Z. Ayanian, Eric Vittinghoff, Feng Lin, Michael G. Shlipak

Abstract—Although improved control of hypertension is known to attenuate progression of chronic kidney disease (CKD), little is known about the adequacy of hypertension treatment in adults with CKD in the United States. Using data from the Fourth National Health and Nutrition Survey, we assessed adherence to national hypertension guideline targets for patients with CKD (blood pressure <130/80 mm Hg), we assessed control of systolic (<130 mm Hg) and diastolic (<80 mm Hg) blood pressure, and we evaluated determinants of adequate blood pressure control. Presence of CKD was defined as glomerular filtration rate <60 mL/min per 1.73 m² or presence of albuminuria (albumin:creatinine ratio >30 μg/mg). Multivariable logistic regression with appropriate weights was used to determine predictors of inadequate hypertension control and related outcomes. Among 3213 participants with CKD, 37% had blood pressure <130/80 mm Hg (95% confidence interval [CI], 34.5% to 41.8%). Of those with inadequate blood pressure control, 59% (95% CI, 54% to 64%) had systolic >130 mm Hg, with diastolic ≤80 mm Hg, whereas only 7% (95% CI, 3.9 to 9.8%) had a diastolic pressure >80 mm Hg, with systolic blood pressure ≤130 mm Hg. Non-Hispanic black race (odds ratio [OR], 2.4; 95% CI, 1.5 to 3.9), age >75 years (OR, 4.7; 95% CI, 2.7 to 8.2), and albuminuria (OR, 2.4; 95% CI, 1.4 to 4.1) were independently associated with inadequate blood pressure control. We conclude that control of hypertension is poor in participants with CKD and that lack of control is primarily attributable to systolic hypertension. Future guidelines and antihypertensive therapies for patients with CKD should target isolated systolic hypertension. (Hypertension. 2005;45:1119-1124.)

Key Words: kidney ■ race

Progression of chronic kidney disease (CKD) to end-stage renal disease (ESRD) is a major public health problem in the United States. Prevalence of CKD is high,1 and rates of ESRD have nearly doubled in the last 2 decades.2 This accelerated incidence of ESRD far exceeds the rate of increase in the prevalence of CKD.3 CKD has also been associated with increased risk of cardiovascular outcomes and mortality.4

Hypertension is associated with more rapid progression of CKD.5a Several studies have shown that treating hypertension in patients with CKD and proteinuria may attenuate the decline in glomerular filtration rate (GFR).7–9 The Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) and the National Kidney Foundation Kidney Disease Outcome and Quality Initiative (NKF/KDOQI) identify CKD as a high-risk group warranting intensive hypertension treatment.10,11 National guidelines recommend pharmacological therapy and lifestyle modification to achieve a blood pressure goal of <130/80 mm Hg for patients with CKD.10,11 The prevalence and predictors of inadequate blood pressure control have not been well elucidated in adults with CKD.

Guidelines for hypertension treatment in patients with CKD have focused equally on the control of systolic and diastolic blood pressure.10,11 However, recent data in the general population suggest that the prevalence of isolated systolic hypertension is high, especially among the elderly.12,13 Wide pulse pressure (systolic minus diastolic blood pressure) is also prevalent and has been shown to be a marker of arterial stiffness14,15 as well as an independent risk factor for cardiovascular disease.16,17 Although advanced CKD (including ESRD) has been associated with arterial stiffness,18–20 the prevalence of isolated systolic hypertension and wide pulse pressure in the CKD population is unknown.

Using the Fourth National Health and Nutrition Examination Survey (NHANES IV), we aimed to determine the prevalence of inadequate blood pressure control in adults.
with CKD, the clinical and demographic predictors of inadequate control, and the relative adequacy of control of systolic and diastolic pressure.

Methods

Overview
We evaluated prevalence and determinants of inadequate blood pressure control in persons with CKD using data from NHANES IV, a complex, stratified, multistage probability sample of noninstitutionalized US civilians between 1999 and 2002. Adults >60 years of age, low-income individuals, Mexican Americans, and non-Hispanic blacks were oversampled in NHANES IV.

Study Population
We estimated GFR for all adult participants (age >20 years) in NHANES IV with the Modification of Diet in Renal Disease equation, using calibrated serum creatinine. Adults with estimated GFRs <60 mL/min per 1.73 m² or proteinuria (urine albumin/creatinine ratio ≥30 μg/mg) were included. We excluded participants with missing values for serum creatinine (n=1076) or missing blood pressure readings (n=154).

Covariate Definitions
Based on self-report, race/ethnicity was coded in NHANES IV as non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, and other/multiracial. We grouped Mexican American and other Hispanic into 1 category. Poverty was defined as income less than $20,000 per year. Low educational level was defined by noncompletion of 12th grade. Primary language was the language spoken in the home. Insurance status was defined as any coverage. Diabetes was defined as self-report of physician diagnosis or as current or past user of insulin or oral hypoglycemic agent. We excluded diabetes diagnoses made during pregnancy. Obesity was defined as body mass index >30 kg/m².

Outcomes
Blood pressure was measured by a trained technician using a mercury sphygmomanometer and calculated as the average of 3 or 4 measurements, excluding the first measurement. Adequate blood pressure control was defined as systolic blood pressure ≤130 and diastolic blood pressure ≤80 mm Hg per national guidelines. Pulse pressure was calculated as the difference between systolic and diastolic blood pressure; wide pulse pressure was defined as >80 mm Hg.

Statistical Analysis
We compared the characteristics of participants who had adequate control (blood pressure <130/80 mm Hg) with those who were poorly controlled. Categorical variables were expressed as proportions with 95% confidence intervals (95% CIs), and continuous variables were expressed as mean±SD and compared using recommended survey procedures for NHANES IV. We evaluated the association of demographic and clinical characteristics with hypertension control using multivariable logistic regression. Race, age, ethnicity, and insurance and poverty status were principal predictors of interest. Multivariable models also included predictors significantly associated with poor control in unadjusted analysis (P<0.05) or those believed to affect hypertension control in clinical practice (serum creatinine, obesity). We report adjusted odds ratios (ORs) with 95% CIs using model parameter coefficients and SEs, respectively. Two-tailed P values <0.05 were considered significant. All analyses were completed using STATA 8.0 to incorporate adequate sample weights and adjust for clustering and stratification of the sample design.

Results

Characteristics
Among adult participants in NHANES IV (n=15,211), 3213 participants had a GFR of <60 mL/min per 1.73 m² or albuminuria (weighted prevalence of 16%; 95% CI, 15% to 17%), representing 47.2 million Americans. Of participants with CKD, 27% had diabetes (95% CI, 22% to 31%). The average age for the CKD cohort was 56 years, and 60% were women and 72% were white.

Blood Pressure Control
Among participants with CKD, only 37% had blood pressure controlled to <130/80 mm Hg (95% CI, 35% to 42%). Of those with poor control (>130/80 mm Hg), 48% (95% CI, 40% to 53%) had systolic pressure >150 mm Hg. Using a less stringent target of <140/90 mm Hg, 56% of participants with CKD (95% CI, 52% to 60%) had controlled blood pressure.

Systolic hypertension accounted for most of the inadequate control. Among participants with CKD and suboptimal control (>130/80 mm Hg), 59% (95% CI, 54% to 64%) had systolic >130 mm Hg, with diastolic ≤80 mm Hg, whereas only 7% (95% CI, 4% to 10%) had a diastolic pressure >80 mm Hg, with systolic pressure ≤130 mm Hg (Figures 1 and 2). Mean pulse pressure for the CKD cohort was 67 mm Hg (95% CI, 64 to 69). Of those not achieving target levels of <130/80 mm Hg, 44% (95% CI, 38% to 49%) had a pulse pressure >80 mm Hg.

Predictors of Blood Pressure Control
Adults with CKD who did not meet blood pressure targets (<130/80 mm Hg) were older and twice as likely to be non-Hispanic black (Table 1). Inadequate blood pressure control was also associated with the presence of albuminuria and diabetes. Serum creatinine, insurance status, primary language, poverty, and health care utilization patterns were not significantly associated with hypertension control in univariate analyses.
In multivariable analyses, non-Hispanic black race remained independently associated with inadequate blood pressure control (Table 2). Non-Hispanic blacks with CKD had 2-fold odds of inadequate blood pressure control (OR, 2.4; 95% CI, 1.5 to 3.9) than whites. Age >75 years was associated with 4-fold odds of poor blood pressure control in adjusted analyses, and albuminuria was associated with a 2-fold odds of poor control. A diagnosis of diabetes was not independently associated with inadequate control in adjusted analysis.

Predictors of Wide Pulse Pressure
Among all participants with CKD, age 60 to 75 years was associated with a 6-fold odds of wide pulse pressure (>80 mm Hg), and age >75 years was associated with a 13-fold higher odds of wide pulse pressure in the univariate analyses (Table 3). Race and presence of albuminuria were not significantly associated with wide pulse pressures. In multivariable analyses, age remained strongly and independently associated with wide pulse pressure, despite adjustment for race and ethnicity, albuminuria, serum creatinine, diabetes, and obesity.

Discussion
Although CKD patients are at high risk for cardiovascular disease and there is evidence that blood pressure control reduces the rate of cardiovascular complications and attenuates the rate of GFR decline in those with proteinuria, adequate control remains suboptimal. In this sample of Americans with CKD, 37% achieved the blood pressure target advocated by national guidelines (<130/80 mm Hg). These results are consistent with previous studies that document adherence rates to hypertension control guidelines between 25% and 45% in nationally representative samples of non-CKD patients, in which targets are higher (<140/90 mm Hg). Isolated systolic hypertension was the primary cause of inadequate control. Previous studies have documented a high prevalence of systolic hypertension (systolic pressure >140 mm Hg, with diastolic <90 mm Hg) in the general population, and data from clinical trials have documented...
TABLE 3. Predictors of High Pulse Pressure (>80 mm Hg) in Adults With CKD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
<th>P value</th>
<th>Adjusted OR (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–60</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–75</td>
<td>6.3 (3.4–11.7)</td>
<td>&lt;0.001</td>
<td>6.1 (3.0–12.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;75</td>
<td>13.1 (6.4–26.8)</td>
<td>&lt;0.001</td>
<td>17.0 (7.1–39.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>0.91 (0.61–1.4)</td>
<td>0.66</td>
<td>0.98 (0.6–1.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.64 (0.4–0.9)</td>
<td>0.49</td>
<td>0.94 (0.6–1.6)</td>
<td>0.9</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.6 (0.4–0.87)</td>
<td>0.01</td>
<td>0.8 (0.4–1.5)</td>
<td>0.5</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1.0</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1–1.5</td>
<td>1.2 (0.8–1.8)</td>
<td>0.31</td>
<td>1.1 (0.7–1.6)</td>
<td>0.8</td>
</tr>
<tr>
<td>&gt;1.5</td>
<td>1.6 (0.9–2.9)</td>
<td>0.11</td>
<td>1.1 (0.5–2.2)</td>
<td>0.8</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>1.3 (0.8–2.2)</td>
<td>0.19</td>
<td>2.2 (1.3–3.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.9 (1.0–3.7)</td>
<td>0.06</td>
<td>1.7 (0.8–3.9)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*Adjusted for age, race, serum creatinine, albuminuria, diabetes, and obesity.

beneficial effects from treating isolated systolic hypertension in the elderly.29–31 Because high systolic pressure is so prevalent in CKD and is a determinant of CKD progression,52 systolic blood pressure control should be the focus of antihypertensive therapy in CKD.

The association of CKD with isolated systolic hypertension (and wide pulse pressure) may be explained by increased vascular stiffness. Wide pulse pressure appears to be a marker of vascular stiffness and cardiovascular calcification, a predictor of cardiovascular risk in the elderly,14,15,33 and it is associated with increased mortality in patients with renal disease.19,34 Given the observed high prevalence of wide pulse pressure in CKD, vascular stiffness should be considered a potential mediator for the high cardiovascular risk of patients with CKD. It is unknown whether attempts to narrow the pulse pressure in patients with CKD would be associated with favorable or adverse outcomes.

Our findings suggest that non-Hispanic black race is an important determinant of inadequate control among NHANES IV participants with CKD. Higher prevalence rates of hypertension for non-Hispanic blacks when compared with whites have been reported in NHANES IV.35 Data on adequate control are conflicting, with some studies reporting similar rates of control for non-Hispanic blacks and whites,25,27 whereas others show lower rates of control for non-Hispanic blacks.28,36 Our finding that non-Hispanic black race is associated with lower rates of control in participants with CKD may reflect the fact that successful blood pressure control in this group may be more difficult and requires more antihypertensive medications when compared with whites.37 Adequate blood pressure control in non-Hispanic blacks is critical because they have a 5-fold risk of progression from CKD to ESRD when compared with whites.38 The observed disparity in blood pressure control in this study may partially explain the higher rates of progression to ESRD in non-Hispanic blacks. Hispanics had similar blood pressure control to non-Hispanic whites in this study. Despite some evidence that ESRD rates are rising faster in Hispanics than in non-Hispanic whites,2 there are few published data on the burden of CKD in Hispanics.

Although older age is associated with increased rates of complications from CKD,39,40 age >60 years was an independent predictor of inadequate blood pressure control in CKD. The mechanism for this association may be increased arterial stiffness because older age was associated with wider pulse pressure. Alternatively, treatment thresholds may vary by age; physicians may be less likely to add an additional antihypertensive agent in the elderly because of fear of adverse effects or a belief that higher systolic pressure is a normal phenomenon associated with aging. Some studies have suggested that clinicians are more likely to treat high diastolic pressure than high systolic pressure,12,41 and they may be reluctant to treat isolated systolic hypertension for fear of excessively lowering diastolic pressure.12

Our study suggests that new guidelines should focus on reducing systolic blood pressure in adults with CKD. Low adherence may be attributable to lack of awareness of the presence of CKD, because only 10% of this cohort reported awareness of the diagnosis,4 or to the challenge to the clinician of choosing an appropriate antihypertensive regimen, typically requiring multiple medications. Treating systolic hypertension is beneficial in the elderly,12,29–31 and JNC VII recommends thiazide diuretics as the first choice for the treatment of systolic hypertension.10 Randomized clinical trials of patients with CKD have shown that adequate control is possible, but it requires close follow-up, a multidisciplinary team, and, on average, 3 to 4 antihypertensive medications.7,8,37 JNC VII suggests adding additional agents depending on the CKD diagnosis and other comorbidities (especially angiotensin-converting enzyme [ACE] inhibitors and angiotensin receptor blockers) to achieve targets,10 but data for the preferred treatment of isolated systolic hypertension in CKD are scant, with a few studies showing beneficial effects of losartan and candesartan.42–44 Despite evidence of the benefit
of ACE inhibitors and ARBs in patients with CKD, studies suggest their use remains relatively low in the United States.\textsuperscript{45,46}

This study has some limitations. NHANES has a cross-sectional design, which prevents our drawing conclusions on the temporal relationships of these observations. In addition, NHANES does not include institutionalized adults, and therefore, some of the sickest members of the population are excluded from these analyses. Adequate information on prescription medication use for the whole time period is not available, limiting conclusions regarding drug use for hypertension treatment in adults with CKD. We defined CKD as GFR $< 60$ mL/min per 1.73 m$^2$ or albuminuria per NKF and JNC VII definitions.\textsuperscript{10,11} NHANES IV participants with mild decrease in GFR ($>60$ mL/min per 1.73 m$^2$) but no albuminuria were not considered to have CKD in these analyses. Spot urine albumin and creatinine were generally not repeated, and urine albumin and creatinine were not considered to have CKD in these analyses. Spot urine albumin and creatinine were generally not repeated, and we are unable to adequately account for variability in the excretion of albumin in this sample, which may bias the results to increased prevalence of CKD. Because albuminuria is a marker of severity of kidney disease and is strongly associated with inadequate blood pressure control, this inclusion criterion may have biased our study toward a lower adherence to blood pressure control guidelines in the GFR group $>60$ mL/min per 1.73 m$^2$.

Perspectives

Adherence to established blood pressure targets is low for participants with CKD, despite growing evidence that control of hypertension can slow the decline of GFR, reduce proteinuria, and reduce the incidence of cardiovascular complications in CKD.\textsuperscript{5,46} Because the CKD population is characterized by wide pulse pressure and isolated systolic hypertension, more aggressive campaigns focusing on systolic hypertension in this population are needed, and the role of vascular stiffness in the treatment of hypertension in CKD should be explored. Because non-Hispanic blacks and older Americans with CKD are at increased risk for complications and have particularly inadequate blood pressure control, public health efforts should be directed at identifying barriers to hypertension control in these populations. Efforts to treat hypertension in CKD should focus on lowering systolic blood pressure preferentially to bridge the gap between evidence and clinical practice.

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References

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