

Ambulatory Blood Pressure Phenotypes in Adults Taking Antihypertensive Medication with and without CKD

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Abstract

Background and objectives Recent guidelines recommend out-of-clinic BP measurements.

Design, setting, participants, & measurements We compared the prevalence of BP phenotypes between 561 black patients, with and without CKD, taking antihypertensive medication who underwent ambulatory BP monitoring at baseline (between 2000 and 2004) in the Jackson Heart Study. CKD was defined as an albumin-to-creatinine ratio ≥ 30 mg/g or eGFR < 60 ml/min per 1.73 m². Sustained controlled BP was defined by BP at goal both inside and outside of the clinic and sustained uncontrolled BP as BP above goal both inside and outside of the clinic. Masked uncontrolled hypertension was defined by controlled clinic-measured BP with uncontrolled out-of-clinic BP.

Results CKD was associated with a higher multivariable-adjusted prevalence ratio for uncontrolled versus controlled clinic BP (prevalence ratio, 1.44; 95% CI, 1.02 to 2.02) and sustained uncontrolled BP versus sustained controlled BP (prevalence ratio, 1.66; 95% CI, 1.16 to 2.36). There were no statistically significant differences in the prevalence of uncontrolled daytime or nighttime BP, nondipping BP, white-coat effect, and masked uncontrolled hypertension between participants with and without CKD after multivariable adjustment. After multivariable adjustment, reduced eGFR was associated with masked uncontrolled hypertension versus sustained controlled BP (prevalence ratio, 1.42; 95% CI, 1.00 to 2.00), whereas albuminuria was associated with uncontrolled clinic BP (prevalence ratio, 1.76; 95% CI, 1.20 to 2.60) and sustained uncontrolled BP versus sustained controlled BP (prevalence ratio, 2.02; 95% CI, 1.36 to 2.99).

Conclusions The prevalence of BP phenotypes defined using ambulatory BP monitoring is high among adults with CKD taking antihypertensive medication.

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Introduction

The prevalence of high BP, defined as systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg measured in a clinic setting, is higher among adults with versus without CKD (1,2). Ambulatory BP monitoring provides more detailed information on an individual's BP level compared with measurements obtained in the clinic (3). The prevalence of several BP phenotypes that can be determined using ambulatory BP alone or in conjunction with BP measured in the clinic setting, including out-of-clinic uncontrolled BP (daytime, nighttime, and sustained uncontrolled BP), diurnal BP patterns (nondipping BP pattern), and a mismatch between clinic and out-of-clinic controlled BP status (white-coat effect and masked uncontrolled hypertension) are high among adults with CKD (4,5). In an observational follow-up of participants enrolled in the African American Study of Kidney Disease, higher daytime and nighttime systolic BP were each associated with a higher risk for the doubling of serum creatinine and cardiovascular disease events after adjustment for BP measured in a clinic setting (6).

In an analysis of data from the Chronic Renal Insufficiency Cohort study, participants with masked hypertension or masked uncontrolled hypertension had a lower eGFR, higher level of proteinuria, and were more likely to have cardiovascular target-organ damage than their counterparts with controlled clinic and out-of-clinic BP (7).

In prior studies, adults with high daytime and nighttime systolic BP had lower levels of eGFR, a higher prevalence of left ventricular hypertrophy, and a higher risk for cardiovascular disease (8,9). However, these studies were restricted to adults with established CKD, and there are few published data reporting whether phenotypes defined on the basis of ambulatory BP monitoring differ between adults with and without CKD. We compared the prevalence of BP phenotypes based on clinic BP and ambulatory BP monitoring among adults with and without CKD, reduced eGFR, and albuminuria who were taking antihypertensive medication. Additionally, we determined whether these BP phenotypes were associated with left ventricular hypertrophy among adults with

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CKD. For comparison, we assessed these associations among adults without CKD.

Materials and Methods

Study Population

This analysis was based on data from the Jackson Heart Study, a community-based cohort of black adults designed to investigate risk factors for cardiovascular disease. Details of the Jackson Heart Study have been described previously (10–12). Briefly, from 2000 to 2004, 5306 adults aged 21–94 years from the three counties that make up the Jackson, Mississippi Metropolitan Statistical Area were enrolled in the Jackson Heart Study. All participants were invited to complete 24-hour ambulatory BP monitoring at the completion of their baseline study visit, and 1148 participants agreed. We included 561 participants taking antihypertensive medication (Supplemental Figure 1). The current analysis was restricted to participants taking antihypertensive medication as only 31 of 175 (18%) participants with CKD who completed ambulatory BP monitoring were not taking antihypertensive medication. The Jackson Heart Study protocol was approved by the institutional review boards of the participating institutions. All participants provided written informed consent. With institutional board approval, data for replicating this analysis can be obtained through the Jackson Heart Study coordinating center.

Clinical Covariates

The baseline examination consisted of interviewer and self-administered questionnaires to assess age, sex, education, marital status, medical history, medication use within the 2 weeks preceding each participant's study visit, and health behaviors including alcohol consumption, smoking status, and physical activity. Height and weight were measured, and body mass index was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Fasting plasma glucose, hemoglobin A1C, and total and HDL cholesterol were quantified using standardized methods (11,13). Diabetes mellitus was defined as a glycated hemoglobin $\geq 6.5\%$, fasting plasma glucose ≥ 126 mg/dl, or the use of glucose-lowering medication (14).

CKD

Urinary albumin was measured with a Dade Behring BN II nephelometer (Dade Behring, Newark, DE) (15). Serum and urine creatinine levels were measured using a multipoint enzymatic spectrophotometric assay on a Vitros 950 Ortho Clinical Diagnostics analyzer and biochemically calibrated to an isotope-dilution mass spectrometry-traceable method (16). eGFR was calculated using the CKD Epidemiology Collaboration equation (17). Albuminuria was defined by an albumin-to-creatinine ratio ≥ 30 mg/g and reduced eGFR as levels < 60 ml/min per 1.73 m². CKD was defined by the presence of albuminuria or reduced eGFR.

Clinic Blood Pressure and Ambulatory Blood Pressure Measurements

Clinic BP was measured two times during the baseline exam following a standardized protocol using a Hawksley

random zero sphygmomanometer (Hawksley & Sons, Lancing, UK) and Littman stethoscope (3M; St Paul, MN). BP was calibrated to an oscillometric device as described previously (18,19). The mean of these two measurements was calculated. Following the exam, ambulatory BP monitoring was conducted with the SpaceLabs 90207 Oscillometric device (Medifacts International, Rockville, MD). The monitor was programmed to measure BP every 20 minutes throughout the recording period. The International Database of Ambulatory BP in relation to Cardiovascular Outcomes criteria of ten or more valid daytime (10 AM to 8 PM) and five or more valid nighttime (midnight to 6 AM) systolic BP and diastolic BP measurements were applied to define a complete ambulatory BP monitoring recording (20,21). The following three types of phenotypes were evaluated using clinic BP and ambulatory BP monitoring: (1) uncontrolled BP, (2) diurnal BP patterns, and (3) a mismatch in uncontrolled BP between clinic and out-of-clinic measurements (Table 1).

Cardiovascular Target-Organ Damage

The Jackson Heart Study examination center was equipped with four echocardiography machines (Sonos 4500; Phillips Medical Systems, Andover, MA), and certified sonographers performed two-dimensional transthoracic echocardiograms according to the American Society of Echocardiography and the European Association of Cardiovascular Imaging recommendations. Left ventricular mass (in grams) was calculated using the formula: $0.8 \times (1.04 \times [(\text{intraventricular septal thickness in diastole} + \text{left ventricular internal diameter at end diastole} + \text{posterior wall thickness in diastole})^3 - (\text{left ventricular internal diameter at end diastole})^3]) + 0.6$. Left ventricular mass index was calculated by dividing left ventricular mass by estimated body surface area. Left ventricular hypertrophy was defined as left ventricular mass index of ≥ 96 g/m² in females and ≥ 116 g/m² in males (22).

Statistical Analyses

We calculated summary statistics for the characteristics of participants taking antihypertensive medication included and not included in this analysis and by CKD status for those included in this analysis. The prevalence of each BP phenotype was calculated for participants with and without CKD, separately, and the statistical significance of the differences was assessed using chi-squared tests. The prevalence of white-coat effect was calculated among participants with clinic systolic BP ≥ 140 mm Hg or clinic diastolic BP ≥ 90 mm Hg, whereas the prevalence of masked uncontrolled hypertension was calculated among participants with clinic systolic BP < 140 mm Hg and clinic diastolic BP < 90 mm Hg. The multivariable-adjusted association between CKD and each BP phenotype was calculated using Poisson regression models with four levels of progressive adjustment. For white-coat effect, masked uncontrolled BP, and sustained uncontrolled BP, the reference category was sustained controlled BP (clinic systolic BP < 140 mm Hg, clinic diastolic BP < 90 mm Hg, daytime systolic BP < 135 mm Hg, and daytime diastolic BP < 85 mm Hg). In model 1, we adjusted for age and sex. Model 2 included adjustment for age, sex, education,

Table 1. Definitions of phenotypes using clinic BP and ambulatory BP monitoring

BP Phenotype	Clinic Measurements	Ambulatory BP Monitoring Measurements
Uncontrolled BP		
Uncontrolled clinic BP	Mean systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg	Not applicable
Uncontrolled daytime BP	Not applicable	Mean daytime systolic BP ≥ 135 mm Hg or diastolic BP ≥ 85 mm Hg
Uncontrolled nighttime BP	Not applicable	Mean nighttime systolic BP ≥ 120 mm Hg or diastolic BP ≥ 70 mm Hg
Sustained uncontrolled BP	Mean systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg and	Mean daytime systolic BP ≥ 135 mm Hg or diastolic BP ≥ 85 mm Hg
Diurnal BP pattern		
Nondipping BP	Not applicable	Nighttime to daytime decline in systolic BP $\leq 10\%$
Mismatch between uncontrolled clinic and out-of-clinic BP		
White-coat effect	Mean systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg	Mean daytime systolic BP < 135 mm Hg and diastolic BP < 85 mm Hg
Masked uncontrolled hypertension	Mean systolic BP < 140 mm Hg and diastolic BP < 90 mm Hg	Mean daytime systolic BP ≥ 135 mm Hg or diastolic BP ≥ 85 mm Hg
Sustained controlled BP—defined as mean clinic systolic BP < 140 mm Hg, mean clinic diastolic BP < 90 mm Hg, mean daytime systolic BP < 135 mm Hg, and mean daytime diastolic BP < 85 mm Hg—was used as a reference group for analyses of white-coat effect, masked uncontrolled hypertension, and sustained uncontrolled BP.		

cigarette smoking, physical activity, alcohol consumption, and body mass index. Model 3 included additional adjustment for total and HDL cholesterol, diabetes, and history of stroke and myocardial infarction. For uncontrolled daytime and nighttime BP and nondipping BP pattern, model 4 included additional adjustment for clinic systolic BP and diastolic BP. Model 4 was not conducted for the other outcomes because clinic BP is part of their definition.

Next, for participants with and without CKD, separately, we calculated the prevalence of left ventricular hypertrophy among those with and without each BP phenotype. Poisson regression models with sandwich estimators were used to calculate prevalence ratios for left ventricular hypertrophy associated with each BP phenotype for participants with and without CKD, separately, after adjustment for covariates with the four levels of adjustment described above. We evaluated the presence of effect modification for participants with and without CKD using multiplicative interaction terms (e.g., CKD \times masked uncontrolled hypertension).

In secondary analyses, we assessed the association of reduced eGFR and albuminuria, separately, with each ambulatory BP monitoring phenotype. The association between each BP phenotype and left ventricular hypertrophy was assessed by reduced eGFR and albuminuria, separately, as described above for CKD. Sensitivity analyses were conducted by (1) using 24-hour BP rather than daytime BP to define the BP phenotypes, (2) defining a complete ambulatory BP monitoring recording using the European Society of Hypertension criteria ($\geq 70\%$ of planned BP readings, ≥ 20 daytime BP readings, and seven or more asleep readings), and (3) using the 2017 American College of Cardiology/American Heart Association (AHA) BP guideline thresholds for defining uncontrolled BP (Supplemental Table 1). All variables with missing data (Supplemental Table 2) were imputed with ten data sets using chained equations (23). All analyses were conducted using SAS version 9.4 (SAS Institute,

Cary, NC) and Stata version 13 (Stata Statistical Software, College Station, TX).

Results

Characteristics of participants included and not included in this analysis are provided in Supplemental Table 3. The distribution of participants included in this analysis by level of eGFR and albuminuria and CKD stage are presented in Supplemental Table 4. Among participants included in this analysis, 26% had CKD (Table 2).

Blood Pressure Phenotypes among Participants with and without CKD

The prevalence of uncontrolled clinic and nighttime BP, nondipping BP pattern, and sustained uncontrolled BP were each higher among participants with versus without CKD (Figure 1). In the fully adjusted models, having CKD was associated with higher prevalence of uncontrolled clinic BP (prevalence ratio, 1.44; 95% confidence interval [CI], 1.02 to 2.02), and sustained uncontrolled BP versus sustained controlled BP (prevalence ratio, 1.66; 95% CI, 1.16 to 2.36) (Table 3). After multivariable adjustment, there was no evidence of associations between CKD and uncontrolled daytime or nighttime BP, a nondipping BP pattern, white-coat effect, and masked uncontrolled hypertension.

Participants with reduced eGFR were more likely than their counterparts without reduced eGFR to have a nondipping BP pattern (Figure 2, top panel). Participants with albuminuria were more likely than their counterparts without albuminuria to have uncontrolled clinic, daytime, and nighttime BP; a nondipping BP pattern; and sustained uncontrolled BP (Figure 2, bottom panel). Reduced eGFR was associated with a higher prevalence of masked uncontrolled BP versus sustained controlled BP (prevalence ratio, 1.42; 95% CI, 1.00 to 2.00) after multivariable adjustment (Table 4, top panel). After multivariable adjustment, albuminuria was associated with higher prevalence of uncontrolled clinic BP (prevalence ratio, 1.76; 95% CI, 1.20 to 2.60) and sustained uncontrolled BP versus

Table 2. Characteristics of Jackson Heart Study participants taking antihypertensive medication in the analytic sample by CKD status

Characteristics	No CKD (n=417)	CKD (n=144)
Age, yr	62 (9)	64 (10)
Male, n (%)	113 (27)	45 (31)
Less than high school education, n (%)	82 (20)	42 (29)
Current smoking, n (%)	36 (9)	12 (8)
Physical activity score, activity units	8 (3)	7 (3)
Alcohol consumption, n (%)		
None	304 (73)	118 (82)
Moderate	105 (25)	25 (17)
Heavy	8 (2)	2 (1)
Body mass index, kg/m ²	32 (6)	33 (7)
History of stroke, n (%)	16 (4)	15 (10)
History of myocardial infarction, n (%)	20 (5)	12 (8)
Diabetes, n (%)	126 (30)	66 (46)
Total cholesterol, mg/dl	199 (38)	202 (42)
HDL cholesterol, mg/dl	54 (16)	52.7 (14)
eGFR, ml/min per 1.73 m ²	83 (14)	63 (24)
Albuminuria, mg/g	6 (4, 9)	35 (7, 105)
Clinic BP, mm Hg		
Systolic BP	129 (14)	134 (18)
Diastolic BP	74 (8)	74 (9)
Daytime BP, mm Hg		
Systolic BP	130 (13)	135 (16)
Diastolic BP	78 (9)	78 (11)
Nighttime BP, mm Hg		
Systolic BP	122 (14)	130 (19)
Diastolic BP	68 (10)	71 (12)

Numbers reported in table are mean (SD) or N (%) except albuminuria which is median (25th, 75th percentiles).

sustained controlled BP (prevalence ratio, 2.02; 95% CI, 1.36 to 2.99) (Table 4, bottom panel).

Sensitivity Analyses

The prevalence and prevalence ratios for BP phenotypes defined using 24-hour BP for participants with versus

without CKD are provided in Supplemental Table 5 and participants with versus without reduced eGFR and albuminuria in Supplemental Table 6. When using the European Society of Hypertension criteria for defining a complete ambulatory BP monitoring recording, participants with CKD (n=116) were more likely than their counterparts without CKD (n=338) to have uncontrolled

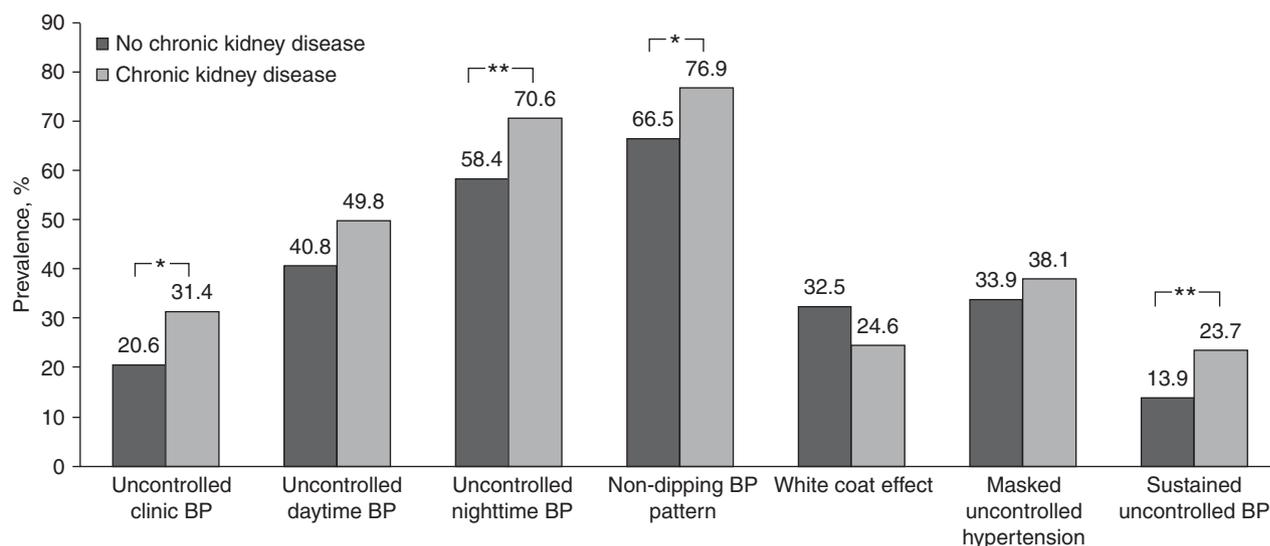


Figure 1. | Prevalence of clinic and ambulatory BP monitoring BP phenotypes among Jackson Heart Study participants with and without CKD taking antihypertensive medication (n=561). CKD was defined as an albumin-to-creatinine ratio ≥ 30 mg/g or eGFR < 60 ml/min per 1.73 m². The prevalence of white-coat effect was calculated among participants with mean clinic systolic BP ≥ 140 mm Hg or mean clinic diastolic BP ≥ 90 mm Hg. The prevalence of masked uncontrolled hypertension was calculated among participants with clinic mean systolic BP < 140 mm Hg and mean clinic diastolic BP < 90 mm Hg. The prevalence of sustained uncontrolled BP was calculated among the full population. * $P < 0.05$, ** $P < 0.01$.

Table 3. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes comparing participants with versus without CKD

BP Phenotypes	Number of Participants		Prevalence Ratio (95% CIs)			
	Without CKD (n=417)	With CKD (n=144)	Model 1 ^a	Model 2 ^b	Model 3 ^c	Model 4 ^d
Uncontrolled clinic BP ^e	86	45	1.39 (0.99 to 1.95)	1.45 (1.03 to 2.04)	1.44 (1.02 to 2.02)	—
Uncontrolled daytime BP	170	72	1.19 (0.97 to 1.46)	1.26 (1.02 to 1.56)	1.23 (1.00 to 1.52)	1.08 (0.88 to 1.33)
Uncontrolled nighttime BP	243	102	1.18 (1.02 to 1.37)	1.17 (1.01 to 1.36)	1.14 (0.98 to 1.33)	1.07 (0.92 to 1.24)
Nondipping BP pattern	277	111	1.13 (1.00 to 1.29)	1.10 (0.96 to 1.25)	1.10 (0.97 to 1.25)	1.09 (0.96 to 1.24)
White-coat effect ^{e,f}	28	11	1.13 (0.58 to 2.19)	1.24 (0.63 to 2.46)	1.25 (0.66 to 2.39)	—
Masked uncontrolled hypertension ^{e,f}	112	38	1.15 (0.86 to 1.53)	1.28 (0.96 to 1.69)	1.24 (0.94 to 1.64)	—
Sustained uncontrolled BP ^{e,f}	58	34	1.53 (1.08 to 2.18)	1.65 (1.16 to 2.35)	1.66 (1.16 to 2.36)	—

CKD was defined as urine albumin-to-creatinine ratio ≥ 30 mg/g or eGFR < 60 ml/min per 1.73 m².

^aModel 1 included adjustment for age and sex.

^bModel 2 included adjustment for age, sex, education, smoking status, physical activity, alcohol consumption, and body mass index.

^cModel 3 included adjustment for the variables in model 2 and history of stroke, history of myocardial infarction, diabetes, and total and HDL cholesterol.

^dModel 4 included adjustment for the variables in model 3 and clinic systolic and diastolic BP.

^eModel 4 not performed because clinic systolic and diastolic BP were used to define these phenotypes.

^fThe prevalence ratios for white-coat effect, masked uncontrolled hypertension, and sustained uncontrolled BP are compared with sustained controlled BP.

clinic BP, uncontrolled nighttime BP, a nondipping BP pattern, and sustained uncontrolled BP (Supplemental Figure 2). The prevalence of BP phenotypes by reduced eGFR and albuminuria status are provided in Supplemental Figure 3. Multivariable-adjusted prevalence ratios comparing participants with versus without CKD are provided in Supplemental Table 7 and with and without eGFR and albuminuria in Supplemental Table 8. The prevalence and prevalence ratios for BP phenotypes, defined using BP thresholds from the 2017 American College of Cardiology/AHA BP guideline, comparing participants with and without CKD are provided in Supplemental Figure 4 and Supplemental Table 9 and with and without reduced eGFR and albuminuria in Supplemental Figure 5 and Supplemental Table 10.

Blood Pressure Phenotypes and Cardiovascular Target-Organ Damage Stratified by CKD Status

The prevalence of left ventricular hypertrophy among participants with and without each BP phenotype is shown for participants with and without CKD, separately, in Supplemental Table 11. There was no evidence of differences in the associations of BP phenotypes with left ventricular hypertrophy for participants with and without CKD (all *P* values for interaction > 0.05 ; Supplemental Table 12). The prevalence of left ventricular hypertrophy among participants with and without each BP phenotype is shown for participants with and without reduced eGFR and with and without albuminuria in Supplemental Table 13. In a fully adjusted model, the association between uncontrolled nighttime BP and left ventricular hypertrophy was stronger for participants with versus without reduced eGFR (*P* value for interaction = 0.046; Supplemental Table 14).

Discussion

In this study, having CKD was associated with uncontrolled clinic BP and sustained uncontrolled BP after multivariable adjustment. Although the prevalence of uncontrolled daytime and nighttime BP, nondipping BP, white-coat effect, and masked uncontrolled BP were high among participants with CKD, these phenotypes were not more common compared with those without CKD after multivariable adjustment. Reduced eGFR was associated with a higher prevalence of masked uncontrolled hypertension, whereas albuminuria was associated with a higher prevalence of uncontrolled clinic BP and sustained uncontrolled BP after multivariable adjustment. Among participants with CKD, uncontrolled daytime and nighttime BP and masked uncontrolled hypertension were associated with a higher prevalence of left ventricular hypertrophy.

Prior studies have examined BP phenotypes using clinic measurements and ambulatory BP monitoring in adults with CKD (7,24,25). The International Database of Ambulatory BP in Renal Patients estimated the prevalence of white-coat effect, masked uncontrolled hypertension, and sustained uncontrolled BP in 7518 adults with CKD from four countries (25). The prevalence of masked uncontrolled hypertension ranged from 6% in a Spanish cohort to 35% in a study of black patients from the United States. Participants in the United States cohort had a higher prevalence of masked uncontrolled hypertension and sustained uncontrolled BP compared with the Italian and Spanish cohorts (25). In a meta-analysis comprising six studies with 980 participants who had CKD, 40% of those with controlled clinic BP had masked hypertension and 30% of those with uncontrolled clinic BP had white-coat hypertension (26).

Participants with masked hypertension or masked uncontrolled hypertension had lower eGFR (-3.2 ml/min per

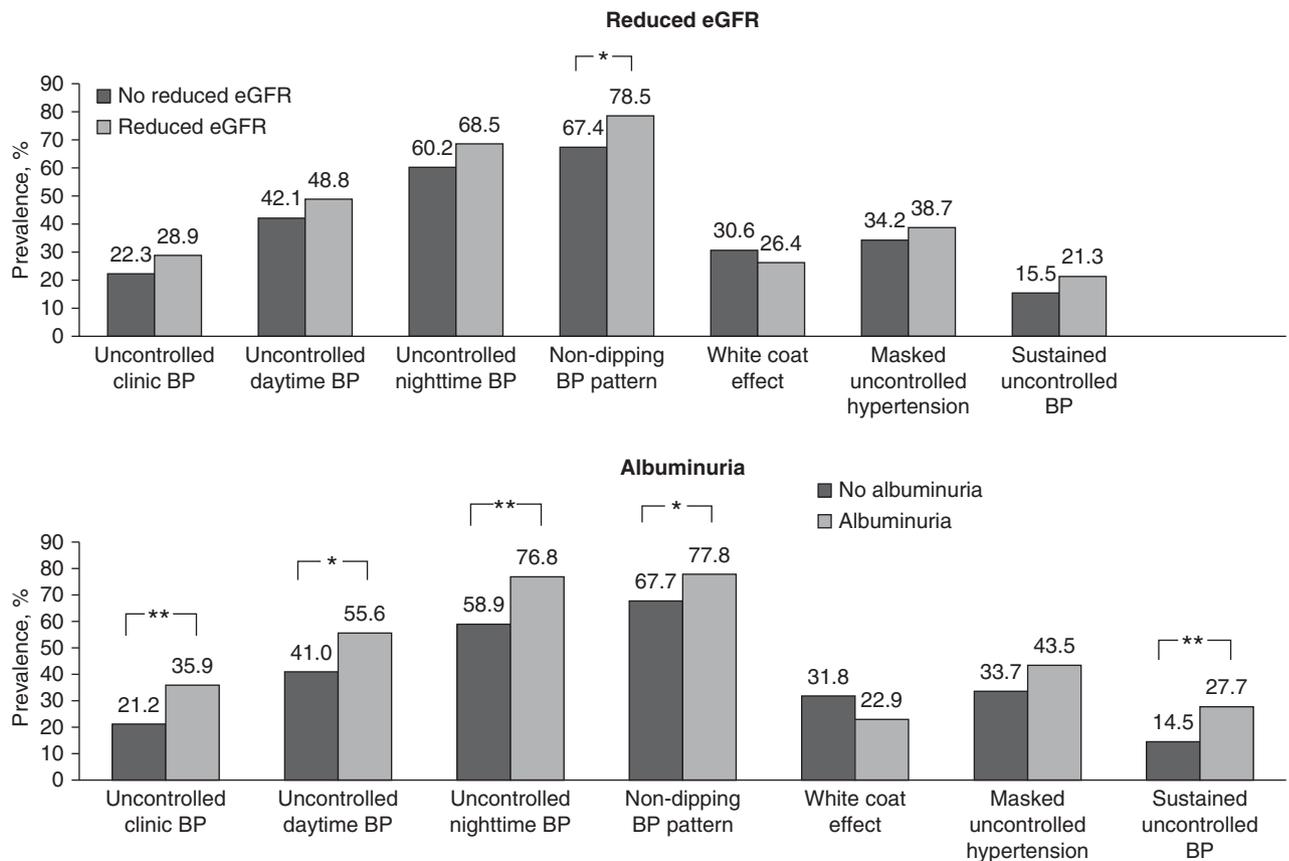


Figure 2. | Prevalence of clinic and ambulatory BP monitoring BP phenotypes among Jackson Heart Study participants with and without reduced eGFR and participants with and without albuminuria. (Top panel) Prevalence among participants with and without reduced eGFR. Reduced eGFR was defined by levels <60 ml/min per 1.73 m². (Bottom panel) Prevalence among patients with and without albuminuria. Albuminuria was defined by an albumin-to-creatinine ratio ≥ 30 mg/g. The prevalence of white-coat effect was calculated among participants with mean clinic systolic BP ≥ 140 mm Hg or mean clinic diastolic BP ≥ 90 mm Hg. The prevalence of masked uncontrolled hypertension was calculated among participants with clinic mean systolic BP <140 mm Hg and mean clinic diastolic BP <90 mm Hg. The prevalence of sustained uncontrolled BP was calculated among the full population. * $P < 0.05$, ** $P < 0.01$.

1.73 m²; 95% CI, -5.5 to -0.9 ml/min per 1.73 m²) than their counterparts with controlled clinic and ambulatory BP in the Chronic Renal Insufficiency Cohort study (7). In a cross-sectional study among patients with CKD at the Roudebush Veteran Affairs Administration Medical Center, masked uncontrolled hypertension was associated with higher urinary albuminuria compared with patients who were normotensive without CKD (27). In this study, reduced eGFR was associated with masked uncontrolled hypertension whereas albuminuria was associated with sustained uncontrolled BP after multivariable adjustment. In this study, the association of CKD with sustained uncontrolled BP appeared to be due to the presence of albuminuria. Given the strong associations of out-of-clinic BP phenotypes including uncontrolled daytime and nighttime BP and sustained uncontrolled BP with higher cardiovascular risk, future studies should evaluate using BPs from ambulatory BP monitoring to guide the titration of antihypertensive medication among adults with CKD (28,29).

Mojón *et al.* (30) analyzed data from 10,271 Spanish adults with hypertension to assess the circadian BP patterns between those with and without CKD. Compared

with participants without CKD, those with CKD had higher ambulatory systolic BP regardless of antihypertensive medication use and were more likely to have a nondipping BP pattern (61% versus 43%) and a rising nighttime BP pattern defined by mean asleep systolic BP greater than mean daytime systolic BP (18% versus 7%) (30). The prevalence of the rising nighttime BP pattern was 8% among those with stage 1 CKD compared with 35% among those with stage 5 CKD (30). Consistent with the study by Mojón *et al.* (30), Jackson Heart Study participants with versus without CKD were more likely to have uncontrolled nighttime BP, nondipping BP, and sustained uncontrolled BP.

An association of masked uncontrolled hypertension with left ventricular hypertrophy has been reported in both individuals with and without CKD (7,31–37). Also, in the African American Study of Kidney Disease, participants with higher nighttime systolic BP were more likely to have left ventricular hypertrophy, as well as higher levels of proteinuria and lower eGFR (6). Similar findings were reported in the Chronic Renal Insufficiency Cohort study, where masked uncontrolled hypertension and sustained uncontrolled BP were both associated with higher left

Table 4. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes among participants with and without reduced eGFR (top panel) and with and without albuminuria (bottom panel)

BP Phenotypes	Number of Participants		Prevalence Ratios (95% CIs)			
			Model 1 ^a	Model 2 ^b	Model 3 ^c	Model 4 ^d
Reduced eGFR (without reduced eGFR, n=472; with reduced eGFR, n=89)						
Uncontrolled clinic BP ^e	105	26	1.05 (0.72 to 1.55)	1.10 (0.75 to 1.61)	1.08 (0.73 to 1.58)	—
Uncontrolled daytime BP ^e	198	44	1.13 (0.88 to 1.45)	1.23 (0.96 to 1.57)	1.21 (0.94 to 1.55)	1.10 (0.87 to 1.40)
Uncontrolled nighttime BP	284	61	1.10 (0.94 to 1.30)	1.10 (0.93 to 1.29)	1.10 (0.93 to 1.29)	1.05 (0.89 to 1.24)
Nondipping BP pattern	318	70	1.12 (0.98 to 1.28)	1.09 (0.95 to 1.24)	1.10 (0.96 to 1.26)	1.09 (0.95 to 1.25)
White-coat effect ^{e,f}	32	7	0.99 (0.43 to 2.28)	1.05 (0.45 to 2.47)	1.04 (0.45 to 2.36)	—
Masked uncontrolled hypertension ^{e,f}	125	25	1.26 (0.90 to 1.78)	1.45 (1.04 to 2.02)	1.42 (1.00 to 2.00)	—
Sustained uncontrolled BP ^{e,f}	73	19	1.16 (0.75 to 1.78)	1.30 (0.84 to 2.01)	1.30 (0.85 to 1.99)	—
Albuminuria (without albuminuria, n=478; with albuminuria, n=83)						
Uncontrolled clinic BP ^e	101	30	1.72 (1.19 to 2.49)	1.76 (1.22 to 2.55)	1.76 (1.20 to 2.60)	—
Uncontrolled daytime BP ^e	196	46	1.33 (1.05 to 1.67)	1.36 (1.07 to 1.72)	1.30 (1.03 to 1.66)	1.09 (0.84 to 1.40)
Uncontrolled nighttime BP	281	64	1.28 (1.09 to 1.50)	1.27 (1.08 to 1.50)	1.21 (1.02 to 1.44)	1.10 (0.93 to 1.31)
Nondipping BP pattern	324	64	1.15 (0.98 to 1.36)	1.12 (0.95 to 1.31)	1.12 (0.96 to 1.32)	1.11 (0.94 to 1.30)
White-coat effect ^{e,f}	32	7	1.45 (0.65 to 3.26)	1.62 (0.72 to 3.69)	1.62 (0.72 to 3.65)	—
Masked uncontrolled hypertension ^{e,f}	127	23	1.26 (0.90 to 1.76)	1.34 (0.97 to 1.83)	1.26 (0.92 to 1.73)	—
Sustained uncontrolled BP ^{e,f}	69	23	2.01 (1.40 to 2.89)	2.06 (1.42 to 2.99)	2.02 (1.36 to 2.99)	—

Reduced eGFR was defined as levels <60 ml/min per 1.73 m². Albuminuria was defined as an albumin-to-creatinine ratio ≥30 mg/g.

^aModel 1 included adjustment for age and sex.

^bModel 2 included adjustment age, sex, education, smoking status, physical activity, alcohol consumption, and body mass index.

^cModel 3 included adjustment for the variables in model 2 and history of stroke, history of myocardial infarction, diabetes, and total and HDL cholesterol.

^dModel 4 included adjustment for the variables in Model 3 and clinic systolic and diastolic BP.

^eModel 4 not performed because clinic systolic and diastolic BP were used to define these phenotypes.

^fThe prevalence ratios for white-coat effect, masked uncontrolled hypertension and sustained uncontrolled BP are compared with sustained controlled BP.

ventricular mass index. In two separate studies conducted in China, a reverse dipping BP pattern was associated with higher left ventricular mass index (35,36). In this study, uncontrolled daytime and nighttime BP and masked uncontrolled hypertension were associated with left ventricular hypertrophy among participants with CKD. These findings highlight the importance of controlling BP, both in the clinic and outside of the clinic, for preventing cardiovascular end-organ damage.

There are several strengths of this study. The Jackson Heart Study is one of the largest community-based studies with black participants to have conducted ambulatory BP monitoring. The study population is well characterized with a large number of covariates collected, allowing us to adjust for potential confounders. There are several limitations that should be mentioned. The modest sample size may have led to results that were not statistically significant. Although not all of the differences in BP phenotypes were statistically significant, the differences in point estimates were in the direction suggesting that people with versus without CKD were more likely to have phenotypes associated with high cardiovascular disease risk. The majority of participants had stages 1 through 3 CKD. The prevalence of the BP phenotypes we studied may be higher in patients with more severe CKD. Only a single

assessment of eGFR and albuminuria were available, and we were unable to confirm the presence of CKD. In addition, too few participants with CKD were not taking antihypertensive medication to study this population.

In this community-based sample of black patients taking antihypertensive medication, the prevalence of phenotypes based on clinic BP and ambulatory BP monitoring was high among adults with CKD. Having CKD was associated with a higher prevalence of uncontrolled clinic BP and sustained uncontrolled BP after multivariable adjustment. Albuminuria was associated with a higher prevalence of several BP phenotypes. This study highlights the high prevalence of hypertension phenotypes defined based on clinic BP and ambulatory BP monitoring among adults with CKD taking antihypertensive medication.

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Disclosures

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Supplemental Material

This article contains the following supplemental material online at <http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.08840719/-/DCSupplemental>.

Supplemental Table 1. Definitions of phenotypes using clinic BP and ambulatory BP monitoring using 24-hour BP (top panel) and awake BP in the 2017 American College of Cardiology/American Heart Association guideline.

Supplemental Table 2. Number and percentage of Jackson Heart Study participants included in the analysis with missing data prior to multiple imputation ($n=561$).

Supplemental Table 3. Characteristics of Jackson Heart Study participants taking antihypertensive medication included and not included in the current analysis.

Supplemental Table 4. Number of participants according to their stage of CKD.

Supplemental Table 5. Prevalence and prevalence ratios for uncontrolled 24-hour BP, white coat effect, masked uncontrolled hypertension and sustained uncontrolled BP using 24-hour BP from ambulatory BP monitoring comparing participants with versus without CKD.

Supplemental Table 6. Prevalence and prevalence ratios for uncontrolled 24-hour BP, white coat effect, masked uncontrolled hypertension and sustained uncontrolled BP defined using 24-hour BP from ambulatory BP monitoring comparing participants with and without reduced eGFR (top panel) and with and without albuminuria (bottom panel).

Supplemental Table 7. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes using European Society of Hypertension criteria to define a complete ambulatory BP monitoring recording and considering daytime BP comparing participants with versus without CKD.

Supplemental Table 8. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes using the European Society of Hypertension criteria to define a complete ambulatory BP monitoring

recording and considering daytime BP comparing participants with and without reduced eGFR (top panel) and with and without albuminuria (bottom panel).

Supplemental Table 9. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes comparing participants with versus without CKD with BP thresholds from the 2017 American College of Cardiology/American Heart Association BP guideline used to define uncontrolled BP.

Supplemental Table 10. Prevalence ratios for clinic and ambulatory BP monitoring phenotypes comparing participants with versus without reduced eGFR (top panel) and with and without albuminuria (bottom panel) with BP thresholds from the 2017 American College of Cardiology/American Heart Association BP guideline used to define uncontrolled BP.

Supplemental Table 11. Prevalence of left ventricular hypertrophy among participants with and without CKD and phenotypes defined by clinic and ambulatory BP monitoring BP.

Supplemental Table 12. Prevalence ratios for left ventricular hypertrophy associated with clinic and ambulatory BP monitoring BP phenotypes among participants with and without CKD.

Supplemental Table 13. Prevalence of left ventricular hypertrophy stratified by BP phenotype based on clinic measurements and ambulatory BP monitoring and reduced eGFR (top panel) and albuminuria (bottom panel).

Supplemental Table 14. Prevalence ratios for left ventricular hypertrophy associated with BP phenotypes based on clinic measurements and ambulatory BP monitoring among participants with and without reduced eGFR (top panel) and with and without albuminuria (bottom panel).

Supplemental Figure 1. Exclusion criteria applied in the current analysis of BP phenotypes in the Jackson Heart Study.

Supplemental Figure 2. Prevalence of BP phenotypes among Jackson Heart Study participants with and without CKD taking antihypertensive medication using the European Society of Hypertension criteria to define a complete ambulatory BP monitoring recording.

Supplemental Figure 3. Prevalence of BP phenotypes among Jackson Heart Study participants with and without reduced eGFR (top panel) and participants with and without albuminuria (bottom panel) taking antihypertensive medication using the European Society of Hypertension criteria to define a complete ambulatory BP monitoring recording.

Supplemental Figure 4. Prevalence of clinic and ambulatory BP monitoring BP phenotypes among Jackson Heart Study participants taking antihypertensive medication with and without CKD with BP thresholds from the 2017 American College of Cardiology/American Heart Association BP guideline used to define uncontrolled BP.

Supplemental Figure 5. Prevalence of clinic and ambulatory BP monitoring BP phenotypes among Jackson Heart Study participants taking antihypertensive medication with and without reduced eGFR (top panel) and with and without albuminuria (bottom panel) with BP thresholds from the 2017 American College of Cardiology/American Heart Association BP guideline used to define uncontrolled BP.

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