

Associations of Blood Pressure Dipping Patterns With Left Ventricular Mass and Left Ventricular Hypertrophy in Blacks: The Jackson Heart Study

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Background—Abnormal diurnal blood pressure (BP), including nondipping patterns, assessed using ambulatory BP monitoring, have been associated with increased cardiovascular risk among white and Asian adults. We examined the associations of BP dipping patterns (dipping, nondipping, and reverse dipping) with cardiovascular target organ damage (left ventricular mass index and left ventricular hypertrophy), among participants from the Jackson Heart Study, an exclusively black population—based cohort.

Methods and Results—Analyses included 1015 participants who completed ambulatory BP monitoring and had echocardiography data from the baseline visit. Participants were categorized based on the nighttime to daytime systolic BP ratio into 3 patterns: dipping pattern (≤0.90), nondipping pattern (>0.90 to ≤1.00), and reverse dipping pattern (>1.00). The prevalence of dipping, nondipping, and reverse dipping patterns was 33.6%, 48.2%, and 18.2%, respectively. In a fully adjusted model, which included antihypertensive medication use and clinic and daytime systolic BP, the mean differences in left ventricular mass index between reverse dipping pattern versus dipping pattern was 8.3 ± 2.1 g/m² (P<0.001) and between nondipping pattern versus dipping pattern was -1.0 ± 1.6 g/m² (P=0.536). Compared with participants with a dipping pattern, the prevalence ratio for having left ventricular hypertrophy was 1.65 (95% CI, 1.05–2.58) and 0.96 (95% CI, 0.63–1.97) for those with a reverse dipping pattern and nondipping pattern, respectively.

Conclusions—In this population-based study of blacks, a reverse dipping pattern was associated with increased left ventricular mass index and a higher prevalence of left ventricular hypertrophy. Identification of a reverse dipping pattern on ambulatory BP monitoring may help identify black at increased risk for cardiovascular target organ damage. (*J Am Heart Assoc.* 2017;6:e004847. DOI: 10. 1161/JAHA.116.004847.)

Key Words: ambulatory blood pressure monitoring • black • dipping • diurnal variation • left ventricular hypertrophy • left ventricular mass

In healthy adults, blood pressure (BP) is characterized by a circadian pattern during a 24-hour period with levels that are normally highest while awake and fall during sleep. Ambulatory BP monitoring (ABPM) can be used to assess the

circadian pattern of BP. 1,2 Based on the nighttime to daytime systolic BP (SBP) ratio, individuals can be categorized by dipping status into nondipping BP status (SBP ratio >0.90) or dipping BP status (SBP ratio ≤0.90). However, in some

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individuals there may be an excess rise or fall in nighttime BP relative to daytime BP. 4,5 Some investigators 6 have proposed that dipping status should be further categorized into 4 dipping patterns 4 : extreme dipping pattern (SBP ratio $\leq\!0.80$), dipping pattern (0.80< SBP ratio $\leq\!0.90$), nondipping pattern (0.90< SBP ratio $\leq\!1.00$), and reverse dipping pattern (SBP ratio $>\!1.00$), as these patterns may provide more prognostic information than dipping dichotomized as nondipping BP or dipping BP status.

Prior studies have demonstrated that nondipping and reverse dipping patterns are associated with increased mortality and cardiovascular events when compared with a dipping pattern. 5,7-12 Also, an association between nondipping BP status and subclinical target organ damage, including left ventricular mass index (LVMI) and left ventricular hypertrophy (LVH), has been previously demonstrated. 13-16 However, less is known about the association between reverse dipping pattern with LVMI or LVH. The prior studies 17,18 that have examined the association between reverse dipping patterns and LVMI have provided conflicting results. These studies were conducted mostly among adults who had untreated hypertension. Neither study 17,18 included blacks, who are known to have a high prevalence of hypertension and hypertensionrelated cardiovascular target organ damage, 19-21 including increased LVMI and a higher prevalence of LVH compared with whites.²² In addition, blacks are also more likely to have nondipping BP and higher nighttime BP compared with whites. 23,24

In the current study, we examined the association of BP dipping patterns with LVMI and LVH among participants in the Jackson Heart Study (JHS), a large population-based cohort study comprised exclusively of blacks. We examined these associations for the overall population and for participants taking and not taking antihypertensive medication, separately. In secondary analyses, we also examined the associations of nighttime BP with LVMI and LVH.

Methods

Study Population

The JHS enrolled 5306 noninstitutionalized blacks, 21 years and older, between 2000 and 2004 from the Atherosclerosis Risk in the Community (ARIC) site in Jackson, MS, and a representative sample of urban and rural Jackson, MS, metropolitan tri-county (Hinds, Madison, and Rankin counties) residents, volunteers, randomly selected individuals, and secondary family members of enrolled participants. The current analyses were restricted to 1148 participants who underwent 24-hour ABPM following the baseline examination in 2000–2004. Participants who did not meet the International Database of Ambulatory Blood Pressure in Relation to

Cardiovascular Outcome 26 (IDACO) criteria for complete ABPM (n=102; described below), did not have complete echocardiography data on LVMI (n=27), or were missing clinic BP values at the baseline visit (n=4) were excluded, leaving a final sample size of 1015 participants.

The JHS was approved by the institutional review boards of the University of Mississippi Medical Center, Jackson State University, and Tougaloo College. The institutional review boards at Columbia University and University of Alabama at Birmingham approved the use of JHS data for the current analysis. All participants provided written informed consent.

Data Collection and Clinical Covariates

A detailed description of the data collection, methodology, and specimen collection and processing from examination 1 has been previously described and is available in Data S1. ^{27,28} Data were collected during an in-home interview, clinic examination, and a 24-hour ABPM period. During the in-home interview, trained staff administered questionnaires to collect self-reported information on sociodemographics, selected health behaviors (eg, alcohol consumption, current smoking, and physical activity), and prior diagnosed comorbid conditions. During the clinic examination, trained technicians measured height, weight, and BP, and collected blood and urine samples. Antihypertensive medication use was defined by self-report. After the clinic examination, participants were given the opportunity to complete ABPM.

Clinic BP Measurement

Clinic BP measurements were taken using a Hawksley random zero sphygmomanometer (Hawksley and Sons Ltd, Lancing, United Kingdom) and an appropriately sized BP cuff. Cuff size was determined by measuring the upper-arm circumference. At each visit, participants rested for at least 5 minutes in a seated, upright position with their back and arms supported, feet flat on the floor, and legs uncrossed prior to having their BP measured. Trained staff conducted 2 BP measurements in the right arm. One minute elapsed between the 2 measurements. The JHS Coordinating Center conducted quality control by semiannual training and retraining of staff, monitoring digit preference for each technician, and comparing mean BP measurements within and between trained technicians. The 2 clinic-measured BP measurements were averaged for analysis. As previously described, BP measurements were calibrated using robust regression to an oscillometric device (Omron HEM-907XL, Omron Healthcare Inc., Lake Forest, IL).²⁹ Prevalent clinic hypertension was defined as a mean clinic SBP ≥140 mm Hg, mean clinic diastolic BP (DBP) ≥90 mm Hg, or antihypertensive medication use.

Ambulatory BP Monitoring

Participants were fitted with an ABPM device (Spacelabs 90207, Spacelabs, Redmond, WA) on their nondominant arm following the baseline examination. Ambulatory BP was recorded every 20 minutes. After 24 hours, the device was removed and data were downloaded onto a computer and processed with Medifacts International's Medicom software (Rockville, MD). IDACO criteria were used to define whether the ABPM period was complete. Specifically, participants were considered to have a complete ABPM if they had ≥10 daytime (10 AM-8 PM) and ≥5 nighttime (12 AM-6 AM) SBP and DBP measurements.²⁶ Mean daytime SBP and DBP and mean nighttime SBP and DBP were calculated by averaging the readings during the daytime and nighttime periods, respectively. Mean 24-hour BP was defined by averaging all available BP measurements from ABPM.

The nighttime to daytime SBP ratio was defined as mean nighttime SBP divided by mean daytime SBP. Dipping was categorized into 3 patterns based on the nighttime to daytime SBP ratio: dipping pattern (\leq 0.90), nondipping pattern (>0.90 to \leq 1.00), and reverse dipping pattern (>1.00). Because of the small sample size (n=38) of participants with an extreme dipping pattern (\leq 0.80), these participants were included in the dipping pattern category (\leq 0.90).

Echocardiography

Certified sonographers performed 2-dimensional transthoracic echocardiography (Sonos-4500, Philips Medical Systems, Amsterdam, Netherlands) using standardized protocols.²⁷ Echocardiograms were reviewed for clinical interpretation and analytical measurements by experienced cardiologists on networked image workstations (Vericis; Camtronics Medical Systems, Hartland, WI).²⁷ Left ventricular dimensions including left ventricular internal diameter in diastole (mm), interventricular septal thickness in diastole (IVSd, mm), and posterior wall thickness in diastole (PWTd, mm), were assessed according to American Society of Echocardiography (ASE) recommendations.³⁰

Calculation of LVMI and LVH

Left ventricular mass, LVMI, and LVH were derived according to ASE and European Society of Cardiovascular Imaging recommendations. Left ventricular mass was calculated using the ASE formula: $0.8 \times (1.04 \times ((IVSD+LVEDD+PWTD)^3-(L-VEDD)^3))+0.6$. LVMI was calculated as left ventricular mass/body surface area. LVH was defined as increased LVMI $\geq 96 \text{ g/m}^2$ in women and $\geq 116 \text{ g/m}^2$ in men).

Statistical Analyses

Participant characteristics were calculated for the overall analytical sample and stratified into 3 dipping patterns (dipping, nondipping, and reverse dipping). Values were expressed as mean±SD or percentages. Using ANOVA, mean differences±standard error (SE) in LVMI between participants with dipping (referent), nondipping, and reverse dipping patterns were determined. In addition to an unadjusted model, 4 adjusted models were conducted using ANCOVA. Model 1 included adjustment for age, sex, and body mass index (BMI). Model 2 included the variables in model 1 plus diabetes mellitus, education level achieved, alcohol consumption, smoking status, physical activity, reduced estimated glomerular filtration rate (<60 mL/min per 1.73 m²), and antihypertensive medication use. Model 3 included adjustment for the variables in model 2 plus mean clinic SBP. Model 4 included adjustment for the variables in model 3 plus mean daytime SBP. The prevalence of LVH between participants with dipping, nondipping, and reverse dipping patterns was also calculated. Prevalence ratios (PRs) and 95% Cls for having LVH were determined using Poisson regression models with sandwich estimators before and after adjustment for covariates as described for models 1 to 4 above, with the dipping pattern serving as the reference group. In secondary analyses, the differences in LVMI and prevalence of LVH between participants with dipping, nondipping, and reverse dipping patterns were calculated by substituting mean daytime SBP with mean 24-hour SBP in model 4. In this model, the association of mean 24-hour SBP with LVMI and LVH was also examined.

Mean differences in LVMI by quartiles of nighttime SBP and quartiles of nighttime DBP, separately, were also calculated using ANCOVA and Poisson regression. For these analyses, the lowest quartile of nighttime SBP and DBP were the referent groups. In analyses for nighttime SBP, mean differences in LVMI were calculated before and after adjustment for covariates in models 1 to 4. In the analyses for nighttime DBP, model 3 included adjustment for mean daytime DBP instead of mean daytime SBP, and model 4 included adjustment for mean clinic DBP instead of mean clinic SBP. PRs and 95% CIs for having LVH associated with quartiles of nighttime SBP and DBP were determined using Poisson regression models with sandwich estimators before and after adjustment for covariates as described for models 1 to 4 above.

Subgroup analyses were conducted by repeating the analyses among participants taking and not taking antihypertensive medication, separately. The tests for interaction between antihypertensive medication use and

dipping BP as well as nighttime SBP and nighttime DBP on LVMI and LVH were calculated in models including the full population, main effect terms, and multiplicative interaction terms (eg, dipping pattern×antihypertensive medication use). *P*<0.05 was considered to be statistically significant. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Baseline Characteristics

Among the participants included in this analysis, the mean \pm SD age was 59.1 ± 10.9 years, 67.9% were women, 63.0% had prevalent clinic hypertension, and 56.8% were taking antihypertensive medication (Table 1). The prevalence

Table 1. Characteristics of Jackson Heart Study Participants Included in the Current Analysis, Overall, and Stratified by BP Dipping Patterns

	Overall (N=1015)	Dipping (n=341)	Nondipping (n=489)	Reverse Dipping (n=185)	P Value*
Sociodemographic characteristics					·
Age, y	59.1±10.9	57.7±10.9	58.9±11.2	62.4±9.7	<0.001
Female sex, %	67.9	68.9	65.0	73.5	0.096
Education <high %<="" school,="" td=""><td>18.8</td><td>15.6</td><td>19.1</td><td>23.8</td><td>0.069</td></high>	18.8	15.6	19.1	23.8	0.069
Clinical characteristics					
Body mass index, kg/m ²	31.1±6.5	30.0±6.0	31.5±6.7	32.1±6.4	<0.001
Diabetes mellitus, %	24.1	18.6	23.3	36.1	<0.001
Low-density lipoprotein cholesterol, mg/dL	125.8±36.0	128.5±36.5	124.8±33.9	123.6±40.0	0.251
High-density lipoprotein cholesterol, mg/dL	54.0±15.1	55.0±15.6	53.5±14.7	53.1±15.2	0.291
Estimated glomerular filtration rate <60 mL/min per 1.73 m², %	10.9	7.7	10.3	18.1	0.001
Health behaviors					
Alcohol use					
Nondrinker, %	69.7	63.9	69.9	80.0	<0.001
Moderate drinker, %	28.1	32.6	28.2	19.5	0.006
Heavy drinker, %	2.2	3.5	1.8	0.5	0.064
Current smoking, %	10.0	11.7	8.4	10.8	0.260
Total physical activity score	8.3±2.6	8.5±2.5	8.3±2.6	7.9±2.6	0.063
High risk for sleep apnea, %	67.2	61.6	67.9	75.7	0.004
BP-related characteristics					
Clinic BP					
Mean systolic BP, mm Hg	127.7±15.9	126.3±15.6	127.8±15.7	130.3±16.9	0.028
Mean diastolic BP, mm Hg	74.5±8.5	74.3±8.8	74.5±8.3	74.9±8.7	0.766
Prevalent clinic hypertension [†] , %	63.0	58.4	60.3	78.8	<0.001
Antihypertensive medication use, %	56.8	52.1	53.2	74.9	<0.001
Ambulatory BP					
Mean daytime systolic BP, mm Hg	129.4±13.5	130.9±13.3	128.6±13.4	128.9±14.1	0.039
Mean daytime diastolic BP, mm Hg	77.9±9.3	79.6±9.3	77.2±9.1	76.6±9.6	<0.001
Mean nighttime systolic BP, mm Hg	121.1±15.8	112.0±11.9	121.9±13.3	135.6±16.4	<0.001
Mean nighttime diastolic BP, mm Hg	68.4±9.8	63.6±8.6	69.0±8.7	75.6±9.7	<0.001
Mean 24-h systolic BP, mm Hg	126.3±13.7	123.5±12.6	126.1±13.4	132.1±15.0	<0.001
Mean 24-h diastolic BP, mm Hg	74.1±8.9	73.2±8.7	74.0±8.8	76.2±9.3	<0.001

Data are presented as mean \pm SD or percentage. Dipping blood pressure (BP) (\leq 0.90), nondipping BP (>0.90 to \leq 1.00), and reverse BP dipping (>1.00). Nighttime to daytime systolic BP (SBP) ratio is defined as mean nighttime SBP divided by mean daytime SBP.

^{*}Analysis of variance P value comparing differences between participants with dipping, nondipping, and reverse dipping patterns.

[†]Prevalent clinic hypertension is defined as a mean clinic SBP ≥140 mm Hg or mean clinic diastolic BP ≥90 mm Hg or self-report of current antihypertensive medication use.

of dipping, nondipping, and reverse dipping patterns was 33.6%, 48.2%, and 18.2%, respectively. Among the 3 dipping patterns, reverse dipping was associated with the oldest age, highest body mass index and clinic SBP, and the highest proportion of women, diabetes mellitus, reduced estimated glomerular filtration rate, non-alcohol use, high risk for sleep apnea, prevalent clinic hypertension, and antihypertensive medication use.

Associations of BP Dipping Patterns With LVMI and LVH

In an unadjusted model, compared with participants with a dipping pattern, mean \pm SE LVMI was 9.9 \pm 2.1 g/m² higher for participants with a reverse dipping pattern (P<0.001) and 1.6 ± 1.6 g/m² lower for participants with a nondipping pattern (P=0.312, Table 2). In a fully adjusted model including daytime SBP, compared with participants with a dipping pattern, mean \pm SE LVMI was 8.3 \pm 2.1 g/m² higher for participants with a reverse dipping pattern (P<0.001) and 1.0 ± 1.6 g/m² lower for participants with a nondipping pattern (P=0.536). In a fully adjusted model controlling for mean 24-hour SBP instead of mean daytime SBP (Table S1), compared with participants with a dipping pattern, mean \pm SE LVMI was $5.1\pm2.1 \text{ g/m}^2$ higher for participants with a reverse dipping pattern (P=0.02) and 2.6 ± 1.6 g/m² lower for participants with a nondipping pattern (P=0.113). In this model, higher mean 24-hour SBP was associated with higher LVMI (P<0.001, Table S2).

Among participants taking antihypertensive medication, the prevalence of a dipping pattern, nondipping pattern, and reverse dipping pattern was 30.8%, 45.4%, and 23.8%, respectively. Among participants not taking antihypertensive medication, the prevalence of a dipping pattern, nondipping pattern,

and reverse dipping pattern was 37.1%, 52.3%, and 10.5%, respectively. Among participants taking and not taking antihypertensive medication, those with reverse dipping pattern had 11.0 ± 2.8 and 2.1 ± 3.4 g/m² higher LVMI, respectively, compared with their counterparts with a dipping pattern in a fully adjusted model including mean daytime SBP (interaction P=0.068, Table 3). In a fully adjusted model including mean 24-hour SBP instead of mean daytime SBP, compared with participants with a dipping pattern, those with a reverse dipping pattern had 7.7 ± 2.8 g/m² higher and 1.0 ± 3.4 g/m² lower LVMI among those taking and not taking antihypertensive medication, respectively (interaction P=0.096, Table S3).

The prevalence of LVH for participants with a dipping pattern, nondipping pattern, and reverse dipping pattern was 11.1%, 10.6%, and 22.2%, respectively (Table 4). The PR for having LVH for reverse dipping pattern versus dipping pattern was 1.99 (95% CI, 1.33–2.98) in an unadjusted model. In a fully adjusted model including mean daytime SBP, the PR for having LVH for reverse dipping pattern versus dipping pattern was 1.65 (95% CI, 1.05–2.58). The PR for having LVH was 1.21 (95% CI, 0.76–1.92) in a fully adjusted model when adjusting for mean 24-hour SBP instead of mean daytime SBP (Table S4). In this latter model, higher mean 24-hour SBP was associated with an increased PR for having LVH (1.32 [95% CI, 1.15–1.51], Table S5).

In a fully adjusted model including mean daytime SBP, the PRs for having LVH among participants with a reverse dipping pattern versus a dipping pattern were 1.78 (95% CI, 1.07–2.95) and 1.48 (95% CI, 0.52–4.16) among those taking and not taking antihypertensive medication, respectively (interaction P=0.904, Table 5). In a fully adjusted model including mean 24-hour SBP instead of mean daytime SBP, the PRs for having LVH among participants with a reverse dipping pattern versus dipping pattern were 1.39 (95% CI, 0.83–2.33) and

Table 2. Differences in LVMI Between Participants With Nondipping and Reverse Dipping Versus Dipping BP Patterns

	Dipping BP Patterns*			P Value	
	Dipping (n=341)	Nondipping (n=489)	Reverse Dipping (n=185)	Nondipping vs Dipping	Reverse Dipping vs Dipping
LVMI, g/m ²	78.2±20.8	76.6±21.2	88.1±29.7	0.312	<0.001
	Difference±standard	error			
Unadjusted	0 (Ref)	-1.6±1.6	9.9±2.1	0.312	<0.001
Model 1	0 (Ref)	-2.5±1.6	8.1±2.1	0.116	<0.001
Model 2	0 (Ref)	-1.8±1.6	7.0±2.1	0.282	<0.001
Model 3	0 (Ref)	-1.9±1.6	6.9±2.1	0.245	0.001
Model 4	0 (Ref)	-1.0±1.6	8.3±2.1	0.536	<0.001

Data are presented as mean±SD or unadjusted/adjusted mean difference compared with referent (Ref) group±standard error. Nighttime to daytime systolic blood pressure (SBP) ratio is defined as mean nighttime SBP/mean daytime SBP. Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive medication use. Model 3 includes additional adjustment for mean clinic SBP. Model 4 includes additional adjustment for mean daytime SBP. BP indicates blood pressure; LVMI, left ventricular mass index. *Dipping pattern is based on the nighttime to daytime SBP ratio and defined by 3 patterns: dipping (≤0.90), nondipping (>0.90 to ≤1.00), and reverse dipping (>1.00).

Table 3. Differences in LVMI Among Participants With Dipping, Nondipping, and Reverse Dipping BP Patterns Stratified by Antihypertensive Medication Use

	Dipping BP Patterns*				
	Among Participants 1	Taking Antihypertensive Medic	ation [†]	P Value	
	Dipping (n=173)	Nondipping (n=255)	Reverse Dipping (n=134)	Nondipping vs Dipping	Reverse Dipping vs Dipping
LVMI, g/m ²	80.2±21.2	78.1±20.3	90.9±30.3	0.347	<0.001
	Difference±standa	rd error	·		
Unadjusted	0 (Ref)	-2.2±2.3	10.7±2.7	0.347	<0.001
Model 1	0 (Ref)	-2.9±2.3	9.7±2.7	0.213	<0.001
Model 2	0 (Ref)	-2.1±2.4	9.7±2.8	0.384	<0.001
Model 3	0 (Ref)	-2.4±2.4	9.5±2.8	0.328	<0.001
Model 4	0 (Ref)	-1.2±2.4	11.0±2.8	0.609	<0.001
	Among Participants I	Not Taking Antihypertensive M	Medication	P Value	
	Dipping (n=159)	Nondipping (n=224)	Reverse Dipping (n=45)	Nondipping vs Dipping	Reverse Dipping vs Dipping
LVMI, g/m ²	75.8±20.2	74.1±21.3	77.0±20.5	0.439	0.737
	Difference±standa	rd error			
Unadjusted	0 (Ref)	-1.7±2.2	1.2±3.5	0.439	0.737
Model 1	0 (Ref)	-2.4±2.1	0.7±3.4	0.264	0.850
Model 2	0 (Ref)	-0.9±2.2	0.8±3.5	0.663	0.812
Model 3	0 (Ref)	-1.0±2.2	0.6±3.5	0.653	0.855
Model 4	0 (Ref)	-0.5±2.1	2.1±3.4	0.820	0.533

Data are presented as mean±SD or unadjusted/adjusted mean difference compared with referent (Ref) group±standard error. Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, and estimated glomerular filtration ratio <60 mL/min per 1.73 m². Model 3 includes additional adjustment for mean clinic systolic blood pressure (SBP). Model 4 includes additional adjustment for mean daytime SBP. BP indicates blood pressure; LVMI, left ventricular mass index.

0.92 (95% CI, 0.33–2.59) among those taking and not taking antihypertensive medication, respectively (interaction P=0.504, Table S6).

The PRs for having LVH among participants with a nondipping pattern versus their counterparts with a dipping pattern were not statistically significant in an unadjusted model (0.95 [95% CI, 0.64–1.42], Table 4) or a fully adjusted model including either mean daytime SBP (0.96 [95% CI, 0.63–1.47], Table 4) or mean 24-hour SBP (0.82 [95% CI, 0.54–1.26], Table S4). In a fully adjusted model including mean daytime SBP, the PRs for having LVH among participants with a nondipping pattern versus dipping pattern were 0.96 (95% CI, 0.58–1.60) and 1.04 (95% CI, 0.47–2.31) among those taking and not taking antihypertensive medication, respectively (interaction P=0.777, Table 5).

Association of Nighttime BP With LVMI and LVH

Higher quartiles of nighttime SBP and DBP were each associated with higher LVMI in unadjusted and fully adjusted

models (Table 6). In an unadjusted model, the PRs for having LVH associated with quartiles 2, 3, and 4 versus quartile 1 of nighttime SBP were 1.21 (95% CI, 0.65–2.23), 2.13 (95% CI, 1.23–3.69), and 3.40 (95% CI, 2.04–5.69), respectively (Table 7). The unadjusted PRs for LVH associated with quartiles 2, 3, and 4 versus quartile 1 of nighttime DBP were 0.80 (95% CI, 0.48–1.34), 0.96 (95% CI, 0.59–1.57), and 1.79 (95% CI, 1.17–2.72), respectively. The associations of higher quartiles of nighttime SBP and DBP with LVH were not statistically significant in fully adjusted models.

The association between higher quartiles of nighttime SBP and LVMI did not differ between participants taking versus not taking antihypertensive medication (interaction P=0.853, Table S7). In contrast, the association between higher quartiles of nighttime DBP and LVMI was stronger among participants taking versus not taking antihypertensive medication (interaction P<0.001, Table S8). Higher quartiles of nighttime SBP (Table S9) and nighttime DBP (Table S10) were not associated with a statistically significant increased prevalence of LVH among participants taking and not taking antihypertensive medication.

^{*}Dipping pattern is based on the nighttime to daytime SBP ratio and defined by 3 patterns: dipping (\leq 0.90), nondipping (>0.90 to \leq 1.00), and reverse dipping (>1.00). Nighttime to daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

[†]The overall test for interaction between antihypertensive medication use and dipping patterns on left ventricular mass index (LVMI) is P=0.086. The test for interaction between antihypertensive medication use and nondipping pattern is P=0.068.

Table 4. Prevalence and Prevalence Ratios for LVH Associated With Dipping Patterns

	Dipping Patterns*	Dipping Patterns*			
	Dipping (n=341)	Nondipping (n=489)	Reverse Dipping (n=185)		
LVH, %	11.1	10.6	22.2		
	Prevalence ratio (95% CI)				
Unadjusted	1 (Ref)	0.95 (0.64–1.42)	1.99 (1.33–2.98)		
Model 1	1 (Ref)	0.91 (0.62–1.34)	1.66 (1.11–2.49)		
Model 2	1 (Ref)	0.89 (0.58–1.37)	1.48 (0.95–2.32)		
Model 3	1 (Ref)	0.88 (0.57–1.35)	1.47 (0.94–2.29)		
Model 4	1 (Ref)	0.96 (0.63–1.47)	1.65 (1.05–2.58)		

Left ventricular hypertrophy (LVH) is defined as left ventricular mass index \ge 96 g/m² in women and \ge 116 g/m² in men according to the American Society of Echocardiography recommendations. Nighttime to daytime systolic blood pressure (SBP) ratio is defined as mean nighttime SBP/mean daytime SBP. Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive medication use. Model 3 includes additional adjustment for mean clinic SBP. Model 4 includes additional adjustment for mean daytime SBP. Ref indicates referent.

Discussion

In the current population-based study of blacks, participants with a reverse dipping BP pattern had higher LVMI and a

higher prevalence of LVH when compared with their counterparts with a dipping BP pattern. These associations were present after multivariable adjustment for demographics, cardiovascular risk factors, antihypertensive medication use,

Table 5. Prevalence Ratios for Having LVH Associated With Dipping Patterns Stratified by Antihypertensive Medication Use

	Dipping Patterns*		
	Among Participants Taking Ant	ihypertensive Medication [†]	
	Dipping (n=173)	Nondipping (n=255)	Reverse Dipping (n=134)
LVH, %	14.5	12.6	24.6
	Prevalence ratio (95% CI)		
Unadjusted	1 (Ref)	0.87 (0.53–1.41)	1.70 (1.07–2.72)
Model 1	1 (Ref)	0.87 (0.53–1.42)	1.64 (1.02–2.65)
Model 2	1 (Ref)	0.89 (0.53–1.50)	1.63 (0.98–2.70)
Model 3	1 (Ref)	0.88 (0.53–1.48)	1.61 (0.97–2.67)
Model 4	1 (Ref)	0.96 (0.58–1.60)	1.78 (1.07–2.95)
	Among Participants Not Taking	Antihypertensive Medication	
	Dipping (Ref) (n=159)	Nondipping (n=224)	Reverse Dipping (n=45)
LVH, %	7.6	6.7	11.1
	Prevalence ratio (95% CI)	·	
Unadjusted	1 (Ref)	0.89 (0.43–1.84)	1.47 (0.55–3.96)
Model 1	1 (Ref)	0.85 (0.42–1.72)	1.16 (0.43–3.15)
Model 2	1 (Ref)	0.98 (0.45–2.12)	1.25 (0.41–3.78)
Model 3	1 (Ref)	0.96 (0.44–2.10)	1.21 (0.40–3.61)
Model 4	1 (Ref)	1.04 (0.47–2.31)	1.48 (0.52–4.16)

Left ventricular hypertrophy (LVH) is defined as left ventricular mass index \ge 96 g/m² in women and \ge 116 g/m² in men according to the American Society of Echocardiography recommendations. Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m². Model 3 includes additional adjustment for mean clinic systolic blood pressure (SBP). Model 4 includes additional adjustment for mean daytime SBP. Ref indicates referent.

^{*}Dipping pattern is based on the nighttime to daytime SBP ratio and defined by three 3: dipping (<0.90), nondipping (>0.90 to <1.00), and reverse dipping (>1.00).

^{*}Dipping pattern is based on the nighttime to daytime SBP ratio and defined by 3 patterns: dipping (\leq 0.90), nondipping (>0.90 to \leq 1.00), and reverse dipping (>1.00). Nighttime to daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

[†]The overall test for interaction between antihypertensive medication use and dipping patterns on LVH is P=0.919. The test for interaction between antihypertensive medication use and nondipping pattern is P=0.777. The test for interaction between antihypertensive medication use and reverse dipping pattern is P=0.904.

Table 6. Differences in LVMI Associated With Quartiles (Qs) of Nighttime SBP (Upper Panel) and Nighttime DBP (Lower Panel)

	Quartiles of Nighttime	Quartiles of Nighttime SBP				
	Q1 (n=253)	Q2 (n=259)	Q3 (n=258)	Q4 (n=245)	P Trend	
Levels of nighttime SBP	<109.5 mm Hg	≥109.5 and <119.4 mm Hg	≥119.4 and <130.8 mm Hg	≥130.8 mm Hg		
LVMI, g/m ²	73.0±18.8	74.7±17.9	80.0±23.5	89.7±28.0	<0.001	
	Difference±standard	Difference±standard error				
Unadjusted	0 (Ref)	1.7±2.0	7.0±2.0	16.7±2.0	<0.001	
Model 1	0 (Ref)	0.4±2.0	4.9±2.0	13.0±2.1	<0.001	
Model 2	0 (Ref)	$-0.3{\pm}2.0$	4.4±2.0	10.4±2.2	<0.001	
Model 3	0 (Ref)	$-0.4{\pm}2.0$	4.3±2.1	10.2±2.3	<0.001	
Model 4	0 (Ref)	-1.4±2.1	2.0±2.3	6.3±2.9	0.026	
	Quartiles of Nighttime DBP					
	Q1 (n=255)	Q2 (n=253)	Q3 (n=256)	Q4 (n=251)	P Trend	
Levels of nighttime DBP	<61.7 mm Hg	≥61.7 and <67.5 mm Hg	≥67.5 and <74.4 mm Hg	≥74.4 mm Hg		
LVMI, g/m ²	76.4±22.9	74.9±19.0	78.7±20.0	87.0±28.2	<0.001	
	Difference±standar	d error		-		
Unadjusted	0 (Ref)	-1.5±2.0	2.3±2.0	10.6±2.0	<0.001	
Model 1	0 (Ref)	-1.2±2.0	2.3±2.0	9.6±2.1	<0.001	
Model 2	0 (Ref)	-2.1±2.0	1.3±2.1	7.0±2.1	<0.001	
Model 3	0 (Ref)	-1.8±2.1	1.8±2.1	7.8±2.2	<0.001	
Model 4	0 (Ref)	-2.4±2.1	0.4±2.3	5.3±2.7	0.013	

Data are presented as mean±SD or unadjusted/adjusted mean difference compared with referent (Ref) group±standard error. Upper panel: Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive mediation use. Model 3 includes model 2 plus additional adjustment for mean clinic systolic blood pressure (SBP). Model 4 includes bodel 3 plus additional adjustment for mean daytime SBP. Lower panel: Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive mediation use. Model 3 includes model 3 plus additional adjustment for mean clinic diastolic blood pressure (DBP). Model 4 includes model 2 plus additional adjustment for mean daytime DBP.

clinic BP, and daytime BP. In contrast, participants with a nondipping versus a dipping pattern did not have higher LVMI or a higher prevalence of LVH. Further, higher nighttime BP was associated with higher LVMI but not the prevalence of LVH.

Although a reverse dipping pattern is associated with increased mortality and cardiovascular events when compared with a dipping pattern, 5,8-12 it is unclear whether a reverse dipping pattern also confers an increased risk for subclinical cardiovascular target organ damage. Among 682 participants with hypertension, the majority of whom were not taking antihypertensive medications in the Korean Ambulatory Blood Pressure Study, there were no differences in LVMI between participants with a reverse dipping or nondipping pattern each versus a dipping pattern. 18 In contrast, in a study of 376 Serbian adults with untreated hypertension, reverse dipping pattern and nondipping BP patterns were each associated with higher LVMI when compared with a dipping BP pattern. ¹⁷ Additionally, 31% of participants with a reverse dipping pattern and 17% of participants with a nondipping pattern had LVH compared with only 9% of participants with a

dipping pattern. These studies 17,18 were not population-based, included mostly individuals who had untreated hypertension, and did not include blacks. Several studies $^{31-36}$ have examined BP dipping in blacks or Caribbean blacks. These studies were typically small, 31,34 were not population-based, $^{31-34,36}$ did not examine reverse dipping $^{31-34}$ or LVMI, $^{31-33}$ and did not consider antihypertensive medication use. $^{31-35}$ The results of our study are novel and extend the findings of these prior studies by demonstrating in a large population-based cohort of blacks that a reverse dipping pattern is associated with higher LVMI and LVH, independent of antihypertensive medication use.

Higher quartiles of nighttime SBP and nighttime DBP were also associated with higher LVMI, highlighting the important contribution of nighttime BP in cardiovascular disease risk. Nighttime BP may be a stronger predictor of cardiovascular events than daytime BP among individuals with treated hypertension^{37,38} and among population-based cohorts.³⁹ In a population-based study of 1682 Italian participants, nighttime SBP was associated with higher left ventricular mass.⁴⁰ Additionally, Yi et al¹⁸ demonstrated that the highest

Table 7. Prevalence and Prevalence Ratios for LVH Associated With Quartiles (Qs) of Nighttime SBP (Upper Panel) and Nighttime DBP (Lower Panel)

	Quartiles of Nighttime S	ВР				
	Q1 (n=253)	Q2 (n=259)	Q3 (n=258)	Q4 (n=245)		
Levels of nighttime SBP	<109.5 mm Hg	≥109.5 and <119.4 mm Hg	≥119.4 and <130.8 mm Hg	≥130.8 mm Hg		
LVH, %	6.7	8.1	14.3	22.9		
	Prevalence ratio (95%	CI)				
Unadjusted	1 (Ref)	1.21 (0.65–2.23)	2.13 (1.23–3.69)	3.40 (2.04–5.69)		
Model 1	1 (Ref)	1.12 (0.61–2.06)	1.87 (1.07–3.28)	2.76 (1.59–4.80)		
Model 2	1 (Ref)	1.03 (0.52–2.04)	1.85 (1.03–3.34)	2.40 (1.31–4.39)		
Model 3	1 (Ref)	1.03 (0.52–2.05)	1.85 (1.29–4.47)	2.40 (1.29–4.47)		
Model 4	1 (Ref)	0.93 (0.46–1.86)	1.43 (0.75–2.75)	1.51 (0.69–3.29)		
	Quartiles of Nighttime DBP					
	Q1 (n=255)	Q2 (n=253)	Q3 (n=256)	Q4 (n=251)		
Levels of nighttime DBP	<61.7 mm Hg	≥61.7 and <67.5 mm Hg	≥67.5 and <74.4 mm Hg	≥74.4 mm Hg		
LVH, %	11.4	9.1	10.9	20.3		
	Prevalence ratio (95	% CI)				
Unadjusted	1 (Ref)	0.80 (0.48–1.34)	0.96 (0.59–1.57)	1.79 (1.17–2.72)		
Model 1	1 (Ref)	0.89 (0.53–1.48)	1.21 (0.74–1.97)	2.24 (1.45–3.46)		
Model 2	1 (Ref)	0.77 (0.44–1.35)	1.04 (0.61–1.79)	1.86 (1.16–2.99)		
Model 3	1 (Ref)	0.80 (0.45–1.41)	1.11 (0.64–1.92)	2.02 (1.24–3.29)		
Model 4	1 (Ref)	0.74 (0.42–1.31)	0.94 (0.53–1.67)	1.49 (0.79–2.78)		

Left ventricular hypertrophy (LVH) is defined as left ventricular mass index ≥96 g/m² in women and ≥116 g/m² in men according to the American Society of Echocardiography recommendations. Upper panel: Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive mediation use. Model 3 includes model 2 plus additional adjustment for mean clinic SBP. Model 4 includes model 3 plus additional adjustment for mean daytime systolic blood pressure (SBP). Lower panel: Model 1 includes adjustment for age, sex, and body mass index. Model 2 includes additional adjustment for diabetes mellitus, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio <60 mL/min per 1.73 m², and antihypertensive mediation use. Model 3 includes model 3 plus additional adjustment for mean clinic diastolic blood pressure (DBP). Model 4 includes model 2 plus additional adjustment for mean daytime DBP. Ref indicates referent.

versus lowest quartile of nighttime SBP was associated with higher LVMI among individuals with untreated and treated hypertension. The results from the current study extend both these findings by demonstrating that higher nighttime BP was associated with increased LVMI, independent of clinic BP and daytime BP among a population-based sample of blacks.

In the current study, the associations of reverse dipping pattern with LVMI and LVH were smaller when adjusting for mean 24-hour SBP instead of mean daytime SBP. These results indicate that the associations of reverse dipping pattern with cardiovascular target organ damage may be explained by higher mean 24-hour SBP levels, and that reverse dipping may represent an ABPM phenotype for which daytime BP but not nighttime BP is controlled. Therefore, among blacks, BP control over the daytime and nighttime periods may be associated with a larger reduction in cardiovascular disease risk compared with BP control only during the daytime period. Some studies^{41–43} have previously

demonstrated that nighttime dosing of antihypertensive medications may improve nighttime and 24-hour BP control and restores dipping BP among adults with nondipping BP. Given the results of the current study, future studies should examine whether nighttime dosing of antihypertensive medications lowers the risk of cardiovascular target organ damage or cardiovascular disease events among blacks with a reverse dipping pattern.

In the current study, 18.2% of participants had a reverse dipping pattern; 23.8% and 10.5% for those taking and not taking antihypertensive medication, respectively. The prevalence of a reverse dipping pattern among participants taking antihypertensive medication was high, which is consistent with the findings of prior studies for which the prevalence ranged from 15.6% to 26.7% among individuals with treated hypertension. 9,18,37,44–46 Although the timing of antihypertensive medication was not recorded in the JHS, it is likely that most participants took their medications during the daytime period. Therefore, the higher prevalence of reverse dipping

pattern among those taking versus not taking antihypertensive medication may be partially explained by the daytime dosing of antihypertensive medication, leading to a reduction in daytime relative to nighttime BP. In the current study, the prevalence of having a high risk of sleep apnea was highest among participants with a reverse dipping pattern. Therefore, another explanation for the high prevalence of reverse dipping pattern is sleep apnea, which is common among individuals with treated hypertension and is associated with higher nighttime BP and a high prevalence of nondipping BP pattern. ^{47–50}

Finally, in the current study, the associations of reverse dipping with LVMI and LVH appeared to be evident only among participants taking antihypertensive medication. Although this finding suggests that reverse dipping may be more benign among those not taking antihypertensive medication, there was no evidence of an interaction between antihypertensive medication and dipping patterns on LVMI and LVH, indicating that the associations of reverse dipping with LVMI and LVH were not modified by antihypertensive medication use.

Study Strengths and Limitations

There are several strengths of the current study. We used data from a large and well-characterized population-based cohort of blacks. The JHS is one of the largest studies of ABPM conducted among blacks. Further, high-quality echocardiography was conducted among JHS participants using standardized procedures. There are also several possible limitations. Participants in JHS underwent ABPM during only one 24-hour period, and the short-term reproducibility of dipping patterns may be limited. The study had only a few participants (n=38) with an extreme dipping pattern. Sleep diaries and information regarding reasons for nighttime awakening, which may impact nighttime BP, were not collected. Lastly, the current analysis was cross-sectional, and we cannot determine the direction of the association between dipping patterns and LVMI and LVH.

Conclusions

Approximately 1 in 5 blacks in the current study had a reverse dipping pattern. Participants with a reverse dipping pattern had higher LVMI and a higher prevalence of LVH compared with participants with a dipping pattern, Further, higher nighttime SBP and DBP values were associated with higher levels of LVMI. The data from the current study suggest that the identification of a reverse dipping pattern on ABPM may identify blacks at increased risk for cardiovascular target organ damage.

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Data S1.

Supplemental Methods

Data Collection & Clinical Covariates

During clinic examination, trained African American interviewers administered standardized questionnaires to assess selected demographic and behavior characteristics: age, sex, education, marital status, socioeconomic status, alcohol consumption, current smoking, and physical activity. 1 Education was measured as the highest level of schooling completed and classified into two categories within this study as "less than high school" or "greater than high school". Physical activity over the past 12 months was assessed using the JHS Physical Activity Cohort (JPAC) survey, a 30item validated guestionnaire.^{2, 3} The JPAC has four index scores that correspond to four physical activity domains (active living, work, sport, and home/life). The total physical activity score was calculated as the sum of the four index scores, with work scores set to 0 for participants who reported no paid or volunteer work during the past year. Higher scores represent more daily physical activity. Current smoking was defined by affirmative responses to the questions "Have you smoked more than 400 cigarettes in your lifetime?" and "Do you now smoke cigarettes?" Daily alcohol consumption was assessed from a validated food frequency questionnaire⁴ and in our study defined as "none": 0 drinks/week, "moderate" consumption: 1-14 and 1-7 alcoholic drinks/week for men and women respectively, and "heavy" consumption: >14 and >7 alcoholic drinks/week for men and women respectively.⁵ Risk of obstructive sleep apnea was assessed using the STOP-BANG questionnaire.^{6, 7} The STOP-BANG questionnaire has 8 questions that assess the following attributes: snoring loudly, breathing cessation

during sleep, tiredness during the daytime, hypertension status, body mass index >35 kg/m², being aged >50 years, and having a neck circumference > 40 cm and being male. Individuals with ≥3 attributes described above were categorized as high risk for obstructive sleep apnea.

Participants were asked to bring any medications taken within 2 weeks prior to the baseline examination to the clinic visit and were transcribed verbatim. Medication coding was performed by a pharmacist using the Medispan dictionary and classified into categories according to the Therapeutic Classification System. Antihypertensive medication use was defined by self-report. Participants were asked to avoid caffeine, eating, heavy physical activity, smoking, and alcohol intake for 12 hours prior to the clinic examination. During the clinic examination, weight and height were measured for each participant. Body mass index was calculated as the weight in kilograms divided by height in meters squared (kg/m²). Fasting blood samples were collected according to standardized procedures⁸ and processed at two central laboratories (University of Mississippi Medical Center and the University of Minnesota).8 Total and high-density lipoprotein (HDL) cholesterol was quantified by an oxidase method and low-density lipoprotein (LDL) cholesterol was calculated using the Freidewald equation.8 Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.9 Reduced eGFR was defined as <60 ml/min/1.73 m². Diabetes was defined as a fasting (≥8 hours) serum glucose ≥126 mg/dL or hemoglobin A1c ≥6.5% or use of insulin or oral hypoglycemic medications within 2 weeks prior to the clinic examination.

Table S1. Differences in left ventricular mass index* between participants with non-dipping and reverse dipping versus dipping blood pressure patterns.

	Dipping BP patterns [†]			P-Value	
	Dipping (N=341)	Non-dipping (N=489)	Reverse dipping (N=185)	Non-dipping versus Dipping	Reverse dipping versus Dipping
LVMI (g/m²)	78.2 ± 20.8	76.6 ± 21.2	88.1 ± 29.7	0.312	<0.001
	Diff	erence ± standard err	or		
	0 (ref)	-2.6 ± 1.6	5.1 ± 2.1	0.113	0.02

Data presented as mean ± standard deviation or unadjusted/adjusted mean difference compared to referent group ± standard error. BP=blood pressure

LVMI=left ventricular mass index

Ref=referent

SBP=systolic blood pressure

^{*}Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and mean 24-hour SBP. ¹Dipping pattern is based on the nighttime-to-daytime SBP ratio and defined by three patterns: dipping (≤0.90), non-dipping (>0.90 to ≤1.00) and reverse dipping (>1.00). Nighttime-to-daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

Table S2. Association between mean 24-hour SBP and left ventricular mass index.

	B coefficient ± standard error*	P-value
Mean 24-hour SBP, per 10 mmHg increase	3.1 ± 0.6	<0.001

B= beta

SBP=systolic blood pressure

*Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and dipping BP patterns. Dipping pattern is based on the nighttime-to-daytime SBP ratio and defined by three patterns: dipping (≤0.90), non-dipping (>0.90 to ≤1.00) and reverse dipping (>1.00). Nighttime-to-daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

Table S3. Differences in left ventricular mass index* among participants with dipping, non-dipping, and reverse dipping blood pressure patterns stratified by antihypertensive medication use.

	D	ipping BP patterns†			
	Among participa	nts taking antihyper	rtensive medication‡	P-1	value
	Dipping	Non-dipping	Reverse dipping	Non-dipping	Reverse dipping
	(N=173)	(N=255)	(N=134)	versus Dipping	versus Dipping
LVMI (g/m²)	80.2 ± 21.2	78.1 ± 20.3	90.9 ± 30.3	0.347	<0.001
	Γ	Difference ± standard	error		
	0 (ref)	-2.9 ± 2.4	7.7 ± 2.8	0.224	0.007
	Among participan	ts not taking antihy	pertensive medication		
	Dipping	Non-dipping	Reverse dipping	Non-dipping	Reverse dipping
	(N=159)	(N=224)	(N=45)	versus Dipping	versus Dipping
LVMI (g/m²)	75.8 ± 20.2	74.1 ± 21.3	77.0 ± 20.5	0.439	0.737
	Γ	Difference ± standard	error		
	0 (ref)	-2.0 ± 2.1	-1.0 ± 3.4	0.361	0.774

Data presented as mean \pm standard deviation or unadjusted/adjusted mean difference compared to referent group \pm standard error.

LVMI=left ventricular mass index Ref=referent

SBP=systolic blood pressure

*Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and mean 24-hour SBP. †Dipping pattern is based on the nighttime-to-daytime SBP ratio and defined by three patterns: dipping (≤0.90), non-dipping (>0.90 to ≤1.00) and reverse dipping (>1.00). Nighttime-to-daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP. ‡The overall test for interaction between antihypertensive medication use and dipping patterns on LVMI is p=0.100. The test for interaction between antihypertensive medication use and non-dipping pattern is p=0.596. The test for interaction between antihypertensive medication use and reverse dipping pattern is p=0.096.

Table S4. Prevalence and prevalence ratios* for left ventricular hypertrophy associated with dipping patterns.

		Dipping patterns [†]	
	Dipping	Non-dipping	Reverse dipping
	(N=341)	(N=489)	(N=185)
LVH, %	11.1%	10.6%	22.2%
	Pre	valence ratio (95% confidence in	iterval)
	1 (ref)	0.82 (0.54 – 1.26)	1.21 (0.76 – 1.92)

Left ventricular hypertrophy defined as LVMI \geq 96 g/m² in females and LVMI \geq 116 g/m² in males according to the American Society of Echocardiography recommendations.

BP=blood pressure

LVH=left ventricular hypertrophy

LVMI=left ventricular mass index

Ref=referent

SBP=systolic blood pressure

*Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and mean 24-hour SBP. ¹Dipping pattern is based on the nighttime-to-daytime SBP ratio and defined by three patterns: dipping (≤0.90), non-dipping (>0.90 to ≤1.00) and reverse dipping (>1.00). Nighttime-to-daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

Table S5. Association between mean 24-hour SBP and left ventricular hypertrophy.

	Prevalence ratio (95% confidence interval)*	P-value
Mean 24-hour SBP, per 10 mmHg	1.32 (1.15 – 1.51)	<0.001
increase		

SBP=systolic blood pressure

^{*}Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and dipping BP patterns.

Table S6. Prevalence ratios* for having left ventricular hypertrophy associated with dipping patterns stratified by antihypertensive medication use.

		Dipping patterns†			
	Among partici	pants taking antihypertens	sive medication‡		
	Dipping	Non-dipping	Reverse dipping		
	(N=173)	(N=255)	(N=134)		
LVH, %	14.5%	12.6%	24.6%		
	Prevalence ratio (95% confidence interval)				
	1 (ref)	0.84 (0.51 – 1.40)	1.39 (0.83 – 2.33)		
	Among participar	nts not taking antihyperter	sive medication		
	Dipping (ref)	Non-dipping	Reverse dipping		
	(N=159)	(N=224)	(N=45)		
LVH, %	7.6%	6.7%	11.1%		
	Prevalence ratio (95% confidence interval)				
	1 (ref)	0.82 (0.36 – 1.88)	0.92 (0.33 – 2.59)		

Left ventricular hypertrophy defined as LVMI \geq 96 g/m² in females and LVMI \geq 116 g/m² in males according to the American Society of Echocardiography recommendations.

LVH=left ventricular hypertrophy

LVMI=left ventricular mass index

Ref=referent

SBP=systolic blood pressure

^{*}Adjusted for age, sex, and body mass index, diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m², antihypertensive medication use, mean clinic SBP, and mean 24-hour SBP. †Dipping pattern is based on the nighttime-to-daytime SBP ratio and defined by three patterns: dipping (≤0.90), non-dipping (>0.90 to ≤1.00) and reverse dipping (>1.00). Nighttime-to-daytime SBP ratio is defined as mean nighttime SBP/mean daytime SBP.

‡The overall test for interaction between antihypertensive medication use and dipping patterns on LVH is p=0.908. The test for interaction between antihypertensive medication use and non-dipping pattern is p=0.333. The test for interaction between antihypertensive medication use and reverse dipping pattern is p=0.504.

Table S7. Differences in left ventricular mass index associated with quartiles of nighttime systolic blood pressure stratified by antihypertensive medication use.

Quartiles of Nighttime SBP							
Among participants taking antihypertensive medication*							
	Q1	Q2	Q3	Q4	P-trend		
	(n=107)	(N=140)	(N=143)	(N=172)	r-trenu		
Levels of	< 109.5	≥109.5 and < 119.4 mmHg	≥119.4 and < 130.8	≥ 130.8			
Nighttime SBP	mmHg		mmHg	mmHg			
LVMI (g/m²)	76.8 ± 21.8	76.3 ± 19.1	81.3 ± 22.4	89.8 ± 27.4	<0.001		
		Difference ± sta	andard error				
Unadjusted	0 (ref)	-0.6 ± 3.0	4.5 ± 3.0	13.0 ± 2.9	<0.001		
Model 1	0 (ref)	-1.2 ± 3.0	3.4 ± 3.0	10.9 ± 2.9	<0.001		
Model 2	0 (ref)	-1.3 ± 3.1	5.2 ± 3.1	10.8 ± 3.1	<0.001		
Model 3	0 (ref)	-1.3 ± 3.2	5.2 ± 3.2	10.9 ± 3.3	<0.001		
Model 4	0 (ref)	-1.6 ± 3.2	4.2 ± 3.4	9.1 ± 3.9	0.020		
	A	Among participants not taking	antihypertensive medic	ation			
	Q1	Q2	Q3	Q4	P-trend		
	(n=142)	(N=113)	(N=107)	(N=66)	P-trena		
Levels of	< 109.5	≥109.5 and < 119.4 mmHg	≥119.4 and < 130.8	≥ 130.8			
Nighttime SBP	mmHg		mmHg	mmHg			
LVMI (g/m²)	70.2 ± 15.9	73.2 ± 16.4	76.6 ± 23.8	86.2 ± 26.8	<0.001		
	Difference ± standard error						

Unadjusted	0 (ref)	3.1 ± 2.5	6.4 ± 2.6	16.0 ± 3.0	<0.001
Model 1	0 (ref)	1.9 ± 2.5	4.3 ± 2.6	12.5 ± 3.1	0.003
Model 2	0 (ref)	0.9 ± 2.6	3.4 ± 2.7	9.8 ± 3.3	0.022
Model 3	0 (ref)	0.8 ± 2.6	3.1 ± 2.8	9.4 ± 3.6	0.056
Model 4	0 (ref)	-1.9 ± 2.7	-1.3 ± 3.2	1.1 ± 4.6	0.767

Data presented as mean ± standard deviation or unadjusted/adjusted mean difference compared to referent group ± standard error. LVMI=left ventricular mass index

Q=quartile

Ref=referent

SBP=systolic blood pressure

Model 1 includes adjustment for age, sex, and body mass index.

Model 2 includes additional adjustment for diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m².

Model 3 includes additional adjustment for mean clinic SBP.

Model 4 includes additional adjustment for mean daytime SBP.

*The overall test for interaction between antihypertensive medication use and quartiles of nighttime SBP on LVMI is p=0.853. The test for interaction between antihypertensive medication use and quartiles 2, 3, and 4 of nighttime SBP, separately are p=0.558, p=0.778, and p=0.921, respectively.

Table S8. Differences in left ventricular mass index associated with quartiles of nighttime diastolic blood pressure stratified by antihypertensive medication use.

		Quartiles of N	lighttime DBP			
	Among participants taking antihypertensive medication*					
	Q1	Q2	Q 3	Q4	P-trend	
	(n=141)	(N=132)	(N=137)	(N=152)	r-tiella	
Levels of	< 61.7 mmHg	≥61.7 and < 67.5 mmHg	≥67.5 and < 74.4 mmHg	≥ 74.4 mmHg		
Nighttime DBP						
LVMI (g/m²)	80.1 ± 24.1	76.9 ± 18.1	78.3 ± 19.7	90.8 ± 28.7	<0.001	
		Difference ± s	standard error			
Unadjusted	0 (ref)	-3.3 ± 2.8	-1.9 ± 2.8	10.7 ± 2.7	<0.001	
Model 1	0 (ref)	-2.4 ± 2.8	-0.8 ± 2.8	11.2 ± 2.9	<0.001	
Model 2	0 (ref)	-2.5 ± 3.0	-1.6 ± 3.0	10.3 ± 3.0	<0.001	
Model 3	0 (ref)	-2.0 ± 3.0	-0.8 ± 3.0	11.6 ± 3.2	<0.001	
Model 4	0 (ref)	-2.1 ± 3.0	-1.1 ± 3.2	11.0 ± 3.7	<0.001	
	Am	ong participants not takir	ng antihypertensive medi	cation		
	Q1	Q2	Q3	Q4	P-trend	
	(n=109)	(N=113)	(N=116)	(N=90)	r-trend	
Levels of	< 61.7 mmHg	≥61.7 and < 67.5 mmHg	≥67.5 and <74.4 mmHg	≥ 74.4 mmHg		
Nighttime DBP						
LVMI (g/m²)	71.8 ± 20.9	72.4 ± 19.6	78.7 ± 20.1	77.6 ± 22.3	0.023	
	Difference ± standard error					

Unadjusted	0 (ref)	0.6 ± 2.8	6.9 ± 2.8	5.8 ± 2.9	0.023
Model 1	0 (ref)	-0.4 ± 2.7	5.1 ± 2.7	3.7 ± 2.9	0.113
Model 2	0 (ref)	-1.5 ± 2.8	5.0 ± 2.8	2.7 ± 3.0	0.086
Model 3	0 (ref)	-1.5 ± 2.8	5.1 ± 2.9	2.9 ± 3.2	0.086
Model 4	0 (ref)	-2.8 ± 2.8	2.2 ± 3.1	-2.3 ± 4.0	0.243

Data presented as mean ± standard deviation or unadjusted/adjusted mean difference compared to referent group ± standard error.

DBP=diastolic blood pressure

LVMI=left ventricular mass index

Q=quartile

Ref=referent

Model 1 includes adjustment for age, sex, and body mass index.

Model 2 includes additional adjustment for diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m².

Model 3 includes additional adjustment for mean clinic DBP.

Model 4 includes additional adjustment for mean daytime DBP.

^{*}The overall test for interaction between antihypertensive medication use and quartiles of nighttime DBP on LVMI is p<0.001. The test for interaction between antihypertensive medication use and quartiles 2, 3, and 4 of nighttime DBP, separately are p=0.989, p=0.158, and p=0.054, respectively.

Table S9. Prevalence and prevalence ratios for left ventricular hypertrophy associated with quartiles of nighttime systolic blood pressure stratified by antihypertensive medication use.

Quartiles of Nighttime SBP						
Among participants taking antihypertensive medication*						
	Q1	Q2	Q3	Q4		
	(n=107)	(N=140)	(N=143)	(N=172)		
Levels of	< 109.5 mmHg	≥109.5 and < 119.4 mmHg	≥119.4 and < 130.8 mmHg	≥ 130.8 mmHg		
Nighttime SBP						
LVH, %	12.2%	10.7%	16.8%	22.1%		
	F	Prevalence ratio (95% confiden	ice interval)			
Unadjusted	1 (ref)	0.88 (0.44 – 1.77)	1.38 (0.74 – 2.59)	1.82 (1.02 – 3.25)		
Model 1	1 (ref)	0.90 (0.45 – 1.80)	1.38 (0.73 – 2.61)	1.84 (1.00 – 3.39)		
Model 2	1 (ref)	0.89 (0.40 – 2.02)	1.74 (0.88 – 3.44)	2.05 (1.05 – 4.02)		
Model 3	1 (ref)	0.91 (0.40 – 2.05)	1.78 (0.89 – 3.55)	2.14 (1.07 – 4.29)		
Model 4	1 (ref)	0.87 (0.38 – 1.97)	1.52 (0.73 – 3.20)	1.62 (0.69 – 3.78)		
	Among par	ticipants not taking antihype	ertensive medication			
	Q1	Q2	Q3	Q4		
	(n=142)	(N=113)	(N=107)	(N=66)		
Levels of	< 109.5 mmHg	≥109.5 and < 119.4 mmHg	≥119.4 and < 130.8 mmHg	≥ 130.8 mmHg		
Nighttime SBP						
LVH, %	2.8%	5.3%	8.4%	19.7%		

Prevalence ratio (95% confidence interval)						
Unadjusted	1 (ref)	1.88 (0.55 – 6.52)	2.99 (0.94 – 9.44)	7.00 (2.37 – 20.63)		
Model 1	1 (ref)	1.66 (0.47 – 5.83)	2.35 (0.72 – 7.66)	4.74 (1.42 – 15.83)		
Model 2	1 (ref)	1.27 (0.33 – 4.85)	1.79 (0.55 – 5.83)	3.19 (0.94 – 10.87)		
Model 3	1 (ref)	1.26 (0.33 – 4.82)	1.78 (0.54 – 5.81)	3.13 (0.91 – 10.79)		
Model 4	1 (ref)	0.93 (0.22 – 3.89)	1.06 (0.28 – 3.96)	1.18 (0.20 – 6.91)		

LVH=left ventricular hypertrophy

Q=quartile

Ref=referent

SBP=systolic blood pressure

Model 1 includes adjustment for age, sex, and body mass index.

Model 2 includes additional adjustment for diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m².

Model 3 includes additional adjustment for mean clinic SBP.

Model 4 includes additional adjustment for mean daytime SBP.

*The overall test for interaction between antihypertensive medication use and quartiles of nighttime SBP on LVH is p=0.530. The test for interaction between antihypertensive medication use and quartiles 2, 3, and 4 of nighttime SBP, separately are p=0.550, p=0.644, and p=0.192, respectively.

Table S10. Prevalence and prevalence ratios for left ventricular hypertrophy associated with quartiles of nighttime diastolic blood pressure stratified by antihypertensive medication use.

		Quartiles of Nighttime I)BP	
	Among pa	rticipants taking antihyperte	ensive medication*	
	Q1	Q2	Q3	Q4
	(n=141)	(N=132)	(N=137)	(N=152)
Levels of	< 61.7 mmHg	≥61.7 and < 67.5 mmHg	≥67.5 and < 74.4 mmHg	≥ 74.4 mmHg
Nighttime DBP				
LVH, %	17.0%	11.4%	11.7%	23.0%
	Pr	evalence ratio (95% confidenc	ce interval)	
Unadjusted	1 (ref)	0.67 (0.37 – 1.22)	0.69 (0.38 – 1.23)	1.35 (0.85 – 2.16)
Model 1	1 (ref)	0.72 (0.39 – 1.31)	0.82 (0.45 – 1.50)	1.74 (1.06 – 2.84)
Model 2	1 (ref)	0.66 (0.34 – 1.28)	0.70 (0.36 – 1.35)	1.62 (0.95 – 2.75)
Model 3	1 (ref)	0.68 (0.35 – 1.33)	0.74 (0.38 – 1.43)	1.74 (1.01 – 2.99)
Model 4	1 (ref)	0.67 (0.34 – 1.30)	0.70 (0.35 – 1.41)	1.59 (0.79 – 3.19)
	Among part	icipants not taking antihype	rtensive medication	
	Q1	Q2	Q3	Q4
	(n=109)	(N=113)	(N=116)	(N=90)
Levels of	< 61.7 mmHg	≥61.7 and < 67.5 mmHg	≥67.5 and < 74.4 mmHg	≥ 74.4 mmHg
Nighttime DBP				
LVH, %	4.6%	5.3%	9.5%	11.1%

Prevalence ratio (95% confidence interval)						
Unadjusted	1 (ref)	1.16 (0.36 – 3.68)	2.07 (0.74 – 5.76)	2.42 (0.86 – 6.83)		
Model 1	1 (ref)	1.26 (0.40 – 3.98)	2.66 (0.96 – 7.37)	2.99 (1.01 – 8.86)		
Model 2	1 (ref)	1.07 (0.32 – 3.66)	2.88 (0.92 – 9.08)	3.03 (0.92 – 9.96)		
Model 3	1 (ref)	1.11 (0.33 – 3.80)	3.10 (0.98 – 9.82)	3.41 (1.02 – 11.5)		
Model 4	1 (ref)	0.92 (0.26 – 3.34)	1.95 (0.57 – 6.64)	1.23 (0.26 – 5.74)		

DBP=diastolic blood pressure

LVH=left ventricular hypertrophy

Q=quartile

Ref=referent

Model 1 includes adjustment for age, sex, and body mass index.

Model 2 includes additional adjustment for diabetes, education level, alcohol consumption, smoking status, physical activity, estimated glomerular filtration ratio < 60 ml/min/1.73m²

Model 3 includes additional adjustment for mean clinic DBP.

Model 4 includes additional adjustment for mean daytime DBP.

^{*}The overall test for interaction between antihypertensive medication use and quartiles of nighttime DBP on LVH is p=0.434. The test for interaction between antihypertensive medication use and quartiles 2, 3, and 4 of nighttime DBP, separately are p=0.445, p=0.115, and p=0.490, respectively.

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